Improvement of the pharmaceutical availability and membrane permeability of furosemide by formulation design

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Yours truly

Jannes van der Merwe (29 November 2020)

Declaration by researcher

I, Jannes van der Merwe, hereby declare that this dissertation, with the title “Improvement of the pharmaceutical availability and membrane permeability of furosemide by formulation design” is my work alone and has never previously been submitted for examination. I declare that all sources utilised in this study have been referenced and acknowledged. I also declare that this dissertation was submitted to the Turnitin software program and that a satisfactory report was released regarding plagiarism.

C.J (Jannes) van der Merwe

“Everything is theoretically impossible, until it is done.”

(Robert A. Heinlein)

“Success is not final; failure is not fatal: It is the courage to continue that counts.”

(Winston S. Churchill)

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List of abbreviations

FDA	Food and Drug Administration
MUPS	Multiple Unit Pellet System
BCS	Biopharmaceutical Classification System
MDT	Mean Dissolution Time
DRi	Initial Dissolution Rate
AUC	Area Under the Curve
(f1)	Difference factor
API	Active Pharmaceutical Ingredient
IPEC	International Pharmaceutical Excipient Council
CDs	Cyclodextrins
α-CD	Alpha-Cyclodextrin
β-CD	Betha-Cyclodextrin
γ-CD	Gamma-Cyclodextrin
HP-β-CD	Hydroxypropyl-Betha-Cyclodextrin
HPMC	Hydroxypropyl Methylcellulose
SBE-β-CD	Sulfobuthylether-Betha-Cyclodextrin
ODTs	Orally Disintegrating Tablets
PVP	Polyvenyl Pirrolidone
HPMCP	Hydroxypropyl Methylcellulose Phthalate
CMC	Carboxymethylcellulose
HPMC-AS	Hydroxypropyl Methylcellulose-Acetate Succinate
TPGS	Tocopherol Polyethelylene Glycol Succinate
SEDDS	Self-Emulsifying Drug Delivery System
SMEDDS	Self-MicroEmulsifying Drug Delivery System
SNEDDS	Self-NanoEmulsifying Drug Delivery System
C_{max}	Maximum concentration
MCC	MicroCrystalline Cellulose
DPPH	2,2-DiPhenyl-1-PicrylHydrazyl
BP	British Pharmacopoeia
RDA	Redundancy Analysis

P_{app}	Apparent permeability coefficient
SD	Standard Deviation
%max	Maximum percentage dissolution
C	Control MUPS tablet formulation
N/A	Not Applicable
L	Lasix®

Abstract

Furosemide is a well-known loop diuretic having weak acidic chemical properties. Furosemide belongs to the Biopharmaceutical Classification System (BCS) class IV because it has poor aqueous solubility and poor membrane permeability characteristics. In this study, the effect of different combinations of functional excipients (i.e. chitosan, sodium lauryl sulphate, NaHCO3 and CaCO3) in the formulation of multiple-unit pellet system (MUPS) tablets has been investigated. Spherical beads (0.5 mm, 0.75 mm and 1 mm) were produced by extrusion-spheronisation consisting of different combinations of excipients, which were compressed to form flat faced, bevelled edge MUPS tablets. Three control MUPS tablet formulations (i.e. containing 0.5 mm, 0.75mm and 1 mm beads) were prepared without the functional excipients. A commercial product (Lasix®) was also included in the study as a reference for purposes of comparison. Each MUPS tablet formulation was evaluated for physical properties (hardness, disintegration, mass variation and friability), whereasthe bead formulations were tested for mucoadhesiveness. Dissolution evaluations were conducted on each MUPS tablet formulation in media with three different pH environments, namely 0.1 M HCl (pH 1.2), citric acid buffer (pH 4.6) and a phosphate buffer (pH 7.4). Ex-vivo permeability studies were performed across excised pig tissues of the pyloric antrum and the duodenal region on selected experimental MUPS tablet formulations; the control MUPS tablet formulations, and (or as well as) the commercial product. Histological analysis was conducted on the tissues after exposure to the selected experimental MUPS tablet formulations, the control MUPS tablet formulation and the commercial product. The dissolution results in the 0.1 M HCl (pH 1.2) showed the highest effect of the excipients on furosemide release when compared to the control formulations and the commercial product. This phenomenon was expected due to the acidic nature of furosemide. All the dissolution parameters showed increased dissolution of furosemide for the MUPS tablet formulations containing the functional excipients as compared to that of the control MUPS tablet formulations as follow: the AUC values of the dissolution curves showed a 4.5–10 fold increase, the %max showed a 60–70% increase and the DR_i exhibited up to a 19 fold increase. Permeability results revealed the selected MUPS tablet formulations had a 2.5 fold higher cumulative percentage transport than the control MUPS tablet formulation without a cytotoxic effect on the tissues. The results from this study showed that the combination of selected functional excipients incorporated into beads that were compressed into MUPS tablet formulations not only increased furosemide release, but also its permeation across excised intestinal tissues.

Keywords: Beads, Biopharmaceutics classification system, Dissolution, Functional excipients, Furosemide, Multiple-unit pellet system, Permeability.

Chapter 1

Introduction

This first chapter contains the introduction to this thesis, the research problem and the aims and objectives.

Introduction

Tablets are the preferred solid oral dosage form for administration of medicines and are also very popular from a formulation point of view (Paul & Sun, 2017). According to a recent study conducted by Dalvi *et al* (2019), 51% (23 out of 45) of newly developed medicinal products were formulated into solid oral dosage forms. Within this group of solid oral dosage forms, 15 of the products were formulated as tablets and registered as such on the United States Food and Drug Administration (FDA) database. Tablets are relatively easily administered and handled by patients, which consequently result in high patient compliance that areassociated with effective treatment. Powder mixtures intended for compression into tablets should, amongst other properties, have sufficient flow properties in order to ensure uniform filling of the die during the compression cycle that will provide tablets of uniform mass. Good powder flow properties are also needed to ensure that an acceptable manufacturing speed can be maintained. The mechanical properties of the tablet should likewise comply with certain parameters to withstand abrasion during normal handling (Dalvi *et al.,* 2019:87; Paul & Sun., 2017:111-112; Worku *et al.,* 2017:191-192).

A modern approach, which is currently being implemented to improve the flow and functionality of powder mixtures intended for tableting, is the formulation of beads/pellets and compression of these beads/pellets into multiple unit pellet system (MUPS) tablets. MUPS tablets are also often utilised for the formulation of modified release solid oral dosage forms. The variation (e.g. mass uniformity) between tablets will most likely be lower because of the improved particle flow and the particle size distribution will furthermore be narrower compared to that of a normal powder or granule mixture. A notable advantage of a MUPS tablet is the relatively fast distribution of the evenly shaped and small sized beads/pellets throughout the stomach and the small intestine after disintegration, providing a more even drug absorption from the gastro-intestinal tract. However, despite the advantages associated with MUPS tablets as a dosage from, the compression of beads into tablets is known to present a challenge and ongoing research that generates knowledge regarding MUPS tablet compression is essential (Novika *et al.,* 2017:447-448; Patel *et al.,* 2018:220-221; Osei-Yeboah *et al.,* 2017:591-593).

Furosemide, an anthranilic derivate, is a high ceiling loop diuretic that can be classified as a weak acidic drug with a narrow absorption window in the gastro-intestinal tract that is located in the stomach and proximal small intestine (i.e. the duodenum). Protonation of the drug molecules predominantly occurs in the stomach and in the duodenum, favouring the absorption of the unionised molecules across the epithelial membrane. The extent of

furosemideabsorption further down the gastro-intestinal tract is relatively low and highly variable due to the molecules being mostly in the ionised form (Laulicht *et al.,* 2011:314-316). Furosemide is classified as a class IV drug according to the Biopharmaceutical Classification System (BCS). Itis a drug that has poor membrane permeability and poor aqueous solubility with a bioavailability varying between 20 and 60% (Han *et al.,* 2016:192-193; Nielsen *et al.,* 2015:334-335; Provenza *et al.,* 2014:209-209; Shariare *et al.,* 2019:96-105).

1.1 IMPORTANCE OF SOLUBILITY OF DRUGS FORMULATED INTO SOLID ORAL DOSAGE FORMS

The solubility of a drug refers to the quantity of the drug that can dissolve in a specified volume of a solvent under specified conditions. Solubility of the drug is one of the key factors that determines if it will reach the target area in the body in therapeutic quantities. Sufficient solubility is a prerequisite for acceptable bioavailability; and consequently also the pharmacological effect of the drug. When a solid oral dosage form is poorly formulated in such a way that it has a detrimental influence on the dissolution and bioavailability of the drug, the effectiveness of the drug treatment will be compromised. It is therefore important that various formulation factors should be carefully considered in order to optimise the performance of the dosage form in terms of drug release and delivery (Shergill *et al.,* 2016:3-4).

According to recent studies, the majority of newly developed drugs show inadequate aqueous solubility and poor permeability. The BCS is based on two key factors that determine the bioavailability of a drug administered by the oral route, namely drug solubility and membrane permeability. The BCS classifies drugs into four groups according to their solubility and permeability characteristics. Class I represents substances that are highly soluble/highly permeable, class II represents substances that show low solubility and high permeability, class III represents substances with high solubility and low permeability and class IV represents substances that have low solubility and low permeability. A drug can be classified as highly membrane permeable when 90% or more of the administered drug dose is absorbed. A substance can be classified as highly soluble when the highest dose of this specific drug is soluble in 250 ml or less of an aqueous medium at a fixed temperature of 37°C and at a pH range of 1–7.5 (Butt *et al.,* 2019:619-621).

To improve the solubility, permeability and bioavailability of a BCS class IV drug such asfurosemide, thorough investigation and research need to be done regarding particle type, excipients and the formulation design of the tablet that is being manufactured. It has become evident that the physical and the chemical properties within the dosage form need to be optimised and manipulated to enhance the solubility and permeability of a drug in this BCS class (Volkova *et al.,* 269:492-493).

1.2 MULTIPLE UNIT PELLET SYSTEMS AS SOLID ORAL DOSAGE FORMS

A MUPS (Multiple Unit Pellet System) drug delivery system consists of spherically shaped particles (i.e. beads/pellets) compressed into a tablet or filled into hard gelatine capsules. This formulation approach is commonly used to achieve modified drug release and can also be used to manipulate in which part of the gastro-intestinal tract the drug will be released for most effective absorption. The beads/pellets act as miniature drug depots, each containing a fraction of the drug dose to make up the total dose in the dosage form. This dosage form is thus acting as a multi-unit drug delivery system formulated in such a way to disintegrate in order to release the beads/pellets as sub-units before the drug is released from each bead. By employing a film coating on the beads/pellets or by utilising matrix forming excipients within the beads, the release of the drug can be modified (Mc-Gillicuddy *et al*., 2016:387-388).

The advantages of MUPS as drug delivery systems over conventional single-unit solid oral dosage forms include the following:

- The probability of gastro-intestinal tract wall irritation is lower than that of single-unit solid oral dosage forms because of the even distribution of beads/pellets throughout the gastro-intestinal tract.
- There is more flexibility possible with a MUPS as a dosage form than with a single-unit dosage form. For example, two or more incompatible drugs can be incorporated in the same dosage form.
- The risk of dose dumping is lowered. Once the MUPS tablet or capsule disintegrates, every single bead within this dosage form must disintegrate and/or dissolve on its own before the drug is released.
- The inter-subject variability in terms of drug delivery is lower than that of single-unit dosage forms. This ensures more accurate and consistent dosing (Mc-Gillicuddy *et al*., 2016:387-388).

Certain disadvantages associated with the use of MUPS include:

- The production of the beads/pellets is an additional step to tableting and contributes to a time-consuming process with potential challenges to produce acceptable tablets.
- The process of the production of beads and tableting is more expensive compared to conventional tablets.
- Compressing beads/pellets into an acceptable tablet may be challenging and certain problems may arise during this process.
- MUPS tablets may have a lower mechanical strength than conventional tablets produced from powder mixtures (Shajahan *et al*., 2010:2-4).

1.3 FORMULATION STRATEGIES TO OVERCOME POOR SOLUBILITY AND MEMBRANE PERMEABILITY PROPERTIES

There are certain formulation strategies that can be employed to improve the poor solubility and membrane permeability characteristics associated with BCS Class IV drugs. Specific formulation approaches to improve both the solubility and permeability of Class IV drugs (e.g. furosemide) are discussed in more detail in the sections below. Other examples of Class IV drugs include amphotericin B, ritonavir, paclitaxel and acetazolamide (Ghadi& Dand, 2017:71-73).

1.3.1 Addition of functional excipients

The addition of certain excipients to the dosage form that can enhance the solubility and permeability of the drug is considered a formulation strategy. Excipients added to oral formulations to improve solubility include cyclodextrin (for the formation of inclusion complexes), pH adjusting excipients and wetting agents such as surfactants (Loftsson *et al*., 2005; Saharan *et al.*, 2009).

1.3.2 pH adjusting excipients

The pH of aliquid in direct contact with solid drug particles (i.e. the so-called stagnant diffusion layer) has an important influence on the solubility of the drug when it is a weak acid or base. These excipients can manipulate the pH in the stagnant diffusion layer and thereby have a beneficial influence on the solubility of the drug by forcing the equilibrium towards the ionised form of the molecules. The type of adjusting excipient used in a formulation depends on whether an acidic or more basic environment is required by the drug for the best possible solubility and dissolution. Examples of pH adjusting excipients to be used to create an acidic environment include citric acid, tartaric acid and carbonic acid. Examples of pH adjusting excipients to be used to create a basic environment include sodium bicarbonate and calcium carbonate (Martins *et al.,* 2017:10-13; Kataoka *et al.,* 2016:103-105; Adachi *et al.,* 2015:225-228).

1.3.3 Wetting agents

Wetting agents are frequently used to enhance the wettability of a drug. The wetting agent attracts fluid to the solid oral dosage form, allowing more contact between the drug particle and the solvent. This can possibly lead to a faster dissolution rate of the drug providing a higher concentration of the drug in this area, which can possibly lead to a higher percentage of drug permeating the epithelial membranes that can then move into the systemic circulation. A common wetting agent that is frequently used in the formulation of dosage forms is sodium lauryl sulphate (Lee *et al.,* 2001:125-127; Moore *et al.,* 2010:37-40).

1.3.4 Muco-adhesive excipients

Providing intimate contact of the drug delivery system with the absorptive membranes is advantageous to the absorption process. This can be achieved by adding bioadhesive characteristics to a drug delivery system. Muco-adhesion describes adhesion involving the mucous coating on the surface of the gastro-intestinal tract epithelium and an adhesive polymeric device (Vasir *et al*., 2003:13-17). A typical example of a polymeric excipient that has been shown to impart muco-adhesive properties to a delivery system is chitosan (De Bruyn, 2018:53-55).

2. RESEARCH PROBLEM

Solubility problems do not only complicate the oral delivery of newly developed chemical entities, but also hamper the delivery of a substantial number of existing drugs. As a consequence, different formulation approaches are receiving renewed interest in order to overcome the limited solubility and permeability of drugs, specifically drugs that fall within the BCS Class IV. Furosemide is used frequently as a diuretic and although it is used with success in most patients with oedematous conditions, problems are still arising with regards to variable bioavailability as a result of its poor aqueous solubility. Furthermore, furosemide exhibits poor permeability across the human gastro-intestinal epithelium and is best absorbed from the stomach and the upper small intestine or duodenum (i.e. the optimal absorption window). Furosemide will be used as a model compound to investigate the employment of formulation approaches to improve its dissolution rate and consequently also its intestinal permeability.

3. AIM OF THE STUDY

The aim of this study is to improve the dissolution rate of furosemide by means of formulation approaches via different mechanisms including improvement of the solubility in the microenvironment (diffusion layer) as a result of inclusion or pH adjusting excipients, improvement of wettability as a result of the inclusion of a surfactant and increasing the surface area as a result of pellet size variations. A secondary aim is to improve the membrane permeation of furosemide because of a larger concentration gradient that will occur due to the increased dissolution rate and by the addition of a mucoadhesive agent to prolong the contact time between the bead particles and the intestinal lumen. In order to reach this aim, the following objectives are set to:

- Produce beads/pellets of different sizes (i.e. 0.5 mm. 0.75 mm and 1.0 mm) and different compositions using extrusion-spheronisation.
- Vary the concentration of functional excipients (i.e. pH adjusting excipients, surfactant and mucoadhesive agents) in the bead formulations according to an experimental design layout.

- Prepare MUPS tablets consisting of the different bead/pellet formulations.
- Evaluate the physical properties of the different MUPS tablet formulations by means of weight variation, crushing strength, disintegration, friability and muco-adhesive properties.
- Evaluate the dissolution behaviour of the different MUPS tablet formulations using three different dissolution media and processing the data by calculating different dissolution parameters including maximum dissolution percentage ($\%_{max}$), initial dissolution rate (DR_i), area under the curve (AUC) and the difference factor (f_1).
- Conduct *ex vivo* permeability studies using excised pig pyloric antrum as well as duodenum tissue mounted in the Sweetana-Grass diffusion apparatus.
- Conduct histological evaluations to investigate tissue integrity in the presence of the selected functional excipients.

In this study, 36 bead formulations were developed and compressed to form 9 mm flat faced bevelled edge tablets. These formulations differed either in terms of particle size or combinations and concentrations of functional excipients included. Functional excipients comprised chitosan as muco-adhesive agent to prolong contact time between the bead particles and the intestinal mucosa; pH-adjusting excipients ($NaHCO_3$ and $CaCO_3$) to increase the micro-environmental pH around drug particles after disintegration of the tablets for optimal dissolution of the weak acidic drug, furosemide; and a surfactant/wetting agent, sodium lauryl sulphate, to increase moisture uptake into the MUPS tablet and into the bead and drug particles in order to increase the dissolution rate of furosemide. By studying the individual and combined effects that these functional excipients had on the rate and extent of furosemide dissolution and permeability in different pH environments, new information regarding the optimal formulation of furosemide tablets could be obtained.

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Chapter 2

Review article

This chapter of this thesis is presented in the form of a review article, which was published in the journal “MDPI journal Molecules” on the 25th of April 2020. Author guidelines regarding this journal can be found in “Annexure L” of this document. This article’s main focus was to highlight the role of functional excipients in solid oral dosage forms to overcome poor drug dissolution and bioavailability.

pharmaceutics

MDPI

Review

The Role of Functional Excipients in Solid Oral Dosage Forms to Overcome Poor Drug Dissolution and Bioavailability

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Abstract: Many active pharmaceutical ingredients (APIs) exhibit poor solubility and low dissolution rates in aqueous environments such as the luminal fluids of the gastrointestinal tract. The oral bioavailability of these compounds is usually very low as a result of their poor solubility properties. In order to improve the bioavailability of these poorly soluble drugs, formulation strategies have been applied as a means to improve their aqueous solubility and dissolution rates. With respect to formulation approaches, excipients can be incorporated in the formulation to assist in the dissolution process of the drug, or specialized dosage forms can be formulated that improve dissolution rate through various mechanisms. This paper provides an overview of selected excipients (e.g., alkalinizing agents, surfactants and sugars) that can be used in formulations to increase the dissolution rate as well as specialized dosage forms such as self-emulsifying delivery systems and formulation techniques such as inclusion complexes and solid dispersions. These formulation approaches are discussed with available examples with specific reference to positive outcomes in terms of drug solubility and bioavailability enhancement.

Keywords: solubility; bioavailability; excipients; dissolution

1. Introduction

Pharmacologically active compounds or drugs (also referred to as active pharmaceutical ingredients; APIs) are usually not administered to patients on their own as single compounds, but are formulated into carefully designed dosage forms. Pharmaceutical dosage forms provide a platform for repeatable accurate dosing, quality, efficacy, safety, stability as well as high patient acceptance and compliance [1]. Initially, dosage forms were made by simply adding pharmacologically inert substances (also referred to as excipients) to the API to make up the required volume of an acceptable dosing unit. However, progress in pharmaceutical technology has led to the selection and production of excipients that fulfil specific functions, beyond just making up volume, such as assisting in production of the dosage form and optimizing drug delivery from novel dosage forms. In fact, the functions of excipients in dosage forms are related to all the different aspects of the final product including its manufacturability, the stability of the API, dose uniformity, effective delivery of the API to the systemic circulation after administration, as well as acceptable organoleptic properties for maximum compliance by the patient [2].

Pharmaceutical excipients are usually included in dosage forms in larger quantities than the API and can make up to about 90% of the total mass/volume of medicinal products [2,3]. The International Pharmaceutical Excipient Council (IPEC) classified pharmaceutical excipients based on safety data

into two classes namely 'new chemical excipients' and 'established excipients'. The latter class is sub-divided into the following sub-classes: 'existing chemical excipients', 'existing chemical excipients—first administration to humans' and 'new modifications or combinations of existing excipients'.Thesedifferentclassesofpharmaceuticalexcipientshavedifferentrequirementsinterms of safety evaluation [1]. Awareness of the importance of excipient quality and safety, especially in pediatric patients, was intensified by the death of 84 children in 2008 due to inclusion of glycerin contaminated with diethylene glycol in teething powders [4]. Consequently, updates on regulatory requirements for pharmaceutical excipients are continuously introduced worldwide to ensure the safety of patients[5].

The excipient class 'new chemical excipients' can be sub-divided into 'modified excipients' (i.e., existing excipients that are modified with respect to purity and/or physical properties such as particlesize),'co-processedexcipients'(i.e.,twoormoreexistingexcipientswhichareformulatedinto a new excipient with physical properties that cannot be obtained by a simple physical mixture and is produced through processes such as spray drying) and 'novel excipients' (i.e., new chemical entities used for the first time in a drug product which may include known excipients that are chemically modified)[6].

With the progress in the development of novel drug delivery systems, more sophisticated excipients are needed to impart certain properties into the final product. The term 'multifunctional excipients' refer to excipients (which can be co-processed for example) that fulfil multiple roles in a dosage form or drug delivery system, for example a direct-compressible filler material that also functions as a binder and/or disintegrant. The term 'high functionality excipients' refers to a single excipientthatprovidesadditionalfunctionstoinnovativedrugdeliverysystemstoimprovetheoverall performance of the product with significant economic benefits. An example of a high functionality excipient is one that can provide better flow, act as a disintegrant and simultaneously allow a higher drug loading in the dosage form due to its high compressibility[7].

Itisestimatedthatapproximately40%ofcurrentmedicationdispensedtopatientsinpharmacies exhibit relatively poor aqueous solubility properties. Furthermore, approximately 90% of newly discovered therapeutic compounds, which are in the development phase, have also been reported to exhibit poor aqueous solubility. For these drugs, functional excipients are needed to assist in overcoming their poor physico-chemical properties. Specialty excipients are used to produce dosage forms that can reduce the number of doses by modifying the rate of drug release or improve drug deliverybytargetingdrugreleaseinaspecificregioninthegastrointestinaltractwheredrugabsorption is the highest. Functional excipients are also used to re-formulate existing drugs in order to produce more effective products that are more cost-effective[6,8].

Aqueous solubility and membrane permeability were identified as the two key factors that influencethebioavailabilityofadrugasoutlinedintheBiopharmaceuticsClassificationSystem(BCS). As mentioned before, many promising new drugs exhibit poor solubility, and some also exhibit poor membrane permeability [9]. Generally, a drug that exhibits an aqueous solubility lower than 0.1 mg permLislikelytoexperiencelimitedbioavailability,anditsrateofabsorptionwillbegovernedbythe dissolution rate[10].

Poor aqueous solubility, and consequently also poor dissolution rate, is a major challenge specificallyinthesystemicdeliveryoforallyadministeredBCSclassIIandIVdrugs.Physico-chemical techniques that have been employed to improve the solubility of these drugs include formation of pro-drugs, formation of salts, co-precipitation, solvent evaporation and size reduction (or micronisation). Formulation strategies that have been investigated for the same purpose include melt extrusion/granulation, formation of solid dispersions and formation of inclusion complexes. Furthermore,excipientssuchassurfactants,polymers,super-disintegrantsandmultifunctionalfillers have been included in dosage forms to increase the apparent solubility of drugs[11,12].

Figure 1is a schematic representation of different classes of functional excipients and techniquesusingfunctionalexcipientsthatimproveeitherthesolubility/dissolutionand/ormembrane permeation/absorption and thereby also the bioavailability of poorly solubleAPIs.

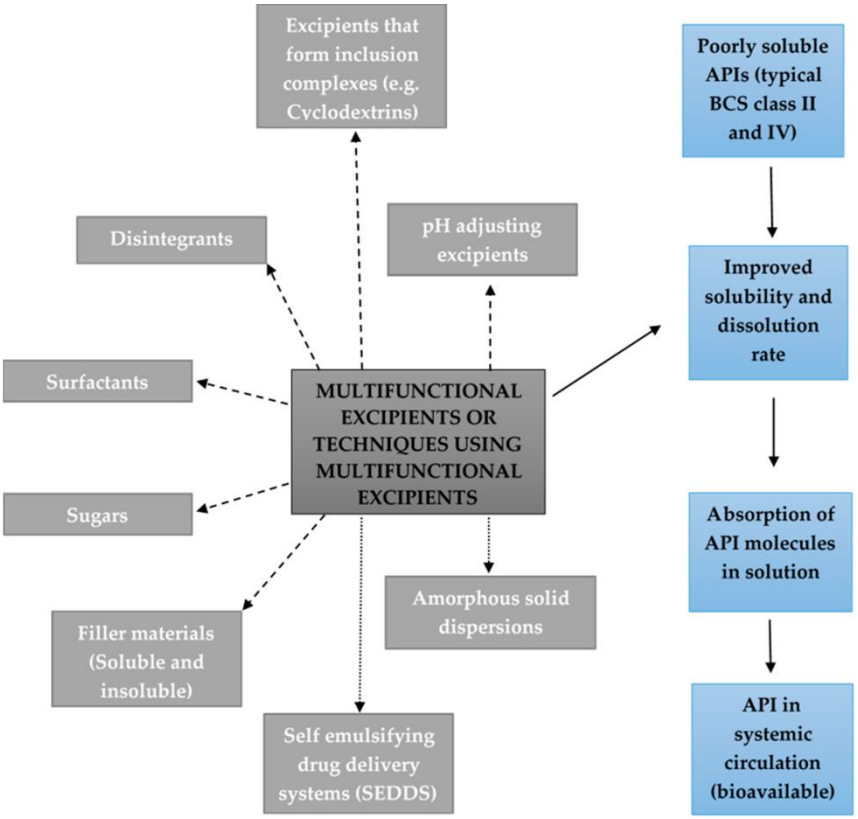

Figure 1. Different classes of functional excipients and techniques using functional excipients that influenceeitherthesolubility/dissolutionand/ormembranepermeation/absorptionandconsequently the bioavailability of poorly soluble active pharmaceutical ingredients(APIs).

2. Excipients Added to Solid Oral Dosage Forms to Improve Drug Solubility and/orDissolution

2.1. Excipients that Form Inclusion Complexes with DrugMolecules

The term 'complex formation' or 'complexation' refers to the binding of two or moreindividual molecules to form a combined chemical product, which act as a single chemical unit. One of the mostfrequentlyemployedcomplexationreactionsinpharmaceuticalsciencesiscomplexationofdrug molecules with cyclodextrin molecules. Cyclodextrin is developed through an enzymatic reaction withstarchtoformacrystallineandnon-hygroscopiccone-shapedmoleculethathasidealproperties for complexation with certain API molecules. Cyclodextrin molecules form inclusion complexes with hydrophobic, non-polar molecules by accommodating them in the hydrophobic cavity of the cone[13,14].

Cyclodextrins(CDs)arecharacterizedbyatoroidalshapewithalipophiliccenterandahydrophilic outer surface. There are three natural cyclodextrins, namely α-cyclodextrin (αCD), β-cyclodextrin (βCD)andγ-cyclodextrin(γCD),whichhavesix,sevenandeightglucoseunits,respectively.Themost frequent application of forming inclusion complexes between cyclodextrin and an API is toincreasetheapparentaqueoussolubilityoftheAPI(specificallythosebelongingtoBSCclassIIandIV).Othe r applications of complex formation include improvement of drug stability, minimization of adverse drugeffectsorside-effectsandimprovementoforganolepticpropertiessuchastasteandsmell[14–17]. Itisimportanttonote,however,thatnotallinclusioncomplexformationsalwaysprovideanincrease in API solubility and/orabsorption.

Cyclodextrinshavebeenwidelyemployedassolubilityanddissolutionmodifyingexcipientsin variousoraldosageforms.Thesedosageformsincludeconventionalimmediatereleasetablets,orally disintegratingtablets,effervescenttablets,andmodifiedreleasedosageformsincludingslowrelease or sustained release drug delivery systems [18–20]. Cyclodextrins are often preferred over organic solvents as a means to enhance solubility and dissolution due to their safety and because they are well tolerated. In addition, advances in genetic engineering, technology and process innovations led to the production of αCD, βCD as well as γCD as pharmaceutical excipients on economically and commerciallyacceptablescales.However,duetotherelativelylowsolubilityaswellasnephrotoxicity of βCD, it is not suitable for parenteral administration. Consequently, more soluble and less toxic cyclodextrin derivatives have been developed, which include hydroxypropyl-β-cyclodextrin (HP-β-CD) and sulfobutylether-β-cyclodextrin (SBE-β-CD)[16].

ExamplesofthebeneficialeffectsofcyclodextrinsasfunctionalexcipientsonAPIsarehighlighted by Conceição et al. [14], which include the increased solubility of carbamazepine by means of complexation with HP-β-CD. The effect of complexation of carbamazepine with HP-β-CD is further illustrated by a study conducted by Kou et al. [17]. A complex of HP-β-CD with carbamazepine waspreparedinthepresenceof0.1%hydroxypropylmethylcellulose(HPMC).Theformedcomplex had increased the solubility of carbamazepine up to 95 times when compared to the drug alone. Furthermore, the complexation of carbamazepine with HP-β-CD rendered a 1.5-fold increase in the bioavailability of carbamazepine in beagle dogs when compared with an immediate-release commercially available carbamazepine tablet. The HP-β-CD-containing formulation rendered a maximumplasmaconcentration(C_{max})of4951.04±1585.21ng/mLandareaunderthecurve($AUC_{0-\infty}$) of 8597.85 ± 2786.18 ng▪h/mL in comparison to a C_{max} of 3577.99 ± 1444.90 ng/mL and $AUC_{0-\infty}$of 6000.65 ±2227.61 ng▪h/mL for the commercially available formulation. The improvement in bioavailability was attributed to an increase in dissolution rate of the HP-β-cyclodextrin complex containing formulation[17].

In a study by Desai et al. [21], orally disintegrating tablets (ODTs) were prepared containing an inclusion complex between eslicarbazepine and β-CD, which was prepared by using a solid dispersion technique. The ODT formulation exhibited 100% dissolution within 60 min compared to 72% dissolution for a commercially available tablet formulation. In an in vivo study in rabbits, theODTformulationexhibitedanimprovedbioavailabilityincomparisontothecommerciallyavailable formulation as characterized by a T_{max} of 2 h, C_{max} of 6661.34 ng/mL and $AUC_{0-\infty}$of 49,887.9 ng/mL▪h in comparison to a T_{max} of 4 h, C_{max} of 2534.39 ng/mL and $AUC_{0-\infty}$of 23,684.7 ng/mL▪h for the commercial formulation[21].

2.2. Disintegrants

Solid oral dosage forms, regardless of their drug release mechanism,have to undergoadisintegrationprocess.Inclusionofadisintegrantinsolidoraldosageformsusuallypromotesfaste rand/ormoreextensivedissolutionincomparisontoaformulationthatdoesnotcontainadisintegrant. A disintegrant is therefore an essential component in solid oral dosage formstoensure maximumpharmaceuticalavailabilityand,consequently,alsoacceptabledrugbioavailability[21,22].Mech anismsthroughwhichdisintegrantsbreakdosageformsupintosmallerpartsincludeswelling, heat generation due to increased interaction between particles, exothermicwickingaction, particlerepulsionandrecoveryofparticledeformation.Theswellingmechanismentailsthattheparticlesofth edisintegrantswellandexpandwhenexposedtomoisture.Thiswillcausetheneighboringparticles to be pushed away causing expansion of the dosage form leading to its disintegration.Itis importanttoensuresufficientvoidsinthedosageformwhenformulatingwithaswellingdisintegrantto allow enough moisture to enter into the dosage form to initiate the swelling process [23].

In a comparative study between jackfruit starch and croscarmellose sodium done by Suryadevara et al. [24], the excipients were investigated as superdisintegrants in the formulation of irbesartan(BCSclassIIdrug)containingfastdisintegratingtabletsviawetgranulation.Irbesartanand

other excipient concentrations were kept constant with the only variables being the jackfruit starch and croscarmellose sodium concentration. These two disintegrants were investigated at 2.5%, 5% and 10% w/w concentrations in the tablets. Irbesartan oral dosage forms provided a delayed and prolonged pharmacological action due to its poor solubility in intestinal fluids. The need for a fast hypotensive action exists for this drug, and a fast disintegrating tablet providing high concentrations of the drug in the gastro-intestinal tract rapidly may fulfill this need. The tablet formulation containing 5% w/w jackfruit starch as superdisintegrant delivered an extent of 97.5% dissolution compared to the pure irbesartan formulation, which achieved only 43.4% dissolution after 60 min. The inclusion of jackfruit starch resulted in a 2.25-fold increase in the extent of dissolution of irbesartan and a 1.17-fold higher dissolution extent than the commercially available irbesartan product. The formulation containing croscarmellose sodium as superdisintegrant rendered an extent of dissolution of 97.9%. This dissolution rate is 2.26-fold higher than the pure irbesartan formulation and 1.18-fold higher than the product which is currently on the market. The results of this study clearly indicated that the inclusion of a superdisintegrant provided the required fast disintegrating action allowing a larger surface area for contact with the gastro-intestinal fluids at an earlier time point, which in turn provided a higher concentration of irbesartan available for absorption[24].

In another study conducted by Husseiny et al. [25], valsartan was formulated into a fast disintegrating tablet using sodium starch glycolate and crospovidone in different concentrations. According to recent research, valsartan proved to be a promising candidate for the treatment of pediatric hypertension, especially in patients suffering from either diabetes or renal impairment[26]. In the results obtained from this study, it was shown that all tablet formulations containing the highest percentage of superdisintegrant (5% *w/w*) could disintegrate within 2 min. The dissolution results indicated that both sodium starch glycolate (5% *w/w*) and crospovidone (5% *w/w*) formulations exhibited the highest percentage dissolution and also the fastest initial dissolution rate. In vivo antihypertensive activity results of the tablet formulations were in agreement with the disintegration and dissolution results, indicating that the tablet formulations containing 5% *w/w* sodium starch glycolate and 5% *w/w* crospovidone exhibited the best blood pressure lowering results. The tablet formulations lowered the arterial blood pressure by 60 and 20 mm Hg, respectively, for the formulation containing 5% *w/w* crospovidone and 5% *w/w* sodium starch glycolate within the first hour after oral administration. The reference oral suspension formulation only managed to lower the arterial blood pressure by 10 mm Hg throughout the 3 h duration of the in vivo evaluation. The fast disintegrating tablet formulations exhibited an antihypertensive effect after only 15 min post administration, whereas the oral suspension formulation exhibited the first sign of antihypertensive action 60 min after oral administration. The early disintegration and release of active ingredient from the fast disintegrating tablet formulations contributed to the early onset of action and was most likely mediated by faster and more efficient absorption of valsartan[25].

Disintegration of a solid oral dosage form and the dissolution of the active ingredient after the disintegration process is known to be crucial and can be the rate-limiting step for drug absorption. Inclusion of disintegrants in solid oral dosage forms have been proven to increase the disintegration rate of solid oral dosage forms and consequently increase the percentage dissolution, bioavailability and the pharmacological effect of certain active ingredients.

2.3. pH Adjusting Excipients

The pH of the boundary layer (or stagnant diffusion layer) on the surface of solid drug particles is of special importance for the dissolution of weak acidic and basic drugs [27]. It is possible to improve the dissolution rate of weak acidic and basic drugs by including pH-adjusting excipients in a formulation that is capable of changing the pH of the stagnant diffusion layer or micro-environment. pH-adjusting excipients are mixed with the other ingredients of a solid oral dosage form prior to being compressed into tablets or filled into capsule shells. When disintegration of the dosage form takes place, these excipients dissolve in the fluids of the gastrointestinal tract. These excipients then cause

a pH adjustment of the stagnant diffusion layer due to provision of H^+ or OH^- ions (depending on whetherdecreasingorincreasingofpHisdesired)thatfavorsthedissolutionoftheactiveingredient by forcing its molecules to exist more in the ionized state[28–30].

Examples of pH-adjusting excipients that can be used to improve the dissolution rate of weak basicdrugsincludeorganicacids(e.g.,citricacid,tartaricacidandcarbonicacid).Afterdisintegration ofasoliddosageform,theorganicaciddissolvesinthesurroundinggastricjuicesandlowersthepH ofthestagnantdiffusionlayersurroundingeachdrugparticle,creatingadesirableenvironmentforthe dissolutionandconsequentlytheabsorptionofalkalinedrugs.Acidicdrugs,ontheotherhand,would exhibitanimprovedsolubilityaswellasdissolutionrateinanalkalinemicro-environmentsincethey will exist more in the ionized state[28–30].

Inastudyinvestigatingtheeffectofsodiumbicarbonate($NaHCO_3$)andcalciumcarbonate ($CaCO_3$) on the pharmacokinetics of paracetamol after oral administration to human subjects, it was shownthattheinclusionof$NaHCO_3$(630mg)intabletsresultedinafasterabsorptionofparacetamol asindicatedbyalowerT_{max} valueandhigherC_{max}value.Furthermore,theinclusionof$NaHCO_3$also reducedthevariabilityinabsorption.Theincreaseinabsorptionofparacetamoluponthеinclusionof $NaHCO_3$inthetabletformulationswaspartlyattributedtoanincreaseininvivodissolutionrate.Itis, however,interestingtonotethatthiseffectwasnotseenwiththeinclusionof$CaCO_3$,andthereason for this occurrence is not clear yet [31]. In another study, the combination of Na_2CO_3 (an alkalizing agent)andpoloxamer407(apolymerusedintheformulationofanano-emulsifyingsoliddispersion formulations)withaceclofenac(apoorlywater-soluble,weakacidicdrug)resultedinanincreaseinthe invitrodissolutionrateofthedrug.Theincreaseindissolutionratewasattributedtoacombinationof threemechanisms,namelymodulationofthemicroenvironmentalpH,changingdrugcrystallinityand providingamorefavorablenano-emulsion-formingenvironment[32].Inafollow-upstudy,alsousing aceclofenacasmodeldrug,itwasshownthattheinclusionofNa_2CO_3inabilayeredtabletformulation resulted in an enhanced solubility and higher plasma concentration in comparison to a reference formulationinbeagledogs.Furthermore,itwasillustratedthattheinclusionofNa_2CO_3asalkaliniser rendered improved in vivo drug safety (decreased gastrointestinal bleeding). This improved safety profilewasattributedtotheeffectsofthealkaliseronthemicroenvironmentalpHandareductionin the size of the drug particles[33].

2.4. Amorphous SolidDispersions

The implementation of a solid dispersion as part of a dosage form is considered one ofthemosteffectivewaystoimprovetheaqueoussolubilityofanAPIandconsequentlyitsbioavailability.Aso liddispersiondescribesthedispersionofoneormoreactiveingredient(s)inacarriermatrixmaterial.Thematr ixconsistsofapolymerinmostcases,andexamplesincludePVP(polyvinylpyrrolidone),HPMC (hydroxypropyl methylcellulose), HPMCP (hydroxypropyl methylcellulosephthalate),chitosan,CMC(carboxymethylcellulose),sodiumalginateandsodiumstarchglycolate.Asoliddispersionsystemcontainspotentialenergythatisavailabletoassistinmaximizingdrugrelease.Uponreachingaspecificareainthehumangastro-intestinaltractthatisfavorablefordrugdissolutionandabsorptionduetocertainfavorableenvironmentalproperties,themaximumdrugconcentrationwillbereleasedfromthedispersion.Soliddispersionscanbeprepareusingmethodssuchasspraydrying,freezedrying,co-precipitation,fusionmethods,hotmeltextrusionandsupercriticalfluidprecipitation[34,35].

When composing an amorphous solid dispersion, the drug is dispersed in a polymer matrix in theamorphousstate.Studieshaveshownthattheamorphoussoliddispersionofanactiveingredient increases the solubility and bioavailability compared to the crystalline state of the same drug. In a study conducted by Herbrink et al. [36], it was said that amorphous drug particles have a higher Gibbsfreeenergyincomparisontothecrystallineform,whichincreasedthesolubilityofthedrug.

Thebioavailabilityofthemarketedproduct,Tasigna® nilotinib,isrelativelylowandestimatedatabout 30%, which is also characterized by substantial variability. A solid dispersion of nilotinib was preparedbymeansofspraydrying.NilotinibwasmolecularlydispersedinSoluplus®,apolyethylene

glycol,polyvinylacetateandpolyvinylcaprolactame-basedgraftco-polymerataratioof1:7.Thissolid dispersion exhibited a remarkable increase in the solubility of the drug. Whether the increase in solubilityofthisdrugwillrenderacorrespondingincreaseinbioavailabilityshouldbeinvestigatedby follow up in vivo studies[36].

Inarecentclinicalstudywiththedrugposaconazole,asoliddispersionwasformulatedusinghot meltextrusiontodisperseposaconazoleinhydroxypropylmethylcellulose(HPMC)acetatesuccinate (HPMC-AS)matrix.Hydroxypropylmethylcellulose(HPMC)acetatesuccinateisapolymershowing pH-sensitivereactionsinthehumangastro-intestinaltract.ResultsobtainedbyHensetal.[37]showed that dispersing posaconazole in HPMC-AS caused a supersaturation of the drug throughout the gastro-intestinal tract and an absorption profile less dependent on the gastric pH, fed or fasted state in healthy human test subjects. This study showed that formulating a delayed release formulation provided more sufficient posaconazole release in comparison to an oral solution of posaconazole. This study showed that fasted state absorption of posaconazole was improved drastically, and further absorption along the gastro-intestinal tract was also noted due to the delayed release of posaconazole[37].

Inastudyconductedondutasteride(5-αreductaseinhibitor),commerciallyavailableasAvodart®, the active ingredient was formulated as a solid dispersion. The solid dispersion was prepared using the solvent evaporation method implemented via a vacuum desiccator. Hydrophilic excipients were alsoincludedtoenhancedrugdissolution.Thepowdertypedispersionofdutasterideincombination with tocopherol polyethyleneglycol-1000-succinate, sodium lauryl sulphate and microcrystalline cellulose provedtobeasuccessfulcombinationinenhancingitsdissolutionaswellasitsbioavailability. Tocopherolpolyethyleneglycol-100-succinateisavitamin-Ederivativeandwasusedasasolubilizing agent to enhance drug dissolution. Sodium lauryl sulphate was included as a surfactant to enhance wettability of the solid oral dosage form, and microcrystalline cellulose was included as the carrier to inhibit recrystallization of dutasteride. The carrier medium also provided a stable environment for the active ingredient and for the other excipients. The dutasteride solid dispersion proved to be successful, and a significant increase in dissolution percentage of 10–20% was noted. Thepercentageof bioavailability also increased when compared to the Avodart® soft capsule [38,39].

Curcumin, an extract prepared from *Curcuma longa*, has enjoyed recent attention due to the pharmacological activity which this natural compound exhibited. According to recent research, curcuminprovidesanti-angiogenic,anti-microbial,anti-inflammatory,anti-oxidationandanti-cancer properties [40]. Curcumin can be classified in class IV of the BCS due to its hydrophobic properties andlowwatersolubility[40].Inanattempttoimprovethesolubilityandmembranepermeabilityofcurcumin ,Huangetal.[41]preparedanamorphoussoliddispersionusingChitosan®oligosaccharide as a carrier matrix. This oligosaccharide provided a low viscous, hydrophilic environment and also increased the possibility of improved membrane permeability by means of opening of the tight junctions in the gastro-intestinal epithelium. The results obtained proved that the use of this oligosaccharide attributed immensely to the solubility and permeability of curcumin. Examiningthe resultsofthisstudy,itbecameevidentthatthesolubilityoftheamorphoussoliddispersionwithcurcuminand theChitosan®oligosaccharide revealedsolubilizationresultsof97.85–101.21 µg/mL comparedtothe60.62µg/mLreachedfornormalcurcumin.Theapparentpermeabilityresultsacross biological membranes showed a 1.72- to 4.44-fold increase compared to that of the normalcurcumin. The Chitosan® oligosaccharide proved to be a successful carrier matrix for preparing an amorphous solid dispersion to ensure more efficient delivery of curcumin [41].

2.5. Surfactants

Solubilization of the API in the gastro-intestinal fluids after oral administration is considered a fundamentalstepforoptimalpermeabilityandbioavailability.Inaddition,notallAPIsandexcipients usedintabletformulationspossessgoodaqueouswettabilityproperties,andfunctionalexcipientsare needed to enhance their wettability[42].

Surfactantsareincludedinsolidoraldosageformstoreducetheinterfaceenergybarrierbetween the dissolution medium and the API, which will allow for more efficient wettability. Surfactants are amphiphilicsubstancesthatcontainbothhydrophobic(non-polar)andhydrophilic(polar)functional groups in their molecular structures[43,44].

Surfactants are able to form micelles above the critical micelle concentration (CMC) in aqueous liquidssuchasthefluidsfoundinthegastro-intestinaltract.Thesemicellescanincreasethesolubility of poorly water-soluble active ingredients by incorporating these molecules in the lipophilic cores of the micelles[43].

Anionic surfactants are also known as amphiphilic surfactants because they contain both polar and non-polar functional chemical groups in their structures (e.g., sodium lauryl sulphate (SLS)). Othersurfactantsincludecationicsurfactantsthatarecommonlyusedasdisinfectants(e.g.,cetrimide), non-ionicsurfactants(e.g.,alkylbetaine)andamphoteric/zwitterionicsurfactants(e.g.,polysorbates).

Surfactantsmostcommonlyusedinsolidoraldosageformsare SLS, poloxamers and d-α-tocopherol polyethylene glycol succinate[39,43–45].

It was illustrated in a study that the inclusion of a 5% *w/v* concentration of SLS increased the dissolution rate of celecoxib significantly, and within the first 20 min of the dissolution test, thedissolutionoccurredthreetimesfaster. Sodiumlaurylsulphatehasshowntheabilitytoincreasethe solubilityofdrugssuchastramadolhydrochloride,methocarbamol,diazepam,alprazolam,gabapentin, buspirone and acetaminophen [43]. Increased solubility of the active ingredient only occurred when the CMC was reached[42,43,45].

AccordingtothestudyconductedbyVarmaandPanchagnula[46],theadditionofd-αtocopherol polyethylene glycol succinate (TPGS) to a formulation containing the anti-cancer drug paclitaxel provedtoenhancethesolubilityandbioavailabilityofthisdrugsignificantly.Theaqueoussolubility of paclitaxel increased drastically once the CMC (0.2 mg/mL) of TPGS was reached, and it increased 38-foldwhencombinedwith5mg/mLTPGS.Whenthepaclitaxel–TPGScombinationwasadministered orallytorats,asignificantincreaseindrugabsorptionwasidentified.TheAUCofpaclitaxelincreased 1.5-folduponco-administrationwithTPGS.Thesolubilizationofpaclitaxelledtoahigherconcentration of drug available at the site of absorption, leading to an overall increase in the bioavailability of paclitaxel[46].

InastudyconductedbyStoyanovaetal.[42],thesolubilizationeffectofdifferentsurfactantson the anti-inflammatory drug ibuprofen was investigated. In this study, non-ionic surfactants(Tween® 20, 40, 60 and 80) and anionic surfactants (sodium dodecyl sulphate and sodium lauryl ethoxy (3) sulphate)wereaddedtoseparateibuprofensolutions.Aconstantconcentrationofeachsurfactantwas added to respective ibuprofen solutions, and the strength of the interactions of the surfactants with ibuprofen was analyzed using thermodynamic treatment. It was evident that all of the surfactants analyzedinthisstudyrevealedanincreasedsolubilityofibuprofenthroughsolubilization.Regarding thenon-ionicsurfactants,itwasclearfromtheresultsofthisstudythatanincreasedsolubilizationof ibuprofenoccurredwithanincreasedquantityofcarbonionsfoundinthehydrophobicchainsofthe polysorbates(Tween®).Thesurfactantssodiumdodecylsulphate,sodiumlaurylethoxy(3)sulphate andTween®80revealedanincreasedaqueoussolubilitybyafactorofaround200.Thesurfactantthat showedthehighestincreaseinsolubilityofibuprofenwasTween®80,andthispolysorbatewasalso the only one in this study containing a double bond in the hydrophobic chain[42].

2.6. Self-Emulsifying Drug Delivery Systems(SEDDS)

Self-emulsifying drug delivery systems (SEDDS) represent a type of lipid-based drug delivery system that emulsifies in the gastro-intestinal tract and can be divided into three groups regarding emulsion droplet size after emulsion formation in the gastro-intestinal tract. SEDDS are emulsion deliverysystemsconsistingofdropletsizesof>300nm,whileSMEDDS(self-micoremulsifyingdrug deliverysystem)consistsofdropletsizesof<250nmandSNEDDS(self-nanoemulsifyingdrugdelivery system)consistsofdropletsizesof<100nm.ThegeneraldiscussiononSEDDSinthissectionwillalso

includeinformationregardingSMEDDSandSNEDDS.SEDDSwerespecificallydevelopedtoimprove theslowdissolutionandpoororalabsorptionofhydrophobicandhydrophilicmacromoleculardrugs. SEDDSconsistofanisotropicmixtureoflipids/oils,surfactants,co-surfactantsandco-solvents.Inmost formulations, the surfactant is water soluble while the co-surfactant is lipid soluble. SEDDS are commonlyadministeredorallyintheformofsoftgelatinecapsulesorascompressedtablets.Oncethe slightestagitationisappliedtothedosageforminthegastro-intestinaltract,aself-emulsifyingeffect will be initiated inside the gastro-intestinal tract after administration. The formulation of SEDDS is a relativelynewfield,andtherearestillunresolvedproblemsregardingitsmanufacturingmethodand the optimum combination of excipients. Research is therefore currently being undertaken regarding S-SEDDS(solidself-emulsifyingdrugdeliverysystem)toestablishamorephysicochemicalstableand viable dosage form for oral administration[47–49].

InarecentstudyconductedbyChaudharyetal.[50],thelipophilicBCSclassIIdrugnabumetone wasinvestigatedforpotentialformulationintoSNEDDS.Initiallydifferentformulationswereprepared includingdifferentconcentrationsofthedrug,Tween® 80(surfactant),polyethyleneglycol400(co-surfactant), capryol-90 (oil/lipid) and an aqueous phase of deionized water. The nabumetone (40%*w*/*w*)wasdissolvedinthecapryol-90,thereafterthemixtureofTween® 80andpolyethylene glycol 400 (PEG 400) was added to the oil phase in small controlled quantities, while adding the aqueous deionized water dropwise under continuous vortex conditions until stable SNEDDS were noticeable. According to the results obtained, one formulation was identified to have a droplet size of 55.06 nm (±5.67 nm). This formulation contained 40% *w*/*w* nabumetone, 22% *w*/*w* capryol-90(oil), 16%*w*/*w*Tween® 80and4%*w*/*w*PEG400. Regardingtheinvitrodissolutionstudyresults,this SNEDDSrevealedatotalof95.61%drugreleaseofwhich66%wasreleasedwithinthefirst4hofthe dissolution test. A suspension was made containing the nabumetone commercially available tablet. Thissuspensionexhibiteda48.53%drugrelease,whichimpliesthattheSNEDDSformulationprovided a 1.97-fold increase in drug release over a period of 4 h. The in vivo bioavailability evaluations were done in Wistar rats (weighing 200–250 g). The in vivo bioavailability results were in agreement with the dissolution results, which showed that a C_{max} value of 45.38 ng/mL could be reached with the SNEDDS formulation, while only 23.95 ng/mL was obtained for the commercial tablet suspension, revealing a 1.89-fold increase in C_{max} for the SNEDDS[50].

Anotherexampleofthesuccessfulimplementationofalipid-baseddrugdeliverysystemintheformofSMEDDSwasillustratedbyKangetal.[51],wheresimvastatincontainingSMEDDSwereformulatedandevaluatedcomparedtothecommercialproductZocor®. Simvastatinpossesseshydrophobic properties and exhibits poor dissolution in the human gastro-intestinal tract, resulting in a relatively lowbioavailability.ThedifferentSMEDDSformulationswerepreparedbydissolvingthesimvastatin intheco-surfactant.Thereafter,thesurfactantandtheoilphaseweremixedtogether.Themixtureof surfactantandoilphasewasaddeddropwisetothemixturecontainingsimvastatinandco-surfactant, and during the mixing process, vortexing was applied to ensure adequate mixing. Five SMEDDS formulations were prepared consisting of different concentrations of capryol 90 (oil), lauroglycol 90 (oil),carbitol(co-surfactant),PEG400(co-surfactant),polypropyleneglycol(co-surfactant),cremophor EL(surfactant)anddeionizedwater.InvitrodrugreleasewasevaluatedusingtheUSP2methodwith a buffered medium at a pH of 6.8. In vitro evaluation was done by means of oral administration of the SMEDDS formulations to beagle dogs. Both in vivo and in vitro results of the formulation with the smallest average droplet size of 33 nm revealed much higher drug release than the commercial tabletandrevealedaC_{max}of35.35ng/mLcomparedtothecommercialproductexhibitinga$C_{max}$of 18.19 ng/mL. This formulation showed a relative bioavailability percentage of 159% [51].

2.7. Sugars

Sugars and sugar-containing excipients have been used for many years as multifunctional excipients in directly compressed tablets as well as other solid oral dosage forms. Most frequently usedsugartypeexcipientsincludedirectcompressiblesucrose(95%sucroseand5%sorbitol),sucrose

esters, sucrose laurate (non-ionic surfactant), crystalline maltose, mannitol and glucose. Initially, sucrose-basedexcipientswereutilizedfortastemaskingpurposes,butcurrentlytheyarealsoutilized for additional purposes such as compressibility of tablets, hydrophilic/hydrophobic dual properties and inclusion in nano-suspensions and nanoparticles as sucrose esters[52,53].

In a study regarding the formulation of a solid dispersion containing sucrose laurate and gemfibrozil,thesoliddispersionwasformedviathemeltingtechnique.Thisstudyincludedatoxicity evaluation to prove that the sucrose-based surface active agent did not pose the same toxic effects as many other surfactants. The effect of different concentrations (1%, 5%, 10% and 15% *w/w*) of sucrose laurate was investigated on the dissolution of the drug. Dissolution results revealed that optimal gemfibrozil release occurred using sucrose laurate in concentrations of 5–10%, obtaining 100% gemfibrozil release within 10 min compared to the 30% release reached after 10 min from the gemfibrozil suspension. These results proved a significant increase in the dissolution of gemfibrozil by sucrose laurate. Evaluation of cytotoxicity of sucrose laurate on Caco-2 cells revealed that the concentrations of sucrose laurate that mediated the best gemfibrozil dissolution (5% and 10% *w/w*) were non-toxic[54].

Mannitolismanufacturedviaacatalytichydrogenationprocessofthenaturalsugarsglucoseor fructose.Thisfunctionalexcipientishighlywatersoluble,non-hygroscopic,non-toxicandshowslittle sensitivity to applied heat. Mannitol is generally recognized as safe, and this excipient is frequently usedinthepharmaceuticalmanufacturingofsoliddosageforms.Mannitolconsistsofhighlyporous particleswitharelativelylargesurfacearea.IncorporationofAPIswiththemannitolcreatesahighly porous powder mixture with improved water wettability and dissolution rate. Recent studies have shown that incorporating mannitol in formulations via physical mixtures, melting techniques or kneading methods could increase the dissolution rate of the APIs significantly[55,56].

In a study conducted by Yadav et al. [57], mannitol formulated with ketoprofen by way of three differentmethods(i.e.,melttechnique,physicalmixtureandkneadingmethod)revealedanincrease in ketoprofen dissolution rate, which correlated directly with the concentration of mannitol added. Ketoprofen:mannitol formulations in ratios of 1:1, 1:3 and 1:5 were formulated for each of the three methods, rendering a total of nine formulations. From the results of this study it was clear that all ratiosof1:5(ketoprofen:mannitol)exhibitedthebestresultswithrespecttodrugreleaseafter30minin a pH 1.2 medium. The three mannitol-containing formulations outperformed the pure ketoprofen suspension by at least 51% in all three preparation methods. The highest extent of dissolution after 30minwas72.28%forketoprofenformulatedviathekneadingmethod.Themeltingmethodandthe physical mixture method resulted in drug releases of 66.34% and 63.76%, respectively. According to Yadavetal.[57],theincreaseddissolutionresultswereobtainedduetoahigherwettabilityofthepowder mixture and also because of a smaller particle size obtained after dispersion of the drug in the mannitol creating a higher contact surface area. The contribution of a decrease in particle size to dissolution was also confirmed by a study conducted by Nassab et al. [56], regarding the drug meloxicam, where the particle size of meloxicam was varied and dispersed in mannitol. Results in this study showed an increase in drug release with smaller size particles of meloxicam and with an increase in the concentration of mannitol. Several studies showed that mannitol can increase the dissolutionrateofhydrophobicdrugsviamorethanonemechanism[56,57],suchastheattractionof watermoleculesintothedosageformduetobetterwettabilityofthedosageformthatalsocausesan increase in dissolution rate of the activeingredient.

2.8. Soluble and Insoluble FillerMaterials

A filler is an excipient normally used in solid oral dosage forms to provide sufficient mass and volume. Multifunctional fillers are now used in solid oral dosage forms to fulfill more than one function. Two major groups of pharmaceutical filler materials exist, namely aqueous soluble and aqueousinsolublefillers.Fillersfororalsoliddosageformsarechosentohelpreachthebestpossible drugreleaseprofilefromthedosageformintheenvironmentofthehumangastro-intestinaltract[1,58].

MCC (microcrystalline cellulose) is one of the most frequent used filler materials in the pharmaceutical industry to produce direct compressible tablets and beads. MCC is purified cellulose that is partially depolymerized and is obtained from fibrous plant material (e.g., wood) [58,59]. In a recent study, the antioxidant quercetin was combined with MCC via a crystallization technique called fluid bed crystallization. MCC was placed in the fluid bed followed by a quercetin–acetone mixture of specific concentrations. Quercetin nanorods were then dispersed onto the surfaces of the MCC particles after dehydration. In vitro dissolution testing was conducted over 2 h in 0.1 M HCl to represent the gastric pH of 1.2. The antioxidant effects of the quercetin formulations were evaluated in vitro via utilization of a DPPH (2,2-diphenyl-1-picrylhydrazyl) scavenging assay. A decreased value of DPPH absorbance indicated an increased antioxidant effect by quercetin. The dissolution increased significantly compared to the quercetin control formulation. The top performing formulation indicated more than double the drug release (34.8%) after only 5 min compared to the quercetin control formulation (15.6%). The total drug release after 2 h was 76.2% for the top performing formulation and 56.4% for the quercetin control formulation. The in vitro antioxidant evaluation revealed a constant increase in inhibitory effect, with values being significantly higher than the quercetin control formulation at 20, 60 and 120 min. The dispersion of quercetin particles onto the surface of the MCC decreased the particle size of the drug throughout the mixture, thereby increasing the surface area available for dissolution medium contact and thus increasing the dissolution of the drug and also the antioxidant effect [60].

An example of an aqueous soluble filler that has been used extensively in the pharmaceutical industry for many years is lactose. The most common forms of lactose used in solid oral dosage form formulations are crystalline alpha-lactose monohydrate, beta-lactose (crystalline anhydrous lactose) and amorphous lactose. Uptake of the dissolution medium in a dosage form is of importance to achieve optimal dissolution and bioavailability of the active ingredient inside the dosage form. Formulating a solid oral dosage form with an aqueous soluble diluent that attracts water towards the dosage form may contribute to enhanced dissolution rate of hydrophobic/poorly aqueous soluble APIs [61].

Li et al. [62] used lactose as carrier for a nanodispersion containing bicalutamide. Bicalutamide is a BCS class II drug exhibiting poor solubility in the gastro-intestinal fluids leading to low dissolution and bioavailability. It was stated that the small particle size of this drug caused agglomeration of the powder mixtures, and it was best to keep this drug dispersed in a carrier medium. Nanodispersions were formulated using the liquid precipitation method dispersing the bicalutamide particles onto the surface of the lactose creating a large contact surface area for optimal solubility. Other formulations contained different functional excipients also formulated for enhanced dissolution purposes. All formulations containing functional excipients revealed enhanced dissolution and drug release from the nanodispersions. All formulations exhibited equal or more than 50% drug release within the first 10 min, but the dispersion formulated using lactose as carrier revealed a 94% drug release within 10 min and 99% release within a period of 2 h. An MCC–bicalutamide formulation was also formulated showing less than 50% drug release within 10 min and only 85% release after 2 h. The control bicalutamide formulation only managed 30% release after 10 min and 78% after the 2 h period. The experimental formulations were compared to that of a reference drug product on the market (Casodex®), which showed 60% drug release after 10 min. Not only did the lactose–bicalutamide combination exhibit faster release of the API but also a higher percentage release overall during the 2 h evaluation period. The key to the success in this study was mediated by smaller particles of a poorly aqueous soluble drug dispersed onto aqueous soluble carrier particles attracting water into the formulation [62].

A summary of excipients that have been investigated and used in dosage forms for improvement of drug solubility and dissolution rate is given in Table 1.

Table 1. Summary of functional excipients used in different types of dosage forms to improve drug solubility and dissolution rate.

Excipient	Excipient Subdivision	Drug Example	In Vitro/In Vivo	Dosage Form Type	Reference
Cyclodextrin	β-Cyclodextrin	Eslicarbazepine	in vitro + in vivo	Orodispersable tablet (solid dispersion)	[21]
	HP(2-Hydroxypropyl)-β-Cyclodextrin	Carbamazepine, Naproxen	in vitro + in vivo	Immediate release tablet/ Enteric coated tablet	[14,17]
Disintegrants	Croscarmellose Sodium and Jackfruit starch	Irbesartan	in vitro + in vivo	Direct compressed fast disintegrating tablet	[24]
	Sodium starch glycolate and crospovidone	Valsartan	in vitro + in vivo	Direct compressed fast disintegrating tablets	[25]
pH adjusting excipients	Citric acid	Ketoconazole	in vitro + in vivo	Physical mixture (granules)	[30]
	Tartaric acid	Ketoconazole	in vitro + in vivo	Physical mixture (granules)	[30]
	Sodium Hydrogen Carbonate	Paracetamol	in vitro + in vivo	Controlled release matrix tablet	[33]
	Calcium Carbonate	Paracetamol	in vitro + in vivo	Controlled release matrix tablet	[33]
	di-Sodium Carbonate	Aceclofenac	in vitro + in vivo	Controlled release matrix tablet	[33]
	di-Sodium Carbonate	Aceclofenac	in vitro + in vivo	Nanoemulsifying GUC (Gelucire 44/14)-based solid dispersions	[32]
Solid dispersions	Tocopherol polyethyleneglycol-1000-succinate	Dutasteride	in vitro + in vivo	Physical mixture (solid dispersion)	[38]
	Polyethylene glycol, polyvinyl acetate and polyvinylcaprolactame-based graft co-polymer	Nilotinib	in vitro	Encapsulated physical mixture (spray-dried mixture)	[36]
	Hydroxypropyl methylcellulose acetate succinate	Posaconazole	in vitro + in vivo	Delayed release tablet	[37]
	Chitosan	Curcumin	in vitro + in vivo	Amorphous solid dispersion	[41]

Table 1. *Cont.*

Excipient	Excipient Subdivision	Drug Example	In Vitro/In Vivo	Dosage Form Type	Reference
Surfactant	Sodium lauryl sulphate	Celecoxib, Tramadol, Methocarbamol Diazepam, Alprazolam, Buspirone, Gabapentin and Acetaminophen	in vitro	Direct compressed tablet	[43]
	Tween 20, Tween 40, Tween 60, Tween 80, sodium dodecyl sulphate and sodium lauryl ethoxy (3) sulphate	Ibuprofen	in vitro	Oral solution	[42]
	D-α-tocopherol polyethylene glycol 1000 succinate	Paclitaxel	in vitro + in vivo	Oral mixture	[46]
	D-α-tocopherol polyethylene glycol 1000 succinate	Dutasteride	in vitro + in vivo	Physical mixture (solid dispersion)	[38]
SNEDDS	Capryol-90, Tween 80 and PEG-400	Nabumetone	in vitro + in vivo	Oral SNEDDS	[50]
SMEDDS	capryol 90, lauroglycol 90, carbitol, PEG 400, polypropylene glycol and cremophor EL	Simvastatin	in vitro + in vivo	Oral SMEDDS	[51]
Mucoadhesive/ Mucopenetrating polymer	Chitosan	Telmisartan	in vitro + in vivo	Oral co-crystals	[63]
	Chitosan	Carvedilol	in vitro + in vivo	Oral nanoparticles	[64]
Sugars	Sucrose laurate	Gemfibrozil	in vitro	Oral solid dispersion	[54]
	Mannitol	Ketoprofen	in vitro + in vivo	Oral co-crystals	[57]
	Mannitol	Meloxicam	in vitro + in vivo	Oral co-crystals	[56]
Soluble and insoluble fillers	MCC	Quercetin	in vitro + in vivo	Oral co-crystals	[60]
	Lactose	Bicalutamide	in vitro	Oral nanodispersion	[62]

3. Conclusions

Variousapproachescanbefollowedoremployedtoimprovethedissolutionofapoorlysoluble APIinasolidoraldosageformrangingfromincorporationoffunctionalexcipientstotechniquessuchas preparation of solid dispersions and micronisation of the API particles. Examples of excipients that canincreaseanAPI'ssolubilityanddissolutionrateincludecyclodextrins,disintegrants,pH-adjusting excipients, natural polymers, surfactants, co-surfactants, oils/lipids andsugars.

Several studies have shown that different classes of functional excipients have a definite and beneficialeffectonthesolubility/dissolutionandconsequentlythebioavailabilityofpoorlysolubleAPIs. For certain excipient groups such as super disintegrants and pH-adjusting excipients,invivoand clinical studies seem to be limited. Furthermore, most studies only used a single,poorly soluble APIasrepresentativecompound.Thereisaneedforfurtherresearchtoshowtheapplicabilityof(multi)funct ionalexcipientstoenhancethesolubility/dissolutionandconsequentlythebioavailabilityof a wide variety of poorly soluble APIs. It is of special interest to determine theclinical significanceor value of formulation approaches on drug bioavailability and if they could result indecreasingthedose needed to reach effective blood plasma levels. Considering that approximately 40%ofcurrentmedicationproductscontainAPIsthatexhibitpooraqueoussolubility,andapproximately90 %ofnewly discovered therapeutic compounds in the development phase exhibit pooraqueoussolubility,futureresearchregardingtheidentificationofsolubility-enhancingexcipientsisofcardinalimportance.

IdentifyingthecorrectformulationmethodandusingthesuitableexcipientinrelationtotheAPI mayresultinefficientpharmacologicaltreatmentbymeansofadministratingalowerdose,whichmay have a significant costimplication.

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Chapter 3

Research article

This chapter of this thesis is presented in the form of a research article, which was submitted for publishing in the journal “Pharmaceutical Development and Technology” in November 2020. Author guidelines regarding this journal can be found in “Annexure M” of this document. This article’s main focus was to highlight the effect of functional excipients on the dissolution and membrane permeation of furosemide formulated into multiple-unit pellet system (MUPS) tablets.

Effect of functional excipients on the dissolution and membrane permeation of furosemide formulated into multiple-unit pellet system (MUPS) tablets

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Effect of functional excipients on the dissolution and membrane permeation of furosemide formulated into multiple-unit pellet system (MUPS) tablets

The effect of functional excipients (i.e. chitosan, sodium lauryl sulphate, $NaHCO_3$ and $CaCO_3$) formulated in multiple-unit pellet system (MUPS) tablets has been investigated on the dissolution and permeability of furosemide, a BCS class IVcompound. Spherical beads were produced and compressed intoMUPS tablets. MUPS tablet formulationswere evaluated for hardness, disintegration, mass variation, friability and dissolution (pH 1.2, pH 4.6 and pH 7.4).*Ex-vivo* permeability studies were conducted across excised pig tissues (pyloric antrum and duodenal region) on selected experimental MUPS tablet formulations. Histological analysis was conducted on the tissues after exposure to selected experimental MUPS tablet formulations. Dissolution resultsin the 0.1 M HCl (pH 1.2)showed the highest effect of the excipients on furosemide release. Dissolution parameters showed increased dissolution of furosemide for the MUPS tablet formulations containing functional excipients: a 4.5 – 10 fold increase in the AUC values, the $\%_{max}$showed a 60 – 70% increase and up to a 19 fold increase in DRi was seen. Permeability results revealed a 2.5 fold higher cumulative percentage transport for selected formulations. The results proved that functional excipients incorporated into beads, compressed into MUPS tablet formulations increased furosemide release as well as permeation across excised intestinal tissues.

Keywords: Functional excipients, Furosemide, Multiple-unit pellet system, Dissolution, Permeability

1. Introduction

Oral ingestion remains the route of choice for the administration of medicines, which can be attributed to several factors such as the non-invasive nature and ease-of-use of the oral route of drug administration (Lipp 2013). However, poor aqueous solubility of active pharmaceutical ingredients is a major challenge hampering their successful oral delivery. Although drug discovery is an important and exciting field of research, approximately 40% of newly discovered therapeutic chemical entities exhibit poor aqueous solubility (Lipp 2013; Salappa

et al. 2015). Poor aqueous solubility of a drug may result in several undesirable *in vivo* consequences, which include incomplete release from a dosage form, poor bioavailability and relatively high inter-patient variability. The relatively low bioavailability of these drugs is related to the complex interplay between chemical, physiological and biochemical processes, which are involved during the drug delivery process (Boyd et al. 2019). It has been shown that the two major factors that determine oral drug bioavailability are solubility and membrane permeability as postulated in the Biopharmaceutics Classification System (BCS) (Amidon et al. 1995; Dahan et al. 2016).

Formulation of a solid oral dosage form such as a tablet, which contains a drug that possesses poor aqueous solubility and poor membrane permeation properties, will pose challenges with respect to the drug's systemic delivery. It therefore requires careful consideration and a scientific approach to overcome these challenges in order to ensure efficient drug delivery to reach the required drug plasma concentration (Xu et al. 2018; Sadeghi et al.2019). To improve the systemic delivery of poorly soluble drugs, novel approaches can be used such as pro-drug strategies, salt formation, employment of amorphous solid dispersion technology, formulation of lipid based delivery systems, preparation of inclusion complexes and microemulsion delivery systems (Boyd et al. 2019). A promising formulation approach to improve the solubility as well as dissolution rate of poorly soluble drugs that will also enhance membrane permeation is the inclusion of functional excipients in dosage forms (Grattan et al. 2000; Hamman and Steenekamp 2012; Van der Merwe et al. 2020).

Functional excipients can be described as pharmaceutical excipients that fulfil specific roles in dosage forms such as easing the manufacture process, improve the quality or performance of the product (Moreton, 2006; Fouché et al. 2020). Different classes of functional excipients can be used in formulations, which include substances that enhance membrane permeability;

substances that enhance drug solubility; substances that protect the drug from degradation; substances that improve manufacturing and substances that modify drug release (Hamman and Steenekamp, 2012; Fouché et al.2020). Drugs grouped in class II (low solubility and high permeability) and class IV (low solubility and low permeability) of the BCS are candidates for formulation approaches to change their biopharmaceutical properties. Strategies that have been used to improve dissolution and membrane permeability and consequently also the bioavailability of drugs include particle size reduction, cyclodextrin complexation and pH modification (Grattan et al.2000; Kawabata et al. 2011; van der Merwe et al. 2020). Furthermore, surface active agents such as sodium lauryl sulphate have been shown to improve the wettability and dissolution of poorly soluble drugs (Jung et al.2016; Dun et al. 2018). Inclusion of pH modifying excipients such as sodium bicarbonate, calcium carbonate, ascorbic acid and magnesium oxide have shown to improve the dissolution and absorption of certain drugs (Grattan et al.2000; Adachi et al.2015; Kang et al.2017; Luo et al.2017). Renewed interest has recently been shown in the use of mucoadhesive/bioadhesive polymers as functional excipients to improve drug delivery. The objective by employing mucoadhesive polymers is to prolong contact time with the intestinal mucosal surface and thereby potentially improving membrane permeation (Menzel et al.2016; Khlibsuwanand Pongjanyakul 2016;Banerjee and Mitragotri, 2017; Rojewska et al.2019).

Multiple-unit pellet systems (MUPS) are dosage forms that have shown distinct advantages in drug delivery such as less inter-subject variation in bioavailability, reduced likelihood of dose dumping and lower fluctuations in plasma drug concentrations. Some of these advantages can partly be attributed to the distribution of the drug dose in small discrete units called pellets or beads (Chen et al.2019; Hamman et al.2019; Zheng et al.2019).

Furosemide is a typical poorly soluble drug that exhibits poor, variable and unpredictable

absorption and consequently also variable bioavailability. Furosemide is a weak acidic drug with a narrow absorption window in the gastrointestinal tract and is mainly absorbed from the stomach and upper region of the duodenum (Laulicht et al.2011). Furosemide is an example of a drug belonging to class IV of the BCS (Ghadiand Dand, 2017). Furosemide can be considered a model drug to investigate the influence of functional excipients and formulation design to improve solubility/dissolution and membrane permeation (Provenza et al.2014;Nielsen et al.2015;Han et al.2016; Shariare et al.2019).

The primary aim of this study was to improve the dissolution rate and extent of furosemide by means of formulation approaches including the use of a combination of pH adjusting excipients, a surfactant as well as a mucoadhesive agent in the formulation. The effect of the higher dissolution rate as a result of the formulation adjustments has also been investigated on the membrane delivery of furosemide.

2. Experimental design

The formulation variables investigated consisted of different combinations of pH adjusting excipients (i.e. sodium bicarbonate ($NaHCO_3$) and calcium carbonate ($CaCO_3$), a surfactant/wetting agent (sodium lauryl sulphate) and a mucoadhesive agent (chitosan)). Furthermore, three different bead sizes (i.e. 0.5, 0.75 and 1.0 mm) were prepared for each formulation that were then each compressed into MUPS tablets. The different formulation variables and levels of these variables that were applied in the MUPS tablet formulations are indicated in Table 1. A drug load of 10% w/w furosemide was kept constant throughout all 36 bead formulations, which were used to prepare the MUPS tablets with additional excipients to assist in tablet compression as indicated in Table 2. The control group consisted of three sizes of beads (i.e. 0.5, 0.75 and 1.0 mm) prepared from microcrystalline cellulose (Pharmacel®) containing 10% w/w furosemide that were each used to prepare MUPS tablets with the

additional excipients to assist in tablet compression (Table 2).

Table 1: Composition of the bead formulations indicating the variables (combination of functional excipients) and their levels that were investigated

				Bead size					
				0.5 mm		0.75 mm		1 mm	
				Mucoadhesive excipient (Chitosan)					
				0% w/w	15% w/w	0% w/w	15% w/w	0% w/w	15% w/w
pH adjusting excipients (20% w/w)	$NaHCO_3$:$CaCO_3$ (50:50)	**Wetting agent** Sodium lauryl sulphate	1.0% w/w	1A	1B	1C	1D	1E	1F
			0% w/w	2A	2B	2C	2D	2E	2F
	$NaHCO_3$:$CaCO_3$ (75:25)	**Wetting agent** Sodium lauryl sulphate	1.0% w/w	3A	3B	3C	3D	3E	3F
			0% w/w	4A	4B	4C	4D	4E	4F
	$NaHCO_3$:$CaCO_3$ (25:75)	**Wetting agent** Sodium lauryl sulphate	1.0% w/w	5A	5B	5C	5D	5E	5F
			0% w/w	6A	6B	6C	6D	6E	6F

All the bead formulations outlined in Table 1 (as well as the three control bead formulations) also contained Pharmacel® as filler and Kollidon VA64® (3% w/w) as binder to ensure acceptable bead formation.

3. Materials and methods

3.1 Materials

Furosemide (Batch number 90111045) was purchased from DB Fine Chemicals (Pty) Ltd. (Johannesburg, South Africa). Microcrystalline cellulose (MCC-PH101) (Batch number K0054) was purchased from Gujarat Microwax Pvt. Ltd. (Nandasan Gujarat, India). CombiLac® (Lot number L1434) was a gift from Meggle® (Wasserburg, Germany). Sodium hydroxide pearls (Lot number 1039849), sodium lauryl sulphate (Lot number 1043002), hydrochloric acid 32% w/w (Lot number 1045042) and calcium carbonate (Lot number 101275) were purchased from Merck® (Pty) Ltd. (Gauteng, South Africa). Chitosan (Batch number 030912) and magnesium stearate (Batch number 21203) were purchased from Warren Chem Specialities® (Cape Town, South Africa). Kollidon® VA 64 (Batch number 93520356VO) was a gift from BASF® (Ludwigshafen, Germany). Potassium dihydrogen orthophosphate (dehydrated) (Batch number 30058) and citric acid (dehydrated) (Batch number 9246) were purchased from Associated Chemical Enterprises®. Krebs-Ringer Bicarbonate buffer (Lot number SLBW3493), Lucifer yellow (LY, CAS number 67769-47-5) and sodium chloride (Batch number 038K0096), Hematoxylin (Cat. number: GHS132), Eosin Y (Cat. number: HT110216) were purchased from Sigma Aldrich® (Johannesburg, South Africa). Sodium hydrogen carbonate (Batch number 100215SB) and ethanol 99.9% (Batch number 290819ET) were purchased from Rochelle® chemicals (Johannesburg, South Africa).

3.2 Methods

3.2.1 Preparation of beads by means of extrusion spheronisation

The excipients and furosemide (active ingredient) for each formulation as specified in Table 1 were mixed using a Turbula T2B (WA Bachofen) mixer at 69 rpm for 5 min. The mixed powder blends (100 g) were then transferred to a porcelain mortar and wetted with a wetting

liquid (i.e. water:ethanol = 1:1). A pestle was then used to mix the powder while the wetting liquid was added slowly to the powder mixture. The bead preparation process commenced with extrusion of the wetted powder mass of each formulation with an Extruder 20 (Caleva®, England) through screens with different size openings for each bead size (i.e. 0.5, 0.75 and 1.0 mm, respectively). The extrusion step was followed by spheronisation of the extrudate in a multi-bowl spheroniser (Caleva®, England). The beads were freeze-dried for 48 h using a VirTis® bench top freeze drier (SP Industries Company). The freeze dried beads were then stored in a screw top glass bottle in a dark, cool, dry place until needed for further study.

3.2.2 Preparation of multiple-unit pellet system (MUPS) tablets

3.2.2.1 Mixing process of each formula prior to tablet compression

Before compression of the beads could commence, magnesium stearate (0.25% w/w) and CombiLac® were added to each bead formulation in concentrations as indicated in Table 2. Magnesium stearate was added to serve as lubricant and CombiLac® is a filler that was included to produce tablets with sufficient mechanical strength. Each bead formulation was mixed with the selected excipients (i.e. magnesium stearate and CombiLac®) using a Turbula® mixer (type T2B, Willy A. Bachofen Machinenfabrik, Germany) at a mixing speed of 47 rpm for a duration of 3 min.This specific speed and time was used as the bead particles needed to stay intact for tablet compression.

Table 2: Composition of multiple-unit pellet system (MUPS) tablet formulations

Ingredient	Concentration (% w/w)	Quantity per 580 mg tablet
CombiLac®	30	174 mg
Magnesium stearate	0.25	1.45 mg
Beads containing 10% w/w furosemide	69.75	404.55 mg

The MUPS tablets therefore contained 6.975% w/w furosemide after addition of the selected excipients to the beads as outlined in Table 2.

3.2.2.2 Tablet compression

The MUPS tablets were compressed with a Korsch® XP1 single station tablet press (Korsch AG, Berlin, Germany) connected to a PharmaResearch® unit (Korsch AG, Berlin, Germany). A 10 mm flat faced punch and die set was used. After compression of the MUPS tablets, each formulation's tablets were placed in a separate container and stored in a cool, dry, dark environment until used in the evaluation tests.

3.2.2 Physical evaluation of MUPS tablets

3.2.3.1 Physical tablet evaluation

The physical properties of the MUPS tablets were evaluated using the British Pharmacopoeia(BP) specifications and guidelines for disintegration, friability and mass variation(British Pharmacopoeia 2020). Although an unofficial test, the crushing strength of the tablets was also determined. Disintegration tests were conducted on six tablets from each formulation according to the BP with the Erweka® disintegration apparatus (Type ZT 323, Erweka GmbH, Heusenstamm, Germany). Friability evaluation was conducted on ten tablets from each formulation using an Erweka® friabilator (Type TAR 220, Erweka GmbH,

Heusenstamm, Germany). Crushing strength was evaluated with an Erweka® apparatus (TypeTBH 425 TD, Erweka GmbH, Heusenstamm, Germany) using ten tablets from each formulation and the weight variation was conducted on 20 tablets using a Mettler Toledo® balance (Mettler, Germany, Model MS205DU). All these physical evaluation tests were performed in triplicate.

3.2.3.2 Content uniformity

Five MUPS tablets from each formulation were randomly selected and evaluated for content uniformity. Determination of content uniformity entailed crushing each of the five tablets to a fine powder using a mortar and pestle. After crushing, the crumpled content of each tablet was transferred to a 200 ml volumetric flask with 0.1 M NaOH. Each volumetric flask was placed in an ultrasonic bath for 10 min to ensure complete dissolution of the furosemide. A volume of 4 ml of this dispersion was withdrawn and filtered through a 0.45 µm membrane and diluted to 100 ml in a volumetric flask using distilled water. Each sample was analysed using UV-spectrophotometry, to determine the quantity of furosemide in the solution. This analytical method was validated with regard to linearity, repeatability and selectivity before sample analysis commenced (Hwang et al.2002; British Pharmacopoeia 2020).

3.2.3.3 Mucoadhesion evaluation

The mucoadhesive properties of the beads were evaluated using the "falling liquid film method". Excised pig duodenal tissue was cut open and then mounted onto a channel which was placed at a fixed angle of 15°. A specific quantity of beads (100) was placed on the duodenum and 1 L of distilled water was allowed to flow over the beads from a separating funnel. The beads that were flushed down the intestinal tissue were collected using a small sieve. These beads were counted, the number of beads left on the tissue was also noted. This

test was performed in triplicate for all formulations (de Bruyn et al.2018).

The percentage mucoadhesion was calculated using the following equation:

$$\%\ Mucoadhesion\ = \frac{Quantity\ of\ beads\ left\ on\ tissue}{Total\ bead\ quantity}\ x\ 100 \qquad Equation\ 1$$

3.2.3 Dissolution studies

Dissolution tests were performed using the USP (II) paddle method. The apparatus consisted of a six-station apparatus (Type Distek® 2500, Distek, North Brunswick, NJ, USA) connected to an automated sample withdrawal unit (Type Distek® evolution 4300, Distek, North Brunswick, NJ, USA). A stirring rate of 50 rpm was used during the dissolution test and 900 ml of 0.1 M HCl (pH 1.2), citric acid buffer (pH 4.6) and a phosphate buffer (pH 7.4) were used as dissolution media for each formulation. The medium was kept at a constant temperature of 37± 0.5 °C during the dissolution test. Samples of 5 ml were withdrawn at 2, 5, 10, 15, 30, 60, 90, 120, 180, 240 and 360 min after the tablets were added to the dissolution vessels. After withdrawal, the volume that was withdrawn was replaced with fresh dissolution medium to ensure a constant volume. After the 360 min sample was withdrawn, the stirring rate was increased to 250 rpm for 15 min whereafter the vessels were sonicated for 10 min to ensure complete release and dissolution of the furosemide in the respective media before the last sample was drawn. Dissolution studies were conducted in triplicate for each formulation in each of the dissolution media. The furosemide concentration in the withdrawn samples was determined by means of UV-spectrophotometry. This analytical method was validated with regard to linearity, repeatability and selectivity before sample analysis commenced (Hwang et al.2002; British Pharmacopoeia 2020).

3.2.4.1 Dissolution parameters

The dissolution profiles of the different formulations were processed and characterised by

means of calculating the following parameters:

3.2.4.1.1 Initial dissolution rate (DR_i)

The slope of the first 15 min of the dissolution profile was calculated using Microsoft Excel to represent the initial dissolution rate of the formulations.

3.2.4.1.2 Area under the curve (AUC)

The area under the curve (AUC) gives an indication of the extent of the dissolution that occurred. The AUC for the different dissolution profiles was calculated using the trapezoidal rule with equation 2(Shargel et al. 2012). Ek het hierdie equation oor getik en in gepaste want daar was inligting kort, ek weet nie of dit aanvaarbaar lyk nie?

$$[AUC]_{t_{n-1}}^{t_n} = \frac{C_{n-1} + C_n}{2}(t_n - t_{n-1}) \qquad Equation\ 2$$

Where AUC is the area under curve from time t_n to time, t_{n-1},C_n is the concentration at time n, and $C_{n-1}$is concentration at time, n-1.

3.2.4.1.3 Difference factor (f_1)

The dissolution profiles of the experimental MUPS tablet formulations were compared to the dissolution profile of a commercially available furosemide tablet formulation (Lasix®) by calculating the difference factor (f_1) values. The f_1 value can be used as an approximation of the percent error between two dissolution profiles. When the f_1 is equal to zero, the two dissolution profiles are identical and will increase proportionally with the dissimilarity between the two curves (Moore J.W & Flanner H.H, 1996). The f_1 values were calculated using equation 3.

$$f_1(difference\ factor) = \left\{ \frac{\sum_{t=|}^{n} |R_t - T_t|}{\sum_{t=|}^{n} R_t} \right\} \times 100 \qquad Equation\ 3$$

Where f_1 is the difference factor, R_t is the reference assay at time point *t*, T_t is the test assay at time point *t*, and *n* is the number of pull points.

3.2.4.1.4 Mean dissolution time (MDT)

Mean dissolution time (MDT) is the statistical moment that can be calculated for the cumulative dissolution process and is defined by Equation 4. MDT is the mean time taken for the drug to dissolve under *in vitro* dissolution conditions (Reppas and Nicolaides 2000). On a practical basis, MDT can be estimated from the cumulative mass dissolved versus time profile by employing equation 4.

$$MDT = \frac{\sum_{i=1}^{n} t_{mid} \Delta X_d}{\sum_{i=1}^{n} \Delta X_d} \qquad Equation\ 4$$

Where MDT is the mean dissolution time, i, is the sample number, n, is the total number of sampling times, t_{mid}, is the time at the midpoint, between i and i – 1, and ΔX_d, is the additional mass of drug dissolved between i and i – 1.

3.2.4 Multivariate statistical analysis (redundancy analysis) of dissolution data

Redundancy analysis (RDA), a multivariate statistical technique, was employed to visualise the dissolution data in the form of various response variables (i.e. area under the curve (AUC), initial dissolution rate (DR_i), mean dissolution time (MDT), and disintegration time were related to a set of explanatory variables (formulation variables). Multivariate projection methods such as redundancy analysis can be employed to simplify complex pharmaceutical

data and in effect make visualisation easier (Rajalahti and Kvalheim 2011; Kadel et al. 2019). This statistical method organises multidimensional data into a less dimensional, organised space. The RDA was implemented to ensure that all the different variables of the study were included to reveal a well organised and thorough summary as well as explanation of the data (Ter Braak 1989). The RDA was done using the software program CANOCO for Windows version 5 (Šmilauer and Lepš 2014). Triplots were interpreted according to previously published work (Šmilauer and Lepš, 2014). The angle between the vector arrows was used to indicate the correlation between the individual environmental variables and/or species data. An angle close to 0° indicates a positive correlation between the variables; whereas an angle closer to 90° shows no correlation; and an angle approaching 180° indicates a negative correlation between variables. The perpendicular line between a sample symbol and a particular species arrow can be used to estimate the value of that sample in terms of the variable it is perpendicular to.

3.2.5 Ex vivo permeability evaluation

The permeability of furosemide across excised pig *(Sus scrofa domesticus)* intestinal tissue was tested in a Sweetana-Grass diffusion apparatus to determine the influence of the formulation variables on the membrane delivery of furosemide. For this permeability study, the first part of the duodenum and the pyloric antrum part of the stomach of pig intestinal tissue were used in order to mimic the absorption window of furosemide in the gastrointestinal tract (Gerber et al.2018).

The use of excised pig intestinal tissues in this project was approved by the NWU AnimCare Research Ethics Committee (NWU-00504-20-A5). After the slaughter process at the local abattoir (Potchefstroom abattoir, Potchefstroom, South Africa), the intestinal tissues (pyloric antrum and duodenum) were excised and washed with freshly prepared cold Krebs-Ringer

bicarbonate buffer with a pH of 7.4. The samples were submerged in ice cold Krebs-Ringer bicarbonate buffer and transported on ice to the laboratory. Once in the laboratory, the duodenal tissue was carefully mounted on a glass tube and the serosa was removed followed by an incision along the mesenteric border. The flat duodenal tissue was placed on filter paper and cut into smaller pieces suitable for mounting between the half cells of the Sweetana-Grass diffusion chambers. The same process was followed for preparation of the pyloric antrum stomach tissue, except for removal of underlying tissue together with the serosa. Throughout this preparation process of the tissue, Krebs-Ringer bicarbonate buffer was constantly applied to the tissue to keep it moist.

After the tissue was prepared and cut into the correct sizes, the tissue was placed on the spikes of the apical half-cell. The filter paper was removed and the basolateral half-cell was joined with the apical half-cell. Prior to starting the permeability study, warm (37 ± 0.5°C) Krebs-Ringer bicarbonate buffer was added to both compartments of the diffusion apparatus and a 15 min equilibration period was allowed before the start of the experimental procedure. After the equilibration period, the buffer was removed from both half-cell compartments using suction. The MUPS tablet to be tested was added to the apical compartment together with a biologically relevant transport medium to provide a biologically similar fluid environment in accordance with the type of tissue used from the gastro-intestinal tract (i.e. either pyloric antrum or duodenum excised tissue). A quantity of 40 ml 0.1 M HCl solution (pH 1.2) was added to the apical chamber for the permeability studies across the excised pyloric antrum tissue. For the permeability studies across the excised duodenal tissue, 40 ml of a citrate buffer solution (pH 4.6) was added to the apical chamber. Drug-free Krebs Ringer bicarbonate buffer was added to the basolateral compartment for all permeability evaluation tests. The chambers were perfused with a mixture of 95% O_2 and 5% CO_2 during the permeation experiments. A temperature of 37 ± 0.5°C was maintained throughout the permeability studies using heating

blocks. Samples of 3 ml were withdrawn at 20, 40, 60, 80 and 120 min. After withdrawal of a sample from the basolateral chamber, the chamber was replenished with 3 ml warm (37 ± 0.5°C) Krebs-Ringer bicarbonate buffer solution. Each sample withdrawn was analysed using UV-spectrophotometry, to determine the concentration of furosemide. This analytical method was validated with regard to linearity, repeatability and selectivity (Hwang et al.2002). Equation 5 and 6 were used to calculate the percentage transport and P_{app} (apparent permeability) values, respectively.

$$\%\, Transport = \frac{Concentration\ value\ at\ specific\ time}{Concentration\ value\ of\ donor\ solution}\ x\ 100 \qquad Equation\ 5$$

$$Papp = \frac{dQ}{dt}\ x\ \left(\frac{1}{A.60.100}\right) \qquad Equation\ 6$$

In equation 6, $\frac{dQ}{dt}$ represents the permeability rate per min and the A represents the surface area available (cm^2) in the chamber for membrane permeation (Hwang et al.2002).

The membrane integrity of the two types of excised intestinal tissues mounted in the Sweetana-Grass diffusion apparatus was evaluated by screening for Lucifer yellow permeation. Lucifer yellow is a molecule used as a hydrophilic marker for determining membrane integrity for in vitro permeation models. During the membrane integrity study, a concentration of 50 µg/ml Lucifer yellow was added to the apical compartment together with the specific buffer suitable for the tissue evaluated. Pre-warmed Krebs-Ringer bicarbonate buffer was added to the basolateral compartment. The permeability study was conducted in a similar manner to the permeability studies done for the MUPS tablet test formulations. Samples withdrawn from the basolateral chamber were analysed using a Spectramax® Paradigm (serial number: 33270-1142) multi-mode detection platform plate reader. The excitation wavelength was set at 485 nm and emission wavelength at 530 nm. The integrity of the tissue evaluated was considered viable for permeability testing if the Lucifer yellow transport was equal to or less than 3% (Padmaja et al.2004).

Statistical data analysis of the P_{app} values for all test groups was performed with Statistica® v. 13.3 software by means of ANOVA followed by Tukey HSD post-hoc tests for comparison of multiple groups. Differences were considered statistically significant when $p < 0.05$.

3.2.7 Histological analysis

Excised pig stomach and duodenum tissue samples were histologically evaluated before the onset of the permeability studies (before exposure to the test formulations) and after permeability evaluations (after exposure to chemicals the test formulations). Evaluation of tissue samples from the stomach and duodenum that was only exposed to Krebs-Ringer bicarbonate buffer (negative control group), the control MUPS tablet formulation and the commercial furosemide tablet product (Lasix®) were also analysed histologically. These histological tests were performed in pH 1.2 and 4.6 environments, respectively. The histology procedure entailed fixation of the specific tissue sample in 10% buffered formalin at 4°C for 48 h. The tissue samples were subsequently dehydrated in a graded series of ethanol solutions and thereafter embedded in paraffin wax. Embedded samples were sliced into 5 μm sections that were stained with hematoxylin-eosin (Sigma-Aldrich, Steinheim, USA). After staining, the sections were examined under a Zeiss Axio Z II microscope (Carl Zeiss Microscopy GmbH, Jena, Germany) using the ZEN (blue edition) software.

3.2.8 Ultraviolet-spectrophotometric analysis

The samples obtained from the dissolution studies, permeability studies and the content uniformity samples were analysed for furosemide content using an Analytik Jenna UV-spectrophotometer (Analytik Jena, Jena, Germany). The absorbance of the samples was determined at a wavelength of 273 nm (absorbance maximum). This analytical method was validated with regards to linearity, repeatability and selectivity as previously described (Hwang et al.2002).

4. Results and discussion

4.1 Physical evaluation of MUPS tablets

A summary of the results obtained from the physical evaluation of the MUPS tablets is presented in Table 3. According to the findings of previous studies, the tableting of beads into MUPS tablets can be challenging (Osei-Yeboah et al.2017).

Table 3: Summary of the physical MUPS tablet evaluation results

	Friability %	SD*	Hardness (N)	SD*	Disintegration (sec)	SD*	Average tablet mass (g)	SD*
1A	3.59	0.144	106.10	18.556	439.72	84.737	0.582	0.001
1B	0.80	0.033	141.30	23.113	544.00	99.555	0.583	0.001
1C	0.23	0.009	147.00	21.812	699.89	108.860	0.583	0.002
1D	0.06	0.002	190.90	21.460	879.83	117.355	0.581	0.003
1E	0.29	0.012	164.00	31.833	694.61	160.629	0.580	0.005
1F	0.40	0.016	214.10	22.820	1235.00	154.735	0.583	0.004
2A	0.06	0.002	209.80	27.571	1206.67	89.930	0.584	0.003
2B	0.12	0.005	207.80	30.987	780.22	54.632	0.581	0.003
2C	0.17	0.007	234.10	50.017	778.00	79.296	0.583	0.004
2D	0.06	0.002	268.10	40.090	1026.06	133.464	0.582	0.004
2E	0.00	0.000	287.30	39.780	1415.94	198.730	0.583	0.005
2F	0.00	0.000	281.50	62.038	1128.11	134.984	0.584	0.005
3A	0.29	0.012	118.70	26.026	626.89	74.006	0.583	0.003
3B	0.11	0.005	165.70	24.559	598.83	110.736	0.582	0.003
3C	1.38	0.057	124.90	30.932	661.72	133.337	0.583	0.004
3D	0.17	0.007	198.50	29.830	708.22	102.696	0.583	0.006
3E	0.17	0.007	160.20	28.901	879.39	82.209	0.584	0.006
3F	0.17	0.007	216.30	43.721	720.83	217.267	0.583	0.006
4A	0.06	0.002	195.80	44.596	1366.67	126.340	0.584	0.004
4B	0.17	0.007	255.80	39.991	1086.83	101.044	0.581	0.003
4C	0.11	0.005	224.60	42.277	1245.78	210.499	0.583	0.006
4D	0.17	0.007	230.00	23.636	1128.50	206.763	0.582	0.002
4E	0.23	0.009	241.00	35.969	1064.11	113.927	0.581	0.006
4F	0.06	0.002	281.70	22.755	1369.11	146.715	0.583	0.006
5A	0.12	0.005	217.50	39.127	1139.56	82.999	0.582	0.003
5B	0.23	0.009	215.50	19.381	813.33	87.484	0.583	0.004
5C	0.34	0.014	170.40	21.742	649.28	85.550	0.582	0.003
5D	0.00	0.000	246.70	30.750	1049.61	196.840	0.584	0.003
5E	0.12	0.005	248.60	32.654	845.28	94.460	0.582	0.006
5F	0.06	0.002	267.50	31.419	1084.83	126.547	0.582	0.006
6A	0.12	0.005	225.70	51.088	1155.61	63.838	0.579	0.003
6B	0.00	0.000	263.20	24.894	1175.17	80.098	0.582	0.002
6C	0.17	0.007	266.40	41.175	1292.67	312.348	0.582	0.003
6D	0.17	0.007	258.50	37.913	1011.67	116.602	0.582	0.004
6E	0.06	0.002	307.80	37.956	879.22	249.211	0.584	0.006

6F	0.06	0.002	277.10	45.615	842.22	230.385	0.579	0.006

* SD = standard deviation

4.1.1 Friability

The friability results indicated that all the MUPS tablet formulations passed the test according to BP standards (≤ 1% average mass loss) except for formulation 1A. Friability results revealed an average percentage friability of 0.286 ± 0.012%. The friability results obtained for the 36 MUPS tablet formulations exhibited acceptable percentage friability that indicated the MUPS tablets should be able to withstand physical stresses sufficiently to stay intact during handling (British Pharmacopoeia 2020).

4.1.2 Tablet hardness (crushing strength)

MUPS tablet hardness results are presented in Table 3. The average hardness (crushing strength) values ranged from 106.1 – 307.8 N for the different formulations. The crushing strength values averaged at 217.5 ± 33.3 N for all the formulations. The MUPS tablets were found to be relatively hard, but tablets compressed at lower compression forces did not pass the friability test (tablets with average crushing strength values < 100 N did not pass the friability test, data not shown). It is therefore evident that the MUPS tablets with the specific compositions investigated in this study had to be compressed at relatively high compression forces to render tablets with hardness values in excess of 110 N in order to produce acceptable friability.

4.1.3 Disintegration

The results revealed that the disintegration times ranged from ± 439.72 – 1415.95 sfor the different MUPS tablet formulations. A total of 18 out of the 36 MUPS tablet formulations exhibited disintegration times that exceeded a period of 15 min (which is the limit set by the BP for the disintegration of conventional tablets (British Pharmacopoeia 2020). A total of 50% of the formulations exceeded the disintegration time limit for conventional tablets, which may

be explained by the bead component of the MUPS tablets. Upon disintegration of the tablets, some of the beads remained intact and eroded slowly over time before passing through the sieve in the disintegration apparatus.

4.1.4 Mass variation

All the MUPS tablet formulations complied with the specifications of the BP with regard to mass variation since none of the MUPS tablets deviated with more than 5% from the average weight. The fact that all the MUPS tablet formulations complied with the specification of mass variation is an indication of acceptable material flow into the die and this will contribute to an even distribution of the furosemide dose between the MUPS tablets (British Pharmacopoeia 2020).

4.1.5 Mucoadhesion

One of the reasons for the inclusion of chitosan in the MUPS tablet formulations, is because of its mucoadhesive properties (Karolewicz 2016). The mucoadhesive properties of chitosan may ensure prolonged contact time with the mucosal surface of the stomach and the small intestine, which may potentially increase the extent of furosemide absorption into the systemic circulation. In Table 4, the results obtained for the percentage mucoadhesion for each of the 36 bead formulations are provided.

Table 4: Percentage mucoadhesion of the different bead formulations

Percentage muchoadhesion (%±SD)											
1A	37.3 ± 9.84	**2A**	70.3 ± 3.68	**3A**	82.0 ± 3.27	**4A**	62.0 ± 5.72	**5A**	54.3 ± 5.31	**6A**	66.3 ± 7.59
1B	46.0 ± 16.31	**2B**	89.3 ± 3.30	**3B**	87.0 ± 3.27	**4B**	81.0 ± 5.10	**5B**	70.0 ± 4.32	**6B**	77.0 ± 4.55
1C	40.0 ± 27.53	**2C**	67.0 ± 9.63	**3C**	58.7 ± 8.18	**4C**	74.0 ± 10.20	**5C**	43.0 ± 2.94	**6C**	51.7 ± 4.50
1D	68.7 ± 8.58	**2D**	78.3 ± 9.74	**3D**	75.3 ± 2.49	**4D**	85.0 ± 6.48	**5D**	61.7 ± 3.30	**6D**	70.3 ± 4.19
1E	42.0 ± 20.02	**2E**	87.7 ± 3.30	**3E**	56.7 ± 7.72	**4E**	76.7 ± 9.46	**5E**	49.7 ± 5.79	**6E**	73.3 ± 6.65
1F	47.3 ± 12.55	**2F**	83.3 ± 10.27	**3F**	59.0 ± 3.74	**4F**	76.7 ± 2.49	**5F**	55.3 ± 5.19	**6F**	76.7 ± 6.60

From the results presented in Table 4, formulations 1B – 6B, 1D – 6D and 1F – 6F exhibited higher percentage mucoadhesion values than the other bead formulations. The bead formulations containing chitosan showed a notably higher percentage mucoadhesion than the other formulations. These mucoadhesion results indicated that the inclusion of chitosan into a MUPS tablet may increase the contact period with the intestinal mucosa providing the possibility of a higher percentage of active ingredient being absorbed due to the prolonged contact time with the intestinal mucosa (de Bruyn et al.2018).

According to an investigative review written by (Caramella et al2010) chitosan has been found useful as a mucoadhesive agent and intestinal permeation enhancer. However, chitosan does not produce good mucoadhesive action above the pH of 6.5 because it is a weak base with a pKa value of 6.5. This entails that chitosan undergoes a more sufficient wetting action and gel formation in the lower pH ranges such as those found in the gastric region (Caramella et al.2010; Khlibsuwan R. & Pongjanyakul T. 2016). Chitosan is a cationic polymer that interacts with the anionic substructures of the sialic acid residues in the mucous layer of the intestines via hydrogen bonding, ionic interactions and Van der Waals forces (Nallathambi and Gopal 2013; Karolewicz 2016).

4.2 Dissolution studies

4.2.1 Dissolution parameters

The maximum percentage dissolution ($\%_{max}$) values and the initial dissolution rate (DR_i) values of the different MUPS tablet formulations are given in Table 5, whereas the area under the curve (AUC) and the difference factor (f_1) values are listed in Table 6. The $\%_{max}$, DR_i, AUC and f_1 values of the different control MUPS formulations (consisting of beads with three different sizes without any functional excipients) and the commercial tablet formulation

(Lasix®) are also included in these two tables.

Table 5: Maximum percentage dissolution ($\%_{max}$) and initial dissolution rate (DR_i) values for the MUPS tablets in the different dissolution media

	Maximum percentage dissolution ($\%_{max}$) ± standard deviation (SD)			**Initial dissolution rate (DR_i) ± standard deviation (SD)**		
Formulation	**pH 1.2**	**pH4.6**	**pH 7.4**	**pH 1.2**	**pH4.6**	**pH 7.4**
1A	79.491 ± 14.396	98.112 ± 3.238	98.817 ± 5,926	2.405 ± 0,789	5.790 ± 0.138	4.127 ± 0.184
1B	73.995 ± 2.333	101.778 ± 2.910	103.220 ± 2.254	1.739 ± 0.099	6.736 ± 0.151	5.029 ± 0.410
1C	56.374 ± 2.753	108.782 ± 4.172	100.716 ± 10.454	1.216 ± 0.240	6.271 ± 0.205	5.047 ± 0.407
1D	74.352 ± 0.961	97.107 ± 2.533	102.647 ± 11.317	1.051 ± 0.058	5.704 ± 0.265	5.427 ± 0.625
1E	56.160 ± 1.886	97.687 ± 9.131	105.152 ± 4.263	1.655 ± 0.185	6.232 ± 1.160	7.132 ± 0.630
1F	73.719 ± 2.299	91.002 ± 9.888	89.718 ± 2.490	1.124 ± 0.348	4.321 ± 1.423	3.977 ± 0.600
2A	63.028 ± 2.378	94.629 ± 5.352	93.157 ± 5.213	0.894 ± 0.073	4.364 ± 0.534	4.059 ± 0.131
2B	71.157 ± 1.713	92.162 ± 5.514	104.355 ± 4.561	1.258 ± 0.113	5.360 ± 0.253	5.759 ± 0.309
2C	66.843 ± 1.507	102.012 ± 1.133	97.265 ± 7.185	1.303 ± 0.069	5.867 ± 0.210	5.344 ± 0.169
2D	76.283 ± 1.277	96.801 ± 2.164	101.104 ± 4.801	1.084 ± 0.159	5.362 ± 0.272	5.699 ± 0.318
2E	50.606 ± 2.314	87.056 ± 2.789	89.998 ± 5.786	0.544 ± 0.018	3.195 ± 0.364	3.336 ± 0.127
2F	74.261 ± 1.718	82.741 ± 0.436	83.638 ± 0.817	0.915 ± 0.127	4.050 ± 0.258	3.576 ± 0.210
3A	59.145 ± 0.628	94.528 ± 2.424	106.991 ± 7.115	1.827 ± 0.157	6.037 ± 0.081	5.558 ± 0.676
3B	77.413 ± 1.216	97.805 ± 5.348	106.695 ± 8.791	1.855 ± 0.051	6.081 ± 0.289	6.176 ± 0.246
3C	62.167 ± 2.604	96.360 ± 4.985	96.771 ± 7.172	2.274 ± 0.155	5.077 ± 0.881	5.706 ± 0.531
3D	74.821 ± 2.499	104.860 ± 0.191	96.623 ± 5.873	1.244 ± 0.214	6.042 ± 0.115	5.340 ± 0.156
3E	46.209 ± 3.112	89.278 ± 10.309	90.960 ± 16.695	0.970 ± 0.071	4.036 ± 1.245	3.633 ± 0.472
3F	68.570 ± 4.416	98.274 ± 13.201	94.668 ± 14.093	1.381 ± 0.447	5.293 ± 1.504	5.245 ± 1.147
4A	51.384 ± 1.878	89.349 ± 5.344	89.002 ± 6.028	1.184 ± 0.035	3.481 ± 0.459	4.625 ± 0.235
4B	75.202 ± 1.335	102.043 ± 0.573	98.030 ± 5.282	1.537 ± 0.193	5.733 ± 0.573	5.474 ± 0.251
4C	51.351 ± 0.249	91.282 ± 4.940	100.105 ± 4.299	0.818 ± 0.067	4.372 ± 0.886	4.760 ± 0.527
4D	80.394 ± 0.361	94.767 ± 6.319	102.527 ± 3.450	1.398 ± 0.099	5.280 ± 0.485	5.043 ± 0.469
4E	61.596 ± 0.894	96.786 ± 4.662	94.708 ± 2.534	1.062 ± 0.123	4.414 ± 0.873	5.206 ± 0.481
4F	70.996 ± 1.431	101.420 ± 3.471	103.602 ± 5.638	1.461 ± 0.241	5.467 ± 0.655	5.314 ± 0.999
5A	56.930 ± 3.080	93.037 ± 3.007	91.554 ± 3.823	1.087 ± 0.189	3.043 ± 0.105	3.773 ± 0.763
5B	72.690 ± 2.704	91.943 ± 1.866	105.100 ± 3.096	1.242 ± 0.232	4.602 ± 0.657	5.674 ± 1.211
5C	56.695 ± 1.270	91.916 ± 3.836	94.553 ± 9.914	1.049 ± 0.141	4.640 ± 0.171	5.263 ± 0.490
5D	73.474 ± 1.041	96.732 ± 2.950	97.377 ± 2.543	0.663 ± 0.008	4.161 ± 0.772	4.283 ± 0.353
5E	55.284 ± 0.227	91.128 ± 3.782	94.518 ± 3.123	1.220 ± 0.020	3.593 ± 0.069	3.797 ± 0.499
5F	78.939 ± 0.949	96.974 ± 10.069	101.057 ± 7.644	1.422 ± 0.501	3.015 ± 0.928	2.811 ± 0.598
6A	65.450 ± 4.919	86.325 ± 4.383	97.012 ± 6.033	0.768 ± 0.197	3.645 ± 0.358	4.805 ± 1.169
6B	64.638 ± 3.230	92.393 ± 2.348	90.385 ± 5.646	0.606 ± 0.208	3.853 ± 0.638	4.313 ± 0.492
6C	61.584 ± 2.399	99.084 ± 1.243	102.011 ± 5.641	0.614 ± 0.116	3.233 ± 0.039	3.330 ± 0.214
6D	77.170 ± 0.546	89.273 ± 4.265	104.180 ± 6.310	1.004 ± 0.156	2.721 ± 0.441	3.330 ± 0.214

6E	60.857 ± 2.398	93.634 ± 1.576	101.621 ± 4.733	1.172 ± 0.161	4.045 ± 0.571	5.308 ± 0.781
6F	71.586 ± 1.991	95.885 ± 1.765	99.898 ± 6.798	0.794 ± 0.128	4.797 ± 0.167	5.123 ± 0.894
Lasix®	38,804 ± 0.204	96.798 ± 0.692	106.390 ± 1.790	0.887 ± 0.032	2.941 ± 0.719	5.378 ± 0.019
C (0.5 mm)*	10.021 ± 0.730	34.650 ± 4.066	102.000 ± 6.087	0.110 ± 0.016	0.286 ± 0.024	3.738 ± 0.166
C (0.75 mm)*	11.325 ± 0.388	30.813 ± 2.116	92.219 ± 4.492	0.125 ± 0.006	0.301 ± 0.034	3.404 ± 0.316
C (1.0 mm)*	12.898 ± 1.582	38.298 ± 3.715	98.706 ± 1.383	0.130 ± 0.009	0.395 ± 0.064	4.671 ± 0.085

*C = control MUPS tablet formulation

Table 6: Area under the curve (AUC) and difference factor (f1) values for the dissolution profiles of the MUPS tablet formulations

Formulation	**AUC (µg.min/ml)**			**Difference factor (f1)**		
	pH 1.2	**pH 4.6**	**pH 7.4**	**pH 1.2**	**pH 4.6**	**pH 7.4**
1A	11272.181 ± 2813.573	15159.609 ± 443.583	14686.050 ± 1168.203	1001.532 ± 295.798	426.245 ± 54.699	22.743 ± 4.852
1B	9674.576 ± 29.708	15955.160 ± 336.167	15989.068 ± 570.480	807.749 ± 37.531	468.230 ± 58.744	29.342 ± 9.721
1C	7370.670 ± 656.626	16249.170 ± 537.806	14698.588 ± 1464.784	519.552 ± 71.390	502.472 ± 37.064	20.043 ± 11.631
1D	9394.953 ± 313.524	15079.958 ± 329.456	14767.941 ± 1354.325	645.982 ± 35.741	451.842 ± 56.164	23.307 ± 12.790
1E	7650.999 ± 399.902	14998.580 ± 1758.129	15367.880 ± 815.028	495.803 ± 42.307	340.124 ± 87.675	20.468 ± 7.318
1F	9736.119 ± 523.892	13856.840 ± 1958.218	12273.780 ± 577.235	601.071 ± 42.483	281.466 ± 50.453	18.398 ± 3.107
2A	7769.823 ± 433.310	14199.520 ± 874.470	13437.440 ± 333.300	604.468 ± 53.423	351.132 ± 27.351	9.960 ± 4.987
2B	9482.156 ± 539.797	14078.200 ± 773.791	14977.590 ± 82.027	759.602 ± 68.371	383.692 ± 36.996	25.368 ± 5.123
2C	8349.209 ± 253.249	15611.820 ± 244.737	14752.820 ± 529.344	590.274 ± 36.001	486.243 ± 60.401	25.185 ± 4.713
2D	9819.738 ± 309.189	14759.570 ± 398.091	14881.290 ± 545.447	685.993 ± 49.200	436.694 ± 29.641	26.244 ± 9.931
2E	6271.921 ± 262.373	12906.700 ± 616.275	12995.960 ± 79.599	344.168 ± 58.725	245.707 ± 22.273	17.861 ± 0.895
2F	9491.790 ± 393.318	12694.340 ± 114.455	12637.310 ± 109.217	571.051 ± 87.056	257.154 ± 47.231	19.106 ± 1.365
3A	8205.076 ± 164.301	14761.390 ± 309.603	15291.670 ± 791.537	678.466 ± 37.800	431.542 ± 55.737	22.928 ± 7.352
3B	9834.289 ± 241.040	15369.740 ± 1205.664	15909.280 ± 1335.339	807.670 ± 70.254	465.447 ± 52.617	32.507 ± 11.767
3C	8534.700 ± 276.799	14382.690 ± 1502.963	14453.280 ± 957.880	654.017 ± 32.695	419.647 ± 90.311	21.911 ± 4.832
3D	9198.197 ± 713.599	16105.580 ± 86.968	14553.500 ± 1120.094	634.737 ± 62.455	492.651 ± 62.838	17.075 ± 2.430
3E	6342.842 ± 664.844	13558.320 ± 2131.681	12437.440 ± 1571.736	365.709 ± 27.190	266.255 ± 73.444	22.520 ± 8.440
3F	8557.460 ± 972.049	14722.470 ± 1863.805	14087.080 ± 2133.502	527.918 ± 66.561	320.480 ±66.503	15.894 ± 8.066
4A	6827.616 ± 187.204	13343.620 ± 899.152	12998.710 ± 256.621	528.494 ± 40.426	313.804 ± 51.003	16.827 ± 1.071
4B	10062.450 ± 536.608	15674.200 ± 315.870	13402.520 ± 508.803	810.302 ± 102.663	429.778 ± 93.834	25.212 ± 1.428
4C	6494.405 ± 64.750	13990.400 ± 1259.342	14381.860 ± 508.803	429.091 ± 9.526	388.848 ± 48.061	12.697 ± 2.559
4D	10456.504 ± 141.459	14392.270 ± 1022.749	14782.730 ± 342.872	748.284 ± 15.310	421.923 ± 14.333	19.772 ± 5.323
4E	7837.367 ± 156.110	14610.460 ± 1008.715	14006.040 ± 269.979	466.941 ± 52.177	295.144 ± 19.957	9.929 ± 1.550
4F	9679.771 ± 297.366	15512.610 ± 717.051	14649.760 ± 942.010	611.452 ± 115.428	344.634 ± 82.084	10.409 ± 1.082
5A	7318.167 ± 625.363	13630.820 ± 428.051	13661.890 ± 616.808	551.174 ± 25.171	338.384 ± 47.631	13.305 ± 5.664
5B	9226.180 ± 440.465	13725.350 ± 952.092	15692.610 ± 974.531	707.869 ± 44.085	355.091 ± 28.212	23.603 ± 11.081

5C	7182.369 ± 297.205	13963.330 ± 495.080	13626.340 ± 969.763	488.895 ± 45.540	398.256 ± 52.662	18.655 ± 5.395
5D	9154.487 ± 188.051	14316.140 ± 724.199	13842.360 ± 809.099	603.218 ± 23.901	390.514 ± 50.237	16.716 ± 2.189
5E	7164.362 ± 96.530	13394.210 ± 288.599	13800.390 ± 390.379	429.314 ± 68.396	259.014 ± 43.299	11.850 ± 6.199
5F	10300.876 ± 630.783	13832.580 ± 1455.078	13478.630 ± 952.993	638.808 ± 42.453	262.477 ±60.258	17.980 ± 3.294
6A	7921.044 ± 1305.997	13190.720 ± 930.307	14494.660 ± 2106.151	591.211 ± 156.591	321.461 ± 73.145	13.049 ± 3.530
6B	7723.308 ± 1027.069	13622.380 ± 562.841	13190.460 ± 901.174	563.266 ± 65.194	328.303 ± 44.010	13.677 ±4.900
6C	7481.403 ± 361.948	14263.440 ± 346.894	14572.300 ± 901.174	495.800 ± 35.924	362.963 ± 38.730	14.212 ± .7.923
6D	10177.995 ± 19.524	13058.000 ± 585.167	14663.300 ± 1350.281	712.629 ± 24.674	323.152 ± 8.737	14.980 ± 8.015
6E	7778.827 ± 443.585	14073.430 ± 660.340	14705.590 ± 1183.452	469.915 ± 99.190	285.781 ± 67.632	12.043 ± 5.374
6F	9098.047 ± 493.855	14686.620 ± 186.286	14426.210 ± 1924.287	538.364 ± 115.569	312.111 ± 31.826	12.985 ± 5.624
C (0.5 mm)	1050.087 ± 41.708	3487.540 ± 495.686	14688.193 ± 1081.464	N/A	N/A	N/A
C (0.75 mm)	1117.614 ± 48.569	3170.361 ± 267.267	13643.792 ± 829.734	N/A	N/A	N/A
C (1.0 mm)	1317.614 ± 192.453	4026.415 ± 516.446	15110.784 ± 256.681	N/A	N/A	N/A
Lasix®	4993.940 ± 83.961	13208.390 ± 699.165	16702.803 ± 118,637	N/A	N/A	N/A

N/A = not applicable

Poor aqueous solubility poses a major hurdle in the effective systemic delivery of BCS class IV drugs formulated into solid oral dosage forms such as furosemide. Adequate aqueous solubility and dissolution of the active ingredient in the human gastro-intestinal tract is one of the key factors to ensure that a sufficient concentration of the active ingredient is absorbed and become available at the site of action in order to elicit a pharmacological action in the human body. Without proper dissolution, the active ingredient will not reach the systemic circulation and the specific site of pharmacological action in sufficient quantities (Volkova et al.2018; Kumar 2019; Sanches and Ferreira, 2019; Van der Merwe et al.2020). The low and inconsistent solubility of furosemide in the stomach fluids and in the upper part of the small intestine remains a challenge. An increased dissolution rate of furosemide in this region of the gastro-intestinal tract may lead to an increased concentration gradient and therefore also an increased absorption rate of the drug (Ambrogi et al.2012; Nielsen et al.2013; Nielsen et al.2015).

It is evident from the data presented in Tables 5 and 6 that the effect of the formulation variables on the dissolution of furosemide was the most prominent at a pH of 1.2. The data give a clear indication that the inclusion of functional excipients had a pronounced effect on both the rate

and extent of dissolution of furosemide as indicated by the calculated dissolution parameters. This is specifically evident from the $\%_{max}$ values of furosemide at pH 1.2 after 360 min that ranged from 50.7 ± 2.31 to 80.4% ± 0.36% obtained for the MUPS tablet formulations containing functional excipients in comparison to 10.0 ± 0.73%, 11.3 ± 0.39% and 12.9 ± 1.58% obtained for the control MUPS tablets (without any functional excipients) consisting of 0.5 mm, 0.75 mm and 1.0 mm beads, respectively. The formulations containing functional excipients also exhibited higher $\%_{max}$ values compared to (Lasix®) that exhibited a $\%_{max}$ value of 38.8 ± 0.20%. The AUC values of 6271.9 ± 262.37 –10456.5 ± 141.46 µg.min/ml for the experimental MUPS tablets in comparison to 1050.1 ± 41.71, 1117.6 ± 48.57 and 1317.6 ± 192.45 µg.min/ml for the control MUPS tablets confirmed the trends(increased dissolution in a less acidic environment) Hier was ‘n verduideliking aangevra.of increased dissolution as observed with the $\%_{max}$ values. The inclusion of functional excipients resulted in an approximately 4.5 to 10-fold increase in the AUC-value of furosemide dissolution when compared to Lasix® (AUC = 4993.9 ± 83.96 µg.min/ml), depending on the functional excipient combination incorporated into the MUPS tablet formulation. The difference factor (f_1) values also confirmed that the formulation variables resulted in a significant difference in the dissolution of furosemide as compared to those of the control MUPS tablet formulations. This is indicated with difference factor values that ranged from 429.1 – 1001.5. The B group of MUPS tablet formulations (containing 15% chitosan and different concentrations and ratios of pH adjusting agents) exhibited the highest average difference factor (f_1) value of 742.7 when compared to that of Lasix®.

With regards to the DR_i’s for the dissolution profiles at a pH of 1.2, all the MUPS tablet formulations containing functional excipients exhibited higher DR_i values in comparison to the control MUPS tablet formulations. DR_i values of the MUPS tablet formulations containing functional excipients ranged from 0.544 ± 0.018 – 2.405 ± 0.789% dissolution.min^{-1} in

comparison to 0.11 ± 0.016% dissolution.min^{-1}, 0.125 ± 0.006% dissolution.min^{-1} and 0.130 ± 0.009% dissolution.min^{-1} for the control MUPS tablet formulations (without any functional excipients) prepared from 0.5 mm, 0.75 mm and 1.0 mm beads, respectively. This is a clear indication that the inclusion of functional excipients investigated in this study in the MUPS tablets increased the DR_i of furosemide in a medium with a pH of 1.2.

Examining the dissolution parameter results closely across all three pH environments, the best performing MUPS tablet formulations in terms of an increase in furosemide release based on $\%_{max}$ and DR_i values as compared to the control formulation and Lasix® were formulations 1B and 3B at a pH of 1.2. These two MUPS tablet formulations consisted of beads that contained a combination of sodium bicarbonate and calcium carbonate as pH adjusting agents in ratios of 50:50 and 75:25 as well as 1% w/w sodium lauryl sulphate. The bead sizes investigated in this study did not have a clear effect on the furosemide dissolution behaviour. It has been shown in previous studies that bead size has an influence on dissolution rate (Hamman et al.2019). It appears that the inclusion of functional excipients over shadowed the effect of bead size with regards to the dissolution behaviour of furosemide.

The dissolution profiles of these MUPS tablet formulations (i.e. formulations 1B – 6B) as well as Lasix® (L) and control formulation (C, 0.5 mm beads in MUPS tablet) are presented in Figures 1, 2 and 3 for the respective dissolution media. Due to the fact that these MUPS tablet formulations (1B – 6B) exhibited the largest difference in comparison to the control formulations, these formulations were selected for further investigations regarding *ex vivo* membrane permeation characteristics.

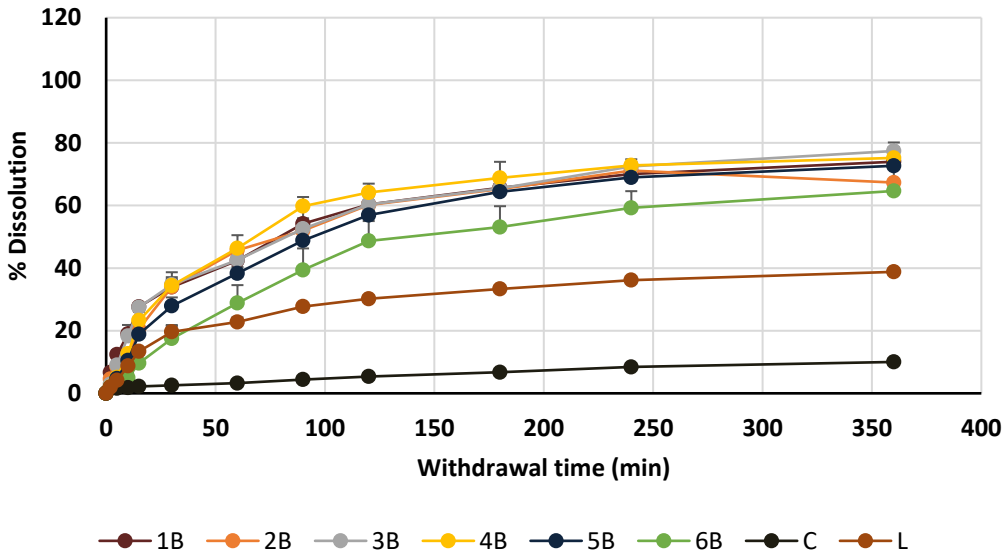


Figure 1: Percentage dissolution of furosemide for MUPS tablet formulations 1B - 6B in the 0.1 M HCl dissolution medium (pH of 1.2) plotted as a function of time. C = control and L = Lasix®

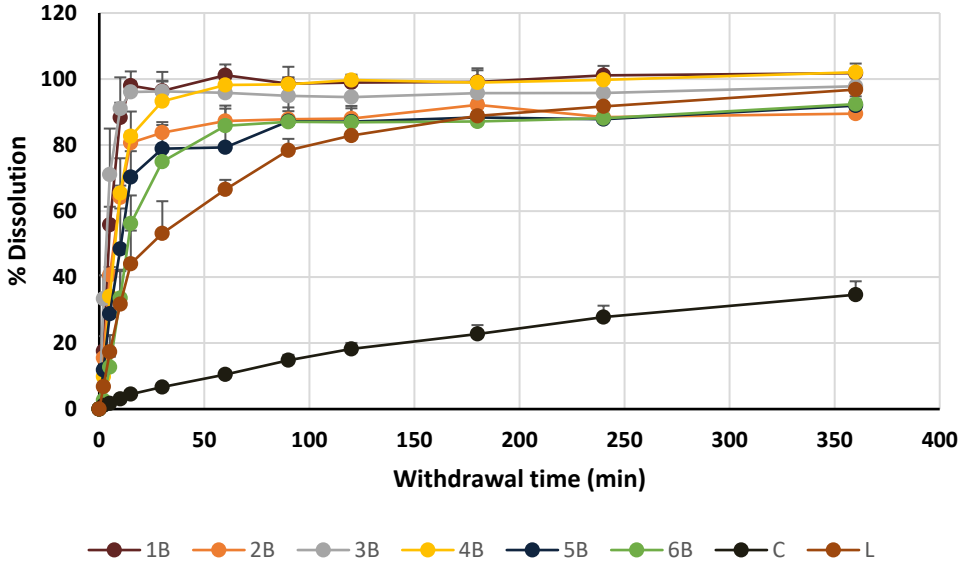


Figure 2: Percentage dissolution of furosemide for MUPS tablet formulations 1B - 6B in the buffer dissolution medium (pH of 4.6) plotted as a function of time. C = control and L = Lasix®

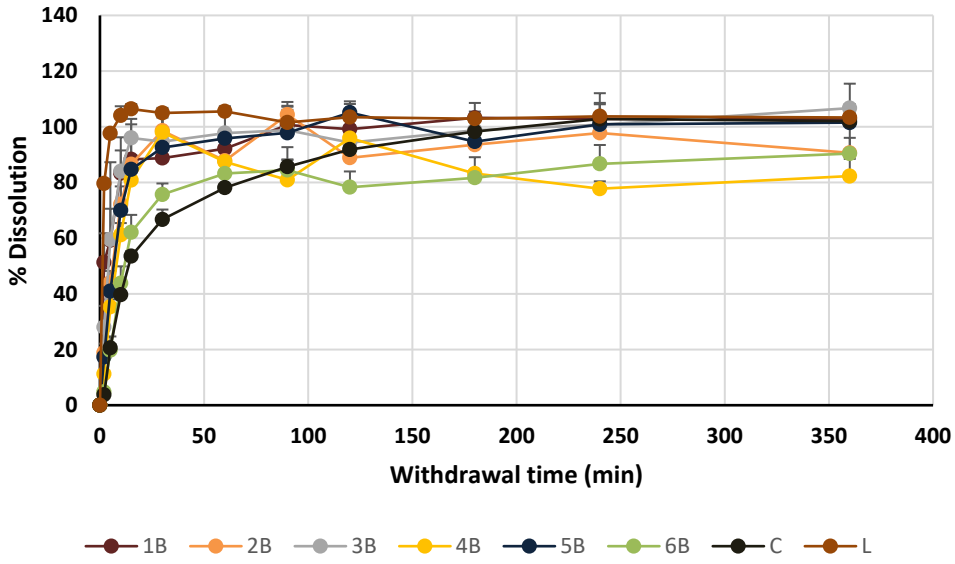


Figure 3: Percentage dissolution of furosemide for MUPS tablet formulations 1B - 6B in the buffer dissolution medium (pH of 7.4) plotted as a function of time. C = control group and L = Lasix®

It is clear from the dissolution graphs (Figures 1, 2 and 3) that all the formulations, including Lasix® (L) and the 0.5 mm control MUPS tablet formulation (C) exhibited in general higher rates and extents of dissolution with an increase in the pH of the dissolution media. This can be explained by the increased solubility of furosemide, a weak acidic drug, in environments with higher pH values. From the dissolution graphs, it is also clear that all the MUPS tablet formulations (1B – 6B) containing functional excipients exhibited distinctive higher rates and extents of dissolution as compared to the control formulation and Lasix® at pH 1.2. From the dissolution graphs (Figure 1), it is evident that the 75:25 ratio of the sodium bicarbonate:calcium carbonate (pH adjusting agents) combination in the MUPS tablet formulations provided the highest increase in furosemide dissolution in a medium with a pH of 1.2.

4.2.2 Multivariate statistical analysis (redundancy analysis) of dissolution data

A redundancy analysis (RDA) triplot, which provides a visual representation regarding the associations between formulation variables and the dissolution parameters, is given in Figure 4.

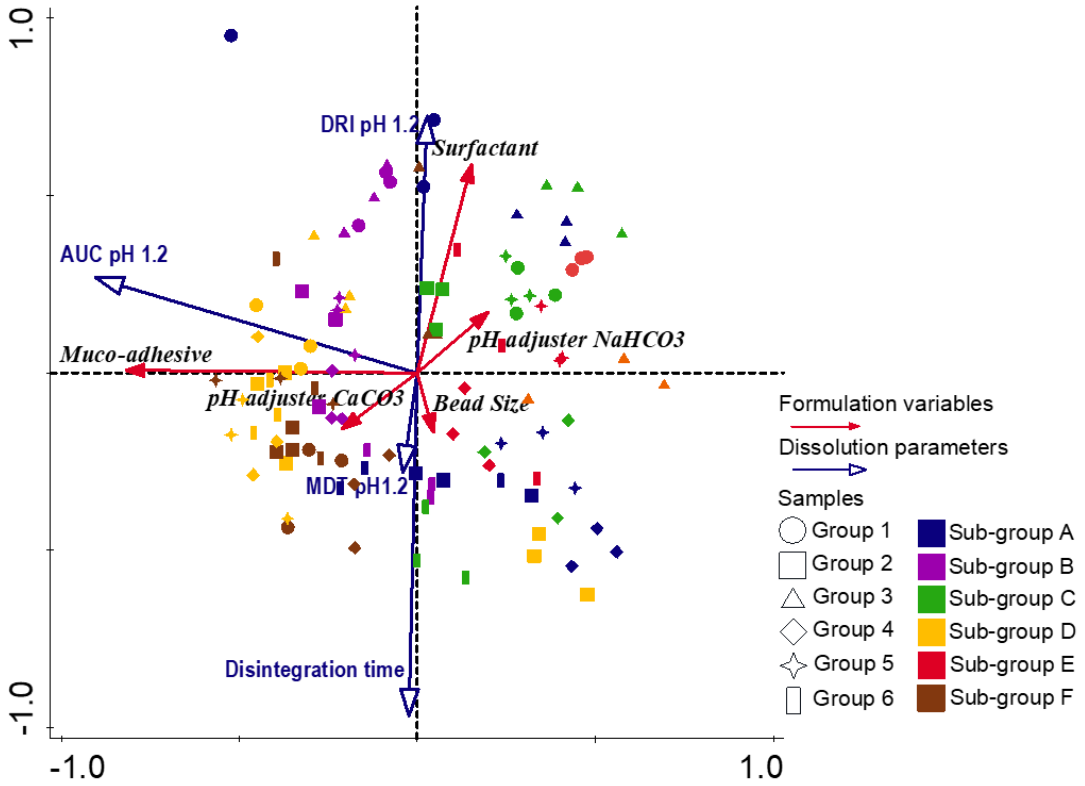


Figure 4: Redundancy analysis (RDA) triplot to indicate the association between formulation variables and dissolution parameters

The RDA analysis of the dissolution parameters indicated that 63.78% of the variation ($p = 0.002$) can be explained by the formulation variables (explanatory variables). The x-axis accounts for 61.7% of this variation and the y-axis accounts for 2.05% of this variation. The x-axis distinguishes between MUPS tablet formulations containing 0% chitosan (positive side of the x-axis) [Groups A, C and E] and MUPS tablet formulations containing 15% chitosan (negative side of the x-axis) [Groups B, D and F]. This indicated that the presence of chitosan

in the chitosan-containing formulations was the driving force with regards to the extent of dissolution as indicated by the AUC values of the dissolution profiles. The narrow angle between the two vector lines namely the dissolution AUC-line and the muco-adhesive line indicated that a positive correlation existed between these two variables. Furthermore, this correlation between chitosan content and the AUC of the dissolution profiles is a strong correlation as perpendicular projection of the environmental vector line (chitosan content) onto the AUC vector line as the environmental vector line extends to almost the complete length of the AUC vector line. The inclusion of chitosan in solid oral dosage forms has been shown to improve the solubility of poorly water-soluble drugs, especially drugs belonging to Class II and IV of the BCS (Lucio and Martínez-Ohárriz, 2017). In recent studies, an enhanced solubility due to an interaction between diflunisal and chitosan has been attributed as the main reason for an increase in the solubility of diflunisal (Lucio and Martínez-Ohárriz, 2017). The interaction between chitosan and diflunisal is due to electrostatic interaction between the anionic drug and the strongly positive charged chitosan at pH values lower than 6.5 (Lucio et al.2014; Lucio and Martínez-Ohárriz, 2017). It is therefore possible that chitosan increased the solubility of furosemide due to a similar interaction between furosemide and chitosan at a pH of 1.2.

The y-axis of the RDA triplot distinguished between MUPS tablet formulations containing 1% sodium lauryl sulphate (positive side of the y-axis) [Groups 1, 3 and 5] and MUPS tablet formulations containing 0% sodium lauryl sulphate (negative side of the y-axis) [Groups 2, 4 and 6]. It is evident from Figure 4 that there exists a positive correlation between the presence of sodium lauryl sulphate and the DR_i, which is a strong correlation (angle between vector lines is less than 15°). It is further clear from Figure 4 that there exists a strong negative correlation (angle between vector lines is close to 180°) between mean dissolution time (MDT) and DR_i. This is to be expected as a higher DR_i (faster initial release) will result in a decrease in the

MDT value. Surfactants such as sodium lauryl sulphate have been shown to improve the dissolution of poorly soluble drugs. The DR_i of celecoxib was significantly improved by the inclusion of sodium lauryl sulphate in the formulation, which mediated better wettability of celecoxib (Dun *et al*., 2018:139-140). The positive correlation (angle between vector lines are closer to 0°) between the increased DR_i and the inclusion of sodium lauryl sulphate in the furosemide MUPS tablets are therefore likely attributable to an improved wettability as furosemide is known to be poorly water wettable (Kumar and Rajeshwarrao 2011; Incecayir 2015; Dun et al.2018).

According to the RDA triplots of the dissolution behaviour of furosemide at the higher pH-values of 4.6 and 7.4, the contribution of the formulation variables to the dissolution of furosemide was less pronounced. Since furosemide is a weak acidic drug with a higher solubility at higher pH values, the contribution of the formulation variables in the improvement of the solubility and dissolution of furosemide at pH 4.6 and pH 7.4 became lower. This is confirmed by the low variation exhibited in the redundancy analyses namely 19.1% and 12.6% for pH 4.6 and 7.4, respectively (data not shown).

4.3 Ex-vivo permeability

Ex-vivo permeation evaluations were conducted for MUPS tablet formulations 1B – 6B, the control MUPS tablet formulation and Lasix®. The transport evaluations were only performed in pH environments of 1.2 and 4.6 since no pronounced changes in the dissolution behaviour were noted at a pH 7.4. In addition, the optimal region for absorption of furosemide is in the pyloric region of the stomach and the upper small intestine with pH ranges between 1.2 and 4.6 (Laulicht et al.2011). In Figures 5 and 6, the furosemide permeability results across excised pig intestinal tissues are provided for the evaluations at pH 1.2 and 4.6. Table 7 provides the average maximum percentage transport and the average P_{app} values.

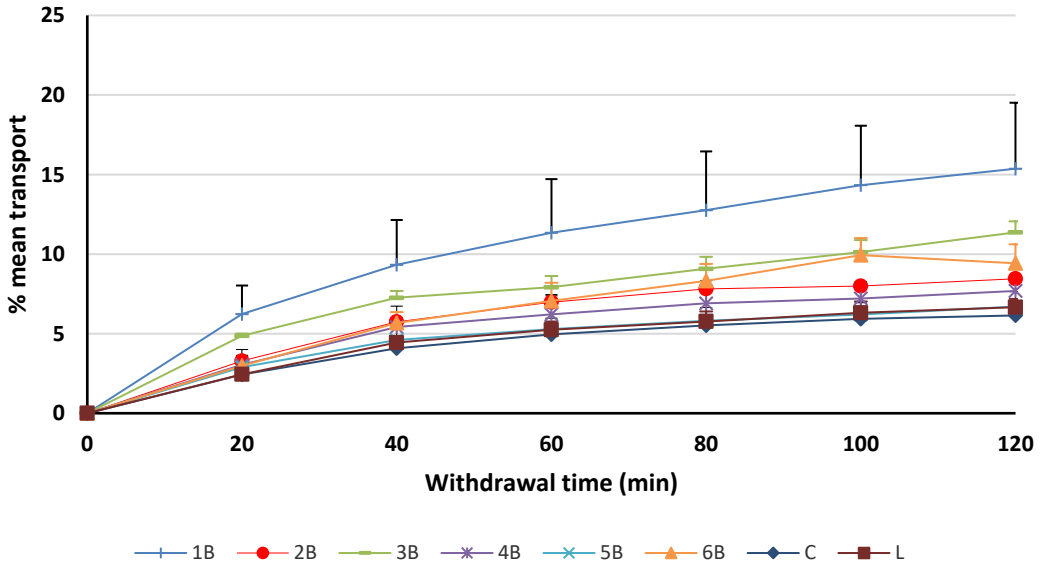


Figure 5: Average percentage transport of furosemide for MUPS tablet formulations 1B – 6B in 0.1 M HCl (pH 1.2) across excised pyloric antrum region of the pig stomach. C = control formulation and L = Lasix®

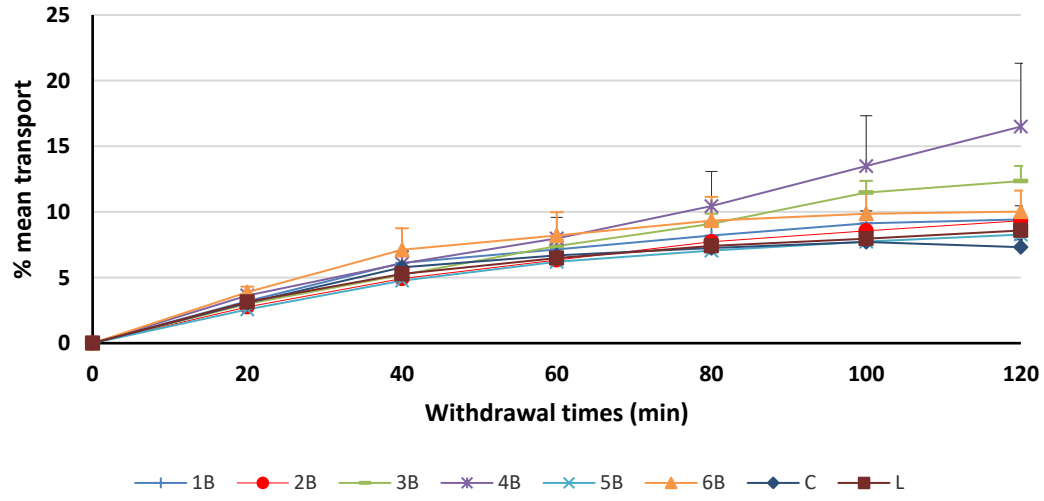


Figure 6: Average percentage transport of furosemide for MUPS tablet formulations 1B – 6B in citric acid buffer (pH 4.6) across excised pig upper small intestine. C = control formulation and L = Lasix®

Table 7: The average maximum percentage transport and the average apparent permeability

coefficient (P_{app}) values for formulations 1B – 6B, the control formulation (C) and Lasix® (L) across excised pig pyloric antrum (pH 1.2) and duodenum (pH 4.6).

	Average maximum percentage transport				Average apparent permeability coefficient			
Formula	**pH 1.2**	**STDEV**	**pH4.6**	**STDEV**	**pH 1.2**	**STDEV**	**pH4.6**	**STDEV**
1B	15.367	4.145	9.429	1.032	3.87348E-06	1.02332E-06	2.48766E-06	2.8431E-07
2B	8.450	0.272	9.326	0.216	2.17046E-06	6.78861E-08	2.4961E-06	2.86854E-08
3B	11.366	0.695	12.348	1.152	2.73605E-06	2.19682E-07	4.05889E-06	3.17637E-07
4B	7.686	0.853	16.497	4.825	1.93779E-06	1.43988E-07	4.33595E-06	1.41499E-06
5B	6.705	0.933	8.273	0.587	1.64689E-06	1.95178E-07	2.2062E-06	1.67959E-07
6B	9.936	1.073	10.021	1.601	2.64173E-06	3.41457E-07	2.60662E-06	4.69998E-07
C	6.146	0.738	7.706	0.616	1.58308E-06	2.13211E-07	1.92503E-06	1.60614E-07
L	6.664	0.521	8.582	0.775	1.71179E-06	1.68178E-07	2.21135E-06	1.80512E-07

It is evident from the data presented in Figures 5 and 6 as well as in Table 7, that the MUPS tablet formulations 1B – 6B exhibited increased furosemide permeation across the excised stomach tissue at pH 1.2 in comparison to the control MUPS tablet formulation and Lasix®. It is clear that MUPS tablet formulation 1B exhibited the highest cumulative percentage permeation (15.4 ± 4.14%) and P_{app} value ($3.87348 \times 10^{-6} \pm 1{,}02332 \times 10^{-06}$) followed by MUPS tablet formulation 3B with a cumulative percentage permeation of 11.4 ± 0.70% and a P_{app} value of $2.7360 \times 10^{-06} \pm 2.19682 \times 10^{-07}$. Therefore, the MUPS tablet formulation 1B exhibited approximately a 2.5 fold higher cumulative percentage furosemide permeation, while MUPS tablet formulation 3B exhibited approximately a 2 fold higher cumulative percentage furosemide permeation in comparison to the control MUPS tablet formulation and Lasix®. The increase in furosemide permeation observed with MUPS tablet formulation 1B was statistically significant in comparison to the control MUPS tablet formulation as well as Lasix® ($p < 0.05$; Tukey HSD test, $\alpha = 0.05$). Although the increase seen in furosemide permeation with MUPS tablet formulation 3B was pronounced, it was however, not statistically significant. It is therefore evident that the inclusion of functional excipients not only resulted in improved dissolution of furosemide at a pH of 1.2, but also improved the permeation of furosemide across

excised pig pyloric antrum tissue. The permeation of furosemide across the stomach tissue observed with MUPS tablet formulation 1B was also significantly higher than the permeation observed with MUPS tablet formulations 4B and 5B ($p < 0.05$; Tukey HSD test, $\alpha = 0.05$). MUPS tablet formulation 4B differs with respect to MUPS tablet formulation 1B in that it did not contain a wetting agent (0% w/w sodium lauryl sulfate) and the ratio of the pH adjusting excipients, $NaHCO_3$ and $CaCO_3$, also differed (ratio of $NaHCO_3$:$CaCO_3$ was 50:50 for formulation 1B and and 75:25 for formulation 4B). In accordance with the dissolution results, the inclusion of a wetting agent (sodium lauryl sulphate) and pH adjusting agents ($NaHCO_3$ and $CaCO_3$) caused an increase in the permeation of furosemide across excised pyloric antrum tissue at a pH of 1.2. This can be explained by the higher concentration gradient created by a higher dissolution rate and extent of the furosemide by the formulation variables investigated in this study. In addition, surface active agents such as sodium lauryl sulphate as well as chitosan (muco-adhesive agent) have been shown to have intestinal drug permeation enhancement effects (Karolewicz 2016; Khlibsuwanand Pongjanyakul 2016; Alizadeh et al.2018; Dun et al.2018).

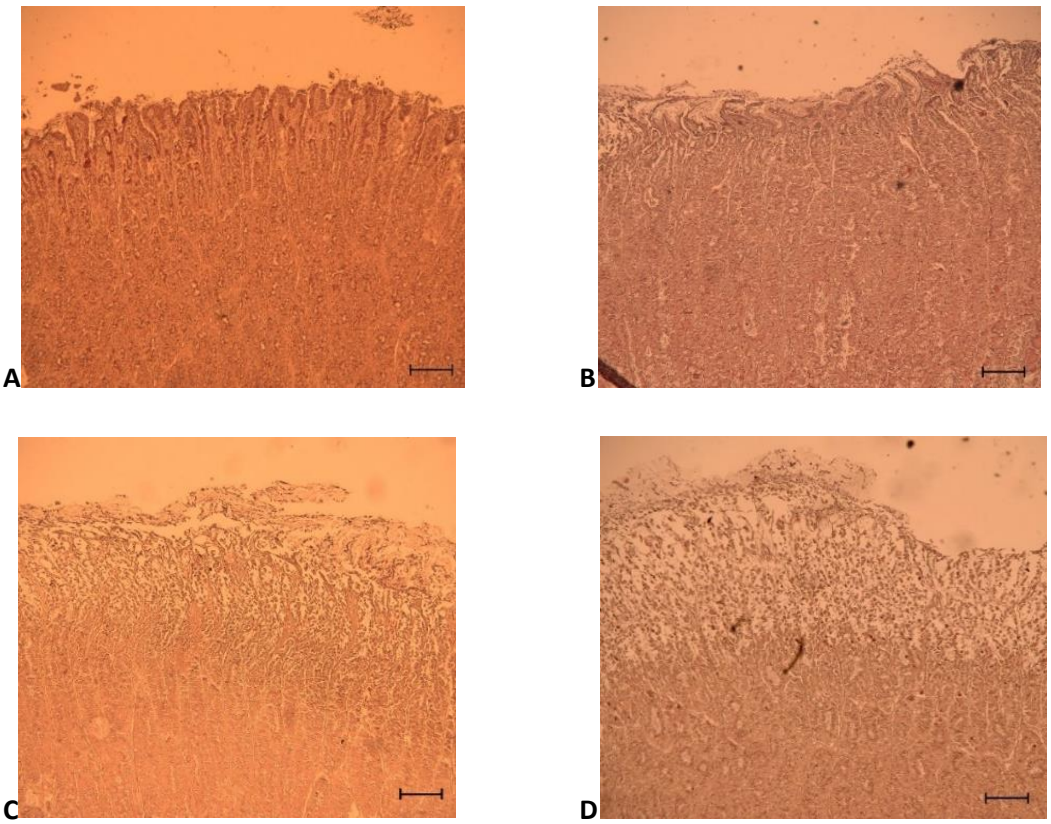
MUPS tablet formulation 3B exhibited the highest average cumulative percentage increase in furosemide permeation with the lowest variability as indicated by the low standard deviation, which is also one of the formulations that showed the highest furosemide dissolution rate and extent.

In general, a tendency towards slightly higher permeation of furosemide across intestinal tissue for all formulations was observed at a pH of 4.6. Similar to the permeation results obtained for pH 1.2, all the MUPS tablet formulations containing functional excipients exhibited higher cumulative percentage permeation values than the control MUPS tablet formulation at pH 4.6. Formulation 4B exhibited the highest percentage cumulative furosemide permeation of 16.5 ±

4.83%. Both MUPS tablet formulations 3B and 4B exhibited a statistically significant higher permeation of furosemide across excised pig duodenal tissue in comparison to the control MUPS tablet formulation and Lasix® ($p < 0.05$; Tukey HSD test, $\alpha = 0.05$). It is therefore evident that at pH of 4.6, the inclusion of functional excipients not only resulted in improved dissolution of furosemide but also improved the transport of furosemide across excised pig duodenal tissue.

4.4 Histological analysis

The MUPS tablet formulations 3B - 6B were selected for the histological analysis because these formulations contained the maximum percentages of the different functional excipients investigated in this study (Table 1). In Figures 7 and 8 images of sections of pyloric antrum and duodenal pig intestinal tissues, respectively, are depicted after exposure to the specific MUPS tablet formulations as well as the untreated control (exposed to transportbufferused).



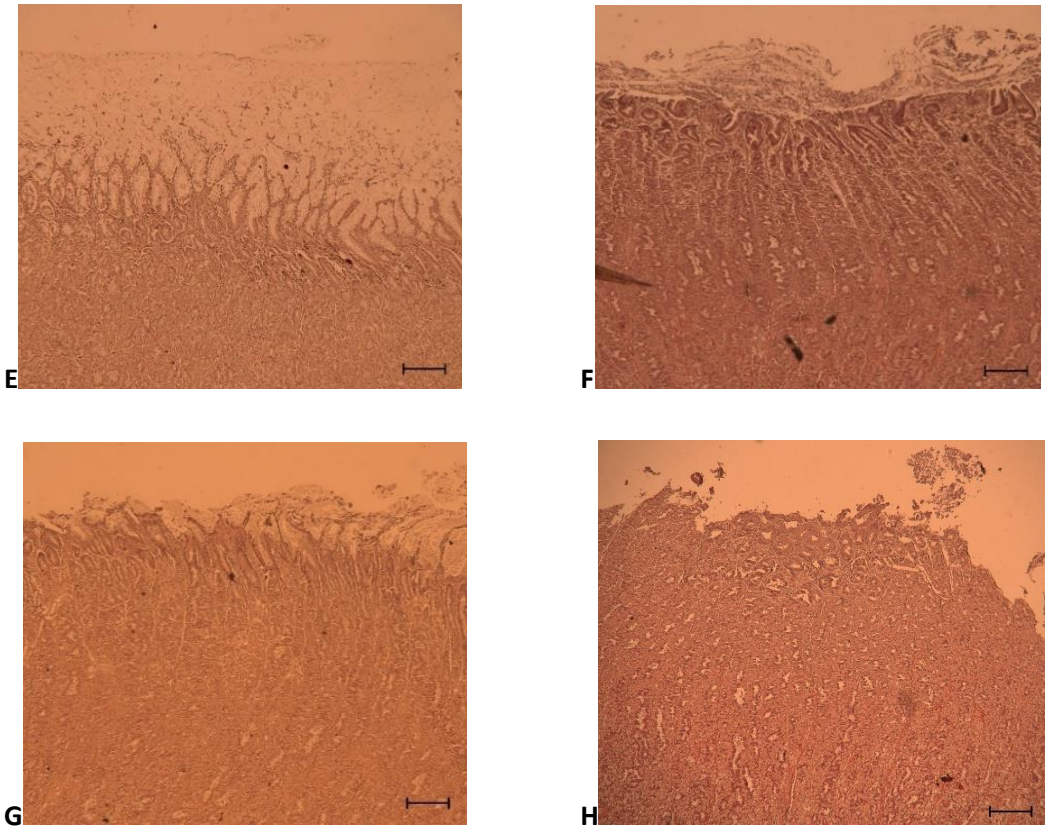
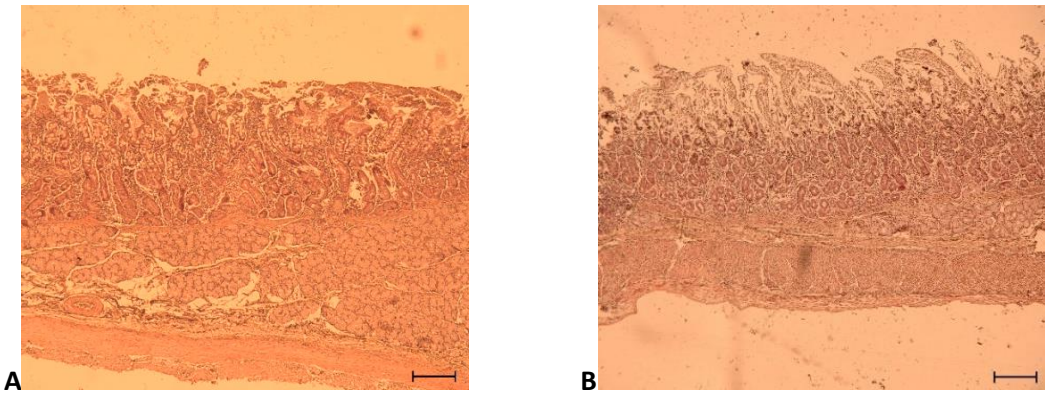


Figure 7: Representative histological sections of excised pig pyloric antrum tissues (scale bars = 200 µm) stained with hematoxylin-eosin after exposure tothe following in the pH 1.2 environment (0.1M HCl solution): A) Tissue sampled before the start of the permeability evaluation, B) Lasix®tablet, C) Control MUPS tablet formulation, D) MUPS tablet formulation 3B, E) MUPS tablet formulation 4B, F) MUPS tablet formulation 5B, G) MUPS tablet formulation 6B, H) the pH 1.2 medium (0.1M HCl solution).



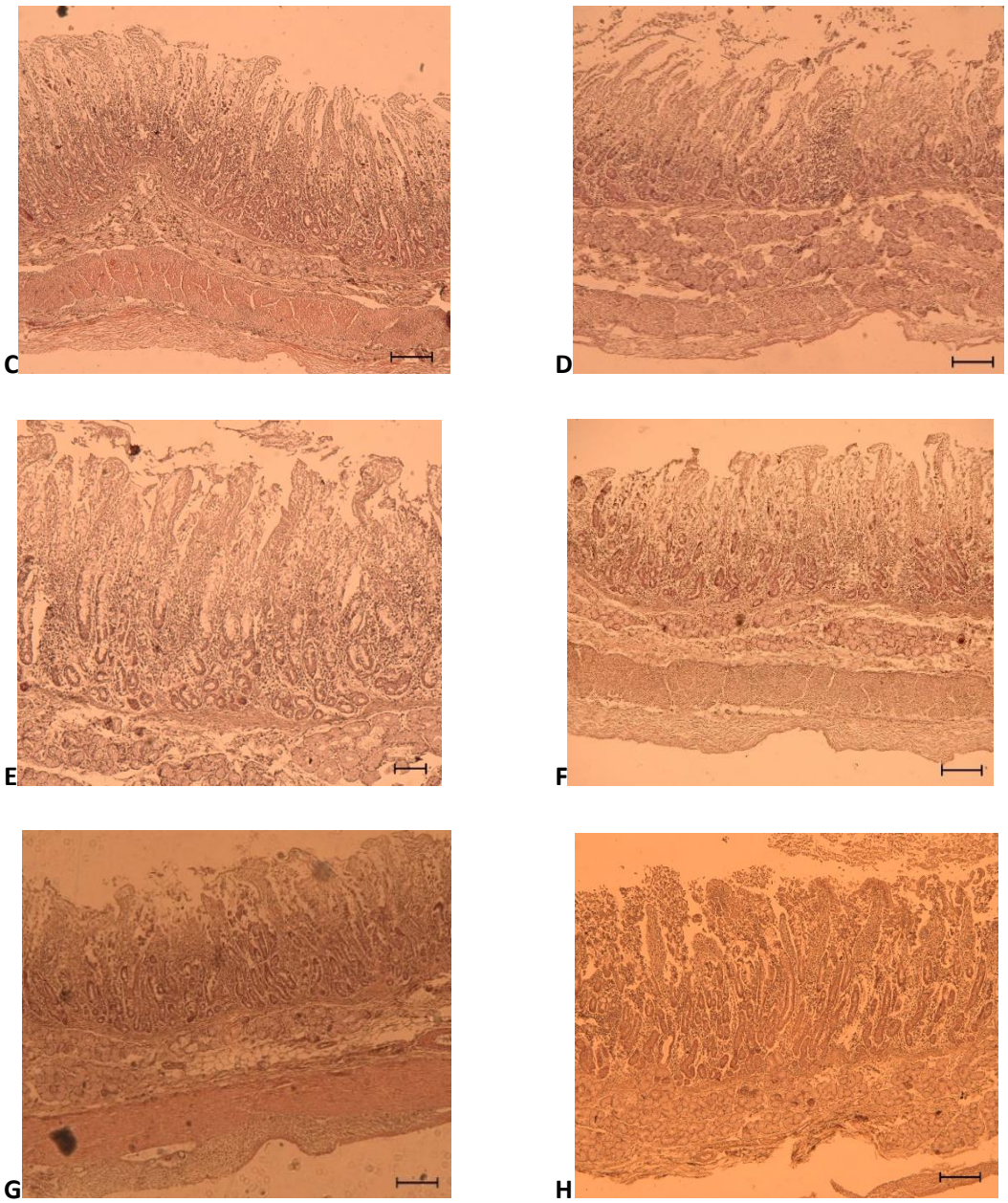


Figure 8: Representative histological sections of excised pig duodenal tissue (scale bars = 200 µm) stained with hematoxylin-eosin after exposure to the following in the pH 4.6 environment (citric acid buffer solution):A) Tissue sampledbefore the start of the permeability study, B) Lasix®tablet, C) MUPS tablet formulation, D) MUPS tablet formulation 3B, E) MUPS tablet formulation 4B, F) MUPS tablet formulation 5B, G) MUPS tablet formulation 6B, H) pH 4.6 medium (citric acid buffer solution).

Based on the data presented in Figures 7 and 8, it is evident that some of the experimental MUPS tablet formulations caused apical damage to the excised tissues to different extents. Important to notice is that the tissue samples exposed for two hours to the corresponding permeation media used in this study (i.e. pH 1.2 – 0.1M HCl and pH 4.6 – citric acid buffer solution) revealed no damage to the tissue. In Table 8, a summary of the important findings related to the histology study is presented.

Table 8: Histological analysis information of excised pyloric antrum and duodenal tissues after exposure to the MUPS tablet formulations

	Pyloric antrum (Stomach)	**Duodenum**
Tissue sampled before the start of permeability study	Intact morphology	Intact morphology
Lasix®	Intact morphology	Intact morphology
Control MUPS tablet formulation	Intact morphology with very little apical damage	Intact morphology
3B	Moderate damage to apical area	Intact morphology with very little apical damage
4B	Moderate damage to apical area	Intact morphology with very little apical damage
5B	Intact morphology	Intact morphology
6B	Intact morphology	Intact morphology
Permeation media	Intact morphology	Intact morphology

Considering the histology results, it evident that the MUPS tablet formulations (3B and 4B) containing the higher concentration of $NaHCO_3$ (Table 1) caused the most damage to the apical part of the pyloric antrum at pH 1.2, whereas the lesions on duodenum (pH 4.6) tissue were observed on the surface area only. Formulations 5B and 6B did not have adverse effects on tissues at both pH 1.2 and pH 4.6. In accordance with these results, the MUPS tablet formulations containing the lower $NaHCO_3$concentration (Table 1) caused less damage to the

apical tissue at both pH environments. It has been previously documented in the literature that $NaHCO_3$ at certain concentrations may cause gastrointestinal side effects and irritation (Kahle et al.2013).

The damage observed in this histological analysis to the apical surfaces of the excised pig tissues for some of the MUPS tablet formulations is not conclusive with respect to the cytotoxicity of these MUPS tablet formulations. Further studies are needed in order to investigate the cytotoxicity of the functional excipients (alone and in combination) on cell cultures and tissues, as well as *in vivo*.

5. Conclusion

Adequate drug solubility is critical to ensure sufficient drug dissolution in orderfor drugs to become pharmaceutically available for membrane permeability and bioavailability. It is evident from the results of this study that the inclusion of functional excipients in MUPS tablets improved the dissolution of furosemide at a pH of 1.2 and 4.6 as well as the permeation of furosemide across excised pig gastric and intestinal tissues during*ex vivo*studies. The most pronounced effects on furosemide dissolution by the inclusion of functional excipients in MUPS tablet formulations was observed at a pH of 1.2. The RDA analysis indicated that the inclusion of the mucoadhesive agent, chitosan, and the wetting agent, sodium lauryl sulphate, contributed the most to the enhanced dissolution of furosemide. However, all formulations evaluated in the pH 1.2 environment exhibited higher DR_i and $\%_{max}$values than the control MUPS tablet formulations as well as Lasix®. This could be attributed to the combination of functional excipients included in the MUPS tablet formulations. The ratio of sodium bicarbonate to calcium carbonate also played a role in dissolution enhancement of furosemide. A higher concentration sodium bicarbonate in relation to calcium carbonate showed a higher effect on furosemide dissolution.

It was anticipated that these increased dissolution profiles of furosemide at a pH of 1.2 should also lead to improved permeation of furosemide across excised pig stomach and intestinal tissue due to the higher concentration of furosemidepresent. Permeability results confirmed that the MUPS tablet formulations could enhance the membrane permeation of furosemide in accordance with the dissolution results. Formulation 3B (containing sodium bicarbonate:calcium carbonate in a ratio of 75:25, 1% w/w sodium lauryl sulphate and 15% w/w chitosan) achieved significantly higher cumulative furosemide permeation in both the pH 1.2 and 4.6 environments and also exhibited the lowest standard deviation values. According to histology analysis, the toxicity of 3B – 6B tablet formulation were low against pyloric antrum and duodenum tissues and with more thorough investigation the safety of these selected excipients combinations can be confirmed.

The application of excised pyloric antrum tissue for permeation evaluation allowed the gathering of valuable information regarding the permeability of furosemide in the stomach, which showed that furosemide absorption in this region can be enhanced by inclusion of functional excipients in MUPS tablet formulations.

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Chapter 4

Final conclusion and future prospects

This chapter contains the final conclusion, remarks and future prospects regarding the results presented in this thesis.

Final conclusion and future prospects

1. FINAL CONCLUSION

Tablets have been the most commonly used solid oral dosage form since the inception of dosage forms to administer dugs. Notwithstanding continuing research to modernise, improve and expand the pharmaceutical world, it still remains the preferred dosage form for effective drug treatment and optimal patient compliance (Lura *et al.,* 2020:1-3). Tablets are convenient to be self-administered by patients during their daily routine and provide a stable, safe and effective dosage form for treatment of numerous acute and chronic illnesses. Tablets do not only consist the drug that is compressed into a compact cylindrical dosage form, but they also contain excipients that are added to constitute the final dosage form. A pharmaceutical excipient is described in the literature as a pharmacologically inactive substance which, when combined with a drug, may serve as a vehicle or impart specific properties to the dosage form to ensure safe and effective treatment (Li *et al.,* 2020:1-4). The combination of a drug with the appropriate excipients is aimed at the formulation of a dosage form suitable for providing a consistent dose to ensure effective treatment of the targeted illness/medical condition. The combination of appropriate and bio-compatible excipients, in the correct ratio, with a specific drug is intended to ensure that the drug molecules reach the targeted site of action in therapeutically sufficient quantities (Lura *et al.,* 2020:1-7; Li *et al.,* 2020:1-8).

Two major characteristics that influence the efficacy of a drug is its solubility and membrane permeability once released from the dosage form. New chemical entities with therapeutic potential are discovered continuously, however, approximately 40% of these compounds exhibit limited and unpredictable bioavailability via the oral route due to poor solubility and membrane permeability, which limit the therapeutic use of these compounds (Volkova *et al.,* 2018:492-494). A number of drugs that are currently commercially available in medicinal products also exhibit poor aqueous solubility and poor membrane permeability. A notable example is furosemide, a weak acidic drug that is used as a loop diuretic in the treatment of hypertension and oedema linked with renal, hepatic and cardiac failure. This drug is of essential value in the pharmaceutical care of numerous patients around the world on a daily basis. Furosemide exhibits poor and variable bioavailability, ranging from approximately 20 to 60%. Furthermore, furosemide exhibits a narrow window of site specific absorption in the gastro-intestinal tract after oral administration. A promising approach to address the poor solubility and permeability of compounds is the use of functional excipients (Volkova *et al.,*

2018:492-494). Manipulating a dosage form throughthe addition of functional excipients to improve poor aqueous solubility and membrane permeability may contribute to more effective therapeutic use of furosemide tablets (Provenza *et al.,* 2014:208-212).

In this study, four functional excipients (chitosan, sodium lauryl sulphate, $NaHCO_3$ and $CaCO_3$) were added in different quantities and combinations in bead and MUPS tablet formulations. Inclusion of these functional excipients was investigated with regards to the potential improvement in the solubility/dissolution and permeability of furosemide. In addition to these functional excipients, other excipients (Kollidon® VA 64 and MCC) were added in order to produce mechanically strong and stable beads/pellets differing in size from 0.5 mm – 1 mm as well as excipients (CombiLac® and magnesium stearate) that were needed to compress 9 mm (diameter) flat faced, bevelled edge MUPS tablets of sufficient mechanical strength to withstand normal handling. The functional excipients were added — in different combinations — to the powder mixtures prior to employing extrusion-spheronisation to prepare beads/pellets. Formulation of MUPS tablets contributed to an accurate and uniform dosage per administration. Each of the 36 MUPS tablet formulations were evaluated with respect to physical characteristics according to BP standards. Official physical evaluations included disintegration, friability, and mass variation. Other non-official physical evaluations included tablet hardness, thickness and diameter. The MUPS tablet formulations were also evaluated with regards to dissolution behaviour. Dissolution testing were conducted at pH 1.2, pH 4.6 and pH 7.4 and *ex-vivo* permeability studies (Sweetana-Grass diffusion method) were performed using tissue from the pyloric antrum (pH 1.2) and ascending duodenum (pH 4.6) of pigs collected at the local abattoir. The *ex vivo* studies were conducted on selected MUPS tablet formulations (1B – 6B) based on dissolution data. Histological analysis was also conducted on selected formulations to evaluate the effect of the functional excipients on the duodenal and pyloric antrum tissue.

Dissolution results indicated that the most pronounced differences were observed in the pH 1.2 environment when comparing the dissolution profiles of the experimental MUPS tablet formulations containing functional excipients with that of the control MUPS tablet formulations as well as that of Lasix® tablets. Notable differences were also observed at pH 4.6, however, the differences decreased with an increase in pH of the dissolution medium and was negligible at a pH of 7.4 due to the inherent improved solubility of furosemide in an alkaline environment. In the pH 1.2 environment, AUC values showed a 4.5 – 10 fold increase compared to the control formulations and the commercial product. Maximum percentage dissolution ($\%_{max}$) results indicated that the Lasix® and the control formulations exhibited a 60 – 70% lower extent of dissolution when compared to that of the experimental MUPS tablet formulations containing functional excipients. Permeability results also exhibited a similar pattern, presenting with a

2.5-fold and a 2-fold increase in the cumulative percentage transport for formulations 1B and 3B respectively in the pH 1.2 environment (pyloric antrum tissue). Formulation 3B revealed the second highest cumulative percentage transport in the pH 1.2 and 4.6 environment with the lowest variability in transport. The improved solubility/dissolution as well as permeability of the formulations containing functional excipients could be linked to two functional excipients in particular, namely sodium lauryl sulphate and chitosan based on an RDA analysis. The inclusion of especially sodium lauryl sulphate, chitosan and the higher concentration of $NaHCO_3$ contributed to the increased solubility of furosemide in the gastro-intestinal tract where weak acidic drugs would normally show poor solubility (pH 1.2 – 4.6). The inclusion of chitosan in the bead, formulations mediated a notable mucoadhesive action which contributed to prolonged contact time of the bead particles with the intestinal mucous membrane and in effect may have contributed to an increase in the permeability of furosemide through the duodenal and pyloric antrum tissue. The inclusion of functional excipients in conjunction with a MUPS approach rendered promising results in improving the solubility/dissolution and permeability of furosemide, a BCS class IV drug, inan acidic pH.

The results of this study indicated that inclusion of functional excipients such as sodium lauryl sulphate, chitosan and $NaHCO_3$ to furosemide MUPS tablets provided promising results in terms of improving the solubility and permeability of furosemide. Furthermore, this study proved that pig pyloric antrum tissue can be used successfully for permeability studies at an acidic pH of 1.2, similar to what is experienced in the stomach. With the addition of this new pemeability evaluation method new and valuable information was obtained regarding furosemide's solubility and permeability profile. This finding may prove promising in studying the permeability of weak acidic drugs at an acidic pH as at an acidic pH the unionised species predominates and this favours permeability.

2. Future prospects

Based on the findings of this study, the following aspects or ideas are recommended for future research:

- Investigate the development and formulation of MUPS tablets containing weak acidic, BCS class IV drugs other than furosemide, to evaluate the effect that the formulation approach used in this study might have on the solubility and permeability of the specific drug in question.
- Investigate the use of chitosan in the formulation of tablets containing weak acidic BCS class IV drugs with an emphasis on the effect of this functional excipient on the solubility and dissolution behaviour of weak acidic drugs.

- Conduct *in vivo* studies with MUPS tablets containing functional excipients to investigate the effect on the absorption and bioavailability of weak acidic drugs as a formulation approach.
- *Ex vivo* studies with pig pyloric antrum tissue for permeability evaluation using the Sweetana-Grass diffusion method. Other weak acidic, BCS class IV drugs having the same poor and variable dissolution in the acidic stomach area can be evaluated using this method.

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Annexure A

Mass variation

In this Annexure the mass variation results for all formulations are displayed.

Table 1: Table of the mass variations results for Formulation 1A-1C

1A			1B			1C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5813	99.8754349	1	0.5821	99.88417485	1	0.583	100.0789645
2	0.5815	99.90979769	2	0.5839	100.3221511	2	0.5788	99.357984
3	0.5835	100.2534255	3	0.5826	99.96997126	3	0.5828	100.0446321
4	0.5819	99.97852326	4	0.5838	100.1758826	4	0.582	99.9073025
5	0.5829	100.1503372	5	0.5825	99.95281198	5	0.5833	100.1304631
6	0.58	99.6520768	6	0.5825	99.95281198	6	0.5827	100.0274659
7	0.5826	100.098793	7	0.5814	99.76405989	7	0.579	99.39231641
8	0.5816	99.92697908	8	0.5831	100.0557677	8	0.5808	99.70130806
9	0.5808	99.78952794	9	0.5818	99.83269701	9	0.5848	100.3879562
10	0.5822	100.0300674	10	0.583	100.0386084	10	0.58	99.56397844
11	0.5815	99.90979769	11	0.5831	100.0557677	11	0.5794	99.46098122
12	0.5831	100.1847	12	0.583	100.0386084	12	0.584	100.2506266
13	0.5823	100.0472488	13	0.5821	99.88417485	13	0.583	100.0789645
14	0.5807	99.77234655	14	0.5834	100.1072455	14	0.5811	99.75280667
15	0.5837	100.2877883	15	0.5829	100.0214491	15	0.582	99.9073025
16	0.5819	99.97852326	16	0.581	99.69542276	16	0.585	100.4222886
17	0.5824	100.0644302	17	0.5836	100.1415641	17	0.5852	100.456621
18	0.5828	100.1331558	18	0.5845	100.2959976	18	0.5847	100.37079
19	0.582	99.99570465	19	0.584	100.2102012	19	0.5838	100.2162942
20	0.5818	99.96134187	20	0.5812	99.72974132	20	0.5854	100.4909534
Average	0.582025	100.00	**Average**	0.582775	100.01	**Average**	0.58254	100.00
SD	0.000939695	0.161452652	**SD**	0.00096675	0.17599883	**SD**	0.00210773	0.361817237
%RSD	**0.161452652**		**%RSD**	0.165887323		**%RSD**	**0.361817237**	

Table 2: Table of the mass variations results for Formulation 1D-1F

1D			1E			1F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5774	99.35558251	1	0.582	100.2644432	1	0.5824	99.8731008
2	0.5834	100.3880271	2	0.586	100.9535459	2	0.5767	98.89563398
3	0.5782	99.49324179	3	0.5706	98.30050046	3	0.5819	99.7873581
4	0.5826	100.2503678	4	0.5862	100.988001	4	0.5781	99.13571355
5	0.5809	99.95784185	5	0.5771	99.42029235	5	0.5802	99.4958329
6	0.5854	100.7321753	6	0.5839	100.5917669	6	0.5856	100.4218541
7	0.5822	100.1815382	7	0.5787	99.69593343	7	0.5857	100.4390026
8	0.5766	99.21792324	8	0.5758	99.19633397	8	0.5871	100.6790822
9	0.5798	99.76856034	9	0.582	100.2644432	9	0.588	100.8334191
10	0.5821	100.1643308	10	0.5746	98.98960316	10	0.5778	99.08426793
11	0.5774	99.35558251	11	0.5812	100.1266226	11	0.5915	101.433618
12	0.5842	100.5256864	12	0.5838	100.5745394	12	0.5832	100.0102891
13	0.5794	99.6997307	13	0.5711	98.3866383	13	0.5793	99.34149604
14	0.5777	99.40720474	14	0.5821	100.2816707	14	0.583	99.97599204
15	0.5814	100.0438789	15	0.5834	100.5056291	15	0.5858	100.4561512
16	0.5856	100.7665901	16	0.5839	100.5917669	16	0.5779	99.10141647
17	0.5823	100.1987456	17	0.5805	100.0060296	17	0.5854	100.387557
18	0.5843	100.5428938	18	0.5806	100.0232572	18	0.5898	101.1420928
19	0.5827	100.2675752	19	0.5817	100.2127605	19	0.5851	100.3361114
20	0.5793	99.68252329	20	0.5841	100.6262221	20	0.5783	99.17001063

Average	0.581145	100.00	**Average**	0.580465	100.00	**Average**	0.58314	100.00
SD	0.002789543	0.480008164	**SD**	0.004502429	0.775659027	**SD**	0.004316114	0.740150605
%RSD	0.480008164		**%RSD**	0.775659027		**%RSD**	0.740150605	

Table 3: Table of the mass variations results for Formulation 2A-2C

2A			2B			2C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5877	100.680109	1	0.5862	100.9262766	1	0.5846	100.1988208
2	0.5843	100.0976479	2	0.581	100.0309907	2	0.5832	99.95886466
3	0.5822	99.73789252	3	0.5804	99.92768844	3	0.5894	101.0215275
4	0.5858	100.354616	4	0.5771	99.35952619	4	0.5879	100.7644316
5	0.584	100.0462543	5	0.5802	99.89325436	5	0.5888	100.9186892
6	0.5857	100.3374848	6	0.5819	100.185944	6	0.5781	99.08473879
7	0.5805	99.44666198	7	0.5817	100.1515099	7	0.5843	100.1474016
8	0.5807	99.4809244	8	0.5855	100.8057574	8	0.5822	99.78746743
9	0.5833	99.92633581	9	0.5777	99.46282841	9	0.5792	99.27327574
10	0.5891	100.9199459	10	0.5814	100.0998588	10	0.5836	100.0274236
11	0.5817	99.65223648	11	0.5802	99.89325436	11	0.5828	99.89030577
12	0.5819	99.6864989	12	0.5829	100.3581144	12	0.5814	99.65034965
13	0.5847	100.1661727	13	0.5808	99.99655659	13	0.5823	99.80460716
14	0.5834	99.94346701	14	0.58	99.85882029	14	0.5867	100.558755
15	0.5803	99.41239957	15	0.5752	99.03240247	15	0.5765	98.81050322
16	0.587	100.5601905	16	0.5816	100.1342929	16	0.5822	99.78746743
17	0.5826	99.80641735	17	0.5793	99.73830102	17	0.5884	100.8501303
18	0.588	100.7315026	18	0.5785	99.60056472	18	0.5889	100.9358289
19	0.5783	99.06977541	19	0.5812	100.0654247	19	0.5838	100.061703
20	0.5834	99.94346701	20	0.5836	100.4786337	20	0.5745	98.46770876
Average	0.58373	100.00	**Average**	0.58082	100.00	**Average**	0.58344	100.00
SD	0.00285972	0.489904625	**SD**	0.002620084	0.451100921	**SD**	0.004199048	0.719705113
%RSD	0.489904625		**%RSD**	0.451100921		**%RSD**	0.719705113	

Table 4: Table of the mass variations results for Formulation 2D-2F

2D			2E			2F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5788	99.48435889	1	0.5732	98.30976494	1	0.5838	99.93067502
2	0.5836	100.3093847	2	0.584	100.1620773	2	0.5754	98.49282358
3	0.5782	99.38123066	3	0.5849	100.3164367	3	0.5894	100.8892426
4	0.5838	100.3437607	4	0.5759	98.77284304	4	0.5815	99.5369776
5	0.5852	100.5843933	5	0.5832	100.024869	5	0.5924	101.402761
6	0.5783	99.3984187	6	0.5827	99.93911381	6	0.581	99.45139121
7	0.5876	100.9969062	7	0.5936	101.8085772	7	0.5786	99.04057651
8	0.584	100.3781368	8	0.5796	99.40743155	8	0.5808	99.41715665
9	0.5697	97.92024751	9	0.5834	100.0591711	9	0.5874	100.5468971
10	0.5853	100.6015813	10	0.5858	100.4707961	10	0.581	99.45139121
11	0.5861	100.7390856	11	0.584	100.1620773	11	0.5875	100.5640143
12	0.5839	100.3609488	12	0.5795	99.39028051	12	0.5895	100.9063599
13	0.5778	99.31247851	13	0.5772	98.99580657	13	0.5723	97.96218793
14	0.5844	100.446889	14	0.582	99.81905652	14	0.5866	100.4099588
15	0.586	100.7218976	15	0.5814	99.71615028	15	0.5868	100.4441934
16	0.5844	100.446889	16	0.5794	99.37312946	16	0.5829	99.77661951
17	0.5806	99.79374355	17	0.5898	101.1568377	17	0.5877	100.5982489
18	0.5791	99.535923	18	0.5881	100.86527	18	0.5851	100.1531996
19	0.5788	99.48435889	19	0.5915	101.4484054	19	0.5858	100.2730206
20	0.5804	99.75936748	20	0.5819	99.80190548	20	0.5886	100.7523044

Average	0.5818	100.00	**Average**	0.583055	100.00	**Average**	0.584205	100.00
SD	0.004229595	0.726984355	**SD**	0.005089564	0.872913126	**SD**	0.005039786	0.862674308
%RSD	0.726984355		**%RSD**	0.872913126		**%RSD**	0.862674308	

Table 5: Table of the mass variations results for Formulation 3A-3C

3A			3B			3C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5837	100.1776321	1	0.5828	100.1555263	1	0.5801	99.43179383
2	0.5826	99.98884436	2	0.5826	100.1211559	2	0.5874	100.6830472
3	0.5799	99.52545631	3	0.5782	99.36500571	3	0.5819	99.74032207
4	0.5823	99.9373568	4	0.5817	99.9664888	4	0.5859	100.4259404
5	0.5805	99.62843143	5	0.5811	99.86337741	5	0.5805	99.50035566
6	0.583	100.0574944	6	0.5825	100.1039706	6	0.5802	99.44893429
7	0.5805	99.62843143	7	0.5824	100.0867854	7	0.5807	99.53463658
8	0.5874	100.8126453	8	0.5823	100.0696002	8	0.5753	98.60905188
9	0.5844	100.2977697	9	0.5817	99.9664888	9	0.5879	100.7687495
10	0.5768	98.99341817	10	0.5785	99.41656141	10	0.5823	99.8088839
11	0.5825	99.97168184	11	0.5864	100.7741947	11	0.59	101.1286991
12	0.585	100.4007449	12	0.5831	100.207082	12	0.5853	100.3230976
13	0.5866	100.6753452	13	0.5777	99.27907956	13	0.5868	100.5802045
14	0.5832	100.0918195	14	0.5829	100.1727116	14	0.585	100.2716763
15	0.5791	99.38815614	15	0.5829	100.1727116	15	0.5829	99.91172664
16	0.5838	100.1947946	16	0.5799	99.65715464	16	0.5801	99.43179383
17	0.5807	99.66275647	17	0.5889	101.2038254	17	0.5919	101.4543678
18	0.587	100.7439953	18	0.5796	99.60559895	18	0.582	99.75746253
19	0.5805	99.62843143	19	0.5806	99.77745126	19	0.5795	99.32895109
20	0.5838	100.1947946	20	0.5821	100.0352297	20	0.5826	99.86030527
Average	0.582665	100.00	**Average**	0.581895	100.00	**Average**	0.583415	100.00
SD	0.002734242	0.469264832	**SD**	0.002609593	0.448464522	**SD**	0.004045046	0.693339339
% RSD	0.469264832		**% RSD**	0.448464522		**% RSD**	0.693339339	

Table 6: Table of the mass variations results for Formulation 3D-3F

3D			3E			3F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5924	101.5574775	1	0.5777	98.90683719	1	0.5763	98.8482286
2	0.5856	100.3917266	2	0.5803	99.35197788	2	0.5816	99.75729612
3	0.5878	100.7688813	3	0.5946	101.8002517	3	0.5809	99.6372306
4	0.579	99.26026247	4	0.5729	98.08503899	4	0.5893	101.0780169
5	0.5759	98.72881719	5	0.5851	100.1737761	5	0.5814	99.72299169
6	0.5885	100.8888851	6	0.5869	100.4819504	6	0.5816	99.75729612
7	0.5873	100.6831643	7	0.5866	100.430588	7	0.5796	99.41425178
8	0.5886	100.9060285	8	0.5822	99.677273	8	0.5734	98.3508143
9	0.5755	98.66024361	9	0.5767	98.73562923	9	0.5875	100.7692769
10	0.5904	101.2146096	10	0.5954	101.937218	10	0.5869	100.6663636
11	0.5833	99.99742849	11	0.5927	101.4749566	11	0.5866	100.614907
12	0.5807	99.5517002	12	0.5802	99.33485708	12	0.5823	99.87736165
13	0.5702	97.75164362	13	0.5814	99.54030663	13	0.5919	101.5239745
14	0.5888	100.9403153	14	0.5893	100.8928495	14	0.5725	98.19644435
15	0.5782	99.1231153	15	0.5811	99.48894425	15	0.595	102.0556932
16	0.5808	99.56884359	16	0.5846	100.0881721	16	0.5768	98.93398969
17	0.5806	99.5345568	17	0.5823	99.6943938	17	0.5802	99.51716508
18	0.5864	100.5288738	18	0.5895	100.9270911	18	0.5774	99.036903
19	0.5876	100.7345945	19	0.5863	100.3792256	19	0.5905	101.2838435
20	0.5787	99.20883228	20	0.5759	98.59866287	20	0.5886	100.9579513
Average	0.583315	100.00	**Average**	0.584085	100.00	**Average**	0.583015	100.00
SD	0.005900069	1.011472212	**SD**	0.006196202	1.060839115	**SD**	0.006269414	1.075343526
% RSD	1.011472212		**% RSD**	1.060839115		**% RSD**	1.075343526	

Table 7: Table of the mass variations results for Formulation 4A-4C

4A			4B			4C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5804	99.3197861	1	0.5766	99.25635199	1	0.5744	98.50712993
2	0.589	100.7914439	2	0.5787	99.61784755	2	0.5901	101.1996124
3	0.5796	99.1828877	3	0.5809	99.99655719	3	0.5879	100.8223219
4	0.5819	99.57647059	4	0.5833	100.409695	4	0.5772	98.98731789
5	0.5805	99.3368984	5	0.5795	99.75556015	5	0.5859	100.4793305
6	0.5862	100.3122995	6	0.579	99.66948977	6	0.5708	97.88974541
7	0.588	100.6203209	7	0.5813	100.0654135	7	0.5882	100.8737706
8	0.5839	99.91871658	8	0.5876	101.1499002	8	0.5759	98.76437348
9	0.5872	100.4834225	9	0.581	100.0137713	9	0.5871	100.6851253
10	0.587	100.4491979	10	0.5818	100.1514839	10	0.5852	100.3592835
11	0.5891	100.8085561	11	0.5836	100.4613372	11	0.5851	100.3421339
12	0.5788	99.0459893	12	0.579	99.66948977	12	0.5825	99.8962451
13	0.5892	100.8256684	13	0.5769	99.30799422	13	0.5866	100.5993775
14	0.5862	100.3122995	14	0.5792	99.70391792	14	0.5843	100.2049374
15	0.5777	98.85775401	15	0.5806	99.94491496	15	0.5899	101.1653133
16	0.5821	99.61069519	16	0.5821	100.2031261	16	0.5888	100.976668
17	0.5907	101.0823529	17	0.5779	99.48013496	17	0.5913	101.4054073
18	0.5822	99.62780749	18	0.5845	100.6162639	18	0.5747	98.55857864
19	0.5837	99.88449198	19	0.5817	100.1342698	19	0.5772	98.98731789
20	0.5841	99.95294118	20	0.5832	100.3924809	20	0.579	99.29601015
Average	**0.584375**	**100.00**	**Average**	**0.58092**	**100.00**	**Average**	**0.583105**	**100.00**
SD	0.003891404	0.665908733	**SD**	0.002711884	0.466825755	**SD**	0.006182018	1.060189441
%RSD	0.665908733		**%RSD**	0.466825755		**%RSD**	1.060189441	

Table 8: Table of the mass variations results for Formulation 4D-4F

4D			4E			4F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5844	100.3330701	1	0.5888	101.3800288	1	0.5867	100.5656496
2	0.5839	100.2472273	2	0.5825	100.29529	2	0.5808	99.55433665
3	0.583	100.0927102	3	0.5843	100.6052154	3	0.5844	100.171409
4	0.5777	99.1827765	4	0.5824	100.2780719	4	0.5774	98.97154611
5	0.5795	99.4918106	5	0.5704	98.21190286	5	0.5719	98.02879671
6	0.5809	99.73217045	6	0.576	99.17611509	6	0.5891	100.9770312
7	0.5849	100.4189129	7	0.584	100.5535611	7	0.5925	101.5598217
8	0.5828	100.0583731	8	0.5798	99.83040196	8	0.5758	98.69729174
9	0.5806	99.68066477	9	0.5799	99.84762003	9	0.5872	100.6513541
10	0.5842	100.298733	10	0.5802	99.89927426	10	0.5806	99.52005485
11	0.5815	99.83518182	11	0.5843	100.6052154	11	0.5807	99.53719575
12	0.5867	100.727947	12	0.5797	99.81318388	12	0.5899	101.1141584
13	0.5794	99.47464204	13	0.5817	100.1575454	13	0.5786	99.17723689
14	0.584	100.2643958	14	0.5928	102.0687518	14	0.5809	99.57147755
15	0.585	100.4360814	15	0.5851	100.74296	15	0.5831	99.94857731
16	0.5809	99.73217045	16	0.5701	98.16024863	16	0.5933	101.6969489
17	0.5819	99.90385606	17	0.5808	100.0025827	17	0.5831	99.94857731
18	0.5837	100.2128902	18	0.5712	98.34964746	18	0.5752	98.59444635
19	0.5798	99.54331628	19	0.5797	99.81318388	19	0.5928	101.6112444
20	0.5844	100.3330701	20	0.582	100.2091996	20	0.584	100.1028454
Average	0.58246	100.00	**Average**	0.580785	100.00	**Average**	0.5834	100.00
SD	0.002347989	0.403115933	**SD**	0.005672489	0.976693443	**SD**	0.006135402	1.051663013
%RSD	0.403115933		**%RSD**	0.976693443		**%RSD**	1.051663013	

Table 9: Table of the mass variations results for Formulation 5A-5C

5A			5B			5C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5821	100.0730649	1	0.5832	100.0034295	1	0.5776	99.24910219
2	0.5844	100.4684747	2	0.579	99.28324017	2	0.5767	99.09445504
3	0.5794	99.60888812	3	0.5853	100.3635241	3	0.5852	100.5550114
4	0.58	99.71203851	4	0.5833	100.0205768	4	0.5807	99.78177569
5	0.5786	99.47135428	5	0.5807	99.57474536	5	0.5861	100.7096586
6	0.5767	99.14471139	6	0.5895	101.0837134	6	0.5837	100.2972662
7	0.5813	99.93553101	7	0.5832	100.0034295	7	0.5809	99.81614173
8	0.5824	100.12464	8	0.587	100.6550293	8	0.582	100.0051549
9	0.5815	99.96991447	9	0.5861	100.500703	9	0.5777	99.2662852
10	0.5862	100.7779258	10	0.5776	99.04317706	10	0.5839	100.3316322
11	0.5844	100.4684747	11	0.5748	98.56305086	11	0.5845	100.4347303
12	0.5812	99.91833928	12	0.5855	100.3978189	12	0.5819	99.98797189
13	0.5773	99.24786178	13	0.5813	99.67762955	13	0.5842	100.3831813
14	0.5826	100.1590235	14	0.5883	100.8779451	14	0.5785	99.40374933
15	0.5839	100.382516	15	0.5823	99.84910319	15	0.5827	100.125436
16	0.579	99.5401212	16	0.5856	100.4149662	16	0.5815	99.91923982
17	0.5781	99.38539562	17	0.5816	99.72907164	17	0.5845	100.4347303
18	0.5867	100.8638845	18	0.5857	100.4321136	18	0.5837	100.2972662
19	0.5854	100.640392	19	0.586	100.4835557	19	0.5838	100.3144492
20	0.5823	100.1074483	20	0.5776	99.04317706	20	0.5796	99.59276251
Average	0.581675	100.00	**Average**	0.58318	100.00	**Average**	0.58197	100.00
SD	0.002929141	0.503570077	**SD**	0.003854266	0.660905083	**SD**	0.002758737	0.474034283
%RSD	0.503570077		**%RSD**	0.660905083		**%RSD**	0.474034283	

Table 10: Table of the mass variations results for Formulation 5D-5F

5D			5E			5F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5851	100.1154981	1	0.5872	100.9168793	1	0.5865	100.7351173
2	0.5921	101.3132566	2	0.5887	101.1746711	2	0.5919	101.6626018
3	0.5838	99.89305728	3	0.5798	99.64510668	3	0.5753	98.81144585
4	0.5827	99.70483809	4	0.5883	101.1059266	4	0.5847	100.4259558
5	0.5829	99.73905976	5	0.5799	99.6622928	5	0.5801	99.63587647
6	0.5852	100.132609	6	0.5773	99.21545376	6	0.5953	102.2465735
7	0.5847	100.0470548	7	0.5837	100.3153652	7	0.5879	100.9755762
8	0.5828	99.72194892	8	0.5801	99.69666503	8	0.5749	98.74274329
9	0.5841	99.94438978	9	0.5695	97.87493663	9	0.579	99.44694445
10	0.5835	99.84172477	10	0.5771	99.18108152	10	0.5781	99.29236371
11	0.5798	99.20862386	11	0.5844	100.4356681	11	0.5779	99.25801244
12	0.5794	99.14018052	12	0.573	98.47645072	12	0.5769	99.08625605
13	0.5851	100.1154981	13	0.5835	100.280993	13	0.5823	100.0137405
14	0.5907	101.0737049	14	0.5845	100.4528542	14	0.5758	98.89732404
15	0.5803	99.29417804	15	0.5857	100.6590876	15	0.5837	100.2541994
16	0.5857	100.2181632	16	0.5868	100.8481349	16	0.5811	99.80763285
17	0.5884	100.6801557	17	0.5792	99.54198998	17	0.5797	99.56717392
18	0.5845	100.0128331	18	0.5731	98.49363684	18	0.585	100.4774827
19	0.5836	99.85883561	19	0.5922	101.7761852	19	0.5887	101.1129813
20	0.5841	99.94438978	20	0.5833	100.2466208	20	0.5796	99.54999828
Average	0.584425	100.00	**Average**	0.581865	100.00	**Average**	0.58222	100.00
SD	0.0031709	0.542567439	**SD**	0.005867509	1.008396907	**SD**	0.005663326	0.972712404
%RSD	0.542567439		**%RSD**	1.008396907		**%RSD**	0.972712404	

Table 11: Table of the mass variations results for Formulation 6A-6C

6A			6B			6C		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5796	100.1269726	1	0.5829	100.233	1	0.5826	100.1013728
2	0.5779	99.83329446	2	0.5852	100.6284982	2	0.5802	99.68900878
3	0.58	100.1960734	3	0.5829	100.233	3	0.5801	99.67182694
4	0.5794	100.0924222	4	0.5792	99.59676379	4	0.5781	99.32819024
5	0.5769	99.66054261	5	0.5816	100.0094576	5	0.5777	99.2594629
6	0.5814	100.4379259	6	0.5827	100.1986089	6	0.5828	100.1357365
7	0.5781	99.86784483	7	0.5816	100.0094576	7	0.5825	100.084191
8	0.5818	100.5070267	8	0.5838	100.3877602	8	0.584	100.3419185
9	0.5812	100.4033756	9	0.581	99.90628412	9	0.5813	99.87800897
10	0.5786	99.95422076	10	0.5827	100.1986089	10	0.5791	99.50000859
11	0.5757	99.45324039	11	0.5806	99.83750183	11	0.5803	99.70619062
12	0.5744	99.22866299	12	0.5873	100.9896053	12	0.5849	100.496555
13	0.5798	100.161523	13	0.5799	99.71713281	13	0.5807	99.77491796
14	0.5804	100.2651741	14	0.5795	99.64835051	14	0.5812	99.86082713
15	0.5783	99.9023952	15	0.5829	100.233	15	0.5828	100.1357365
16	0.5758	99.47051558	16	0.5771	99.23565674	16	0.5803	99.70619062
17	0.5854	101.1289333	17	0.5799	99.71713281	17	0.589	101.2010103
18	0.579	100.0233215	18	0.5788	99.5279815	18	0.5829	100.1529183
19	0.5745	99.24593817	19	0.5811	99.9234797	19	0.5879	101.0120101
20	0.5791	100.0405967	20	0.5802	99.76871953	20	0.5818	99.96391815
Average	0.578865	100.00	**Average**	0.581545	100.00	**Average**	0.58201	100.00
SD	0.002643617	0.456689719	**SD**	0.002354497	0.404869335	**SD**	0.002870155	0.493145299
%RSD	0.456689719		**%RSD**	0.404869335		**%RSD**	0.493145299	

Table 12: Table of the mass variations results for Formulation 6D-6F

6D			6E			6F		
Tablet no.	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**	**Tablet no.**	**mass (g)**	**%MV**
1	0.5823	100.1212184	1	0.5845	100.0753347	1	0.5819	100.4687621
2	0.5841	100.4307121	2	0.5847	100.1095778	2	0.5822	100.5205591
3	0.5782	99.41626046	3	0.5838	99.95548403	3	0.5885	101.6082944
4	0.5767	99.15834902	4	0.5715	97.84953601	4	0.583	100.6586842
5	0.5881	101.1184759	5	0.5744	98.34606034	5	0.5735	99.01844834
6	0.5779	99.36467817	6	0.5913	101.2395987	6	0.5742	99.13930782
7	0.59	101.4451637	7	0.5902	101.0512619	7	0.5914	102.108998
8	0.5778	99.34748407	8	0.5898	100.9827757	8	0.589	101.6946226
9	0.5836	100.3447416	9	0.5808	99.44183817	9	0.5749	99.2601673
10	0.5799	99.70856008	10	0.5844	100.0582132	10	0.5739	99.0875109
11	0.5791	99.57100732	11	0.5877	100.6232236	11	0.579	99.96805857
12	0.5778	99.34748407	12	0.5831	99.83563333	12	0.5838	100.7968093
13	0.5808	99.86330694	13	0.5812	99.51032428	13	0.5714	98.65586989
14	0.5768	99.17554312	14	0.5909	101.1711126	14	0.5831	100.6759498
15	0.5843	100.4651003	15	0.5815	99.56168887	15	0.5711	98.60407296
16	0.5867	100.8777586	16	0.5902	101.0512619	16	0.5772	99.65727704
17	0.5806	99.82891875	17	0.5761	98.63712632	17	0.5834	100.7277467
18	0.5785	99.46784274	18	0.5803	99.35623052	18	0.5794	100.0371211
19	0.5842	100.4479062	19	0.5876	100.6061021	19	0.5704	98.48321348
20	0.5845	100.4994885	20	0.5872	100.537616	20	0.5724	98.82852629
Average	0.581595	100.00	**Average**	0.58406	100.00	**Average**	0.579185	100.00
SD	0.003930913	0.675884979	**SD**	0.005614024	0.96120669	**SD**	0.006384131	1.102261148
%RSD	0.675884979		**%RSD**	0.96120669		**%RSD**	1.102261148	

Annexure B

Crushing strength

In this Annexure the crushing strength results in Newton for all formulations are displayed. The diameter and the thickness of the tablets in each formula tested are also given.

Table 1: Crushing strength results for Formulation 1A-1D

	1A				1B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,350	10,020	87,000		5,470	10,020	135,000
	5,320	10,050	93,000		5,410	10,020	157,000
	5,330	10,060	122,000		5,410	10,010	152,000
	5,320	10,040	137,000		5,410	10,030	152,000
	5,340	10,040	113,000		5,460	10,020	119,000
	5,330	10,050	126,000		5,530	10,030	136,000
	5,370	10,040	104,000		5,310	10,020	185,000
	5,340	10,040	87,000		5,450	10,030	122,000
	5,300	10,040	83,000		5,530	10,040	104,000
	5,290	10,020	109,000		5,380	10,030	151,000
Average	5,329	10,040	106,100	**Average**	5,436	10,025	141,300
SD	0,023	0,012	18,556	**SD**	0,067	0,008	23,113
%RSD	0,437	0,124	17,489	**%RSD**	1,236	0,085	16,358
	1C				**1D**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,200	10,010	182,000		5,280	10,000	197,000
	5,210	10,020	165,000		5,240	10,000	201,000
	5,220	10,000	157,000		5,240	10,010	218,000
	5,200	10,010	149,000		5,320	10,010	172,000
	5,260	10,010	172,000		5,200	10,010	196,000
	5,240	10,010	131,000		5,180	10,010	151,000
	5,230	10,020	140,000		5,180	10,010	206,000
	5,150	10,010	134,000		5,220	10,010	213,000
	5,220	10,010	114,000		5,140	10,010	188,000
	5,230	10,010	126,000		5,220	10,010	167,000
Average	5,216	10,011	147,000	**Average**	5,222	10,008	190,900
SD	0,030	0,006	21,812	**SD**	0,052	0,004	21,460
%RSD	0,566	0,057	14,838	**%RSD**	0,996	0,042	11,242

Table 2: Crushing strength results for Formulation 1E-1F

	1E				1F		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,150	10,010	175,000		5,120	9,990	243,000
	5,130	10,000	196,000		4,980	10,000	191,000
	5,150	10,030	162,000		5,100	10,010	247,000
	5,150	10,020	176,000		5,090	10,000	176,000
	5,150	10,000	188,000		5,040	9,990	211,000
	5,130	10,020	116,000		5,120	10,000	229,000
	5,080	10,000	181,000		5,080	10,000	227,000
	5,190	10,010	123,000		5,040	10,000	198,000
	5,150	10,010	200,000		5,050	10,000	216,000
	5,170	10,010	123,000		5,060	10,000	203,000
Average	5,145	10,011	164,000	**Average**	5,068	9,999	214,100
SD	0,029	0,010	31,833	**SD**	0,043	0,006	22,820
%RSD	0,559	0,099	19,410	**%RSD**	0,851	0,057	10,659

Table 3: Crushing strength results for Formulation 2A-2B

	2A				2B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,230	10,020	256,000		5,390	9,620	194,000
	5,240	10,000	240,000		5,400	9,620	203,000
	5,220	10,010	195,000		5,390	9,610	217,000
	5,210	10,020	171,000		5,400	9,630	171,000
	5,170	10,010	215,000		5,380	9,620	206,000
	5,200	10,000	228,000		5,360	9,600	273,000
	5,200	10,010	223,000		5,390	9,600	208,000
	5,210	10,010	175,000		5,330	9,620	189,000
	5,200	10,010	201,000		5,380	9,620	243,000
	5,220	10,010	194,000		5,380	9,610	174,000
Average	5,210	10,010	209,800	**Average**	5,380	9,615	207,800
SD	0,019	0,007	27,571	**SD**	0,021	0,010	30,987
%RSD	0,373	0,067	13,142	**%RSD**	0,392	0,101	14,912

Table 4: Crushing strength results for Formulation 2C-2F

	2C				2D		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,300	10,010	243,000		5,250	9,990	328,000
	5,350	10,010	277,000		5,280	10,010	277,000
	5,330	10,020	227,000		5,250	9,980	232,000
	5,310	10,010	273,000		5,190	9,980	273,000
	5,320	10,010	296,000		5,200	9,980	326,000
	5,280	10,000	280,000		5,270	10,010	219,000
	5,280	10,020	165,000		5,270	10,010	242,000
	5,290	10,010	209,000		5,250	9,990	299,000
	5,290	10,000	224,000		5,270	10,000	223,000
	5,320	10,020	147,000		5,200	10,000	262,000
Average	5,307	10,011	234,100	**Average**	5,243	9,995	268,100
SD	0,023	0,007	50,017	**SD**	0,034	0,013	40,090
%RSD	0,436	0,074	21,365	**%RSD**	0,642	0,127	14,953
	2E				**2F**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,220	9,970	280,000		5,200	9,970	306,000
	5,090	9,960	333,000		5,200	9,970	347,000
	5,090	9,960	298,000		5,150	9,970	282,000
	5,080	9,960	291,000		5,320	9,990	197,000
	5,110	9,960	358,000		5,340	9,980	191,000
	5,090	9,970	260,000		5,290	10,010	264,000
	5,020	9,970	230,000		5,210	9,960	373,000
	5,030	9,950	295,000		5,330	9,990	226,000
	5,160	9,960	294,000		5,170	9,970	330,000
	5,130	9,960	234,000		5,160	9,960	299,000
Average	5,102	9,962	287,300	**Average**	5,237	9,977	281,500
SD	0,059	0,006	39,780	**SD**	0,075	0,016	62,038
%RSD	1,150	0,063	13,846	**%RSD**	1,429	0,157	22,038

Table 5: Crushing strength results for Formulation 3A-3D

	3A				3B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,280	9,980	162,000		5,300	9,980	178,000
	5,280	9,980	99,000		5,410	9,980	153,000
	5,330	9,980	123,000		5,420	9,990	171,000
	5,270	9,990	104,000		5,400	9,990	198,000
	5,280	9,980	116,000		5,410	9,980	145,000
	5,310	9,980	83,000		5,310	9,980	198,000
	5,240	9,990	115,000		5,380	10,000	131,000
	5,250	9,990	165,000		5,330	9,980	160,000
	5,280	9,990	112,000		5,290	9,990	187,000
	5,250	9,980	108,000		5,360	9,990	136,000
Average	5,277	9,984	118,700	**Average**	5,361	9,986	165,700
SD	0,028	0,005	26,026	**SD**	0,050	0,007	24,559
%RSD	0,521	0,052	21,926	**%RSD**	0,932	0,070	14,821
	3C				**3D**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,210	9,980	159,000		5,230	9,970	204,000
	5,370	9,980	126,000		5,260	9,970	200,000
	5,230	9,970	149,000		5,260	9,980	125,000
	5,310	9,990	112,000		5,250	9,980	201,000
	5,220	9,980	97,000		5,240	9,970	207,000
	5,310	9,980	131,000		5,160	9,980	216,000
	5,210	9,980	177,000		5,260	9,980	221,000
	5,330	9,990	97,000		5,270	9,980	221,000
	5,270	9,990	76,000		5,170	9,980	219,000
	5,220	9,970	125,000		5,220	9,980	171,000
Average	5,268	9,981	124,900	**Average**	5,232	9,977	198,500
SD	0,058	0,007	30,932	**SD**	0,039	0,005	29,830
%RSD	1,106	0,074	24,765	**%RSD**	0,736	0,048	15,028

Table 6: Crushing strength results for Formulation 3E-3F

	3E				3F		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,110	9,980	177,000		5,200	10,000	160,000
	5,100	9,980	132,000		5,270	10,000	148,000
	4,970	10,010	171,000		5,140	10,020	249,000
	5,050	9,980	176,000		5,230	10,000	239,000
	5,000	9,980	153,000		5,070	10,000	179,000
	5,060	9,980	147,000		5,270	10,000	182,000
	5,060	10,010	136,000		5,170	10,000	241,000
	5,020	9,990	223,000		5,120	9,990	247,000
	4,930	9,980	124,000		5,120	10,000	256,000
	5,030	10,020	163,000		5,150	9,990	262,000
Average	5,033	9,991	160,200	**Average**	5,174	10,000	216,300
SD	0,056	0,016	28,901	**SD**	0,067	0,008	43,721
%RSD	1,108	0,160	18,041	**%RSD**	1,299	0,082	20,213

Table 7: Crushing strength results for Formulation 4A-4B

	4A				4B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,130	9,960	132,000		5,300	9,990	209,000
	5,070	9,960	144,000		5,230	9,970	328,000
	5,060	9,960	207,000		5,280	9,970	275,000
	5,140	9,960	198,000		5,260	9,980	273,000
	5,080	9,960	242,000		5,270	9,980	278,000
	5,170	9,950	257,000		5,210	10,000	225,000
	5,040	9,970	211,000		5,200	9,960	240,000
	5,040	9,950	148,000		5,240	9,960	215,000
	5,070	9,940	243,000		5,220	9,960	296,000
	5,040	10,000	176,000		5,210	10,000	219,000
Average	5,084	9,961	195,800	**Average**	5,242	9,977	255,800
SD	0,046	0,016	44,596	**SD**	0,034	0,016	39,991
%RSD	0,914	0,160	22,777	**%RSD**	0,647	0,157	15,634

Table 8: Crushing strength results for Formulation 4C-4F

	4C				4D		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,020	9,970	203,000		5,180	9,970	203,000
	5,020	9,970	241,000		5,110	9,980	260,000
	5,020	9,950	267,000		5,200	9,960	256,000
	5,120	9,970	248,000		4,900	9,980	193,000
	5,020	9,980	151,000		5,150	9,980	237,000
	4,980	9,960	188,000		5,190	9,980	223,000
	5,120	9,970	242,000		5,190	9,960	218,000
	5,030	9,980	179,000		4,920	9,970	234,000
	4,980	9,970	243,000		4,910	10,000	216,000
	5,120	9,970	284,000		4,900	9,980	260,000
Average	5,043	9,969	224,600	**Average**	5,065	9,976	230,000
SD	0,056	0,009	42,277	**SD**	0,138	0,012	23,636
%RSD	1,106	0,088	18,823	**%RSD**	2,725	0,118	10,277
	4E				**4F**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	4,880	9,990	199,000		4,550	9,980	311,000
	4,880	9,970	278,000		4,490	9,980	275,000
	4,880	9,990	244,000		4,590	9,980	293,000
	4,870	9,990	222,000		4,710	10,000	329,000
	4,790	9,980	184,000		5,160	9,980	263,000
	4,920	10,000	278,000		4,500	9,980	283,000
	4,810	9,990	222,000		5,160	9,970	267,000
	4,890	9,980	282,000		4,530	9,970	264,000
	4,880	9,960	276,000		5,160	9,970	269,000
	4,860	9,970	225,000		5,130	10,050	263,000
Average	4,866	9,982	241,000	**Average**	4,798	9,986	281,700
SD	0,038	0,012	35,969	**SD**	0,311	0,024	22,755
%RSD	0,788	0,123	14,925	**%RSD**	6,485	0,242	8,078

Table 9: Crushing strength results for Formulation 5A-5D

	5A				5B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	4,640	9,970	279,000		4,820	9,990	243,000
	4,660	9,980	287,000		4,770	9,980	201,000
	4,640	9,980	188,000		4,820	9,970	235,000
	4,650	9,980	200,000		4,830	10,000	220,000
	5,270	9,980	187,000		4,830	9,970	220,000
	5,270	10,000	194,000		4,810	9,970	205,000
	5,280	9,980	224,000		4,830	9,980	215,000
	5,190	9,960	241,000		4,820	9,960	173,000
	5,230	9,960	195,000		4,820	10,000	223,000
	5,230	9,990	180,000		4,790	9,980	220,000
Average	5,006	9,978	217,500	**Average**	4,814	9,980	215,500
SD	0,310	0,012	39,127	**SD**	0,020	0,013	19,381
%RSD	6,186	0,123	17,990	**%RSD**	0,406	0,134	8,993
	5C				**5D**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,360	9,980	207,000		5,220	9,970	207,000
	5,380	10,000	150,000		5,220	9,970	211,000
	5,380	9,990	157,000		5,260	9,970	309,000
	5,360	9,980	189,000		5,230	9,970	254,000
	5,340	10,000	158,000		5,210	9,950	245,000
	5,350	10,000	155,000		5,180	9,970	255,000
	5,350	10,000	177,000		5,210	9,990	274,000
	5,320	9,980	201,000		5,180	9,990	251,000
	5,350	10,000	147,000		5,210	9,990	244,000
	5,360	10,010	163,000		5,290	10,000	217,000
Average	5,355	9,994	170,400	**Average**	5,221	9,977	246,700
SD	0,018	0,011	21,742	**SD**	0,033	0,015	30,750
%RSD	0,332	0,108	12,759	**%RSD**	0,641	0,150	12,465

Table 10: Crushing strength results for Formulation 5E-5F

	5E				5F		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,320	9,970	209,000		5,210	9,980	221,000
	5,380	9,970	291,000		5,250	9,960	271,000
	5,350	9,990	259,000		5,230	9,980	277,000
	5,340	9,970	253,000		5,230	9,990	314,000
	5,350	9,970	281,000		5,190	9,990	282,000
	5,330	9,960	263,000		5,330	9,980	263,000
	5,300	9,960	252,000		5,220	9,990	279,000
	5,300	9,980	237,000		5,350	10,020	243,000
	5,300	9,960	260,000		5,190	9,990	304,000
	5,270	10,000	181,000		5,320	10,000	221,000
Average	5,324	9,973	248,600	**Average**	5,252	9,988	267,500
SD	0,032	0,013	32,654	**SD**	0,059	0,015	31,419
%RSD	0,608	0,134	13,135	**%RSD**	1,131	0,155	11,745

Table 11: Crushing strength results for Formulation 6A-6B

	6A				6B		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,190	10,020	236,000		5,270	10,000	293,000
	5,220	9,990	358,000		5,140	9,990	240,000
	5,220	9,990	210,000		5,110	9,980	264,000
	5,200	10,000	216,000		5,280	9,980	249,000
	5,230	10,030	187,000		5,220	9,990	302,000
	5,220	10,000	206,000		5,200	9,990	254,000
	5,220	10,000	190,000		5,180	9,990	243,000
	5,180	10,000	222,000		5,170	9,980	228,000
	5,230	10,010	249,000		5,170	9,980	270,000
	5,210	10,010	183,000		5,190	9,980	289,000
Average	5,212	10,005	225,700	**Average**	5,193	9,986	263,200
SD	0,017	0,013	51,088	**SD**	0,053	0,007	24,894
%RSD	0,324	0,127	22,635	**%RSD**	1,019	0,070	9,458

Table 12: Crushing strength results for Formulation 6C-6F

	6C				6D		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,170	9,990	232,000		5,200	9,990	235,000
	5,170	9,990	253,000		5,110	9,980	239,000
	5,180	9,990	277,000		5,190	9,990	254,000
	5,180	9,990	285,000		5,240	9,970	268,000
	5,170	9,990	250,000		5,220	9,970	338,000
	5,150	9,990	344,000		5,180	9,990	249,000
	5,150	10,000	214,000		5,210	9,990	305,000
	5,210	10,010	309,000		5,170	10,030	209,000
	5,140	9,980	218,000		5,170	9,990	229,000
	5,140	10,010	282,000		5,200	9,980	259,000
Average	5,166	9,994	266,400	**Average**	5,189	9,988	258,500
SD	0,022	0,010	41,175	**SD**	0,035	0,017	37,913
%RSD	0,420	0,097	15,456	**%RSD**	0,683	0,169	14,667
	6E				**6F**		
	Thickness (mm)	**Diameter (mm)**	**Hardness (N)**		**Thickness (mm)**	**Diameter (mm)**	**Hardness (N)**
	5,400	10,000	280,000		5,230	9,990	303,000
	5,300	9,980	334,000		5,420	9,990	353,000
	5,440	9,990	289,000		5,260	9,970	317,000
	5,430	10,000	319,000		5,310	9,980	256,000
	5,360	10,000	222,000		5,580	10,000	207,000
	5,380	10,000	292,000		5,320	9,990	265,000
	5,390	9,980	339,000		5,320	9,980	304,000
	5,220	10,000	325,000		5,390	9,980	213,000
	5,300	10,000	329,000		5,310	9,990	290,000
	5,290	9,990	349,000		5,320	9,980	263,000
Average	5,351	9,994	307,800	**Average**	5,346	9,985	277,100
SD	0,071	0,008	37,956	**SD**	0,099	0,008	45,615
%RSD	1,323	0,084	12,331	**%RSD**	1,846	0,085	16,462

Annexure C

Disintegration time

In this Annexure the disintegration test results done on all formulas are given.

Table 1: Table of the disintegration test results for Formulation 1A-1F

1A		1B		1C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	6:02	1	7:55	1	10:34
2	6:52	2	8:17	2	10:36
3	7:18	3	8:24	3	10:51
4	7:30	4	8:30	4	11:36
5	8:12	5	8:33	5	11:54
6	8:14	6	6:01	6	9:24
7	8:44	7	8:18	7	9:45
8	8:44	8	5:58	8	12:40
9	5:10	9	9:10	9	8:04
10	5:50	10	12:34	10	10:58
11	7:15	11	7:40	11	11:18
12	8:50	12	10:28	12	10:20
13	9:17	13	11:30	13	13:25
14	8:20	14	9:16	14	11:25
15	8:40	15	10:14	15	14:40
16	4:02	16	10:28	16	13:57
17	6:05	17	9:55	17	13:55
18	6:50	18	10:01	18	14:36
Average	**7:19**	**Average**	**9:04**	**Average**	**11:39**
1D		**1E**		**1F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	13:50	1	6:02	1	13:18
2	13:57	2	11:51	2	15:56
3	11:10	3	6:20	3	18:50
4	15:15	4	12:30	4	19:45
5	12:55	5	12:55	5	19:57
6	16:20	6	13:18	6	20:07
7	16:40	7	13:10	7	20:53
8	14:11	8	13:40	8	20:48
9	17:35	9	10:50	9	22:35
10	14:51	10	8:25	10	23:01
11	11:55	11	14:40	11	23:20
12	12:24	12	9:17	12	23:09
13	16:26	13	9:55	13	23:27
14	13:02	14	9:30	14	20:04
15	14:10	15	13:55	15	19:55
16	14:47	16	14:10	16	20:15
17	16:21	17	14:57	17	22:20
18	18:48	18	12:48	18	22:44
Average	**14:42**	**Average**	**11:34**	**Average**	**20:34**

Table 2: Table of the disintegration test results for Formulation 2A-2F

2A		2B		2C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	17:28	1	10:38	1	11:00
2	18:23	2	12:40	2	11:32
3	19:36	3	12:54	3	11:49
4	20:01	4	13:10	4	12:01
5	20:17	5	13:13	5	14:18
6	23:37	6	13:45	6	10:58
7	17:22	7	11:25	7	11:41
8	20:10	8	12:02	8	12:10
9	20:20	9	12:24	9	12:18
10	20:50	10	12:42	10	12:21
11	21:10	11	13:01	11	13:01
12	22:10	12	13:17	12	13:32
13	21:40	13	13:24	13	13:42
14	19:36	14	13:51	14	14:35
15	18:50	15	14:10	15	14:44
16	20:23	16	13:50	16	14:20
17	20:11	17	13:25	17	14:50
18	19:56	18	14:13	18	14:32
Average	**20:06**	**Average**	**13:00**	**Average**	**12:58**
2D		**2E**		**2F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	12:45	1	18:30	1	7:50
2	14:27	2	19:50	2	16:48
3	16:20	3	22:32	3	18:36
4	16:50	4	23:45	4	19:10
5	16:41	5	24:31	5	19:55
6	17:38	6	25:02	6	20:28
7	17:10	7	26:20	7	16:54
8	18:10	8	27:25	8	17:40
9	20:20	9	27:50	9	17:40
10	19:30	10	27:03	10	19:30
11	19:50	11	27:26	11	21:40
12	21:02	12	28:38	12	22:14
13	16:25	13	19:50	13	12:50
14	13:40	14	18:32	14	17:37
15	14:36	15	19:30	15	16:44
16	18:50	16	21:50	16	20:44
17	16:45	17	22:23	17	21:22
18	16:50	18	23:50	18	20:46
Average	**17:06**	**Average**	**23:35**	**Average**	**18:14**

Table 3: Table of the disintegration test results for Formulation 3A-3F

3A		3B		3C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	08:33	1	06:41	1	07:15
2	08:00	2	09:30	2	08:49
3	08:21	3	09:34	3	11:24
4	10:10	4	11:12	4	11:44
5	10:00	5	12:36	5	12:09
6	10:35	6	11:54	6	12:52
7	09:21	7	06:57	7	07:52
8	09:26	8	07:34	8	06:50
9	11:10	9	08:06	9	08:05
10	10:50	10	08:21	10	09:38
11	12:20	11	08:33	11	11:43
12	11:00	12	10:18	12	12:30
13	11:28	13	10:06	13	13:25
14	11:38	14	11:35	14	13:10
15	10:41	15	11:05	15	13:21
16	10:57	16	11:45	16	13:08
17	11:42	17	12:09	17	11:56
18	11:52	18	11:43	18	12:40
Average	**10:26**	**Average**	**09:58**	**Average**	**11:01**
3D		**3E**		**3F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	09:33	1	12:35	1	08:44
2	09:51	2	14:30	2	08:44
3	12:10	3	14:34	3	10:51
4	13:18	4	12:30	4	14:44
5	14:37	5	12:00	5	14:48
6	14:40	6	14:00	6	16:25
7	08:30	7	14:50	7	07:02
8	10:50	8	14:34	8	07:50
9	10:36	9	15:30	9	08:51
10	11:07	10	15:00	10	08:00
11	10:39	11	15:55	11	08:25
12	11:42	12	16:00	12	08:40
13	12:10	13	16:10	13	12:24
14	13:22	14	16:00	14	14:49
15	14:17	15	16:15	15	15:00
16	11:59	16	16:07	16	16:35
17	10:44	17	14:44	17	16:45
18	12:23	18	12:35	18	17:18
Average	**11:48**	**Average**	**14:39**	**Average**	**11:59**

Table 4: Disintegration test results for Formulation 4A-4F

4A		4B		4C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	18:22	1	14:16	1	14:20
2	19:55	2	14:28	2	14:59
3	21:40	3	16:42	3	17:08
4	22:10	4	16:44	4	17:26
5	22:20	5	16:14	5	17:44
6	22:12	6	19:00	6	19:17
7	24:20	7	17:37	7	19:19
8	24:40	8	18:10	8	20:24
9	21:09	9	19:22	9	20:14
10	21:18	10	18:48	10	21:17
11	22:00	11	19:36	11	21:41
12	22:06	12	19:42	12	23:03
13	22:08	13	19:04	13	27:07
14	23:56	14	19:21	14	24:15
15	26:28	15	18:59	15	24:30
16	27:00	16	19:09	16	22:19
17	24:56	17	19:27	17	26:19
18	23:20	18	19:24	18	22:22
Average	**22:46**	**Average**	**18:06**	**Average**	**20:45**
4D		**4E**		**4F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	12:30	1	13:46	1	19:35
2	16:54	2	16:30	2	20:24
3	16:44	3	16:59	3	20:56
4	15:55	4	13:57	4	21:22
5	14:16	5	16:06	5	22:20
6	15:50	6	16:09	6	22:22
7	19:04	7	17:24	7	19:44
8	20:30	8	17:35	8	20:01
9	20:56	9	17:50	9	20:31
10	21:22	10	17:55	10	21:11
11	22:23	11	18:36	11	22:33
12	23:17	12	18:25	12	24:54
13	13:14	13	18:17	13	25:05
14	18:35	14	19:36	14	25:15
15	19:40	15	19:33	15	25:46
16	20:27	16	19:45	16	25:48
17	24:40	17	19:54	17	26:15
18	22:18	18	20:57	18	26:42
Average	**18:48**	**Average**	**17:44**	**Average**	**22:49**

Table 5: Disintegration results for Formulation 5A-5F

5A		5B		5C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	16:48	1	11:16	1	08:55
2	16:36	2	11:53	2	10:30
3	17:25	3	12:43	3	10:50
4	18:31	4	11:46	4	11:10
5	18:45	5	11:26	5	11:30
6	19:01	6	12:34	6	12:50
7	19:06	7	12:06	7	07:17
8	19:48	8	13:19	8	08:17
9	20:01	9	13:34	9	10:38
10	20:01	10	13:56	10	09:50
11	20:38	11	13:34	11	11:20
12	17:21	12	14:31	12	10:50
13	17:47	13	15:26	13	10:50
14	17:47	14	14:28	14	11:50
15	20:18	15	15:30	15	11:10
16	20:36	16	15:35	16	12:20
17	20:42	17	15:10	17	12:20
18	20:41	18	15:13	18	12:20
Average	**18:59**	**Average**	**13:33**	**Average**	**10:49**
5D		**5E**		**5F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	12:10	1	11:32	1	14:33
2	12:16	2	11:46	2	14:53
3	13:20	3	12:05	3	15:10
4	14:55	4	12:45	4	15:51
5	16:45	5	12:35	5	16:12
6	17:00	6	13:23	6	17:34
7	15:34	7	13:56	7	17:30
8	13:40	8	15:02	8	17:45
9	15:27	9	15:24	9	17:23
10	19:03	10	14:49	10	18:30
11	19:09	11	14:57	11	18:07
12	18:48	12	15:23	12	19:08
13	19:34	13	17:38	13	19:22
14	20:44	14	13:15	14	19:36
15	21:35	15	13:27	15	21:00
16	21:20	16	14:33	16	20:40
17	21:05	17	15:05	17	20:40
18	22:28	18	16:00	18	21:33
Average	**17:29**	**Average**	**14:05**	**Average**	**18:04**

Table 6: Disintegration test results for Formulation 6A-6F

6A		6B		6C	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	17:28	1	18:20	1	19:40
2	17:59	2	18:31	2	18:47
3	18:12	3	18:46	3	19:35
4	18:18	4	19:15	4	20:10
5	18:30	5	19:30	5	19:47
6	18:34	6	18:25	6	20:42
7	18:49	7	20:00	7	20:37
8	18:56	8	21:11	8	21:48
9	18:31	9	18:43	9	23:40
10	19:02	10	19:27	10	22:34
11	19:08	11	20:36	11	27:36
12	20:05	12	21:22	12	24:00
13	19:45	13	16:22	13	23:13
14	20:35	14	18:45	14	24:46
15	20:11	15	20:10	15	26:00
16	21:10	16	20:12	16	25:51
17	20:41	17	20:58	17	26:05
18	20:47	18	22:00	18	28:09
Average	**19:15**	**Average**	**19:35**	**Average**	**22:56**
6D		**6E**		**6F**	
Tablet no.	**Time (min)**	**Tablet no.**	**Time (min)**	**Tablet no.**	**Time (min)**
1	14:45	1	09:34	1	07:45
2	14:45	2	10:24	2	08:05
3	14:32	3	11:30	3	07:49
4	14:08	4	11:50	4	10:58
5	16:08	5	09:27	5	10:47
6	15:36	6	09:52	6	11:12
7	16:05	7	11:09	7	11:41
8	16:55	8	11:28	8	14:20
9	17:01	9	14:30	9	14:35
10	17:43	10	14:52	10	15:07
11	19:20	11	16:30	11	15:40
12	20:18	12	15:45	12	15:51
13	15:55	13	16:42	13	16:05
14	16:25	14	17:12	14	16:45
15	17:01	15	18:05	15	18:28
16	17:10	16	20:55	16	18:52
17	18:11	17	21:05	17	19:13
18	21:32	18	22:56	18	19:27
Average	**16:51**	**Average**	**14:39**	**Average**	**14:02**

Annexure D

Friability

In this Annexure the friability results for all formulations are given.

Table 1: Table of the friability results for Formulation 1A-1F

1A				1D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.880	5.680	0.401	0.141	5.810	5.810	0.000	0.000
5.580	5.340	0.301	0.170	5.850	5.840	0.171	0.007
5.550	5.380	0.363	0.120	5.780	5.780	0.000	0.000
	Average	0.355	0.144		**Average**	0.057	0.002
1B				**1E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.770	0.859	0.035	5.850	5.840	0.171	0.007
5.810	5.770	0.688	0.028	5.860	5.840	0.341	0.014
5.820	5.770	0.859	0.035	5.800	5.780	0.345	0.014
	Average	0.802	0.033		**Average**	0.286	0.012
1C				**1F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.840	5.830	0.171	0.007	5.880	5.860	0.340	0.014
5.830	5.810	0.343	0.014	5.890	5.860	0.509	0.021
5.780	5.770	0.173	0.007	5.840	5.820	0.342	0.014
	Average	0.229	0.009		**Average**	0.397	0.016

Table 2: Table of the friability test results for Formulation 2A-2F

2A				2D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.850	5.850	0.000	0.000	5.830	5.830	0.000	0.000
5.820	5.810	0.172	0.007	5.800	5.790	0.172	0.007
5.790	5.790	0.000	0.000	5.810	5.810	0.000	0.000
	Average	0.057	0.002		**Average**	0.057	0.002
2B				**2E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.810	0.172	0.007	5.890	5.890	0.000	0.000
5.790	5.790	0.000	0.000	5.820	5.820	0.000	0.000
5.780	5.770	0.173	0.007	5.860	5.860	0.000	0.000
	Average	0.115	0.005		**Average**	0.000	0.000
2C				**2F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.860	5.860	0.000	0.000	5.830	5.830	0.000	0.000
5.830	5.820	0.172	0.007	5.820	5.820	0.000	0.000
5.810	5.790	0.344	0.014	5.780	5.780	0.000	0.000
	Average	0.172	0.007		**Average**	0.000	0.000

Table 3: Table of the friability test results for Formulation 3A-3F

3A				3D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.810	0.172	0.007	5.810	5.810	0.000	0.000
5.810	5.790	0.344	0.014	5.820	5.810	0.172	0.007
5.820	5.800	0.344	0.014	5.840	5.820	0.342	0.014
	Average	0.287	0.012		**Average**	0.171	0.007
3B				**3E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.810	0.172	0.007	5.810	5.810	0.000	0.000
5.840	5.830	0.171	0.007	5.800	5.790	0.172	0.007
5.830	5.830	0.000	0.000	5.810	5.790	0.344	0.014
	Average	0.114	0.005		**Average**	0.172	0.007
3C				**3F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.800	5.710	1.052	0.064	5.820	5.810	0.172	0.007
5.820	5.750	0.603	0.049	5.840	5.820	0.342	0.014
5.810	5.730	0.777	0.057	5.810	5.810	0.000	0.000
	Average	0.811	0.057		**Average**	0.171	0.007

Table 4: Table of the friability test results for Formulation 4A-4F

4A				4D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.790	5.790	0.000	0.000	5.830	5.830	0.000	0.000
5.770	5.760	0.173	0.007	5.860	5.840	0.341	0.014
5.820	5.820	0.000	0.000	5.810	5.800	0.172	0.007
	Average	0.058	0.002		**Average**	0.171	0.007
4B				**4E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.820	0.000	0.000	5.810	5.800	0.172	0.007
5.810	5.800	0.172	0.007	5.840	5.830	0.171	0.007
5.830	5.810	0.343	0.014	5.780	5.760	0.346	0.014
	Average	0.172	0.007		**Average**	0.230	0.009
4C				**4F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.860	5.850	0.171	0.007	5.850	5.850	0.000	0.000
5.870	5.870	0.000	0.000	5.870	5.860	0.170	0.007
5.840	5.830	0.171	0.007	5.840	5.840	0.000	0.000
	Average	0.114	0.005		**Average**	0.057	0.002

Table 5: Table of the friability test results for Formulation 5A-5F

5A				5D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.800	5.790	0.172	0.007	5.840	5.840	0.000	0.000
5.780	5.770	0.173	0.007	5.860	5.860	0.000	0.000
5.830	5.830	0.000	0.000	5.820	5.820	0.000	0.000
	Average	0.115	0.005		**Average**	0.000	0.000
5B				**5E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.840	5.830	0.171	0.007	5.860	5.860	0.000	0.000
5.860	5.840	0.341	0.014	5.840	5.830	0.171	0.007
5.800	5.790	0.172	0.007	5.800	5.790	0.172	0.007
	Average	0.228	0.009		**Average**	0.115	0.005
5C				**5F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.810	5.790	0.344	0.014	5.810	5.810	0.000	0.000
5.770	5.760	0.173	0.007	5.830	5.830	0.000	0.000
5.830	5.800	0.515	0.021	5.880	5.870	0.170	0.007
	Average	0.344	0.014		**Average**	0.057	0.002

Table 6: Table of the friability test results for Formulation 6A-6F

6A				6D			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.790	5.790	0.000	0.000	5.820	5.820	0.000	0.000
5.820	5.820	0.000	0.000	5.820	5.810	0.172	0.007
5.800	5.780	0.345	0.014	5.830	5.810	0.343	0.014
	Average	0.115	0.005		**Average**	0.172	0.007
6B				**6E**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.820	5.820	0.000	0.000	5.850	5.850	0.000	0.000
5.820	5.820	0.000	0.000	5.840	5.830	0.171	0.007
5.800	5.800	0.000	0.000	5.820	5.820	0.000	0.000
	Average	0.000	0.000		**Average**	0.057	0.002
6C				**6F**			
M1 (gram)	**M2 (gram)**	**% Friability**	**SD**	**M1 (gram)**	**M2 (gram)**	**% Friability**	**SD**
5.850	5.840	0.171	0.007	5.800	5.800	0.000	0.000
5.840	5.820	0.342	0.014	5.800	5.790	0.172	0.007
5.800	5.800	0.000	0.000	5.780	5.780	0.000	0.000
	Average	0.171	0.007		**Average**	0.057	0.002

Annexure E

Mucoadhesion

In this Annexure the mucoadhesion test results for all formulations are given.

Table 1: Table of the mucoadhesion results for Formulation 1-3

Formula 1		Formula 2		Formula 3	
Formula	**Quantity of beads left on tissue**	**Formula**	**Quantity of beads left on tissue**	**Formula**	**Quantity of beads left on tissue**
1A1	50.000	2A1	70.000	3A1	82.000
1A2	36.000	2A2	66.000	3A2	86.000
1A3	26.000	2A3	75.000	3A3	78.000
Average	**37.333**	**Average**	**70.333**	**Average**	**82.000**
1B1	24.000	2B1	85.000	3B1	83.000
1B2	51.000	2B2	90.000	3B2	91.000
1B3	63.000	2B3	93.000	3B3	87.000
Average	**46.000**	**Average**	**89.333**	**Average**	**87.000**
1C1	69.000	2C1	70.000	3C1	69.000
1C2	48.000	2C2	77.000	3C2	58.000
1C3	3.000	2C3	54.000	3C3	49.000
Average	**40.000**	**Average**	**67.000**	**Average**	**58.667**
1D1	79.000	2D1	92.000	3D1	78.000
1D2	69.000	2D2	70.000	3D2	76.000
1D3	58.000	2D3	73.000	3D3	72.000
Average	**68.667**	**Average**	**78.333**	**Average**	**75.333**
1E 1	67.000	2E 1	83.000	3E 1	64.000
1E 2	41.000	2E 2	90.000	3E 2	60.000
1E 3	18.000	2E 3	90.000	3E 3	46.000
Average	**42.000**	**Average**	**87.667**	**Average**	**56.667**
1F1	40.000	2F1	95.000	3F1	64.000
1F2	65.000	2F2	70.000	3F2	55.000
1F3	37.000	2F3	85.000	3F3	58.000
Average	**47.333**	**Average**	**83.333**	**Average**	**59.000**

Table 2: Table of the mucoadhesion test results for Formulation 4-6

Formula 4		Formula 5		Formula 6	
Formula	**Quantity of beads left on tissue**	**Formula**	**Quantity of beads left on tissue**	**Formula**	**Quantity of beads left on tissue**
4A1	62.000	5A1	48.000	6A1	69.000
4A2	55.000	5A2	54.000	6A2	74.000
4A3	69.000	5A3	61.000	6A3	56.000
Average	**62.000**	**Average**	**54.333**	**Average**	**66.333**
4B1	83.000	5B1	74.000	6B1	72.000
4B2	86.000	5B2	72.000	6B2	76.000
4B3	74.000	5B3	64.000	6B3	83.000
Average	**81.000**	**Average**	**70.000**	**Average**	**77.000**
4C1	88.000	5C1	39.000	6C1	58.000
4C2	70.000	5C2	44.000	6C2	48.000
4C3	64.000	5C3	46.000	6C3	49.000
Average	**74.000**	**Average**	**43.000**	**Average**	**51.667**
4D1	94.000	5D1	58.000	6D1	76.000
4D2	79.000	5D2	61.000	6D2	69.000
4D3	82.000	5D3	66.000	6D3	66.000
Average	**85.000**	**Average**	**61.667**	**Average**	**70.333**
4E 1	89.000	5E 1	42.000	6E 1	64.000
4E 2	66.000	5E 2	51.000	6E 2	77.000
4E 3	75.000	5E 3	56.000	6E 3	79.000
Average	**76.667**	**Average**	**49.667**	**Average**	**73.333**
4F1	80.000	5F1	48.000	6F1	78.000
4F2	76.000	5F2	59.000	6F2	68.000
4F3	74.000	5F3	59.000	6F3	84.000
Average	**76.667**	**Average**	**55.333**	**Average**	**76.667**

Annexure F

Content uniformity

In this Annexure the content uniformity for all formulations are given. Five tablets from each formula were evaluated for content uniformity.

Table 1: Table of the content uniformity results for Formulation 1A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1A1**	**1A2**	**1A3**	**1A4**	**1A5**
	0,4382	0,4344	0,4356	0,4289	0,4546
	0,4415	0,4517	0,4556	0,4315	0,4197
	0,4433	0,4466	0,4357	0,4497	0,4273
	0,4488	0,4233	0,4321	0,4257	0,4318
Average	0,44295	0,439	0,43975	0,43395	0,43335
	0,210142164	0,208211115	0,20857777	0,205742305	0,205448981
Assay percentage	**101,093603**	**100,1646284**	**100,341016**	**98,97695202**	**98,83584196**
Content uniformity	**99,88240828**				

Table 2: Table of the content uniformity results for Formulation 1B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1B1**	**1B2**	**1B3**	**1B4**	**1B5**
	0,4399	0,4306	0,4578	0,4296	0,457
	0,4367	0,4322	0,461	0,4532	0,4596
	0,4409	0,4404	0,4531	0,4292	0,4612
	0,4674	0,4631	0,4631	0,4575	0,4603
Average	0,446225	0,441575	0,45875	0,442375	0,459525
	0,211743224	0,209469964	0,217866362	0,209861062	0,218245238
Assay percentage	**101,8638288**	**100,7702258**	**104,8095014**	**100,9583725**	**104,9917686**
Content uniformity	**102,6787394**				

Table 3: Table of the content uniformity results for Formulation 1C

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1C1**	**1C2**	**1C3**	**1C4**	**1C5**
	0,4084	0,4598	0,4512	0,4109	0,4364
	0,4111	0,4595	0,4531	0,4355	0,4114
	0,4457	0,4547	0,4526	0,428	0,4131
	0,4424	0,4599	0,4554	0,4126	0,4369
Average	0,4269	0,458475	0,453075	0,42175	0,42445
	0,202295749	0,217731921	0,215092006	0,199778052	0,201098009
Assay percentage	**97,31890875**	**104,744826**	**103,4748354**	**96,10771402**	**96,74270931**
Content unifromity	**99,67779868**				

Table 4: Table of the content uniformity results for Formulation 1D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1D1**	**1D2**	**1D3**	**1D4**	**1D5**
	0,474	0,445	0,45	0,4549	0,4587
	0,4681	0,4439	0,4544	0,4538	0,4596
	0,4652	0,4485	0,4506	0,458	0,4571
	0,4739	0,4491	0,4525	0,4577	0,442
Average	0,4703	0,446625	0,451875	0,4561	0,45435
	0,223512848	0,211938774	0,214505358	0,216570848	0,215715319
Assay percentage	**107,5258702**	**101,9579022**	**103,1926152**	**104,1862653**	**103,7746943**
Content uniformity	**104,1274694**				

Table 5: Table of the content uniformity results for Formulation 1E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1 E1**	**1 E2**	**1 E3**	**1 E4**	**1 E5**
	0,4273	0,4168	0,4438	0,4204	0,4069
	0,4288	0,4174	0,4217	0,4436	0,4119
	0,447	0,415	0,4201	0,4307	0,4384
	0,4353	0,412	0,4217	0,424	0,4356
Average	0,4346	0,4153	0,426825	0,429675	0,4232
	0,206060073	0,196624819	0,202259083	0,203652372	0,200486918
Assay percentage	**99,12982126**	**94,59078081**	**97,30126999**	**97,9715428**	**96,44873001**
Content uniformity	**97,08842897**				

Table 6: Table of the content uniformity results for Formulation 1F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**1F1**	**1F2**	**1F3**	**1F4**	**1F5**
	0,4481	0,4391	0,4499	0,3983	0,4036
	0,4498	0,4337	0,4665	0,3933	0,4046
	0,4474	0,4345	0,4512	0,3972	0,4026
	0,4657	0,4324	0,4478	0,402	0,4038
Average	0,45275	0,434925	0,45385	0,3977	0,40365
	0,214933122	0,206218957	0,215470883	0,18802065	0,190929446
Assay percentage	**103,3984008**	**99,20625588**	**103,6571025**	**90,45155221**	**91,8508937**
Content uniformity	**97,71284102**				

Table 7: Table of the content uniformity results for Formulation 2A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2A1**	**2A2**	**2A3**	**2A4**	**2A5**
	0,4524	0,4633	0,4547	0,4617	0,446
	0,4523	0,4596	0,4489	0,4607	0,4486
	0,4554	0,4628	0,4445	0,4675	0,4493
	0,4493	0,4627	0,4446	0,4643	0,4491
Average	0,45235	0,4621	0,448175	0,46355	0,44825
	0,214737573	0,219504087	0,212696527	0,220212953	0,212733193
Assay percentage	**103,3043274**	**105,5973659**	**102,3224365**	**105,9383819**	**102,3400753**
Content uniformity	**103,9005174**				

Table 8: Table of the content uniformity results for Formulation 2B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2B1**	**2B2**	**2B3**	**2B4**	**2B5**
	0,4578	0,4412	0,4626	0,4575	0,43322
	0,4533	0,4601	0,4682	0,4597	0,4376
	0,4544	0,4393	0,4603	0,4626	0,4287
	0,4541	0,4379	0,4587	0,458	0,4327
Average	0,4549	0,444625	0,46245	0,45945	0,433055
	0,2159842	0,210961027	0,219675193	0,218208573	0,205304764
Assay percentage	**103,9040452**	**101,4875353**	**105,6796802**	**104,9741298**	**98,76646284**
Content uniformity	**102,9623706**				

Table 9: Table of the content uniformity results for Formulation 2C

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2C1**	**2C2**	**2C3**	**2C4**	**2C5**
	0,4341	0,4602	0,4598	0,4095	0,4323
	0,4313	0,4441	0,4572	0,4107	0,4526
	0,4283	0,4461	0,4588	0,4056	0,4381
	0,4309	0,4485	0,4608	0,4072	0,43
Average	0,43115	0,449725	0,45915	0,40825	0,43825
	0,20437346	0,213454281	0,218061911	0,193178263	0,20784446
Assay percentage	**98,31843838**	**102,6869708**	**104,9035748**	**92,93273754**	**99,98824083**
Content uniformity	**99,76599247**				

Table 10: Table of the content uniformity results for Formulation 2D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2D1**	**2D2**	**2D3**	**2D4**	**2D5**
	0,454	0,428	0,4295	0,434	0,4188
	0,4307	0,4363	0,4332	0,4328	0,4375
	0,4281	0,4319	0,4114	0,4576	0,4375
	0,4298	0,4284	0,4293	0,4395	0,4405
Average	0,43565	0,43115	0,42585	0,440975	0,433575
	0,20657339	0,20437346	0,201782432	0,20917664	0,205558978
Assay percentage	**99,37676388**	**98,31843838**	**97,07196613**	**100,6291157**	**98,88875823**
Content uniformity	**98,85700847**				

Table 11: Table of the content uniformity results for Formulation 2E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2 E1**	**2 E2**	**2 E3**	**2 E4**	**2 E5**
	0,4884	0,4293	0,4676	0,4506	0,447
	0,4883	0,427	0,4677	0,4551	0,4506
	0,4856	0,4272	0,4696	0,4666	0,4451
	0,4793	0,4264	0,4711	0,4596	0,4455
Average	0,4854	0,427475	0,469	0,457975	0,44705
	0,230894834	0,202576851	0,222877312	0,217487485	0,212146545
Assay percentage	**111,0771402**	**97,45413923**	**107,2201317**	**104,6272342**	**102,0578551**
Content uniformity	**104,4873001**				

Table 12: Table of the content uniformity results for Formulation 2F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**2F1**	**2F2**	**2F3**	**2F4**	**2F5**
	0,469	0,4359	0,4624	0,4293	0,4647
	0,4606	0,4364	0,4648	0,4278	0,4608
	0,4545	0,4367	0,4581	0,4322	0,4574
	0,4611	0,434	0,4584	0,4299	0,4617
Average	0,4613	0,43575	0,460925	0,4298	0,46115
	0,219112988	0,206622277	0,218929661	0,203713481	0,219039657
Assay percentage	**105,4092192**	**99,40028222**	**105,3210254**	**98,00094073**	**105,3739417**
Content uniformity	**102,7010818**				

Table 13: Table of the content uniformity results for Formulation 3A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3A1**	**3A2**	**3A3**	**3A4**	**3A5**
	0,4118	0,4241	0,4282	0,4319	0,4343
	0,427	0,4244	0,4305	0,417	0,4474
	0,4305	0,4181	0,4321	0,4162	0,4477
	0,4129	0,4181	0,4321	0,4183	0,4311
Average	0,42055	0,421175	0,430725	0,42085	0,440125
	0,199191404	0,199496949	0,204165689	0,199338066	0,208761097
Assay percentage	**95,82549389**	**95,97248354**	**98,21848542**	**95,89604892**	**100,4292098**
Content uniformity	**97,26834431**				

Table 14: Table of the content uniformity results for Formulation 3B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3B1**	**3B2**	**3B3**	**3B4**	**3B5**
	0,4631	0,4665	0,4508	0,4584	0,4473
	0,4605	0,4684	0,4474	0,4455	0,4492
	0,4578	0,466	0,4465	0,4562	0,4501
	0,455	0,4672	0,4457	0,4558	0,4479
Average	0,4591	0,467025	0,4476	0,453975	0,448625
	0,218037467	0,221911788	0,212415425	0,215531992	0,21291652
Assay percentage	**104,8918156**	**106,7556444**	**102,187206**	**103,6865005**	**102,428269**
Content uniformity	**103,9898871**				

Table 15: Table of the content uniformity results for Formulation 3C

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3C1**	**3C2**	**3C3**	**3C4**	**3C5**
	0,4193	0,4492	0,4376	0,434	0,4393
	0,4186	0,4466	0,4339	0,4257	0,4373
	0,4354	0,4472	0,4335	0,4253	0,4391
	0,4278	0,4472	0,4337	0,4238	0,4378
Average	0,425275	0,44755	0,434675	0,4272	0,438375
	0,20150133	0,212390981	0,206096738	0,202442411	0,207905569
Assay percentage	**96,93673565**	**102,1754468**	**99,14746002**	**97,38946378**	**100,0176388**
Content uniformity	**99,13334901**				

Table 16: Table of the content uniformity results for Formulation 3D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3D1**	**3D2**	**3D3**	**3D4**	**3D5**
	0,4639	0,4331	0,4348	0,4473	0,4412
	0.0.4610	0,4326	0,4305	0,4496	0,4333
	0,4598	0,4322	0,4303	0,4464	0,4344
	0,4588	0,4325	0,431	0,4475	0,4402
Average	0,460833333	0,4326	0,43165	0,4477	0,437275
	0,218884848	0,205082326	0,204617897	0,212464312	0,207367809
Assay percentage	**105,2994669**	**98,65945437**	**98,4360301**	**102,2107244**	**99,75893697**
Content uniformity	**100,8729225**				

Table 17: Table of the content uniformity results for Formulation 3E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3 E1**	**3 E2**	**3 E3**	**3 E4**	**3 E5**
	0,4168	0,4412	0,4431	0,4054	0,43
	0,4178	0,4322	0,4392	0,4068	0,4251
	0,4144	0,4407	0,4421	0,4078	0,425
	0,4158	0,43	0,4417	0,3988	0,4237
Average	0,4162	0,436025	0,441525	0,4047	0,42595
	0,197064805	0,206756717	0,20944552	0,191442763	0,201831319
Assay percentage	**94,80244591**	**99,46495767**	**100,7584666**	**92,09783631**	**97,09548448**
Content uniformity	**96,84383819**				

Table 18: Table of the content uniformity results for Formulation 3F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**3F1**	**3F2**	**3F3**	**3F4**	**3F5**
	0,4517	0,4658	0,4562	0,4618	0,4649
	0,4534	0,4663	0,4582	0,4621	0,4639
	0,4564	0,4669	0,457	0,4627	0,4628
	0,4557	0,465	0,455	0,4625	0,4625
Average	0,4543	0,466	0,4566	0,462275	0,463525
	0,215690876	0,221410693	0,216815284	0,21958964	0,220200731
Assay percentage	**103,7629351**	**106,5145814**	**104,303857**	**105,638523**	**105,9325024**
Content uniformity	**105,2304798**				

Table 19: Table of the content uniformity results for Formulation 4A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4A1**	**4A2**	**4A3**	**4A4**	**4A5**
	0,4456	0,4473	0,4435	0,4571	0,4515
	0,4421	0,4474	0,4438	0,4565	0,4509
	0,4387	0,4464	0,4508	0,4568	0,4513
	0,4409	0,4461	0,4475	0,4559	0,4521
Average	0,441825	0,4468	0,4464	0,456575	0,45145
	0,209592182	0,212024326	0,211828777	0,216803062	0,214297587
Assay percentage	**100,8290216**	**101,9990593**	**101,9049859**	**104,2979774**	**103,0926623**
Content uniformity	**102,4247413**				

Table 20: Table of the content uniformity results for Formulation 4B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4B1**	**4B2**	**4B3**	**4B4**	**4B5**
	0,4501	0,4604	0,453	0,4378	0,4647
	0,449	0,4568	0,4527	0,4413	0,4502
	0,4494	0,4545	0,4522	0,439	0,4512
	0,4521	0,4555	0,4587	0,439	0,4525
Average	0,45015	0,4568	0,45415	0,439275	0,45465
	0,213662052	0,216913059	0,215617545	0,208345555	0,215861981
Assay percentage	**102,7869238**	**104,3508937**	**103,7276576**	**100,2293039**	**103,8452493**
Content uniformity	**102,9880056**				

Table 21: Table of the content uniformity results for Formulation 4C

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4C1**	**4C2**	**4C3**	**4C4**	**4C5**
	0,4202	0,418	0,4041	0,4391	0,4112
	0,4367	0,4195	0,4075	0,4571	0,4129
	0,4215	0,4175	0,4066	0,458	0,4145
	0,4225	0,4189	0,4049	0,4585	0,4119
Average	0,425225	0,418475	0,405775	0,453175	0,412625
	0,201476886	0,198176992	0,191968301	0,215140893	0,195317083
Assay percentage	**96,92497648**	**95,33748824**	**92,35065851**	**103,4983537**	**93,9616651**
Content uniformity	**96,41462841**				

Table 22: Table of the content uniformity results for Formulation 4D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4D1**	**4D2**	**4D3**	**4D4**	**4D5**
	0,4685	0,4132	0,4266	0,4485	0,4512
	0,4656	0,4102	0,4264	0,4458	0,4525
	0,4673	0,4228	0,4219	0,4463	0,4536
	0,4679	0,4239	0,4257	0,4449	0,4533
Average	0,467325	0,417525	0,42515	0,446375	0,45265
	0,22205845	0,197712562	0,201440221	0,211816555	0,214884235
Assay percentage	**106,8261994**	**95,11406397**	**96,90733772**	**101,8991063**	**103,3748824**
Content uniformity	**100,824318**				

Table 23: Table of the content uniformity results for Formulation 4E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4 E1**	**4 E2**	**4 E3**	**4 E4**	**4 E5**
	0,4172	0,4176	0,4313	0,426	0,422
	0,4167	0,4156	0,4305	0,4248	0,4202
	0,4232	0,4285	0,4353	0,4221	0,4226
	0,4245	0,4255	0,4315	0,4239	0,4219
Average	0,4204	0,4218	0,43215	0,4242	0,421675
	0,199118073	0,199802495	0,204862333	0,200975791	0,199741386
Assay percentage	**95,79021637**	**96,11947319**	**98,55362183**	**96,68391345**	**96,09007526**
Content uniformity	**96,64746002**				

Table 24: Table of the content uniformity results for Formulation 4F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**4F1**	**4F2**	**4F3**	**4F4**	**4F5**
	0,4442	0,4263	0,4102	0,4166	0,4174
	0,4414	0,413	0,428	0,417	0,4285
	0,4361	0,417	0,4268	0,4126	0,4179
	0,4372	0,4227	0,4227	0,4132	0,4186
Average	0,439725	0,41975	0,421925	0,41485	0,4206
	0,208565548	0,198800305	0,199863604	0,196404826	0,199215847
Assay percentage	**100,3351364**	**95,63734713**	**96,14887112**	**94,48494826**	**95,83725306**
Content uniformity	**96,48871119**				

Table 25: Table of the content uniformity results for Formulation 5A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5A1**	**5A2**	**5A3**	**5A4**	**5A5**
	0,4504	0,4159	0,4197	0,4276	0,4355
	0,451	0,42	0,4203	0,4301	0,4403
	0,4494	0,4127	0,4236	0,4251	0,4395
	0,445	0,4174	0,4265	0,425	0,4352
Average	0,44895	0,4165	0,422525	0,42695	0,437625
	0,213075404	0,197211467	0,200156928	0,202320192	0,207538914
Assay percentage	**102,5047037**	**94,87300094**	**96,28998119**	**97,33066792**	**99,84125118**
Content uniformity	**98,16792098**				

Table 26: Table of the content uniformity results for Formulation 5B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5B1**	**5B2**	**5B3**	**5B4**	**5B5**
	0,4581	0,4229	0,4182	0,4538	0,418
	0,4508	0,4294	0,4184	0,457	0,422
	0,4487	0,433	0,4201	0,4584	0,4179
	0,4516	0,4299	0,4234	0,4555	0,4181
Average	0,4523	0,4288	0,420025	0,456175	0,419
	0,214713129	0,203224608	0,198934745	0,216607513	0,19843365
Assay percentage	**103,2925682**	**97,76575729**	**95,70202258**	**104,203904**	**95,46095955**
Content uniformity	**99,28504233**				

Table 27: Table of the content uniformity results for Formulation 5C

40mg/200ml - 200µg/ml	y = 51.138x + 0.0131
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH	x = y-0.0131/51.138

4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5C1**	**5C2**	**5C3**	**5C4**	**5C5**
	0,4178	0,4337	0,4172	0,4187	0,4206
	0,4188	0,4351	0,4195	0,4207	0,4209
	0,4205	0,439	0,4199	0,4195	0,4211
	0,4277	0,4327	0,4189	0,4198	0,421
Average	0,4212	0,435125	0,418875	0,419675	0,4209
	0,199509171	0,206316731	0,198372541	0,19876364	0,199362509
Assay percentage	**95,97836312**	**99,25329257**	**95,43156162**	**95,61970837**	**95,90780809**
Content uniformity	**96,43814675**				

Table 28: Table of the content uniformity results for Formulation 5D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5D1**	**5D2**	**5D3**	**5D4**	**5D5**
	0,4571	0,4371	0,4549	0,4307	0,4227
	0,4616	0,4447	0,4546	0,4304	0,4205
	0,4529	0,4388	0,4475	0,4312	0,4225
	0,4524	0,4481	0,4489	0,4309	0,4219
Average	0,456	0,442175	0,451475	0,4308	0,4219
	0,21652196	0,209763288	0,214309809	0,204202354	0,199851383
Assay percentage	**104,1627469**	**100,9113358**	**103,0985419**	**98,23612418**	**96,14299153**
Content uniformity	**100,5103481**				

Table 29: Table of the content uniformity results for Formulation 5E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5 E1**	**5 E2**	**5 E3**	**5 E4**	**5 E5**
	0,4231	0,4278	0,41	0,4284	0,4281
	0,4184	0,4204	0,4102	0,4289	0,4287
	0,4166	0,42	0,4105	0,4189	0,4269
	0,4215	0,4257	0,4104	0,4278	0,4285
Average	0,4199	0,423475	0,410275	0,426	0,42805
	0,198873636	0,200621358	0,194168231	0,201855763	0,202857953
Assay percentage	**95,67262465**	**96,51340546**	**93,40898401**	**97,10724365**	**97,58936971**
Content uniformity	**96,05832549**				

Table 30: Table of the content uniformity results for Formulation 5F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**5F1**	**5F2**	**5F3**	**5F4**	**5F5**
	0,4217	0,4178	0,425	0,4152	0,4482
	0,4266	0,4195	0,4297	0,4163	0,4485
	0,4199	0,4118	0,4266	0,4168	0,4526
	0,4224	0,4151	0,4233	0,4155	0,4518
Average	0,42265	0,41605	0,42615	0,41595	0,450275
	0,200218037	0,196991474	0,201929094	0,196942587	0,213723161
Assay percentage	**96,31937912**	**94,76716839**	**97,14252117**	**94,74365005**	**102,8163217**
Content uniformity	**97,15780809**				

Table 31: Table of the content uniformity results for Formulation 6A

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6A1**	**6A2**	**6A3**	**6A4**	**6A5**
	0,4577	0,4499	0,425	0,4233	0,4417
	0,4465	0,4627	0,4233	0,4223	0,4401
	0,433	0,4585	0,4283	0,4197	0,4414
	0,4356	0,4508	0,4237	0,42	0,4383
Average	0,4432	0,455475	0,425075	0,421325	0,440375
	0,210264383	0,216265302	0,201403555	0,19957028	0,208883316
Assay percentage	**101,1523989**	**104,0392756**	**96,88969897**	**96,00776105**	**100,4880056**
Content uniformity	**99,71542803**				

Table 32: Table of the content uniformity results for Formulation 6B

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6B1**	**6B2**	**6B3**	**6B4**	**6B5**
	0,4138	0,426	0,4545	0,4165	0,4255
	0,4135	0,4255	0,4398	0,4211	0,4221
	0,4149	0,4182	0,4462	0,4136	0,4229
	0,4176	0,4249	0,4485	0,4255	0,4249
Average	0,41495	0,42365	0,44725	0,419175	0,42385
	0,196453713	0,200706911	0,212244319	0,198519203	0,200804685
Assay percentage	**94,5084666**	**96,55456256**	**102,1048918**	**95,50211665**	**96,60159925**
Content uniformity	**97,05432738**				

Table 33: Table of the content uniformity results for Formulation 6C

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6C1**	**6C2**	**6C3**	**6C4**	**6C5**
	0,436	0,4459	0,4185	0,4399	0,4295
	0,4369	0,4518	0,4169	0,4304	0,4293
	0,4371	0,4532	0,4171	0,4254	0,43
	0,4403	0,4559	0,4143	0,4204	0,4288
Average	0,437575	0,4517	0,4167	0,429025	0,4294
	0,207514471	0,214419805	0,197309242	0,203334604	0,203517932
Assay percentage	**99,829492**	**103,1514581**	**94,92003763**	**97,81867357**	**97,90686736**
Content uniformity	**98,72530574**				

Table 34: Table of the content uniformity results for Formulation 6D

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6D1**	**6D2**	**6D3**	**6D4**	**6D5**
	0,427	0,465	0,4614	0,455	0,4168
	0,4229	0,4656	0,4608	0,4535	0,4173
	0,4245	0,4601	0,4612	0,4538	0,4178
	0,4237	0,4608	0,46	0,4542	0,418
Average	0,424525	0,462875	0,46085	0,454125	0,417475
	0,201134675	0,219882964	0,218892995	0,215605323	0,197688118
Assay percentage	**96,76034807**	**105,7796331**	**105,3033866**	**103,721778**	**95,1023048**
Content uniformity	**101,3334901**				

Table 35: Table of the content uniformity results for Formulation 6E

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6 E1**	**6 E2**	**6 E3**	**6 E4**	**6 E5**
	0,4351	0,4269	0,4333	0,4422	0,4216
	0,436	0,4234	0,4371	0,447	0,4239
	0,4337	0,4222	0,4298	0,4433	0,4267
	0,4339	0,4281	0,4361	0,4393	0,4263
Average	0,434675	0,42515	0,434075	0,44295	0,424625
	0,206096738	0,201440221	0,205803414	0,210142164	0,201183562
Assay percentage	**99,14746002**	**96,90733772**	**99,00634995**	**101,093603**	**96,78386642**
Content uniformity	**98,58772342**				

Table 36: Table of the content uniformity results for Formulation 6F

40mg/200ml - 200µg/ml			y = 51.138x + 0.0131		
Mother solution contains 1 tablet diluted in 200ml 0.1M NaOH			x = y-0.0131/51.138		
4ml of the mother solution was diluted in 100ml of distilled water			m	51,138	
Theoretical furosemide concentration to be 8µg/ml			c	0,0131	
Theoretical average absorbance value at 273nm					
0,4121	**0,008314756**	**0,207868904**			
Formula	**6F1**	**6F2**	**6F3**	**6F4**	**6F5**
	0,4218	0,4237	0,4229	0,4189	0,4309
	0,4234	0,4219	0,4226	0,4183	0,4311
	0,4207	0,4235	0,4236	0,4205	0,4319
	0,4225	0,4241	0,4235	0,4209	0,43
Average	0,4221	0,4233	0,42315	0,41965	0,430975
	0,199949157	0,200535805	0,200462474	0,198751418	0,204287907
Assay percentage	**96,19002822**	**96,47224835**	**96,43697084**	**95,61382879**	**98,27728128**
Content uniformity	**96,5980715**				

Annexure G

Dissolution results

In this Annexure the dissolution results for all formulations are provided which were evaluated in three pH environments (1.2, 4.6 and 7.4).

Dissolution results Formulation 1A

Table 1: Table containing the spectrophotometric values and dissolution data of formula 1A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,02
m	0,05

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	0,066	0,070	0,070	0,050	0,049	0,051	0,376	0,306	0,283	1,930	1,544	7,234	4,289	3,430	16,076	7,932	5,769	72,737
5	0,315	0,309	0,325	0,216	0,203	0,204	0,603	0,610	0,585	7,128	4,854	13,091	15,840	10,787	29,092	18,573	7,719	41,558
10	0,675	0,653	0,672	0,353	0,354	0,357	0,646	0,665	0,663	14,514	7,958	14,391	32,253	17,685	31,980	27,306	6,804	24,918
15	1,041	1,057	1,058	0,469	0,423	0,428	0,787	0,857	0,837	22,669	9,787	18,011	50,375	21,749	40,023	37,383	11,835	31,659
30	1,432	1,409	1,401	0,752	0,741	0,746	1,025	1,047	1,059	30,383	16,262	22,646	67,519	36,137	50,325	51,327	12,831	24,999
60	1,778	1,831	1,707	0,969	0,920	0,932	1,097	1,046	1,092	38,055	20,414	23,501	84,567	45,363	52,224	60,718	17,095	28,154
90	1,850	1,790	1,851	1,066	1,052	1,096	1,240	1,322	1,311	39,483	23,270	28,079	87,739	51,711	62,399	67,283	15,108	22,455
120	1,958	1,912	1,937	1,226	1,212	1,198	1,379	1,362	1,362	41,904	26,344	29,838	93,120	58,542	66,307	72,656	14,813	20,388
180	1,939	1,963	1,963	1,282	1,294	1,249	1,422	1,406	1,419	42,538	27,809	31,005	94,528	61,797	68,899	75,075	14,058	18,725
240	1,970	2,032	2,035	1,304	1,270	1,277	1,404	1,447	1,443	43,955	28,137	31,505	97,679	62,526	70,011	76,738	15,119	19,702
360	2,040	2,095	1,981	1,332	1,322	1,398	1,496	1,487	1,483	44,747	29,694	32,871	99,437	65,987	73,048	79,491	14,396	18,110
inf	2,062	1,937	1,939	1,373	1,375	1,376	1,540	1,528	1,499	43,747	30,348	33,740	97,214	67,441	74,978	79,878	12,639	15,823

Table 2: Table containing the spectrophotometric values and dissolution data of formula 1A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,02
m	0,05

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,369	0,369	0,369	0,368	0,368	0,369	0,433	0,431	0,431	6,922	6,912	8,068	15,383	15,360	17,930	16,224	1,206	7,433
5	1,114	1,104	1,112	1,070	1,063	1,068	1,161	1,164	1,167	20,438	19,653	21,426	45,417	43,673	47,613	45,568	1,612	3,538
10	1,789	1,804	1,794	1,836	1,818	1,817	1,801	1,812	1,810	33,008	33,521	33,241	73,351	74,492	73,869	73,904	0,466	0,631
15	2,110	2,021	2,077	2,132	2,127	2,129	2,056	2,029	2,030	38,171	39,264	37,617	84,824	87,254	83,594	85,224	1,521	1,785
30	2,097	2,163	2,144	2,159	2,249	2,195	2,202	2,172	2,182	39,565	40,777	40,497	87,923	90,616	89,994	89,511	1,151	1,286
60	2,204	2,242	2,224	2,253	2,266	2,261	2,387	2,366	2,386	41,398	42,073	44,259	91,996	93,496	98,354	94,616	2,714	2,868
90	2,389	2,236	2,389	2,191	2,198	2,196	2,394	2,383	2,311	43,710	41,119	44,188	97,134	91,376	98,196	95,569	2,996	3,135
120	2,328	2,301	2,330	2,250	2,213	2,231	2,408	2,307	2,363	43,609	42,009	44,358	96,910	93,354	98,573	96,279	2,177	2,261
180	2,226	2,270	2,263	2,163	2,185	2,169	2,338	2,400	2,369	42,633	41,152	44,777	94,740	91,448	99,505	95,231	3,308	3,473
240	2,301	2,223	2,287	2,191	2,180	2,187	2,310	2,320	2,319	43,176	41,629	44,057	95,947	92,508	97,904	95,453	2,230	2,337
360	2,387	2,303	2,363	2,179	2,218	2,206	2,448	2,329	2,365	44,872	42,119	45,462	99,715	93,597	101,026	98,112	3,238	3,300
inf	2,374	2,372	2,369	2,156	2,142	2,177	2,401	2,388	2,395	44,328	41,565	45,960	98,507	92,367	102,132	97,669	4,031	4,127

Table 3: Table containing the spectrophotometric values and dissolution data of formula 1A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,02
m	0,05

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,208	0,208	0,207	0,214	0,225	0,219	0,532	0,522	0,529	12,933	13,659	21,391	28,739	30,353	47,535	35,542	8,506	23,931
5	0,627	0,635	0,631	0,665	0,668	0,668	1,053	1,055	1,053	22,839	22,579	29,060	50,754	50,177	64,577	55,169	6,657	12,066
10	1,121	1,125	1,121	1,103	1,119	1,106	1,416	1,448	1,429	27,372	26,542	32,402	60,827	58,982	72,005	63,938	5,753	8,999
15	1,336	1,347	1,346	1,293	1,307	1,304	1,594	1,586	1,591	31,703	29,793	35,707	70,452	66,207	79,350	72,003	5,476	7,606
30	1,543	1,565	1,548	1,461	1,449	1,460	1,723	1,754	1,764	31,876	29,955	35,902	70,835	66,567	79,781	72,394	5,506	7,606
60	1,754	1,666	1,716	1,558	1,583	1,563	1,869	1,849	1,849	35,248	32,348	38,276	78,328	71,884	85,057	78,423	5,378	6,858
90	1,843	1,871	1,861	1,734	1,720	1,724	1,958	2,033	2,010	38,369	35,681	41,366	85,265	79,290	91,925	85,493	5,161	6,037
120	2,024	2,100	2,064	1,737	1,726	1,730	2,034	2,022	2,037	42,657	35,971	42,205	94,793	79,935	93,788	89,506	6,780	7,574
180	2,212	2,114	2,207	1,861	1,853	1,859	2,077	2,692	2,264	45,185	38,699	48,693	100,412	85,998	108,207	98,206	9,200	9,368
240	2,165	2,315	2,276	1,937	1,991	1,974	2,114	2,194	2,184	46,917	41,095	45,353	104,259	91,322	100,784	98,789	5,467	5,534
360	2,216	2,254	2,240	1,927	1,953	1,936	2,120	2,349	2,053	46,860	40,747	45,795	104,134	90,549	101,767	98,817	5,926	5,996
inf	2,062	2,172	2,110	1,903	1,914	1,909	1,996	2,064	1,993	42,648	40,357	42,910	94,773	89,682	95,356	93,270	2,548	2,732

Dissolution results Formulation 1B

Table 4: Table containing the spectrophotometric alues and dissolution data of formula 1B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,107	0,092	0,096	0,155	0,121	0,166	0,097	0,117	0,128	2,554	3,577	2,883	5,676	7,949	6,407	6,678	0,948	14,191
5	0,282	0,264	0,245	0,284	0,266	0,238	0,205	0,178	0,212	6,028	6,017	4,662	13,396	13,371	10,360	12,376	1,426	11,520
10	0,435	0,437	0,408	0,432	0,419	0,420	0,304	0,289	0,296	9,483	9,420	6,739	21,074	20,934	14,976	18,995	2,842	14,961
15	0,559	0,543	0,566	0,622	0,589	0,590	0,527	0,556	0,541	12,239	13,171	11,915	27,198	29,269	26,478	27,649	1,183	4,279
30	0,798	0,766	0,764	0,703	0,709	0,709	0,618	0,609	0,609	16,913	15,472	13,458	37,585	34,383	29,907	33,958	3,149	9,273
60	0,865	0,877	0,865	0,921	0,931	0,937	0,834	0,838	0,818	18,960	20,225	18,096	42,133	44,944	40,214	42,430	1,943	4,578
90	1,104	1,068	1,061	1,182	1,148	1,178	1,120	1,128	1,124	23,433	25,358	24,352	52,074	56,352	54,116	54,181	1,747	3,224
120	1,308	1,324	1,311	1,170	1,126	1,118	1,298	1,271	1,320	28,519	24,844	28,099	63,376	55,208	62,442	60,342	3,650	6,049
180	1,440	1,351	1,346	1,362	1,354	1,356	1,332	1,336	1,335	30,024	29,572	29,051	66,719	65,716	64,557	65,664	0,884	1,346
240	1,472	1,441	1,424	1,435	1,446	1,412	1,474	1,432	1,452	31,594	31,278	31,690	70,210	69,506	70,421	70,046	0,391	0,559
360	1,494	1,364	1,492	1,547	1,561	1,592	1,574	1,501	1,556	31,844	34,286	33,763	70,764	76,190	75,029	73,995	2,333	3,153
inf	1,885	1,881	1,883	1,570	1,563	1,525	1,462	1,452	1,453	35,793	34,170	32,092	79,540	75,934	71,316	75,597	3,366	4,452

Table 5: Table containing the spectrophotometric values and dissolution data of formula 1B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,512	0,509	0,510	0,267	0,266	0,266	0,501	0,496	0,487	9,492	5,061	9,205	21,092	11,246	20,455	17,598	4,499	25,566
5	1,441	1,443	1,442	1,181	1,183	1,176	1,487	1,494	1,467	26,488	21,696	27,221	58,862	48,213	60,491	55,855	5,444	9,747
10	2,159	2,148	2,149	2,041	2,041	2,021	2,291	2,316	2,306	39,540	37,351	42,320	87,866	83,002	94,045	88,304	4,519	5,117
15	2,330	2,381	2,369	2,371	2,392	2,386	2,439	2,423	2,434	43,534	43,894	44,865	96,742	97,542	99,700	97,995	1,249	1,275
30	2,242	2,295	2,279	2,352	2,272	2,284	2,438	2,444	2,446	42,181	42,676	45,313	93,736	94,835	100,696	96,423	3,055	3,168
60	2,343	2,340	2,334	2,427	2,486	2,458	2,512	2,554	2,535	43,627	45,712	47,208	96,948	101,582	104,908	101,146	3,264	3,227
90	2,310	2,309	2,309	2,315	2,404	2,386	2,440	2,404	2,413	43,327	44,356	45,383	96,281	98,569	100,850	98,567	1,865	1,892
120	2,314	2,297	2,310	2,333	2,344	2,341	2,459	2,429	2,431	43,514	44,056	46,001	96,699	97,902	102,224	98,942	2,373	2,398
180	2,294	2,293	2,264	2,248	2,309	2,283	2,401	2,578	2,503	43,325	43,223	47,235	96,278	96,051	104,967	99,099	4,151	4,188
240	2,249	2,315	2,316	2,474	2,463	2,444	2,415	2,413	2,419	43,727	46,732	46,059	97,170	103,848	102,354	101,124	2,862	2,830
360	2,444	2,426	2,436	2,458	2,456	2,454	2,284	2,286	2,289	46,542	46,899	43,960	103,426	104,220	97,689	101,778	2,910	2,859
inf	2,362	2,393	2,387	2,443	2,456	2,439	2,505	2,505	2,483	46,897	46,966	48,026	104,217	104,368	106,724	105,103	1,148	1,092

Table 6: Table containing the spectrophotometric values and dissolution data of formula 1B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,251	0,252	0,251	0,749	0,752	0,746	0,385	0,376	0,379	17,113	28,611	23,541	38,030	63,581	52,314	51,308	10,455	20,378
5	0,835	0,842	0,842	1,357	1,492	1,396	1,169	1,155	1,160	8,826	35,380	35,776	19,613	78,622	79,503	59,246	28,027	47,306
10	0,415	0,415	0,432	1,745	1,744	1,746	1,781	1,725	1,794	32,886	37,612	41,943	73,080	83,583	93,206	83,290	8,219	9,868
15	1,592	1,635	1,637	1,868	1,830	1,844	1,987	2,105	2,103	35,092	40,325	43,763	77,983	89,611	97,252	88,282	7,923	8,974
30	1,726	1,735	1,707	1,951	1,987	1,979	2,121	2,169	2,143	35,284	40,544	44,002	78,408	90,098	97,781	88,762	7,965	8,974
60	1,837	1,808	1,818	2,089	2,129	2,114	2,074	2,155	2,078	37,441	43,528	43,396	83,202	96,729	96,435	92,122	6,308	6,848
90	2,013	1,985	1,991	2,319	2,310	2,316	2,291	2,226	2,274	41,148	47,848	46,855	91,440	106,330	104,123	100,631	6,561	6,520
120	2,029	2,229	2,164	2,204	2,167	2,174	2,160	2,083	2,107	44,266	45,444	44,163	98,370	100,986	98,140	99,165	1,291	1,302
180	2,130	2,238	2,207	2,362	2,236	2,274	2,218	2,172	2,195	45,518	47,859	45,969	101,150	106,354	102,154	103,220	2,254	2,184
240	2,222	2,112	2,194	2,192	2,232	2,294	2,192	2,211	2,198	45,442	47,085	46,316	100,983	104,634	102,924	102,847	1,491	1,450
360	2,163	2,226	2,219	2,137	2,163	2,161	2,208	2,226	2,245	46,225	45,626	47,089	102,722	101,391	104,643	102,919	1,335	1,297
inf	2,058	2,194	2,175	2,209	2,214	2,295	2,132	2,176	2,140	45,953	47,571	45,797	102,117	105,714	101,772	103,201	1,783	1,727

Dissolution results Formulation 1C

Table 7: Table containing the spectrophotometric values and dissolution data of formula 1C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,020	0,019	0,019	0,011	0,012	0,009	0,006	0,008	0,001	0,890	0,713	0,593	1,978	1,584	1,318	1,627	0,271	16,666
5	0,127	0,127	0,124	0,054	0,052	0,048	0,071	0,073	0,071	3,135	1,565	1,998	6,967	3,478	4,441	4,962	1,471	29,646
10	0,164	0,166	0,164	0,182	0,183	0,181	0,240	0,239	0,239	3,967	4,317	5,514	8,815	9,594	12,254	10,221	1,472	14,404
15	0,287	0,279	0,288	0,377	0,368	0,373	0,457	0,453	0,458	6,491	8,332	10,089	14,424	18,516	22,420	18,454	3,265	17,691
30	0,444	0,442	0,444	0,612	0,611	0,611	0,653	0,653	0,657	9,857	13,372	14,293	21,905	29,715	31,761	27,794	4,247	15,279
60	0,625	0,622	0,613	0,763	0,768	0,754	0,795	0,831	0,835	13,602	16,605	17,850	30,226	36,900	39,667	35,598	3,963	11,132
90	0,752	0,756	0,760	0,874	0,880	0,863	0,901	0,898	0,909	16,542	19,009	19,679	36,761	42,243	43,732	40,912	2,998	7,327
120	0,845	0,850	0,856	0,980	0,969	0,972	1,017	1,038	1,016	18,600	21,233	22,315	41,333	47,185	49,589	46,036	3,467	7,531
180	0,972	0,932	0,919	0,997	0,986	0,992	1,123	1,078	1,061	20,597	21,727	23,771	45,772	48,282	52,824	48,959	2,919	5,961
240	0,983	0,984	0,985	1,112	1,104	1,124	1,230	1,168	1,179	21,616	24,397	26,099	48,036	54,216	57,998	53,416	4,106	7,687
360	1,112	1,065	1,061	1,151	1,162	1,189	1,222	1,207	1,217	23,725	25,664	26,716	52,723	57,031	59,370	56,374	2,753	4,884
inf	1,099	1,102	1,098	1,225	1,266	1,228	1,252	1,254	1,252	26,326	27,313	27,648	58,503	60,695	61,439	60,212	1,246	2,070

Table 8: Table containing the spectrophotometric values and dissolution data of formula 1C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,304	0,304	0,304	0,280	0,279	0,281	0,257	0,257	0,257	5,749	5,306	4,893	12,776	11,791	10,874	11,814	0,777	6,573
5	0,881	0,876	0,877	0,809	0,807	0,808	0,907	0,904	0,905	16,208	14,943	16,704	36,018	33,206	37,119	35,448	1,648	4,648
10	1,707	1,703	1,707	1,624	1,608	1,616	1,810	1,818	1,815	31,345	29,715	33,321	69,655	66,033	74,047	69,912	3,277	4,687
15	2,315	2,250	2,274	2,164	2,106	2,165	2,298	2,254	2,269	41,957	39,491	41,858	93,237	87,757	93,017	91,337	2,533	2,773
30	2,641	2,523	2,622	2,468	2,405	2,427	2,298	2,355	2,326	47,927	44,949	43,045	106,505	99,886	95,655	100,682	4,465	4,435
60	2,609	2,444	2,493	2,608	2,595	2,606	2,412	2,311	2,415	46,734	48,279	44,241	103,853	107,287	98,313	103,151	3,697	3,584
90	2,422	2,453	2,476	2,408	2,462	2,443	2,286	2,252	2,297	45,804	45,540	42,647	101,786	101,201	94,772	99,253	3,177	3,201
120	2,656	2,717	2,693	2,642	2,713	2,683	2,466	2,466	2,467	50,384	50,171	46,300	111,965	111,492	102,889	108,782	4,172	3,835
180	2,499	2,564	2,490	2,518	2,503	2,510	2,466	2,401	2,413	47,552	47,372	45,824	105,670	105,272	101,830	104,258	1,724	1,654
240	2,461	2,455	2,460	2,437	2,437	2,411	2,281	2,301	2,291	46,737	46,139	43,609	103,860	102,530	96,908	101,100	3,013	2,980
360	2,395	2,402	2,390	2,487	2,477	2,469	2,291	2,296	2,291	45,834	47,280	43,864	101,854	105,066	97,477	101,466	3,110	3,066
inf	2,311	2,311	2,291	2,396	2,391	2,390	2,336	2,343	2,336	45,155	45,978	44,925	100,345	102,174	99,832	100,784	1,005	0,997

Table 9: Table containing the spectrophotometric values and dissolution data of formula 1C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,267	0,264	0,267	0,163	0,163	0,163	0,140	0,142	0,140	5,641	3,583	3,132	12,535	7,963	6,960	9,153	2,426	26,510
5	0,844	0,852	0,851	0,547	0,539	0,540	0,508	0,491	0,498	17,328	11,179	10,316	38,507	24,842	22,924	28,758	6,938	24,127
10	1,398	1,412	1,419	1,117	1,118	1,117	0,982	0,984	0,984	28,638	22,740	20,054	63,640	50,534	44,564	52,913	7,967	15,057
15	1,840	1,805	1,814	1,608	1,688	1,664	1,508	1,479	1,494	36,993	33,584	30,372	82,207	74,631	67,493	74,777	6,008	8,035
30	2,037	1,930	1,974	1,723	1,755	1,761	1,530	1,533	1,532	40,401	35,637	31,296	89,779	79,193	69,547	79,506	8,263	10,392
60	2,179	2,341	2,294	2,401	1,875	1,904	1,910	1,893	1,897	46,449	42,096	38,836	103,221	93,547	86,302	94,357	6,931	7,345
90	2,290	2,151	2,210	1,976	1,950	1,963	2,018	2,162	2,034	45,610	40,388	42,478	101,355	89,752	94,395	95,167	4,768	5,010
120	2,663	2,837	2,043	2,179	1,834	1,906	2,018	2,153	2,139	51,812	40,810	43,345	115,138	90,689	96,322	100,716	10,454	10,379
180	2,775	2,723	2,741	1,730	2,029	1,930	2,211	2,088	2,063	56,725	39,500	43,931	126,056	87,777	97,624	103,819	16,230	15,633
240	2,093	2,093	2,107	1,766	1,667	1,723	1,764	2,082	1,793	44,057	36,152	39,346	97,903	80,337	87,436	88,559	7,215	8,147
360	2,107	1,780	1,791	1,721	2,223	1,894	1,649	1,944	1,863	40,194	40,885	38,328	89,321	90,855	85,173	88,450	2,400	2,713
inf	2,365	2,209	2,194	1,920	1,904	1,974	1,962	1,904	1,947	43,391	40,834	40,911	96,424	90,741	90,913	92,693	2,639	2,847

Dissolution results Formulation 1D

Table 10: Table containing the spectrophotometric values and dissolution data of formula 1D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,004	0,002	0,001	0,004	0,001	0,003	0,021	0,019	0,023	0,537	0,549	0,927	1,193	1,221	2,059	1,491	0,402	26,969
5	0,031	0,026	0,026	0,055	0,045	0,045	0,075	0,078	0,078	1,078	1,501	2,111	2,395	3,335	4,692	3,474	0,943	27,141
10	0,128	0,127	0,123	0,142	0,145	0,139	0,173	0,175	0,175	3,142	3,476	4,151	6,982	7,723	9,225	7,977	0,933	11,697
15	0,290	0,298	0,307	0,330	0,319	0,321	0,353	0,348	0,345	6,771	7,298	7,828	15,046	16,219	17,396	16,220	0,959	5,915
30	0,552	0,540	0,548	0,569	0,569	0,565	0,568	0,574	0,577	12,005	12,455	12,569	26,677	27,678	27,931	27,429	0,541	1,974
60	0,757	0,754	0,759	0,852	0,840	0,838	0,720	0,725	0,726	16,475	18,300	15,802	36,611	40,667	35,116	37,465	2,345	6,260
90	0,987	0,990	0,984	1,063	1,033	1,108	0,907	0,908	0,910	21,388	23,104	19,754	47,529	51,343	43,897	47,589	3,040	6,388
120	1,155	1,162	1,153	1,285	1,287	1,257	1,221	1,220	1,212	25,063	27,596	26,346	55,695	61,323	58,546	58,521	2,298	3,927
180	1,305	1,310	1,314	1,418	1,395	1,397	1,338	1,345	1,348	28,398	30,412	29,122	63,106	67,581	64,716	65,134	1,851	2,841
240	1,432	1,431	1,434	1,584	1,534	1,542	1,495	1,494	1,494	31,130	33,723	32,446	69,177	74,940	72,101	72,073	2,353	3,265
360	1,508	1,511	1,514	1,546	1,525	1,522	1,576	1,569	1,536	32,942	33,432	34,000	73,205	74,294	75,556	74,352	0,961	1,292
inf	1,588	1,580	1,600	1,535	1,548	1,539	1,563	1,568	1,562	34,241	33,804	34,267	76,091	75,119	76,148	75,786	0,472	0,623

Table 11: Table containing the spectrophotometric values and dissolution data of formula 1D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,117	0,116	0,117	0,217	0,217	0,217	0,159	0,159	0,158	2,340	4,158	3,104	5,200	9,239	6,898	7,112	1,656	23,281
5	0,549	0,546	0,548	0,734	0,730	0,731	0,696	0,698	0,697	10,189	13,543	12,900	22,642	30,096	28,667	27,135	3,230	11,904
10	1,309	1,296	1,298	1,538	1,522	1,527	1,560	1,556	1,557	23,936	28,111	28,622	53,192	62,469	63,605	59,755	4,664	7,806
15	1,892	1,865	1,878	2,041	2,059	2,055	2,078	2,079	2,097	34,569	37,770	38,366	76,821	83,934	85,257	82,004	3,704	4,517
30	2,355	2,348	2,349	2,301	2,207	2,303	2,319	2,308	2,311	43,345	41,956	42,714	96,323	93,236	94,919	94,826	1,262	1,331
60	2,199	2,167	2,177	2,263	2,266	2,660	2,169	2,281	2,186	40,495	44,473	41,124	89,988	98,830	91,386	93,401	3,881	4,155
90	2,246	2,243	2,243	2,337	2,285	2,296	2,278	2,347	2,303	41,865	43,076	43,117	93,033	95,725	95,815	94,857	1,291	1,361
120	2,294	2,257	2,263	2,243	2,383	2,303	2,400	2,355	2,393	42,591	43,377	44,683	94,646	96,393	99,296	96,779	1,918	1,982
180	2,194	2,272	2,264	2,347	2,293	2,303	2,403	2,396	2,377	42,304	43,696	45,096	94,009	97,102	100,212	97,107	2,533	2,608
240	2,217	2,226	2,220	2,330	2,313	2,329	2,257	2,293	2,283	42,128	44,099	43,252	93,618	97,997	96,116	95,910	1,794	1,870
360	2,177	2,191	2,176	2,251	2,288	2,302	2,220	2,221	2,218	41,632	43,541	42,428	92,515	96,757	94,284	94,519	1,740	1,841
inf	2,244	2,251	2,245	2,213	2,210	2,219	2,307	2,302	2,309	43,200	42,566	44,225	96,000	94,591	98,277	96,290	1,519	1,577

Table 12: Table containing the spectrophotometric values and dissolution data of formula 1D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,088	0,086	0,087	0,112	0,110	0,110	0,222	0,219	0,219	2,057	2,533	4,721	4,572	5,628	10,492	6,897	2,578	37,378
5	0,637	0,633	0,638	0,672	0,684	0,680	0,910	0,893	0,897	13,047	13,901	18,348	28,993	30,891	40,774	33,553	5,165	15,393
10	1,106	1,094	1,094	1,107	1,109	1,114	1,577	1,604	1,655	22,358	22,604	32,684	49,684	50,230	72,632	57,515	10,691	18,589
15	1,678	1,676	1,675	1,551	1,577	1,569	2,078	1,965	1,989	34,051	31,850	40,841	75,669	70,778	90,758	79,068	8,503	10,754
30	1,876	1,767	1,839	1,620	1,680	1,694	1,996	1,988	1,983	37,255	33,996	40,623	82,789	75,547	90,273	82,870	6,012	7,255
60	1,946	2,178	2,171	1,853	1,880	1,871	2,139	2,852	2,639	42,875	38,243	51,937	95,278	84,984	115,416	98,559	12,639	12,824
90	2,409	2,144	2,163	2,035	1,964	1,851	2,369	2,656	2,656	45,921	40,094	52,559	102,046	89,098	116,798	102,647	11,317	11,025
120	2,132	2,159	2,139	1,790	1,928	1,809	2,164	2,500	2,464	44,257	38,161	49,156	98,350	84,802	109,237	97,463	9,995	10,255
180	2,101	2,066	2,089	1,869	1,709	1,794	2,261	1,876	1,931	43,342	37,327	42,348	96,315	82,950	94,106	91,124	5,850	6,419
240	2,044	2,063	2,051	1,906	1,754	1,793	2,062	2,003	2,043	42,916	38,073	42,849	95,369	84,607	95,220	91,732	5,039	5,493
360	1,953	2,143	2,037	1,818	1,835	1,821	1,831	2,241	2,194	42,975	38,411	44,120	95,499	85,358	98,045	92,967	5,480	5,895
inf	2,142	2,074	2,089	1,687	1,732	1,741	1,962	1,943	1,956	40,823	36,524	41,657	90,719	81,164	92,572	88,152	4,999	5,670

Dissolution results Formulation 1E

Table 13: Table containing the spectrophotometric values and dissolution data of formula 1E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,034	0,062	0,081	0,083	0,041	0,022	0,013	0,098	0,021	1,727	1,515	1,417	3,839	3,367	3,149	3,452	0,288	8,339
5	0,134	0,138	0,135	0,163	0,164	0,155	0,215	0,214	0,216	3,345	3,863	5,005	7,434	8,585	11,123	9,047	1,541	17,034
10	0,229	0,243	0,253	0,325	0,337	0,314	0,383	0,382	0,395	5,578	7,333	8,626	12,395	16,296	19,169	15,953	2,776	17,404
15	0,456	0,440	0,455	0,554	0,544	0,551	0,548	0,547	0,551	9,984	12,076	12,064	22,188	26,836	26,809	25,278	2,185	8,644
30	0,626	0,620	0,621	0,721	0,731	0,731	0,717	0,700	0,716	13,636	15,867	15,537	30,303	35,260	34,526	33,363	2,184	6,547
60	0,720	0,717	0,717	0,864	0,872	0,871	0,832	0,850	0,850	15,726	18,917	18,401	34,946	42,037	40,892	39,292	3,108	7,911
90	0,853	0,856	0,852	0,955	0,947	0,947	0,942	0,958	0,954	18,639	20,715	20,753	41,421	46,034	46,119	44,525	2,195	4,929
120	0,966	0,958	0,959	1,016	1,014	1,020	1,036	1,028	1,020	20,998	22,231	22,469	46,663	49,403	49,930	48,665	1,432	2,943
180	0,987	0,982	0,975	1,045	1,036	1,045	1,079	1,078	1,087	21,533	22,879	23,708	47,851	50,843	52,684	50,459	1,992	3,947
240	1,029	1,027	1,021	1,084	1,075	1,110	1,139	1,134	1,137	22,581	24,004	25,004	50,181	53,343	55,563	53,029	2,209	4,165
360	1,076	1,131	1,078	1,151	1,153	1,154	1,189	1,187	1,189	24,156	25,448	26,212	53,680	56,551	58,249	56,160	1,886	3,358
inf	1,116	1,115	1,175	1,231	1,210	1,206	1,195	1,270	1,208	26,309	26,901	27,104	58,464	59,781	60,231	59,492	0,749	1,260

Table 14: Table containing the spectrophotometric values and dissolution data of formula 1E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,386	0,387	0,385	0,095	0,094	0,094	0,345	0,338	0,339	0,069	0,050	0,322	0,152	0,111	0,715	0,326	0,275	84,385
5	1,254	1,252	1,252	0,441	0,442	0,442	1,093	1,092	1,093	23,030	8,253	20,119	51,178	18,340	44,709	38,076	14,203	37,301
10	2,159	2,123	2,147	1,080	1,078	1,079	1,946	1,971	1,970	39,347	19,886	36,040	87,439	44,190	80,089	70,573	18,895	26,774
15	2,406	2,421	2,418	1,599	1,594	1,556	2,238	2,212	2,223	44,509	29,166	40,997	98,908	64,812	91,104	84,942	14,586	17,172
30	2,388	2,308	2,345	1,877	1,848	1,863	2,320	2,278	2,293	43,517	34,405	42,551	96,704	76,457	94,557	89,239	9,081	10,176
60	2,247	2,407	2,327	1,997	1,974	1,970	2,337	2,192	2,266	43,387	36,732	42,198	96,416	81,627	93,773	90,606	6,439	7,107
90	2,430	2,532	2,473	1,955	1,994	1,973	2,400	2,339	2,373	46,376	36,816	44,353	103,058	81,813	98,562	94,478	9,141	9,676
120	2,476	2,570	2,483	2,027	2,007	2,033	2,410	2,487	2,463	47,197	37,897	46,092	104,883	84,216	102,426	97,175	9,218	9,486
180	2,507	2,528	2,511	2,046	2,002	2,036	2,406	2,481	2,436	47,556	38,208	46,114	105,680	84,907	102,475	97,687	9,131	9,347
240	2,490	2,582	2,525	1,960	2,004	1,993	2,321	2,361	2,342	48,119	37,638	44,556	106,931	83,641	99,014	96,529	9,669	10,017
360	2,265	2,261	2,270	1,932	1,941	1,930	2,246	2,260	2,249	43,519	36,906	43,161	96,709	82,013	95,914	91,545	6,748	7,372
inf	2,329	2,309	2,306	1,869	1,871	1,851	2,317	2,323	2,299	41,900	35,819	44,498	93,112	79,597	98,884	90,531	8,083	8,928

Table 15: Table containing the spectrophotometric values and dissolution data of formula 1E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,696	0,693	0,696	0,556	0,558	0,554	0,255	0,257	0,259	0,069	0,050	0,322	0,152	0,111	0,715	0,326	0,275	84,385
5	1,565	1,525	1,550	1,361	1,442	1,424	0,707	0,708	0,707	31,324	28,558	14,493	69,609	63,462	32,206	55,092	16,376	29,726
10	2,197	2,287	2,200	2,011	2,080	2,125	1,484	1,492	1,491	45,130	41,981	30,204	100,290	93,291	67,121	86,901	14,275	16,427
15	2,172	2,343	2,284	2,272	2,196	2,234	1,980	1,823	1,906	46,142	45,456	38,655	102,538	101,013	85,901	96,484	7,509	7,783
30	2,339	2,372	2,370	2,394	2,399	2,389	2,111	2,078	2,084	48,275	48,896	42,623	107,278	108,658	94,719	103,552	6,271	6,056
60	2,297	2,398	2,385	2,390	2,377	2,364	2,087	2,243	2,207	48,527	48,818	44,611	107,837	108,485	99,136	105,152	4,263	4,054
90	2,366	2,338	2,361	2,319	2,388	2,310	2,199	1,967	2,095	48,692	48,322	43,014	108,205	107,383	95,588	103,725	5,764	5,557
120	2,162	2,194	2,400	2,334	2,378	2,310	1,971	1,867	1,986	46,885	48,614	40,334	104,189	108,031	89,632	100,617	7,925	7,876
180	2,052	2,160	2,133	2,094	2,360	2,350	1,948	1,916	1,910	44,405	47,423	40,218	98,679	105,385	89,373	97,812	6,566	6,712
240	1,912	2,250	2,196	1,827	2,068	1,950	2,098	1,911	1,965	44,728	41,283	41,768	99,396	91,741	92,817	94,652	3,384	3,575
360	1,676	1,879	1,713	1,765	1,757	1,741	1,678	1,679	1,960	37,694	37,624	37,608	83,764	83,609	83,573	83,649	0,083	0,099
inf	1,943	1,863	1,879	2,018	1,951	1,991	1,867	1,805	1,844	40,905	42,460	39,127	90,899	94,356	86,950	90,735	3,026	3,335

Dissolution results Formulation 1F

Table 16: Table containing the spectrophotometric values and dissolution data of formula 1F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,031	0,027	0,011	0,005	0,012	0,013	0,019	0,011	0,012	0,976	0,704	0,790	2,169	1,565	1,756	1,830	0,252	13,774
5	0,031	0,027	0,029	0,043	0,044	0,046	0,096	0,096	0,094	1,102	1,416	2,495	2,449	3,146	5,544	3,713	1,326	35,712
10	0,092	0,107	0,101	0,116	0,097	0,114	0,241	0,251	0,230	2,592	2,790	5,551	5,759	6,199	12,335	8,098	3,002	37,067
15	0,242	0,243	0,258	0,308	0,313	0,327	0,500	0,499	0,498	5,700	7,138	10,990	12,666	15,862	24,422	17,650	4,963	28,119
30	0,540	0,536	0,537	0,619	0,616	0,618	0,713	0,710	0,719	11,813	13,495	15,559	26,251	29,990	34,575	30,272	3,404	11,244
60	0,850	0,847	0,847	0,952	0,960	0,974	0,947	0,947	0,952	18,377	20,792	20,561	40,837	46,204	45,692	44,244	2,418	5,466
90	1,089	1,102	1,098	1,222	1,228	1,205	1,174	1,169	1,188	23,689	26,276	25,454	52,643	58,391	56,564	55,866	2,398	4,293
120	1,332	1,326	1,314	1,453	1,447	1,446	1,356	1,356	1,357	28,583	31,248	29,358	63,518	69,439	65,241	66,066	2,487	3,764
180	1,256	1,254	1,237	1,428	1,416	1,430	1,464	1,452	1,439	27,170	30,908	31,516	60,379	68,683	70,035	66,366	4,269	6,433
240	1,374	1,384	1,387	1,457	1,474	1,458	1,527	1,515	1,513	30,094	31,877	33,082	66,876	70,838	73,516	70,410	2,727	3,874
360	1,467	1,450	1,462	1,522	1,513	1,520	1,559	1,593	1,569	31,887	33,213	34,421	70,860	73,807	76,490	73,719	2,299	3,119
inf	1,543	1,529	1,530	1,575	1,586	1,580	1,653	1,655	1,654	34,777	34,680	36,286	77,282	77,067	80,635	78,328	1,634	2,086

Table 17: Table containing the spectrophotometric values and dissolution data of formula 1F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,040	0,041	0,041	0,028	0,029	0,029	0,152	0,153	0,153	0,958	0,739	2,993	2,129	1,643	6,652	3,475	2,255	64,906
5	0,291	0,291	0,291	0,151	0,151	0,151	0,791	0,787	0,788	5,514	2,967	14,571	12,253	6,594	32,379	17,075	11,065	64,804
10	0,850	0,851	0,851	0,545	0,549	0,547	1,687	1,704	1,697	15,718	10,178	31,149	34,928	22,617	69,220	42,255	19,718	46,665
15	1,347	1,347	1,346	1,033	1,022	1,029	2,177	2,125	2,165	24,820	18,979	39,680	55,156	42,177	88,178	61,837	19,365	31,317
30	1,879	1,889	1,881	1,604	1,579	1,597	2,273	2,368	2,303	34,710	29,366	42,784	77,133	65,258	95,076	79,156	12,257	15,484
60	2,045	2,049	2,049	1,873	1,827	1,837	2,481	2,462	2,472	37,895	34,112	45,872	84,212	75,805	101,939	87,318	10,893	12,475
90	2,089	2,045	2,063	1,878	1,880	1,880	2,305	2,370	2,328	38,423	34,914	43,634	85,385	77,587	96,964	86,645	7,960	9,187
120	2,152	2,204	2,193	1,918	1,907	1,911	2,465	2,401	2,429	40,765	35,690	45,626	90,588	79,310	101,392	90,430	9,016	9,970
180	2,199	2,216	2,204	1,882	1,876	1,879	2,433	2,445	2,463	41,407	35,288	46,158	92,016	78,417	102,573	91,002	9,888	10,866
240	2,029	2,115	2,106	1,911	1,952	1,944	2,418	2,357	2,303	39,404	36,505	44,812	87,564	81,123	99,582	89,423	7,650	8,555
360	1,998	1,990	1,990	1,812	1,811	1,811	2,471	2,470	2,466	37,964	34,439	47,047	84,364	76,532	104,548	88,481	11,802	13,339
inf	1,968	1,973	1,980	1,809	1,810	1,807	2,453	2,451	2,437	39,689	34,583	46,895	88,199	76,851	104,212	89,754	11,224	12,505

Table 18: Table containing the spectrophotometric values and dissolution data of formula 1F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,052	0,047	0,049	0,054	0,058	0,056	0,069	0,066	0,068	1,306	1,441	1,677	2,902	3,203	3,726	3,277	0,340	10,385
5	0,202	0,194	0,198	0,351	0,352	0,350	0,281	0,283	0,282	4,277	7,350	5,970	9,506	16,332	13,266	13,035	2,792	21,419
10	0,653	0,638	0,641	0,980	0,989	0,984	0,807	0,807	0,806	13,223	20,051	16,494	29,385	44,558	36,654	36,866	6,196	16,807
15	1,030	1,034	1,033	1,465	1,502	1,500	1,276	1,296	1,280	21,064	30,255	26,123	46,810	67,232	58,052	57,365	8,352	14,559
30	1,674	1,697	1,681	2,191	1,921	1,971	1,807	1,740	1,782	34,214	41,189	36,124	76,032	91,531	80,275	82,613	6,540	7,916
60	1,816	1,958	1,926	2,084	1,980	1,989	1,979	1,975	1,977	38,723	41,221	40,334	86,051	91,603	89,631	89,095	2,298	2,580
90	1,863	1,929	1,931	2,126	1,989	1,995	1,964	1,957	1,960	39,086	41,818	40,216	86,858	92,928	89,368	89,718	2,490	2,776
120	1,612	1,574	1,501	1,750	1,756	1,760	1,636	1,575	1,613	32,394	36,425	33,385	71,986	80,945	74,188	75,706	3,812	5,035
180	1,683	1,535	1,579	1,832	1,854	1,841	1,781	1,776	1,780	33,303	38,354	36,991	74,006	85,230	82,203	80,480	4,741	5,891
240	1,536	1,664	1,584	1,666	1,613	1,583	1,635	1,474	1,583	33,385	34,125	32,881	74,189	75,833	73,069	74,364	1,135	1,526
360	1,509	1,490	1,491	1,574	1,617	1,604	1,490	1,481	1,473	31,604	33,867	31,398	70,232	75,260	69,772	71,755	2,486	3,464
inf	1,591	1,544	1,551	1,880	0,800	1,764	1,610	1,611	1,587	32,811	31,703	33,996	72,913	70,452	75,547	72,970	2,081	2,851

Dissolution results Formulation 2A

Table 19: Table containing the spectrophotometric values and dissolution data of formula 2A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,013	0,009	0,006	0,095	0,100	0,095	0,046	0,042	0,041	0,683	2,516	1,390	1,517	5,590	3,089	3,399	1,677	49,350
5	0,182	0,184	0,182	0,113	0,112	0,115	0,061	0,062	0,065	4,328	2,878	1,807	9,618	6,395	4,014	6,676	2,296	34,396
10	0,188	0,189	0,195	0,156	0,152	0,157	0,158	0,162	0,164	4,509	3,768	3,885	10,019	8,373	8,633	9,009	0,723	8,020
15	0,278	0,279	0,284	0,273	0,281	0,279	0,298	0,305	0,308	6,414	6,357	6,882	14,252	14,127	15,294	14,558	0,523	3,593
30	0,407	0,413	0,411	0,450	0,446	0,445	0,466	0,462	0,464	9,172	9,932	10,284	20,381	22,070	22,854	21,769	1,032	4,740
60	0,849	0,845	0,848	0,816	0,814	0,811	0,614	0,617	0,615	18,381	17,679	13,513	40,848	39,286	30,029	36,721	4,775	13,002
90	0,687	0,685	0,688	1,005	1,003	0,999	0,882	0,885	0,875	15,116	21,726	19,144	33,591	48,280	42,542	41,471	6,044	14,575
120	0,972	0,980	0,990	1,121	1,112	1,109	1,114	1,118	1,168	21,353	24,185	24,547	47,452	53,745	54,549	51,915	3,173	6,112
180	1,139	1,143	1,143	0,901	0,901	0,824	1,145	1,141	1,149	24,849	19,314	24,926	55,220	42,919	55,390	51,176	5,839	11,410
240	1,266	1,279	1,268	0,942	0,963	0,957	1,212	1,211	1,218	27,684	21,068	26,494	61,521	46,817	58,876	55,738	6,400	11,482
360	1,356	1,356	1,357	1,233	1,231	1,235	1,298	1,302	1,299	29,632	27,015	28,441	65,850	60,032	63,203	63,028	2,378	3,773
inf	1,357	1,358	1,359	1,308	1,300	1,306	1,330	1,318	1,327	29,214	28,663	29,123	64,920	63,695	64,718	64,444	0,536	0,832

Table 20: Table containing the spectrophotometric values and dissolution data of formula 2A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,118	0,120	0,119	0,099	0,098	0,098	0,143	0,126	0,127	2,383	2,005	2,616	5,296	4,457	5,814	5,189	0,559	10,780
5	0,476	0,474	0,476	0,406	0,402	0,405	0,570	0,589	0,576	8,870	7,578	10,745	19,712	16,840	23,877	20,143	2,889	14,344
10	1,037	1,058	1,047	0,917	0,917	0,916	1,270	1,255	1,261	19,317	16,936	23,230	42,927	37,635	51,622	44,061	5,766	13,087
15	1,503	1,504	1,506	1,333	1,339	1,337	1,794	1,782	1,791	27,732	24,655	32,940	61,628	54,789	73,200	63,205	7,599	12,022
30	1,928	1,848	1,873	1,706	1,686	1,693	2,016	2,028	2,018	34,764	31,318	37,338	77,254	69,595	82,973	76,608	5,481	7,154
60	2,065	2,145	2,126	1,894	1,889	1,890	2,245	2,169	2,189	39,130	35,047	40,825	86,955	77,882	90,721	85,186	5,389	6,326
90	2,114	2,113	2,103	1,997	1,980	1,982	2,390	2,352	2,373	39,303	36,976	44,146	87,340	82,170	98,102	89,204	6,636	7,440
120	2,203	2,239	2,219	1,995	2,054	2,027	2,308	2,332	2,316	41,520	37,884	43,423	92,266	84,187	96,495	90,983	5,106	5,612
180	2,409	2,366	2,379	2,110	2,118	2,120	2,233	2,274	2,293	44,736	39,737	42,709	99,412	88,304	94,908	94,208	4,562	4,843
240	2,236	2,204	2,226	2,076	2,077	2,079	2,186	2,285	2,202	42,019	39,250	42,163	93,375	87,222	93,696	91,431	2,979	3,258
360	2,303	2,378	2,344	2,077	2,044	2,065	2,214	2,386	2,363	44,419	39,180	44,149	98,709	87,067	98,110	94,629	5,352	5,656
inf	2,261	2,263	2,289	2,035	2,040	2,036	2,249	2,246	2,251	41,816	38,930	43,070	92,925	86,512	95,711	91,716	3,852	4,199

Table 21: Table containing the spectrophotometric values and dissolution data of formula 2A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,121	0,163	0,106	0,105	0,121	0,111	0,104	0,157	0,137	2,922	2,558	2,971	6,493	5,684	6,601	6,260	0,409	6,537
5	0,513	0,526	0,519	0,449	0,451	0,441	0,524	0,517	0,521	10,719	9,269	10,746	23,820	20,598	23,880	22,766	1,533	6,735
10	0,921	0,919	0,920	0,840	0,874	0,890	0,966	0,942	0,961	18,787	17,743	19,519	41,748	39,428	43,376	41,518	1,620	3,902
15	1,258	1,257	1,258	1,178	1,394	1,488	1,390	1,328	1,369	25,644	27,543	27,749	56,987	61,206	61,664	59,952	2,105	3,511
30	1,572	1,645	1,629	1,603	1,456	1,454	1,369	1,641	1,494	32,944	30,712	30,675	73,209	68,249	68,166	69,875	2,358	3,374
60	1,510	1,675	1,644	1,398	1,644	1,573	1,560	1,730	1,703	33,005	31,563	34,104	73,344	70,139	75,786	73,090	2,312	3,164
90	1,768	1,591	1,606	1,749	1,746	1,741	1,762	1,729	1,744	34,092	35,868	35,897	75,759	79,706	79,772	78,412	1,876	2,393
120	1,910	2,040	2,013	1,853	2,213	2,063	1,866	1,937	1,940	40,926	42,021	39,483	90,946	93,380	87,740	90,689	2,309	2,547
180	1,819	1,799	1,795	1,754	1,753	1,774	1,789	1,671	1,797	37,482	36,594	36,448	83,293	81,320	80,995	81,869	1,015	1,240
240	1,874	1,888	1,868	2,071	1,973	1,982	2,176	2,160	2,154	39,132	41,758	44,872	86,961	92,796	99,715	93,157	5,213	5,596
360	1,909	1,861	1,894	1,916	1,921	1,909	1,938	2,224	2,013	39,566	40,109	43,008	87,925	89,132	95,574	90,877	3,358	3,695
inf	1,895	1,891	1,879	2,098	1,948	1,983	2,072	1,994	1,979	41,436	42,210	42,374	92,079	93,800	94,164	93,348	0,909	0,974

Dissolution results Formulation 2B

Table 22: Table containing the spectrophotometric values and dissolution data of formula 2B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,092	0,067	0,077	0,063	0,071	0,068	0,077	0,078	0,077	2,144	1,897	2,111	4,764	4,215	4,691	4,557	0,244	5,350
5	0,136	0,134	0,138	0,184	0,184	0,179	0,156	0,156	0,155	3,351	4,326	3,770	7,446	9,614	8,378	8,480	0,888	10,472
10	0,191	0,209	0,199	0,239	0,237	0,256	0,240	0,243	0,246	4,694	5,638	5,616	10,431	12,528	12,481	11,813	0,978	8,277
15	0,369	0,363	0,378	0,451	0,452	0,454	0,428	0,426	0,423	8,295	10,033	9,468	18,433	22,296	21,039	20,589	1,609	7,813
30	0,629	0,625	0,625	0,637	0,631	0,634	0,841	0,844	0,845	13,711	13,894	18,278	30,469	30,876	40,618	33,988	4,691	13,803
60	0,938	0,938	0,941	0,937	0,949	0,941	0,973	0,964	0,961	20,340	20,428	20,952	45,199	45,395	46,561	45,718	0,601	1,315
90	0,845	0,859	0,870	1,153	1,169	1,166	1,172	1,203	1,271	18,752	25,153	26,284	41,672	55,895	58,408	51,991	7,369	14,173
120	1,297	1,297	1,298	1,351	1,332	1,329	1,009	1,281	1,036	28,063	28,959	24,191	62,361	64,353	53,758	60,157	4,598	7,643
180	1,367	1,405	1,409	1,428	1,428	1,424	1,246	1,223	1,219	30,240	30,994	26,851	67,200	68,875	59,668	65,248	4,004	6,137
240	1,484	1,493	1,488	1,507	1,500	1,499	1,417	1,413	1,424	32,377	32,734	30,950	71,950	72,743	68,779	71,157	1,713	2,407
360	1,015	0,976	0,983	1,592	1,556	1,573	1,571	1,571	1,573	22,138	34,407	34,334	49,196	76,460	76,298	67,318	12,814	19,035
inf	1,171	1,130	1,157	1,488	1,512	1,526	1,508	1,509	1,518	30,624	33,226	33,257	68,054	73,836	73,905	71,932	2,742	3,812

Table 23: Table containing the spectrophotometric values and dissolution data of formula 2B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,364	0,366	0,363	0,368	0,375	0,370	0,378	0,384	0,380	6,838	6,964	7,136	15,196	15,475	15,857	15,509	0,271	1,748
5	0,957	0,956	0,957	0,940	0,940	0,939	1,080	1,073	1,077	17,650	17,339	19,824	39,221	38,530	44,054	40,602	2,457	6,053
10	1,537	1,536	1,533	1,476	1,483	1,479	1,705	1,678	1,683	28,263	27,252	31,060	62,806	60,559	69,022	64,129	3,579	5,581
15	1,954	1,959	1,956	1,907	1,852	1,863	2,091	2,058	2,077	36,080	34,572	38,272	80,178	76,826	85,049	80,684	3,376	4,185
30	2,081	2,009	2,010	1,986	1,917	1,915	2,097	2,165	2,125	37,669	35,955	39,457	83,708	79,901	87,682	83,764	3,177	3,793
60	2,063	2,052	2,060	1,972	2,008	2,026	2,268	2,264	2,271	38,333	37,283	42,189	85,185	82,851	93,753	87,263	4,687	5,371
90	2,088	2,134	2,128	2,008	1,998	1,999	2,153	2,253	2,237	39,596	37,483	41,450	87,991	83,295	92,110	87,798	3,602	4,102
120	2,077	2,081	2,080	1,983	2,055	2,050	2,229	2,191	2,196	39,137	38,183	41,508	86,972	84,851	92,241	88,021	3,107	3,530
180	2,251	2,266	2,254	2,017	2,003	2,009	2,313	2,325	2,319	42,581	38,036	43,802	94,625	84,524	97,338	92,162	5,514	5,982
240	2,086	2,040	2,065	1,967	1,972	2,046	2,178	2,235	2,229	39,290	37,974	42,119	87,311	84,387	93,599	88,432	3,843	4,346
360	2,045	2,091	2,063	1,987	2,029	2,016	2,271	2,261	2,188	39,545	38,462	42,821	87,878	85,470	95,157	89,502	4,118	4,601
inf	1,990	1,996	1,994	1,995	1,994	1,986	2,163	2,143	2,138	39,358	38,316	41,375	87,463	85,146	91,945	88,185	2,822	3,201

Table 24: Table containing the spectrophotometric values and dissolution data of formula 2B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a phosphate buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,405	0,423	0,410	0,495	0,500	0,494	0,325	0,315	0,315	8,575	10,244	6,690	19,055	22,764	14,867	18,895	3,226	17,074
5	0,945	0,962	0,956	1,070	1,111	1,104	0,853	0,878	0,860	19,456	22,268	17,633	43,235	49,484	39,185	43,968	4,236	9,635
10	1,765	1,367	1,395	1,512	2,199	2,074	1,303	1,412	1,374	30,649	39,056	27,713	68,108	86,791	61,584	72,161	10,683	14,804
15	2,060	1,806	1,894	2,109	1,818	2,074	1,894	1,772	1,806	39,033	40,708	37,079	86,740	90,463	82,399	86,534	3,295	3,808
30	2,054	2,008	2,044	2,442	2,415	2,440	1,911	2,128	2,137	41,557	49,573	41,976	92,349	110,163	93,280	98,597	8,187	8,303
60	2,071	2,050	2,058	1,933	1,878	1,896	1,808	1,796	1,795	42,269	39,251	37,030	93,931	87,225	82,288	87,815	4,772	5,434
90	2,301	2,351	2,493	2,427	2,182	2,350	2,144	2,142	2,149	48,940	47,807	44,132	108,757	106,237	98,072	104,355	4,561	4,370
120	1,801	1,827	1,806	1,998	1,999	2,018	1,883	2,053	1,903	37,796	41,773	40,403	83,991	92,829	89,785	88,868	3,666	4,125
180	1,866	1,924	1,901	2,002	1,894	1,893	2,039	2,299	2,325	39,714	40,491	46,104	88,253	89,979	102,454	93,562	6,327	6,762
240	2,325	2,050	2,003	2,254	2,203	2,095	2,010	1,973	1,983	44,501	45,788	41,706	98,891	101,750	92,680	97,774	3,786	3,872
360	1,903	2,244	2,193	1,663	1,469	1,639	1,977	2,165	2,092	44,485	34,158	43,718	98,856	75,907	97,151	90,638	10,439	11,518
inf	1,947	1,963	1,982	1,875	1,729	1,699	1,602	1,594	1,543	37,865	37,886	33,980	84,145	84,191	75,511	81,282	4,081	5,020

Dissolution results Formulation 2C

Table 25: Table containing the spectrophotometric values and dissolution data of formula 2C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,018	0,016	0,017	0,028	0,027	0,028	0,013	0,014	0,014	0,847	1,071	0,777	1,882	2,381	1,727	1,997	0,279	13,969
5	0,076	0,074	0,075	0,110	0,110	0,111	0,076	0,078	0,078	2,061	2,815	2,112	4,581	6,255	4,693	5,176	0,764	14,757
10	0,210	0,204	0,208	0,257	0,264	0,259	0,217	0,222	0,220	4,846	5,957	5,101	10,768	13,237	11,335	11,780	1,056	8,963
15	0,368	0,367	0,367	0,418	0,420	0,418	0,396	0,397	0,397	8,232	9,315	8,841	18,293	20,699	19,647	19,546	0,985	5,039
30	0,513	0,513	0,513	0,592	0,563	0,575	0,531	0,530	0,531	11,321	12,679	11,704	25,159	28,176	26,009	26,448	1,270	4,803
60	0,674	0,675	0,674	0,719	0,743	0,720	0,701	0,715	0,713	14,766	15,909	15,511	32,812	35,352	34,469	34,211	1,053	3,078
90	0,831	0,836	0,843	0,937	0,932	0,947	0,899	0,908	0,898	18,247	20,418	19,618	40,550	45,372	43,596	43,173	1,991	4,613
120	1,035	1,005	1,026	1,092	1,096	1,097	1,059	1,059	1,060	22,231	23,806	23,024	49,402	52,903	51,165	51,157	1,429	2,794
180	1,145	1,152	1,152	1,214	1,226	1,226	1,180	1,171	1,173	25,030	26,593	25,572	55,622	59,095	56,826	57,181	1,440	2,519
240	1,264	1,253	1,258	1,285	1,316	1,315	1,307	1,302	1,283	27,443	28,480	28,282	60,983	63,289	62,850	62,374	1,000	1,603
360	1,325	1,347	1,353	1,420	1,414	1,417	1,373	1,360	1,373	29,333	30,974	29,931	65,184	68,831	66,513	66,843	1,507	2,255
inf	1,445	1,450	1,449	1,503	1,504	1,487	1,445	1,443	1,457	32,065	32,836	31,756	71,255	72,968	70,570	71,598	1,009	1,409

Table 26: Table containing the spectrophotometric values and dissolution data of formula 2C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,259	0,258	0,258	0,314	0,312	0,311	0,346	0,346	0,347	4,914	5,903	6,517	10,920	13,118	14,482	12,840	1,468	11,429
5	0,900	0,894	0,897	1,035	1,032	1,033	1,087	1,089	1,087	16,558	19,030	20,028	36,796	42,290	44,507	41,198	3,241	7,868
10	1,644	1,642	1,643	1,820	1,803	1,816	1,818	1,839	1,826	30,211	33,320	33,597	67,136	74,043	74,660	71,947	3,411	4,741
15	1,957	1,953	1,956	2,110	2,144	2,133	2,113	2,146	2,146	36,053	39,247	39,369	80,118	87,215	87,488	84,940	3,412	4,017
30	2,116	2,179	2,135	2,262	2,259	2,260	2,366	2,307	2,346	39,667	41,847	43,300	88,150	92,993	96,223	92,455	3,318	3,588
60	2,274	2,305	2,286	2,302	2,332	2,287	2,342	2,344	2,350	42,519	42,924	43,640	94,487	95,387	96,978	95,618	1,030	1,077
90	2,235	2,290	2,278	2,350	2,311	2,370	2,376	2,330	2,365	42,377	43,822	44,092	94,171	97,382	97,982	96,512	1,673	1,734
120	2,181	2,247	2,227	2,297	2,243	2,270	2,304	2,365	2,343	41,704	42,718	43,969	92,676	94,928	97,708	95,104	2,058	2,164
180	2,326	2,361	2,344	2,396	2,413	2,337	2,378	2,393	2,388	44,208	44,987	45,094	98,239	99,971	100,210	99,473	0,878	0,883
240	2,341	2,340	2,343	2,484	2,428	2,435	2,368	2,396	2,383	44,400	46,449	45,261	98,667	103,219	100,581	100,822	1,866	1,851
360	2,426	2,436	2,428	2,401	2,441	2,436	2,336	2,322	2,436	46,258	46,274	45,184	102,795	102,830	100,410	102,012	1,133	1,110
inf	2,482	2,462	2,490	2,457	2,455	2,457	2,501	2,487	2,477	47,304	47,072	47,671	105,120	104,604	105,936	105,220	0,548	0,521

Table 27: Table containing the spectrophotometric values and dissolution data of formula 2C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,350	0,348	0,349	0,532	0,539	0,539	0,417	0,415	0,416	7,297	11,045	8,639	16,216	24,544	19,197	19,986	3,445	17,238
5	1,072	1,067	1,066	1,269	1,239	1,240	0,948	0,944	0,950	21,725	25,370	19,310	48,279	56,378	42,910	49,189	5,536	11,254
10	1,592	1,607	1,612	1,756	1,846	1,822	1,670	1,647	1,651	32,547	36,674	33,586	72,326	81,499	74,636	76,154	3,895	5,115
15	1,545	1,803	1,594	1,986	1,785	1,750	1,699	1,965	1,581	33,596	37,534	35,617	74,657	83,409	79,148	79,071	3,573	4,519
30	2,014	1,814	1,919	2,268	1,916	2,019	1,917	1,996	1,955	39,155	42,273	39,968	87,010	93,940	88,817	89,923	2,935	3,264
60	2,421	2,272	2,310	2,221	1,946	1,963	1,682	2,021	1,843	47,738	42,022	38,040	106,085	93,381	84,534	94,667	8,845	9,343
90	2,174	2,346	2,341	2,128	1,714	1,794	2,173	1,850	1,854	47,049	38,955	40,451	104,553	86,566	89,891	93,670	7,814	8,342
120	1,986	2,139	2,127	2,054	2,041	2,047	2,032	2,045	1,936	43,247	42,537	41,581	96,104	94,526	92,402	94,344	1,517	1,608
180	2,259	2,173	2,250	2,147	2,241	2,204	1,783	1,934	1,908	46,340	45,759	39,209	102,977	101,686	87,132	97,265	7,185	7,387
240	1,815	1,812	1,821	1,980	2,080	2,049	2,072	2,047	1,816	38,360	42,787	41,484	85,244	95,082	92,188	90,838	4,128	4,544
360	1,926	1,979	1,935	1,740	2,236	2,065	1,822	1,818	1,824	41,176	42,562	38,565	91,502	94,582	85,700	90,594	3,682	4,065
inf	1,863	1,893	1,946	2,276	2,035	2,111	1,957	1,993	1,922	42,454	45,328	41,489	94,343	100,728	92,197	95,756	3,623	3,784

Dissolution results Formulation 2D

Table 28: Table containing the spectrophotometric values and dissolution data of formula 2D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,010	0,010	0,010	0,017	0,017	0,018	0,015	0,014	0,014	0,696	0,853	0,792	1,547	1,896	1,759	1,734	0,144	8,291
5	0,045	0,045	0,045	0,054	0,056	0,055	0,069	0,067	0,068	1,444	1,646	1,922	3,209	3,657	4,271	3,712	0,435	11,724
10	0,149	0,144	0,146	0,143	0,146	0,146	0,199	0,216	0,213	3,565	3,536	4,887	7,923	7,858	10,861	8,881	1,400	15,769
15	0,306	0,306	0,307	0,288	0,289	0,290	0,397	0,398	0,399	6,935	6,582	8,871	15,410	14,626	19,714	16,583	2,237	13,487
30	0,550	0,526	0,537	0,485	0,485	0,486	0,584	0,589	0,588	11,823	10,724	12,880	26,273	23,832	28,623	26,243	1,956	7,455
60	0,839	0,848	0,844	0,791	0,804	0,807	0,890	0,907	0,896	18,304	17,387	19,453	40,676	38,638	43,230	40,848	1,878	4,598
90	1,133	1,138	1,147	1,082	1,101	1,101	1,164	1,162	1,169	24,595	23,655	25,169	54,656	52,566	55,930	54,384	1,387	2,550
120	1,342	1,336	1,345	1,252	1,288	1,277	1,376	1,382	1,382	28,952	27,500	29,807	64,338	61,112	66,237	63,896	2,116	3,311
180	1,422	1,440	1,440	1,373	1,375	1,377	1,466	1,481	1,479	31,069	29,805	31,972	69,043	66,234	71,048	68,775	1,975	2,871
240	1,512	1,518	1,513	1,478	1,477	1,478	1,541	1,537	1,537	32,913	32,113	33,465	73,139	71,362	74,367	72,956	1,234	1,691
360	1,588	1,584	1,609	1,537	1,537	1,535	1,519	1,592	1,658	34,752	33,515	34,715	77,226	74,477	77,145	76,283	1,277	1,674
inf	1,645	1,642	1,622	1,602	1,605	1,604	1,681	1,664	1,664	35,842	35,109	36,587	79,649	78,021	81,305	79,658	1,341	1,683

Table 29: Table containing the spectrophotometric values and dissolution data of formula 2D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,197	0,197	0,196	0,084	0,085	0,086	0,174	0,175	0,174	3,792	1,769	3,384	8,427	3,931	7,521	6,626	1,941	29,296
5	0,761	0,752	0,756	0,593	0,596	0,596	0,633	0,629	0,630	13,992	11,046	11,701	31,093	24,547	26,001	27,214	2,807	10,313
10	1,487	1,478	1,482	1,394	1,393	1,394	1,296	1,295	1,297	27,269	25,622	23,863	60,598	56,938	53,029	56,855	3,090	5,436
15	1,930	1,956	1,946	1,962	1,917	1,936	1,805	1,742	1,750	35,811	35,674	32,530	79,580	79,275	72,288	77,048	3,368	4,371
30	2,248	2,266	2,236	2,162	2,216	2,211	2,037	2,021	2,027	41,571	40,557	37,487	92,381	90,128	83,304	88,604	3,859	4,355
60	2,316	2,320	2,309	2,238	2,239	2,248	2,121	2,198	2,174	42,985	41,600	40,163	95,522	92,444	89,252	92,406	2,560	2,770
90	2,292	2,303	2,298	2,243	2,263	2,254	2,172	2,138	2,156	42,896	42,036	40,220	95,325	93,413	89,378	92,705	2,479	2,674
120	2,281	2,205	2,263	2,291	2,368	2,342	2,265	2,259	2,341	42,255	43,729	42,860	93,900	97,176	95,244	95,440	1,344	1,409
180	2,303	2,269	2,280	2,159	2,159	2,174	2,184	2,156	2,159	43,106	40,876	40,871	95,791	90,836	90,825	92,484	2,338	2,528
240	2,308	2,236	2,296	2,267	2,214	2,209	2,128	2,151	2,163	43,264	42,297	40,739	96,143	93,994	90,532	93,556	2,312	2,471
360	2,429	2,292	2,297	2,295	2,310	2,306	2,275	2,189	2,191	44,572	43,864	42,245	99,048	97,475	93,878	96,801	2,164	2,235
inf	2,302	2,301	2,301	2,285	2,293	2,284	2,235	2,243	2,217	43,610	43,795	42,717	96,911	97,321	94,926	96,386	1,046	1,085

Table 30: Table containing the spectrophotometric values and dissolution data of formula 2D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,421	0,410	0,417	0,263	0,276	0,271	0,491	0,494	0,493	8,639	5,724	10,166	19,199	12,720	22,591	18,170	4,095	22,537
5	1,009	1,086	1,043	0,864	0,856	0,860	1,397	1,216	1,324	21,287	17,549	26,621	47,304	38,997	59,157	48,486	8,273	17,062
10	1,795	2,007	1,821	1,598	1,322	1,469	1,399	1,406	1,405	37,964	29,708	28,579	84,364	66,018	63,508	71,297	9,297	13,039
15	2,141	1,854	1,898	2,040	1,663	1,567	1,954	2,037	2,009	39,971	35,745	40,682	88,825	79,433	90,404	86,221	4,843	5,617
30	1,819	2,100	2,107	1,810	1,980	1,963	2,037	2,038	1,936	41,080	39,161	40,977	91,289	87,024	91,061	89,791	1,959	2,182
60	2,305	1,931	1,941	1,833	1,763	1,657	1,977	2,075	1,937	42,318	36,032	41,043	94,040	80,071	91,207	88,439	6,030	6,818
90	1,973	2,069	2,013	2,131	1,949	1,974	1,960	1,947	1,904	41,730	41,567	40,083	92,734	92,371	89,074	91,393	1,647	1,802
120	2,016	2,116	2,035	2,312	2,370	1,978	2,366	2,285	2,309	42,700	45,831	47,960	94,889	101,847	106,577	101,104	4,801	4,748
180	1,966	2,112	2,108	1,924	2,092	2,035	2,263	2,113	2,097	43,055	42,016	44,964	95,678	93,370	99,920	96,323	2,713	2,816
240	1,903	2,047	2,003	1,799	1,950	1,983	1,935	2,083	1,943	41,727	40,117	41,788	92,726	89,149	92,863	91,580	1,719	1,877
360	1,903	1,762	1,822	1,931	1,921	1,911	2,176	2,314	2,247	38,842	40,533	47,187	86,317	90,073	104,860	93,750	8,005	8,538
inf	1,973	1,993	2,096	1,886	1,904	1,906	1,889	1,895	1,936	41,306	40,300	40,658	91,791	89,556	90,351	90,566	0,925	1,021

Dissolution results Formulation 2E

Table 31: Table containing the spectrophotometric values and dissolution data of formula 2E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,008	0,011	0,010	0,013	0,011	0,011	0,009	0,008	0,008	0,692	0,734	0,663	1,537	1,631	1,474	1,547	0,064	4,163
5	0,019	0,020	0,019	0,022	0,022	0,022	0,016	0,016	0,016	0,903	0,949	0,826	2,007	2,109	1,836	1,984	0,113	5,671
10	0,064	0,068	0,065	0,072	0,070	0,071	0,062	0,062	0,063	1,875	1,986	1,804	4,168	4,414	4,010	4,197	0,166	3,966
15	0,173	0,173	0,173	0,164	0,163	0,165	0,156	0,157	0,157	4,128	3,944	3,793	9,174	8,764	8,428	8,789	0,305	3,471
30	0,324	0,318	0,322	0,309	0,309	0,309	0,315	0,305	0,308	7,266	6,998	7,005	16,147	15,552	15,566	15,755	0,277	1,759
60	0,514	0,513	0,514	0,512	0,512	0,512	0,527	0,523	0,525	11,332	11,288	11,565	25,182	25,085	25,699	25,322	0,270	1,065
90	0,716	0,716	0,717	0,678	0,682	0,681	0,707	0,716	0,714	15,639	14,879	15,546	34,754	33,064	34,546	34,121	0,752	2,205
120	0,839	0,838	0,838	0,777	0,779	0,778	0,827	0,826	0,867	18,281	17,000	18,311	40,625	37,778	40,691	39,698	1,358	3,421
180	0,945	0,951	0,950	0,876	0,860	0,866	0,894	0,907	0,904	20,691	18,978	19,705	45,980	42,173	43,788	43,980	1,560	3,547
240	0,995	0,998	0,998	0,907	0,913	0,907	0,990	0,978	0,980	21,817	19,949	21,497	48,482	44,331	47,772	46,862	1,813	3,868
360	1,099	1,089	1,096	0,974	0,972	0,980	1,058	1,039	1,034	23,981	21,439	22,898	53,290	47,643	50,885	50,606	2,314	4,573
inf	1,147	1,140	1,145	1,035	1,029	1,030	1,069	1,117	1,120	24,061	22,729	24,245	53,469	50,509	53,877	52,618	1,501	2,852

Table 32: Table containing the spectrophotometric values and dissolution data of formula 2E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,029	0,029	0,029	0,032	0,040	0,040	0,052	0,052	0,052	0,745	0,894	1,162	1,655	1,987	2,583	2,075	0,384	18,504
5	0,173	0,171	0,173	0,254	0,250	0,250	0,310	0,310	0,309	3,353	4,795	5,855	7,450	10,655	13,011	10,372	2,279	21,972
10	0,550	0,547	0,548	0,696	0,693	0,694	0,806	0,807	0,805	10,207	12,870	14,906	22,682	28,599	33,124	28,135	4,275	15,196
15	0,977	0,971	0,974	1,141	1,140	1,140	1,284	1,277	1,279	17,999	21,048	23,606	39,999	46,773	52,459	46,410	5,093	10,975
30	1,536	1,544	1,541	1,660	1,662	1,682	1,771	1,746	1,749	28,395	30,757	32,385	63,101	68,350	71,968	67,806	3,640	5,369
60	1,708	1,737	1,710	1,864	1,901	1,894	1,931	1,935	1,950	31,785	34,893	35,889	70,634	77,539	79,753	75,975	3,883	5,111
90	1,968	2,069	1,994	2,027	2,043	2,039	2,059	2,063	2,061	37,269	37,816	38,305	82,821	84,037	85,123	83,993	0,940	1,120
120	1,934	1,899	1,899	1,978	2,081	2,048	2,072	2,095	2,079	35,661	38,011	38,907	79,246	84,468	86,461	83,392	3,042	3,648
180	1,915	1,894	1,898	2,069	2,073	2,071	2,069	2,069	2,071	35,708	38,856	38,886	79,352	86,346	86,414	84,037	3,313	3,942
240	1,938	1,900	1,919	2,080	2,084	2,079	2,094	2,132	2,109	36,205	39,248	39,855	80,455	87,219	88,567	85,414	3,549	4,155
360	1,965	1,984	1,974	2,111	2,114	2,115	2,107	2,119	2,109	37,401	40,048	40,076	83,113	88,995	89,058	87,056	2,788	3,202
inf	1,985	1,987	1,985	2,108	2,107	2,084	2,172	2,180	2,169	39,636	40,015	41,411	88,080	88,921	92,025	89,676	1,697	1,892

Table 33: Table containing the spectrophotometric values and dissolution data of formula 2E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,000	0,000	0,000	0,016	0,016	0,016	0,000	0,000	0,000	0,320	0,639	0,320	0,711	1,421	0,711	0,948	0,335	35,300
5	0,174	0,165	0,171	0,251	0,261	0,257	0,201	0,211	0,206	3,723	5,445	4,445	8,273	12,100	9,879	10,084	1,569	15,563
10	0,571	0,583	0,583	0,675	0,678	0,675	0,646	0,644	0,649	11,912	13,866	13,271	26,470	30,814	29,491	28,925	1,818	6,285
15	1,009	1,006	1,007	1,061	1,058	1,054	1,077	1,144	1,096	20,552	21,580	22,523	45,671	47,956	50,051	47,892	1,789	3,735
30	1,505	1,534	1,521	1,547	1,565	1,549	1,557	1,549	1,550	30,911	31,619	31,575	68,691	70,264	70,166	69,707	0,719	1,032
60	1,781	1,782	1,785	1,699	1,706	1,701	1,726	1,880	1,795	36,336	34,757	36,712	80,747	77,237	81,582	79,855	1,882	2,357
90	1,841	1,875	1,852	1,840	1,737	1,789	1,962	1,852	1,879	37,998	36,677	38,869	84,440	81,505	86,375	84,107	2,002	2,380
120	1,817	1,710	1,801	1,921	1,930	1,920	1,985	1,920	1,936	36,609	39,579	40,062	81,353	87,953	89,027	86,111	3,393	3,940
180	1,854	2,104	1,963	1,954	2,380	2,002	1,710	1,846	1,822	40,757	43,552	37,189	90,571	96,782	82,643	89,998	5,786	6,429
240	1,725	1,861	1,792	1,774	1,813	1,783	1,759	1,892	1,822	37,362	37,350	38,021	83,026	82,999	84,491	83,505	0,697	0,835
360	1,862	1,792	1,797	1,630	1,832	1,698	1,714	1,781	1,773	38,050	36,151	36,858	84,556	80,336	81,908	82,267	1,741	2,117
inf	1,670	1,683	1,661	1,755	1,789	1,757	1,772	1,781	1,791	36,702	37,284	37,558	81,561	82,854	83,463	82,626	0,793	0,960

Dissolution results Formulation 2F

Table 34: Table containing the spectrophotometric values and dissolution data of formula 2F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,007	0,006	0,006	0,011	0,012	0,012	0,009	0,007	0,008	0,624	0,736	0,658	1,387	1,635	1,463	1,495	0,104	6,953
5	0,021	0,022	0,022	0,050	0,047	0,048	0,029	0,028	0,029	0,946	1,505	1,095	2,101	3,345	2,432	2,626	0,526	20,026
10	0,089	0,093	0,093	0,154	0,155	0,155	0,106	0,107	0,107	2,422	3,744	2,733	5,382	8,320	6,074	6,592	1,254	19,030
15	0,254	0,243	0,244	0,334	0,339	0,339	0,262	0,268	0,266	5,679	7,581	6,066	12,620	16,846	13,481	14,316	1,823	12,736
30	0,462	0,457	0,458	0,570	0,576	0,570	0,484	0,483	0,483	10,152	12,546	10,667	22,561	27,881	23,705	24,716	2,286	9,251
60	0,784	0,787	0,790	0,925	0,929	0,922	0,799	0,799	0,799	17,085	20,025	17,349	37,967	44,501	38,554	40,340	2,952	7,317
90	1,110	1,109	1,088	1,196	1,195	1,196	1,049	1,064	1,053	23,788	25,801	22,813	52,862	57,336	50,695	53,631	2,765	5,156
120	1,223	1,238	1,235	1,306	1,339	1,336	1,266	1,284	1,274	26,636	28,684	27,534	59,192	63,742	61,187	61,374	1,862	3,035
180	1,347	1,350	1,347	1,447	1,421	1,431	1,354	1,339	1,343	29,208	31,066	29,161	64,907	69,036	64,803	66,249	1,972	2,976
240	1,406	1,419	1,419	1,515	1,513	1,507	1,454	1,438	1,439	30,763	32,879	31,382	68,361	73,064	69,737	70,388	1,974	2,805
360	1,518	1,520	1,498	1,574	1,584	1,584	1,511	1,499	1,497	32,965	34,506	32,781	73,256	76,679	72,847	74,261	1,718	2,314
inf	1,518	1,514	1,516	1,629	1,622	1,626	1,500	1,504	1,503	33,900	35,635	32,951	75,333	79,188	73,225	75,915	2,469	3,252

Table 35: Table containing the spectrophotometric values and dissolution data of formula 2F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,128	0,128	0,128	0,113	0,115	0,114	0,118	0,119	0,118	2,543	2,290	2,372	5,651	5,088	5,271	5,337	0,234	4,393
5	0,509	0,496	0,498	0,420	0,420	0,420	0,454	0,422	0,437	9,335	7,862	8,185	20,745	17,471	18,190	18,802	1,405	7,474
10	1,062	1,058	1,057	0,942	0,943	0,942	0,922	0,923	0,923	19,537	17,404	17,051	43,417	38,676	37,892	39,995	2,441	6,102
15	1,557	1,600	1,576	1,414	1,384	1,393	1,371	1,366	1,366	29,075	25,765	25,236	64,610	57,255	56,080	59,315	3,775	6,364
30	1,865	1,880	1,866	1,783	1,759	1,760	1,658	1,656	1,673	34,557	32,642	30,726	76,792	72,537	68,279	72,536	3,475	4,791
60	1,917	1,908	1,910	1,879	1,983	1,980	1,939	1,966	1,953	35,492	36,094	36,177	78,870	80,208	80,393	79,823	0,678	0,850
90	1,965	1,950	1,961	1,910	1,908	1,909	1,905	1,912	1,909	36,540	35,590	35,576	81,201	79,089	79,057	79,782	1,003	1,257
120	1,915	1,981	1,987	1,883	1,876	1,879	1,927	1,928	1,930	36,781	35,244	36,123	81,736	78,319	80,273	80,110	1,400	1,747
180	1,978	1,976	1,981	1,961	1,921	1,943	1,917	1,959	1,953	37,293	36,566	36,584	82,874	81,258	81,299	81,810	0,752	0,919
240	1,957	1,945	1,946	2,014	1,937	1,963	1,976	1,981	1,979	36,965	37,308	37,427	82,143	82,908	83,172	82,741	0,436	0,527
360	2,007	1,910	1,943	1,923	1,935	1,931	1,933	1,992	1,963	37,238	36,744	37,337	82,751	81,653	82,971	82,458	0,576	0,699
inf	1,901	1,936	1,903	1,925	1,929	1,921	1,932	1,948	1,938	36,931	36,854	37,105	82,069	81,898	82,455	82,141	0,233	0,284

Table 36: Table containing the spectrophotometric values and dissolution data of formula 2F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,032	0,034	0,031	0,021	0,018	0,019	0,025	0,023	0,023	0,961	0,705	0,793	2,135	1,567	1,763	1,822	0,235	12,919
5	0,242	0,239	0,241	0,204	0,205	0,203	0,262	0,261	0,261	5,135	4,401	5,551	11,411	9,780	12,336	11,176	1,057	9,457
10	0,672	0,684	0,671	0,656	0,654	0,655	0,751	0,742	0,748	13,862	13,442	15,293	30,805	29,871	33,984	31,554	1,761	5,580
15	1,109	1,085	1,090	1,091	1,087	1,085	1,235	1,237	1,235	22,325	22,172	25,150	49,610	49,272	55,889	51,590	3,043	5,898
30	1,488	1,612	1,509	1,648	1,467	1,479	1,562	1,507	1,483	31,272	31,168	30,919	69,493	69,262	68,708	69,154	0,329	0,476
60	1,788	1,707	1,764	1,838	1,838	1,902	1,682	1,697	1,689	35,782	37,893	34,524	79,516	84,207	76,720	80,148	3,089	3,854
90	1,872	1,832	1,839	1,742	1,865	1,824	1,996	1,714	1,840	37,864	37,119	37,929	84,142	82,486	84,287	83,638	0,817	0,977
120	1,723	1,700	1,702	1,745	1,762	1,753	1,755	1,770	1,761	35,287	36,183	36,371	78,416	80,407	80,825	79,882	1,051	1,316
180	1,888	1,906	1,881	2,019	1,737	1,792	1,722	1,679	1,579	39,139	38,298	34,534	86,975	85,106	76,741	82,941	4,450	5,365
240	1,766	1,869	1,861	1,796	1,801	1,797	1,707	1,713	1,720	38,158	37,475	35,773	84,797	83,278	79,496	82,524	2,229	2,701
360	1,622	1,673	1,702	1,704	1,702	1,689	1,912	1,863	1,873	35,033	35,682	39,358	77,850	79,294	87,462	81,535	4,232	5,190
inf	1,648	1,622	1,622	1,689	1,682	1,698	1,663	1,687	1,663	35,182	35,703	35,332	78,182	79,340	78,515	78,679	0,487	0,619

Dissolution results Formulation 3A

Table 37: Table containing the spectrophotometric values and dissolution data of formula 3A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,020	0,020	0,021	0,038	0,038	0,037	0,040	0,043	0,044	0,918	1,282	1,377	2,041	2,848	3,061	2,650	0,439	16,585
5	0,112	0,109	0,109	0,152	0,152	0,152	0,165	0,164	0,164	2,806	3,685	3,946	6,236	8,189	8,768	7,731	1,083	14,014
10	0,282	0,282	0,282	0,378	0,378	0,379	0,374	0,372	0,372	6,419	8,453	8,333	14,265	18,785	18,518	17,189	2,071	12,047
15	0,491	0,491	0,492	0,606	0,605	0,605	0,571	0,570	0,571	10,843	13,251	12,520	24,095	29,448	27,821	27,121	2,241	8,262
30	0,674	0,673	0,674	0,749	0,751	1,751	0,735	0,735	0,735	14,723	23,347	16,040	32,718	51,882	35,645	40,082	8,429	21,031
60	0,820	0,816	0,818	0,894	0,897	0,895	0,858	0,853	0,856	17,817	19,528	18,656	39,593	43,397	41,458	41,483	1,553	3,743
90	0,969	0,973	0,969	0,997	0,991	0,993	0,987	0,984	0,986	21,115	21,691	21,474	46,922	48,202	47,719	47,614	0,528	1,109
120	1,048	1,045	1,046	1,060	1,077	1,077	1,044	1,048	1,046	22,819	23,431	22,851	50,709	52,068	50,781	51,186	0,624	1,220
180	1,124	1,125	1,125	1,130	1,125	1,129	1,104	1,107	1,105	24,584	24,748	24,216	54,631	54,996	53,814	54,480	0,494	0,907
240	1,191	1,182	1,190	1,161	1,161	1,161	1,159	1,165	1,163	26,035	25,568	25,544	57,857	56,817	56,765	57,146	0,503	0,880
360	1,211	1,235	1,225	1,204	1,208	1,208	1,187	1,191	1,191	26,935	26,663	26,248	59,857	59,250	58,330	59,145	0,628	1,061
inf	1,199	1,207	1,209	1,199	1,200	1,198	1,191	1,191	1,191	26,541	26,640	26,422	58,981	59,199	58,715	58,965	0,198	0,336

Table 38: Table containing the spectrophotometric values and dissolution data of formula 3A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,605	0,616	0,613	0,445	0,444	0,449	0,602	0,605	0,606	11,331	8,331	11,206	25,180	18,513	24,902	22,865	3,079	13,468
5	1,497	1,472	1,481	1,232	1,218	1,220	1,522	1,492	1,503	27,250	22,501	27,655	60,555	50,002	61,456	57,337	5,200	9,069
10	2,097	2,002	2,065	1,947	1,949	1,944	2,076	2,068	2,072	37,792	35,775	38,108	83,983	79,501	84,684	82,722	2,296	2,776
15	2,204	2,208	2,209	2,184	2,165	2,170	2,251	2,302	2,300	40,762	40,095	42,178	90,583	89,100	93,728	91,137	1,930	2,117
30	2,264	2,240	2,263	2,245	2,261	2,254	2,358	2,300	2,320	41,872	41,765	43,167	93,048	92,812	95,927	93,929	1,416	1,508
60	2,239	2,137	2,211	2,116	2,094	2,099	2,230	2,164	2,180	41,011	39,264	40,948	91,136	87,254	90,996	89,795	1,798	2,002
90	2,117	2,178	2,165	2,204	2,133	2,141	2,095	2,112	2,204	40,468	40,501	40,175	89,929	90,002	89,278	89,736	0,326	0,363
120	2,247	2,195	2,137	2,139	2,137	2,141	2,194	2,178	2,171	41,398	40,347	41,197	91,996	89,660	91,549	91,068	1,012	1,112
180	2,235	2,240	2,232	2,181	2,120	2,160	2,182	2,267	2,193	42,400	40,840	42,020	94,222	90,756	93,378	92,785	1,476	1,591
240	2,246	2,190	2,203	2,124	2,131	2,131	2,210	2,269	2,209	42,212	40,596	42,521	93,805	90,214	94,492	92,837	1,876	2,020
360	2,236	2,241	2,236	2,171	2,126	2,131	2,282	2,296	2,261	42,887	41,062	43,664	95,305	91,248	97,031	94,528	2,424	2,564
inf	2,237	2,241	2,237	2,184	2,161	2,180	2,210	2,264	2,211	42,679	41,874	42,959	94,842	93,054	95,465	94,454	1,022	1,082

Table 39: Table containing the spectrophotometric values and dissolution data of formula 3A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,282	0,283	0,288	0,276	0,271	0,270	0,469	0,472	0,470	6,008	5,758	9,726	13,351	12,796	21,613	15,920	4,032	25,328
5	0,795	0,811	0,809	0,759	0,757	0,758	1,237	1,245	1,269	16,452	15,514	25,379	36,561	34,475	56,398	42,478	9,880	23,259
10	1,642	1,591	1,597	1,242	1,286	1,264	1,880	1,669	1,694	32,647	25,710	35,465	72,549	57,134	78,810	69,498	9,108	13,106
15	1,956	1,900	1,943	1,411	1,558	1,541	2,117	1,980	1,994	39,282	30,640	41,315	87,293	68,088	91,810	82,397	10,285	12,482
30	2,020	1,920	1,965	1,602	1,641	1,611	1,934	1,956	1,949	40,202	33,100	39,856	89,338	73,555	88,570	83,821	7,266	8,668
60	1,982	1,885	1,933	1,764	1,796	1,781	2,011	2,335	2,294	39,717	36,520	45,410	88,260	81,155	100,911	90,108	8,171	9,068
90	2,069	2,356	2,305	1,890	1,933	1,963	2,141	2,096	2,063	46,138	39,689	43,394	102,528	88,197	96,431	95,719	5,872	6,135
120	2,052	1,994	2,036	1,898	1,903	1,893	1,987	1,961	1,973	42,067	39,291	41,100	93,482	87,313	91,333	90,709	2,557	2,818
180	2,295	2,302	2,299	1,906	1,838	1,869	2,001	2,047	2,037	47,714	38,964	42,416	106,031	86,586	94,257	95,625	7,997	8,363
240	2,263	2,349	2,279	1,921	2,034	1,963	1,956	2,296	2,092	47,938	41,205	44,367	106,528	91,567	98,594	98,896	6,112	6,180
360	2,014	2,147	2,044	2,471	2,402	2,390	2,417	2,403	2,400	43,618	50,388	50,432	96,929	111,973	112,071	106,991	7,115	6,650
inf	2,412	2,411	2,411	2,440	2,441	2,430	2,401	2,400	2,411	50,829	50,975	50,654	112,954	113,278	112,565	112,933	0,292	0,258

Dissolution results Formulation 3B

Table 40: Table containing the spectrophotometric values and dissolution data of formula 3B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,056	0,055	0,056	0,033	0,033	0,033	0,031	0,032	0,031	1,657	1,180	1,145	3,682	2,621	2,544	2,949	0,519	17,608
5	0,209	0,206	0,206	0,159	0,158	0,159	0,144	0,143	0,144	4,839	3,825	3,503	10,753	8,500	7,783	9,012	1,265	14,039
10	0,413	0,411	0,412	0,355	0,357	0,358	0,339	0,339	0,337	9,161	7,991	7,602	20,357	17,757	16,893	18,336	1,472	8,029
15	0,584	0,586	0,583	0,558	0,558	0,558	0,548	0,547	0,547	12,822	12,252	12,030	28,494	27,226	26,734	27,485	0,741	2,697
30	0,738	0,737	0,777	0,724	0,722	0,722	0,673	0,669	0,673	16,370	15,768	14,699	36,377	35,039	32,664	34,693	1,536	4,426
60	0,935	0,935	0,936	0,858	0,852	0,854	0,849	0,856	0,854	20,334	18,620	18,571	45,187	41,379	41,270	42,612	1,821	4,274
90	1,088	1,097	1,095	1,078	1,078	1,081	1,099	1,096	1,094	23,755	23,425	23,781	52,789	52,056	52,847	52,564	0,360	0,685
120	1,238	1,229	1,235	1,186	1,195	1,192	1,327	1,323	1,325	26,829	25,899	28,701	59,621	57,554	63,781	60,319	2,589	4,293
180	1,341	1,333	1,337	1,298	1,298	1,298	1,425	1,427	1,417	29,137	28,278	30,901	64,750	62,839	68,669	65,419	2,427	3,709
240	1,495	1,497	1,495	1,463	1,457	1,461	1,540	1,528	1,536	32,615	31,832	33,411	72,477	70,738	74,247	72,487	1,433	1,976
360	1,611	1,618	1,617	1,564	1,554	1,559	1,611	1,604	1,611	35,301	34,068	35,139	78,447	75,706	78,087	77,413	1,216	1,571
inf	1,621	1,622	1,620	1,569	1,570	1,559	1,619	1,601	1,616	35,162	34,407	35,403	78,138	76,459	78,673	77,757	0,943	1,213

Table 41: Table containing the spectrophotometric values and dissolution data of formula 3B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	1,014	1,015	1,014	0,588	0,588	0,588	0,844	0,846	0,844	18,661	10,909	15,576	41,468	24,242	34,613	33,441	7,081	21,174
5	2,044	2,034	2,041	1,261	1,262	1,261	1,876	1,958	1,946	37,401	23,206	35,337	83,114	51,569	78,526	71,070	13,916	19,580
10	2,361	2,411	2,411	1,893	1,905	1,904	2,351	2,401	2,409	44,064	34,958	43,901	97,920	77,685	97,558	91,055	9,455	10,384
15	2,426	2,442	2,440	2,134	2,117	2,128	2,469	2,457	2,436	45,061	39,263	45,360	100,135	87,251	100,801	96,062	6,236	6,492
30	2,446	2,430	2,494	2,145	2,121	2,131	2,392	2,414	2,398	45,680	39,583	44,651	101,511	87,961	99,224	96,232	5,922	6,154
60	2,371	2,459	2,443	2,101	2,144	2,110	2,375	2,374	2,385	45,341	39,541	44,465	100,758	87,869	98,811	95,812	5,673	5,921
90	2,464	2,467	2,471	1,975	1,978	1,981	2,364	2,380	2,365	46,366	37,200	44,551	103,035	82,666	99,001	94,901	8,806	9,280
120	2,308	2,390	2,364	2,193	2,205	2,000	2,238	2,237	2,311	44,550	40,216	42,834	98,999	89,369	95,186	94,518	3,960	4,189
180	2,445	2,319	2,407	2,040	2,031	2,039	2,414	2,347	2,363	45,452	38,685	45,106	101,003	85,967	100,236	95,736	6,914	7,222
240	2,420	2,416	2,418	2,089	2,060	2,061	2,291	2,290	2,251	46,200	39,496	43,586	102,667	87,769	96,858	95,765	6,131	6,402
360	2,357	2,396	2,384	2,111	2,135	2,113	2,387	2,371	2,384	45,735	40,609	45,693	101,633	90,243	101,540	97,805	5,348	5,468
inf	2,425	2,428	2,399	2,147	2,143	2,161	2,407	2,393	2,389	44,927	41,379	46,220	99,838	91,954	102,712	98,168	4,548	4,633

Table 42: Table containing the spectrophotometric values and dissolution data of formula 3B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,487	0,489	0,488	0,498	0,494	0,500	0,852	0,862	0,861	10,085	10,262	17,485	22,410	22,804	38,856	28,024	7,661	27,339
5	1,140	1,155	1,143	1,154	1,156	1,122	1,724	1,613	1,673	23,293	23,258	33,815	51,762	51,684	75,144	59,530	11,041	18,546
10	1,659	1,614	1,641	1,685	1,732	1,704	2,274	2,218	2,249	33,256	34,638	45,540	73,903	76,974	101,199	84,025	12,208	14,529
15	1,995	2,108	2,039	2,037	2,017	2,094	2,217	2,300	2,301	41,624	41,678	46,303	92,498	92,618	102,896	96,004	4,874	5,077
30	1,988	1,857	1,993	1,994	1,812	1,899	2,398	2,393	2,400	39,836	38,954	49,042	88,525	86,565	108,982	94,691	10,137	10,705
60	1,975	2,383	2,002	1,899	2,045	1,940	2,315	2,355	2,332	43,522	40,362	48,049	96,715	89,694	106,776	97,729	7,011	7,174
90	2,141	2,128	2,142	1,924	1,922	1,930	2,384	2,389	2,400	44,099	39,859	49,446	97,997	88,575	109,880	98,818	8,717	8,821
120	2,438	1,858	2,140	1,849	2,027	2,002	2,118	1,918	1,994	44,505	40,745	42,089	98,900	90,544	93,531	94,325	3,457	3,665
180	1,924	1,905	1,901	2,180	1,987	1,991	2,456	2,387	2,410	40,031	42,827	50,467	88,957	95,172	112,149	98,759	9,802	9,925
240	2,111	2,242	2,002	1,998	1,983	1,991	2,375	2,333	2,399	44,413	41,822	49,767	98,696	92,938	110,593	100,742	7,352	7,297
360	2,415	2,443	2,428	2,006	2,006	2,016	2,407	2,411	2,399	50,858	42,418	50,762	113,018	94,263	112,803	106,695	8,791	8,239
inf	2,296	2,302	2,302	2,002	2,114	1,996	2,409	2,400	2,390	47,468	43,200	50,907	105,485	96,001	113,126	104,871	7,005	6,680

Dissolution results Formulation 3C

Table 43: Table containing the spectrophotometric values and dissolution data of formula 3C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,046	0,046	0,047	0,032	0,031	0,032	0,046	0,045	0,044	1,465	1,160	1,435	3,255	2,578	3,188	3,007	0,305	10,132
5	0,196	0,202	0,203	0,152	0,151	0,152	0,222	0,228	0,226	4,694	3,675	5,223	10,432	8,167	11,607	10,069	1,428	14,179
10	0,483	0,483	0,482	0,392	0,405	0,402	0,512	0,513	0,512	10,639	8,893	11,264	23,643	19,763	25,032	22,813	2,229	9,773
15	0,708	0,708	0,708	0,620	0,618	0,619	0,723	0,720	0,721	15,419	13,534	15,707	34,264	30,076	34,904	33,081	2,141	6,473
30	0,867	0,862	0,863	0,785	0,786	0,786	0,835	0,833	0,832	18,768	17,109	18,140	41,706	38,019	40,310	40,012	1,520	3,799
60	0,960	0,963	0,964	0,905	0,905	0,905	0,939	0,945	0,942	20,933	19,701	20,515	46,517	43,780	45,590	45,296	1,136	2,509
90	1,094	1,090	1,092	0,997	0,996	0,998	1,083	1,084	1,082	23,764	21,730	23,578	52,810	48,290	52,395	51,165	2,040	3,987
120	1,064	1,061	1,063	1,093	1,092	1,093	1,100	1,101	1,102	23,278	23,850	24,085	51,729	53,000	53,521	52,750	0,753	1,427
180	1,071	1,062	1,063	1,106	1,102	1,106	1,139	1,139	1,139	23,456	24,233	25,007	52,124	53,851	55,570	53,848	1,407	2,613
240	1,317	1,319	1,319	1,169	1,161	1,162	1,163	1,166	1,166	28,885	25,603	25,681	64,189	56,895	57,069	59,384	3,398	5,722
360	1,345	1,348	1,344	1,227	1,214	1,222	1,245	1,237	1,237	29,612	26,931	27,383	65,804	59,847	60,850	62,167	2,604	4,188
inf	1,323	1,315	1,326	1,197	1,201	1,202	1,192	1,189	1,192	27,500	26,639	26,505	61,112	59,197	58,901	59,736	0,980	1,640

Table 44: Table containing the spectrophotometric values and dissolution data of formula 3C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,234	0,234	0,233	0,062	0,060	0,060	0,223	0,223	0,223	4,467	1,318	4,269	9,927	2,928	9,487	7,447	3,201	42,978
5	0,945	0,947	0,945	0,344	0,355	0,349	0,804	0,795	0,797	17,439	6,572	14,764	38,754	14,603	32,808	28,722	10,274	35,771
10	1,860	1,850	1,856	0,959	0,957	0,958	1,585	1,643	1,621	34,071	17,681	29,710	75,714	39,292	66,023	60,343	15,402	25,524
15	2,027	2,052	2,051	1,348	1,330	1,339	1,849	1,829	1,831	37,672	24,704	33,876	83,716	54,898	75,280	71,298	12,097	16,967
30	2,253	2,146	2,183	1,489	1,477	1,490	1,981	1,927	1,963	40,624	27,495	36,257	90,275	61,101	80,572	77,316	12,131	15,690
60	2,412	2,297	2,373	1,630	1,611	1,619	2,043	2,028	2,036	43,875	30,102	37,878	97,500	66,894	84,172	82,856	12,530	15,122
90	2,378	2,360	2,370	1,821	1,810	1,811	2,151	2,210	2,194	44,272	33,785	40,798	98,382	75,077	90,662	88,040	9,693	11,010
120	2,337	2,411	2,396	1,958	1,957	1,943	2,244	2,246	2,241	44,728	36,487	42,084	99,394	81,082	93,520	91,332	7,635	8,359
180	2,364	2,363	2,393	2,071	2,067	2,069	2,355	2,282	2,394	44,827	38,802	44,126	99,617	86,227	98,057	94,633	5,978	6,317
240	2,363	2,426	2,421	2,051	2,007	2,044	2,210	2,184	2,194	45,608	38,373	41,678	101,351	85,274	92,618	93,081	6,571	7,060
360	2,372	2,332	2,328	2,139	2,100	2,129	2,342	2,404	2,372	44,773	40,196	45,117	99,496	89,324	100,261	96,360	4,985	5,173
inf	2,382	2,407	2,416	2,120	2,100	2,109	2,197	2,206	2,180	43,028	40,165	42,115	95,619	89,257	93,588	92,821	2,653	2,858

Table 45: Table containing the spectrophotometric values and dissolution data of formula 3C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,163	0,155	0,157	0,270	0,254	0,260	0,129	0,132	0,128	3,487	5,549	2,911	7,750	12,330	6,468	8,849	2,516	28,436
5	0,651	0,658	0,654	0,938	0,959	0,940	0,532	0,526	0,531	13,424	19,263	10,932	29,830	42,807	24,294	32,310	7,759	24,012
10	1,512	1,486	1,491	2,001	1,994	1,997	1,225	1,233	1,229	30,339	40,401	24,977	67,420	89,781	55,505	70,902	14,208	20,039
15	1,751	1,778	1,763	1,935	1,930	1,834	1,462	1,697	1,602	35,859	38,663	32,269	79,687	85,919	71,708	79,105	5,816	7,352
30	2,153	2,326	2,291	2,179	2,239	2,219	1,771	1,822	1,813	45,907	45,134	36,744	102,015	100,299	81,654	94,656	9,220	9,741
60	2,058	2,210	2,194	1,822	1,756	1,882	1,792	1,802	1,806	44,103	37,526	36,911	98,007	83,392	82,025	87,808	7,234	8,238
90	2,174	2,249	2,202	2,372	2,112	2,248	1,914	1,869	1,902	45,425	46,211	39,005	100,944	102,691	86,678	96,771	7,172	7,412
120	2,112	2,260	2,208	1,945	1,719	1,973	1,954	1,968	1,933	45,375	39,161	40,346	100,834	87,025	89,657	92,505	5,987	6,472
180	2,310	2,319	2,213	1,977	2,000	1,933	1,997	1,905	1,963	47,366	41,193	40,634	105,257	91,540	90,297	95,698	6,778	7,083
240	1,934	2,174	2,050	1,747	1,810	1,793	1,821	1,872	1,801	43,058	37,677	38,379	95,684	83,726	85,287	88,232	5,308	6,015
360	1,927	1,944	1,933	1,882	1,865	1,893	1,949	1,763	1,802	40,926	39,813	38,710	90,946	88,473	86,022	88,480	2,010	2,272
inf	1,835	1,810	1,843	2,003	1,995	1,993	2,002	1,963	2,166	41,577	42,355	43,029	92,393	94,122	95,619	94,045	1,318	1,402

Dissolution results Formulation 3D

Table 46: Table containing the spectrophotometric values and dissolution data of formula 3D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,013	0,014	0,014	0,020	0,020	0,020	0,011	0,011	0,011	0,781	0,912	0,726	1,735	2,027	1,613	1,792	0,173	9,678
5	0,057	0,057	0,057	0,094	0,094	0,094	0,041	0,043	0,042	1,686	2,462	1,374	3,748	5,471	3,053	4,091	1,017	24,856
10	0,178	0,179	0,180	0,262	0,261	0,262	0,153	0,153	0,153	4,252	5,990	3,706	9,449	13,312	8,235	10,332	2,164	20,950
15	0,358	0,354	0,356	0,468	0,468	0,469	0,314	0,314	0,314	7,982	10,356	7,097	17,737	23,014	15,770	18,840	3,058	16,232
30	0,530	0,531	0,532	0,556	0,667	0,667	0,462	0,461	0,458	11,698	13,805	10,205	25,996	30,679	22,678	26,451	3,282	12,408
60	0,744	0,744	0,745	0,880	0,880	0,881	0,644	0,636	0,631	16,231	19,125	13,966	36,069	42,500	31,036	36,535	4,692	12,842
90	0,934	0,934	0,935	1,158	1,158	1,158	0,828	0,828	0,829	20,297	25,046	18,047	45,104	55,657	40,103	46,955	6,483	13,808
120	1,121	1,126	1,124	1,305	1,305	1,306	1,079	1,082	1,081	24,371	28,269	23,432	54,158	62,821	52,072	56,350	4,654	8,259
180	1,283	1,283	1,283	1,444	1,440	1,437	1,249	1,253	1,253	27,843	31,254	27,145	61,873	69,454	60,323	63,883	3,990	6,245
240	1,383	1,385	1,381	1,513	1,515	1,512	1,392	1,397	1,394	30,097	32,951	30,276	66,883	73,225	67,281	69,129	2,900	4,196
360	1,536	1,539	1,541	1,614	1,612	1,599	1,477	1,497	1,486	33,515	35,118	32,376	74,477	78,039	71,948	74,821	2,499	3,340
inf	1,462	1,468	1,469	1,505	1,502	1,503	1,439	1,443	1,441	32,262	33,102	31,589	71,693	73,561	70,197	71,817	1,376	1,916

Table 47: Table containing the spectrophotometric values and dissolution data of formula 3D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,168	0,169	0,168	0,136	0,136	0,136	0,244	0,243	0,244	3,279	2,688	4,646	7,288	5,973	10,325	7,862	1,822	23,179
5	0,882	0,885	0,895	0,738	0,765	0,759	1,011	1,026	1,019	16,367	13,939	18,769	36,370	30,975	41,709	36,351	4,382	12,055
10	1,807	1,803	1,810	1,556	1,564	1,570	1,828	1,829	1,766	33,179	28,735	33,214	73,731	63,855	73,809	70,465	4,674	6,633
15	2,027	2,052	2,051	2,045	2,043	2,051	2,172	2,163	2,143	37,655	37,668	39,788	83,677	83,708	88,418	85,268	2,228	2,613
30	2,253	2,146	2,184	2,283	2,200	2,204	2,189	2,360	2,311	40,608	41,194	42,326	90,239	91,542	94,057	91,946	1,585	1,724
60	2,280	2,273	2,274	2,231	2,405	2,293	2,444	2,337	2,377	42,306	42,891	44,357	94,014	95,314	98,571	95,966	1,917	1,997
90	2,341	2,338	2,338	2,373	2,421	2,383	2,546	2,577	2,564	43,695	44,624	47,804	97,101	99,165	106,231	100,832	3,909	3,877
120	2,552	2,435	2,477	2,490	2,564	2,533	2,534	2,528	2,529	46,639	47,349	47,484	103,642	105,220	105,520	104,794	0,824	0,786
180	2,538	2,482	2,474	2,521	2,538	2,473	2,487	2,525	2,493	47,070	47,274	47,217	104,599	105,054	104,927	104,860	0,191	0,183
240	2,480	2,479	2,480	2,481	2,349	2,373	2,499	2,278	2,299	46,989	45,531	44,875	104,421	101,181	99,723	101,775	1,963	1,929
360	2,404	2,486	2,491	2,483	2,480	2,491	2,463	2,474	2,471	46,883	47,301	47,123	104,185	105,112	104,718	104,672	0,380	0,363
inf	2,432	2,397	2,422	2,414	2,400	2,411	2,496	2,479	2,470	46,688	46,162	47,595	103,751	102,583	105,767	104,034	1,315	1,264

Table 48: Table containing the spectrophotometric values and dissolution data of formula 3D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,071	0,062	0,071	0,073	0,075	0,072	0,013	0,018	0,016	1,684	1,787	0,634	3,742	3,970	1,409	3,040	1,157	38,069
5	0,512	0,514	0,515	0,561	0,562	0,563	0,343	0,352	0,347	10,594	11,565	7,275	23,541	25,700	16,167	21,803	4,081	18,719
10	1,162	1,194	1,173	1,270	1,303	1,290	1,010	1,024	1,011	23,909	26,141	20,658	53,130	58,090	45,906	52,375	5,003	9,552
15	1,636	1,862	1,713	1,723	1,664	1,673	1,741	1,491	1,622	35,253	34,271	32,833	78,341	76,158	72,963	75,820	2,209	2,913
30	1,930	1,900	1,873	1,765	2,163	1,922	1,762	1,954	1,893	38,725	39,718	38,046	86,055	88,263	84,546	86,288	1,526	1,769
60	1,862	2,017	1,932	1,905	2,381	1,933	1,940	1,909	1,933	39,657	42,396	39,404	88,126	94,213	87,564	89,968	3,010	3,346
90	1,893	2,177	2,180	2,226	2,387	2,263	1,979	1,986	1,969	42,805	47,002	40,635	95,122	104,449	90,300	96,623	5,873	6,079
120	2,012	1,974	1,989	2,124	1,855	1,928	1,969	2,112	2,103	41,203	40,799	42,516	91,562	90,664	94,480	92,235	1,629	1,766
180	1,856	2,013	1,994	2,405	2,117	2,243	1,735	1,738	1,793	40,672	46,739	36,632	90,381	103,864	81,405	91,883	9,230	10,046
240	1,969	1,926	1,942	2,233	2,200	2,208	2,114	1,759	1,803	40,718	46,162	39,558	90,484	102,582	87,907	93,658	6,398	6,831
360	1,762	1,761	1,770	2,377	2,353	2,302	1,871	1,891	1,880	37,308	49,014	39,548	82,907	108,920	87,885	93,237	11,274	12,092
inf	1,912	1,878	1,892	1,686	1,733	1,969	1,685	1,693	1,643	37,973	38,318	35,607	84,384	85,152	79,127	82,888	2,678	3,230

Dissolution results Formulation 3E

Table 49: Table containing the spectrophotometric values and dissolution data of formula 3E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,009	0,008	0,009	0,009	0,008	0,009	0,007	0,007	0,007	0,676	0,672	0,632	1,503	1,494	1,404	1,467	0,045	3,055
5	0,030	0,031	0,031	0,045	0,046	0,046	0,025	0,025	0,026	1,135	1,454	1,029	2,523	3,231	2,288	2,680	0,401	14,955
10	0,118	0,118	0,118	0,156	0,156	0,154	0,111	0,110	0,111	2,972	3,755	2,811	6,604	8,344	6,246	7,065	0,916	12,969
15	0,284	0,285	0,285	0,326	0,327	0,327	0,285	0,285	0,285	6,480	7,360	6,477	14,399	16,355	14,394	15,049	0,923	6,136
30	0,472	0,473	0,473	0,489	0,488	0,489	0,526	0,526	0,526	10,455	10,797	11,563	23,234	23,993	25,696	24,308	1,030	4,235
60	0,623	0,622	0,623	0,613	0,615	0,613	0,766	0,767	0,767	13,653	13,477	16,678	30,340	29,949	37,063	32,451	3,265	10,062
90	0,738	0,741	0,739	0,704	0,699	0,699	0,899	0,897	0,898	16,168	15,371	19,515	35,929	34,158	43,366	37,818	3,989	10,549
120	0,793	0,797	0,794	0,763	0,763	0,763	0,967	0,967	0,968	17,418	16,756	21,078	38,707	37,236	46,841	40,928	4,224	10,321
180	0,845	0,835	0,842	0,818	0,815	0,814	1,019	1,010	1,010	18,474	17,953	22,141	41,053	39,896	49,202	43,383	4,141	9,546
240	0,865	0,874	0,872	0,843	0,838	0,840	1,029	1,027	1,029	19,187	18,562	22,592	42,637	41,248	50,205	44,697	3,936	8,806
360	0,894	0,897	0,891	0,892	0,899	0,895	1,031	1,032	1,032	19,789	19,819	22,775	43,975	44,042	50,611	46,209	3,112	6,735
inf	0,902	0,901	0,936	0,911	0,910	0,907	1,030	1,029	1,029	21,078	20,214	22,843	46,840	44,920	50,761	47,507	2,431	5,117

Table 50: Table containing the spectrophotometric values and dissolution data of formula 3E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,023	0,022	0,022	0,099	0,098	0,098	0,025	0,025	0,025	0,618	2,002	0,671	1,372	4,450	1,491	2,438	1,424	58,399
5	0,147	0,148	0,149	0,507	0,514	0,511	0,190	0,189	0,189	2,916	9,512	3,663	6,480	21,139	8,140	11,920	6,554	54,983
10	0,599	0,594	0,596	1,384	1,369	1,370	0,664	0,657	0,660	11,080	25,263	12,244	24,621	56,141	27,209	35,990	14,288	39,698
15	1,030	1,029	1,030	2,022	2,010	2,019	1,213	1,211	1,220	19,019	37,093	22,391	42,264	82,429	49,759	58,150	17,438	29,988
30	1,523	1,522	1,523	2,303	2,358	2,357	1,680	1,709	1,690	28,089	43,155	31,209	62,419	95,900	69,354	75,891	14,429	19,013
60	1,755	1,728	1,729	2,525	2,564	2,543	2,185	2,149	2,163	32,141	47,110	39,973	71,425	104,689	88,829	88,314	13,585	15,382
90	1,797	1,789	1,788	2,299	2,294	2,291	1,898	1,940	1,894	33,299	42,832	35,557	73,998	95,183	79,014	82,732	9,039	10,926
120	1,859	1,857	1,858	2,461	2,454	2,484	1,957	1,979	1,963	34,689	46,188	36,767	77,087	102,640	81,705	87,144	11,118	12,758
180	1,871	1,836	1,852	2,365	2,420	2,383	2,018	1,979	1,982	34,789	45,037	37,449	77,309	100,082	83,221	86,871	9,649	11,107
240	1,929	1,947	1,933	2,509	2,457	2,440	2,012	1,953	1,959	36,487	46,718	37,321	81,081	103,818	82,936	89,278	10,309	11,547
360	1,908	1,842	1,876	2,446	2,410	2,428	1,933	2,002	2,002	35,577	46,229	37,594	79,061	102,731	83,542	88,444	10,266	11,608
inf	1,890	1,878	1,884	2,490	2,347	0,427	1,989	1,930	1,963	35,604	34,235	37,460	79,121	76,077	83,245	79,481	2,938	3,696

Table 51: Table containing the spectrophotometric values and dissolution data of formula 3E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,000	0,000	0,000	0,000	0,000	0,000	0,027	0,027	0,027	0,320	0,320	0,859	0,711	0,711	1,908	1,110	0,564	50,831
5	0,190	0,201	0,195	0,146	0,147	0,140	0,264	0,259	0,260	4,218	3,203	5,538	9,373	7,117	12,307	9,599	2,125	22,137
10	0,700	0,700	0,699	0,530	0,523	0,528	0,828	0,826	0,828	14,332	10,867	16,903	31,850	24,150	37,561	31,187	5,495	17,621
15	1,155	1,179	1,165	0,962	0,973	0,967	1,307	1,344	1,310	23,751	19,747	26,851	52,779	43,881	59,669	52,110	6,463	12,402
30	1,555	1,496	1,532	1,303	1,236	1,272	1,406	1,525	1,518	31,096	25,904	30,249	69,103	57,565	67,219	64,629	5,054	7,820
60	1,417	1,630	1,594	1,293	1,279	1,289	1,713	1,714	1,705	31,659	26,382	34,964	70,353	58,628	77,698	68,893	7,853	11,400
90	1,637	1,580	1,609	1,469	1,591	1,574	1,781	1,848	1,822	33,065	31,676	37,283	73,478	70,391	82,851	75,573	5,298	7,010
120	1,601	1,796	1,735	1,502	1,628	1,602	1,657	1,726	1,693	35,281	32,502	34,993	78,403	72,228	77,761	76,131	2,772	3,641
180	1,676	1,697	1,683	1,743	1,637	1,643	2,297	2,495	2,244	34,967	34,622	48,238	77,705	76,937	107,196	87,279	14,086	16,139
240	1,726	1,874	1,763	1,506	1,486	1,513	1,621	1,852	1,783	37,201	31,350	36,631	82,670	69,668	81,401	77,913	5,853	7,513
360	2,064	1,833	1,963	1,523	1,511	1,519	2,383	2,474	2,411	40,711	31,844	50,242	90,468	70,764	111,649	90,960	16,695	18,354
inf	2,097	2,101	2,094	1,596	1,590	1,633	2,401	2,416	2,401	42,590	33,780	50,175	94,644	75,066	111,500	93,737	14,888	15,883

Dissolution results Formulation 3F

Table 52: Table containing the spectrophotometric values and dissolution data of formula 3F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,008	0,008	0,008	0,030	0,031	0,031	0,036	0,035	0,036	0,653	1,131	1,243	1,452	2,514	2,763	2,243	0,568	25,342
5	0,025	0,024	0,025	0,142	0,141	0,142	0,106	0,103	0,104	1,009	3,461	2,683	2,243	7,690	5,962	5,298	2,273	42,897
10	0,099	0,097	0,099	0,346	0,343	0,343	0,284	0,285	0,284	2,557	7,721	6,470	5,683	17,158	14,377	12,406	4,888	39,398
15	0,233	0,233	0,233	0,546	0,545	0,545	0,483	0,485	0,485	5,385	11,982	10,692	11,966	26,626	23,759	20,784	6,344	30,523
30	0,405	0,404	0,405	0,732	0,734	0,734	0,657	0,657	0,658	9,016	15,989	14,380	20,037	35,530	31,955	29,174	6,624	22,705
60	0,622	0,615	0,622	0,895	0,907	0,903	0,818	0,813	0,813	13,570	19,601	17,753	30,154	43,558	39,450	37,721	5,607	14,864
90	0,823	0,778	0,793	0,870	0,870	0,867	0,966	0,963	0,966	17,378	19,020	20,994	38,618	42,268	46,654	42,513	3,285	7,727
120	0,914	0,907	0,907	1,219	1,229	1,228	1,171	1,171	1,171	19,810	26,590	25,431	44,022	59,089	56,513	53,208	6,580	12,366
180	1,037	1,037	1,037	1,290	1,279	1,280	1,241	1,233	1,238	22,588	27,944	26,955	50,194	62,098	59,900	57,398	5,172	9,011
240	1,187	1,175	1,176	1,402	1,382	1,392	1,352	1,350	1,351	25,695	30,375	29,490	57,100	67,501	65,534	63,378	4,511	7,118
360	1,287	1,281	1,291	1,491	1,490	1,488	1,454	1,449	1,475	28,073	32,586	31,910	62,385	72,414	70,911	68,570	4,416	6,440
inf	1,291	1,291	1,299	1,499	1,509	1,494	1,465	1,461	1,459	31,000	32,989	32,132	68,888	73,309	71,403	71,200	1,810	2,543

Table 53: Table containing the spectrophotometric values and dissolution data of formula 3F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,111	0,110	0,110	0,196	0,194	0,194	0,179	0,178	0,197	2,224	3,756	3,572	4,941	8,346	7,938	7,075	1,518	21,455
5	0,682	0,693	0,687	0,734	0,712	0,722	0,884	0,908	0,893	12,730	13,378	16,501	28,289	29,729	36,669	31,562	3,659	11,592
10	1,630	1,654	1,641	0,720	0,723	0,720	1,836	1,860	1,849	30,144	13,424	33,937	66,986	29,830	75,415	57,410	19,803	34,495
15	2,096	2,185	2,174	1,276	1,241	1,249	2,230	2,174	2,202	39,579	23,208	40,551	87,954	51,573	90,114	76,547	17,681	23,098
30	2,200	2,194	2,189	1,788	1,783	1,786	2,295	2,325	2,302	40,576	32,982	42,689	90,168	73,293	94,865	86,109	9,262	10,757
60	2,236	2,453	2,294	1,862	1,893	1,911	2,497	2,262	2,311	43,220	35,028	43,816	96,044	77,841	97,369	90,418	8,910	9,854
90	2,507	2,346	2,393	2,092	1,980	1,982	2,378	2,337	2,393	45,047	37,574	44,284	100,105	83,499	98,410	94,004	7,461	7,937
120	2,282	2,307	2,303	1,966	1,972	1,961	2,399	2,277	2,284	43,156	36,841	43,632	95,902	81,868	96,959	91,576	6,878	7,511
180	2,194	2,343	2,273	1,944	1,975	1,963	2,450	2,388	2,395	42,886	36,931	45,516	95,303	82,068	101,146	92,839	7,981	8,596
240	2,410	2,333	2,376	1,917	1,950	1,927	2,781	2,677	2,653	44,991	36,594	51,085	99,980	81,321	113,521	98,274	13,201	13,433
360	2,228	2,291	2,276	1,894	1,880	1,951	2,261	2,258	2,448	43,268	36,377	44,421	96,151	80,838	98,714	91,901	7,892	8,588
inf	2,225	2,144	2,186	1,839	1,848	1,847	2,170	2,184	2,179	39,931	35,406	42,024	88,736	78,679	93,386	86,934	6,138	7,060

Table 54: Table containing the spectrophotometric values and dissolution data of formula 3F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,069	0,072	0,070	0,077	0,078	0,077	0,000	0,000	0,000	1,719	1,869	0,320	3,821	4,154	0,711	2,895	1,550	53,550
5	0,626	0,640	0,628	0,605	0,612	0,607	0,154	0,156	0,155	12,946	12,491	3,419	28,768	27,757	7,599	21,375	9,750	45,614
10	1,537	1,538	1,535	1,474	1,440	1,439	0,662	0,656	0,659	31,126	29,414	13,514	69,169	65,365	30,031	54,855	17,622	32,124
15	1,751	1,880	1,803	1,878	1,888	1,908	1,135	1,171	1,135	36,793	38,391	23,353	81,761	85,313	51,896	72,990	14,986	20,532
30	1,870	1,969	1,936	1,837	1,878	1,884	1,525	1,673	1,665	39,265	38,088	32,959	87,256	84,641	73,243	81,713	6,084	7,445
60	1,976	1,918	1,936	1,988	1,674	1,973	1,678	1,684	1,681	39,853	38,542	34,340	88,562	85,648	76,311	83,507	5,226	6,258
90	2,042	1,974	1,989	2,072	1,825	1,944	1,558	1,790	1,763	41,240	40,125	34,982	91,644	89,167	77,738	86,183	6,056	7,027
120	2,017	2,070	2,432	2,055	2,067	2,035	1,519	1,498	1,498	44,882	42,441	31,195	99,738	94,314	69,323	87,792	13,246	15,088
180	2,397	2,406	2,389	2,136	2,113	2,099	1,672	1,572	1,704	49,607	43,947	34,249	110,237	97,659	76,108	94,668	14,093	14,887
240	1,802	2,322	2,262	1,917	1,914	1,917	1,561	1,895	1,763	44,501	40,183	36,237	98,892	89,296	80,527	89,572	7,500	8,373
360	2,227	2,232	2,263	1,987	1,981	2,991	1,461	1,398	1,433	46,976	48,465	30,251	104,390	107,701	67,225	93,105	18,350	19,709
inf	2,009	2,136	2,018	1,671	1,642	1,653	1,364	1,359	1,346	36,188	35,437	28,925	80,418	78,749	64,277	74,481	7,247	9,730

Dissolution results Formulation 4A

Table 55: Table containing the spectrophotometric values and dissolution data of formula 4A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,016	0,016	0,016	0,018	0,018	0,018	0,020	0,020	0,019	0,823	0,864	0,904	1,828	1,921	2,008	1,919	0,074	3,833
5	0,072	0,072	0,072	0,074	0,073	0,074	0,076	0,075	0,074	2,006	2,037	2,064	4,458	4,527	4,586	4,524	0,052	1,159
10	0,205	0,205	0,205	0,193	0,192	0,193	0,205	0,206	0,207	4,792	4,540	4,823	10,648	10,090	10,718	10,485	0,281	2,681
15	0,366	0,366	0,366	0,347	0,341	0,342	0,367	0,365	0,366	8,197	7,723	8,197	18,215	17,162	18,216	17,864	0,497	2,781
30	0,530	0,526	0,528	0,506	0,506	0,506	0,530	0,531	0,530	11,638	11,174	11,687	25,862	24,832	25,971	25,555	0,513	2,008
60	0,656	0,657	0,657	0,670	0,664	0,666	0,687	0,683	0,624	14,397	14,602	14,568	31,993	32,448	32,373	32,271	0,199	0,617
90	0,827	0,822	0,827	0,808	0,804	0,808	0,807	0,803	0,803	18,006	17,617	17,570	40,014	39,149	39,045	39,403	0,434	1,102
120	0,884	0,887	0,884	0,850	0,851	0,851	0,846	0,845	0,845	19,354	18,632	18,527	43,009	41,405	41,171	41,862	0,817	1,951
180	0,968	0,971	0,969	0,942	0,933	0,938	0,924	0,923	0,923	21,233	20,543	20,255	47,184	45,651	45,012	45,949	0,912	1,984
240	1,062	1,056	1,058	0,999	1,010	1,007	0,989	0,990	0,990	23,205	22,081	21,758	51,566	49,068	48,352	49,662	1,378	2,774
360	1,104	1,109	1,101	1,021	1,041	1,029	1,009	1,019	1,011	24,300	22,713	22,355	54,000	50,474	49,678	51,384	1,878	3,655
inf	1,173	1,181	1,185	1,086	1,092	1,092	1,080	1,100	1,084	24,733	24,091	24,052	54,963	53,536	53,448	53,982	0,694	1,286

Table 56: Table containing the spectrophotometric values and dissolution data of formula 4A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,040	0,041	0,041	0,074	0,074	0,073	0,062	0,062	0,062	0,954	1,557	1,343	2,120	3,460	2,985	2,855	0,555	19,431
5	0,197	0,196	0,196	0,325	0,321	0,322	0,357	0,360	0,359	3,787	6,089	6,746	8,416	13,530	14,992	12,313	2,819	22,898
10	0,573	0,570	0,572	0,906	0,893	0,897	0,907	0,910	0,909	10,637	16,592	16,785	23,638	36,871	37,300	32,603	6,342	19,451
15	1,015	1,021	1,021	1,288	1,292	1,291	1,366	1,363	1,364	18,823	23,807	25,154	41,830	52,905	55,897	50,211	6,051	12,050
30	1,481	1,488	1,483	1,739	1,762	1,754	1,846	1,835	1,836	27,380	32,327	33,933	60,844	71,837	75,406	69,362	6,197	8,934
60	1,832	1,830	1,831	1,970	1,971	1,976	2,162	2,104	2,137	33,843	36,519	39,476	75,206	81,152	87,725	81,361	5,113	6,284
90	1,903	1,888	1,891	2,045	2,002	2,036	2,194	2,140	2,164	35,171	37,726	40,270	78,158	83,836	89,490	83,828	4,626	5,519
120	2,022	1,978	1,984	2,033	2,029	2,034	2,276	2,150	2,184	37,190	38,005	41,165	82,645	84,456	91,478	86,193	3,809	4,420
180	1,955	1,970	1,965	2,046	2,110	2,094	2,265	2,113	2,176	36,827	39,144	41,054	81,838	86,986	91,231	86,685	3,841	4,430
240	2,008	1,916	1,943	2,222	2,158	2,184	2,290	2,201	2,263	36,882	41,251	42,488	81,960	91,669	94,417	89,349	5,344	5,981
360	1,986	1,944	1,946	2,131	2,163	2,093	2,184	2,190	2,189	37,145	40,404	41,556	82,544	89,786	92,346	88,225	4,151	4,705
inf	2,026	2,019	2,009	2,150	2,149	2,160	2,278	2,014	2,200	40,117	41,057	41,346	89,148	91,237	91,880	90,755	1,166	1,285

Table 57: Table containing the spectrophotometric values and dissolution data of formula 4A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,112	0,129	0,119	0,110	0,110	0,111	0,132	0,136	0,135	2,719	2,529	3,003	6,042	5,619	6,674	6,112	0,433	7,092
5	0,548	0,540	0,544	0,458	0,468	0,459	0,535	0,531	0,533	11,210	9,564	10,992	24,911	21,252	24,427	23,530	1,623	6,896
10	1,254	1,231	1,239	1,018	0,979	0,993	1,175	1,175	1,175	25,223	20,316	23,901	56,051	45,147	53,113	51,437	4,607	8,956
15	1,477	1,444	1,454	1,405	1,333	1,373	1,641	1,465	1,474	29,700	27,897	31,057	65,999	61,993	69,015	65,669	2,876	4,380
30	1,732	2,149	2,135	2,028	2,089	2,004	2,096	2,202	2,074	40,798	41,450	43,166	90,662	92,111	95,925	92,899	2,220	2,390
60	1,618	1,462	1,603	1,798	2,218	1,935	1,661	1,665	1,693	32,130	40,549	34,390	71,400	90,108	76,423	79,310	7,906	9,968
90	1,805	1,586	1,644	1,917	1,888	1,933	1,642	1,741	1,722	34,649	39,341	35,145	76,998	87,424	78,100	80,841	4,677	5,785
120	1,678	1,801	1,946	1,966	2,413	1,994	1,999	1,798	1,844	37,446	43,792	38,914	83,214	97,316	86,475	89,002	6,028	6,773
180	1,677	1,560	1,635	1,451	1,724	1,714	1,540	1,809	1,764	33,957	34,132	35,601	75,459	75,849	79,114	76,808	1,639	2,134
240	1,917	1,994	1,942	1,816	1,662	1,722	1,528	1,784	1,742	40,678	36,387	35,391	90,397	80,860	78,646	83,301	5,098	6,120
360	1,656	1,759	1,693	1,666	1,874	1,763	1,851	1,546	1,734	35,926	37,272	36,092	79,835	82,828	80,204	80,956	1,332	1,646
inf	1,742	1,741	1,750	2,020	1,996	1,994	1,752	1,789	1,776	38,861	42,179	37,524	86,357	93,731	83,387	87,825	4,349	4,951

Dissolution results Formulation 4B

Table 58: Table containing the spectrophotometric values and dissolution data of formula 4B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,021	0,021	0,022	0,017	0,017	0,017	0,026	0,025	0,025	0,938	0,841	1,018	2,084	1,868	2,263	2,072	0,161	7,785
5	0,070	0,070	0,070	0,073	0,072	0,073	0,114	0,114	0,114	1,965	2,013	2,882	4,366	4,474	6,405	5,081	0,937	18,432
10	0,213	0,214	0,214	0,227	0,227	0,227	0,303	0,303	0,301	4,983	5,254	6,849	11,073	11,676	15,220	12,656	1,830	14,457
15	0,419	0,417	0,418	0,449	0,446	0,447	0,576	0,570	0,522	9,287	9,910	12,203	20,638	22,023	27,118	23,260	2,786	11,979
30	0,668	0,664	0,667	0,693	0,693	0,694	0,772	0,774	0,773	14,549	15,120	16,813	32,331	33,599	37,362	34,431	2,136	6,205
60	0,845	0,845	0,846	0,989	0,984	0,985	1,058	1,058	1,059	18,382	21,332	22,885	40,849	47,404	50,857	46,370	4,151	8,951
90	1,203	1,206	1,206	1,200	1,199	1,199	1,334	1,332	1,333	26,015	25,921	28,768	57,811	57,602	63,930	59,781	2,935	4,909
120	1,285	1,284	1,285	1,292	1,302	1,301	1,419	1,411	1,417	27,821	28,131	30,660	61,825	62,514	68,134	64,158	2,825	4,404
180	1,337	1,321	1,333	1,363	1,371	1,370	1,572	1,583	1,577	28,925	29,749	34,207	64,279	66,108	76,015	68,801	5,155	7,493
240	1,477	1,470	1,473	1,475	1,480	1,477	1,575	1,539	1,563	32,091	32,197	34,009	71,313	71,550	75,576	72,813	1,956	2,687
360	1,524	1,525	1,520	1,533	1,530	1,538	1,586	1,581	1,579	33,295	33,550	34,677	73,990	74,555	77,061	75,202	1,335	1,775
inf	1,583	1,581	1,586	1,594	1,594	1,591	1,577	1,579	1,571	34,752	34,972	34,725	77,228	77,716	77,166	77,370	0,246	0,318

Table 59: Table containing the spectrophotometric values and dissolution data of formula 4B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,199	0,201	0,201	0,298	0,298	0,298	0,195	0,196	0,197	3,862	5,633	3,782	8,582	12,517	8,405	9,835	1,898	19,300
5	0,772	0,752	0,759	1,070	1,008	1,073	0,688	0,685	0,686	14,075	19,346	12,717	31,277	42,991	28,261	34,176	6,353	18,590
10	1,510	1,501	1,501	1,964	1,953	1,956	1,347	1,340	1,343	27,662	35,950	24,731	61,471	79,888	54,958	65,439	10,557	16,133
15	2,013	2,011	1,985	2,276	2,213	2,264	1,804	1,803	1,803	36,882	41,476	33,230	81,961	92,170	73,845	82,659	7,497	9,070
30	2,384	2,268	2,294	2,440	2,410	2,414	2,059	2,089	2,076	42,764	44,798	38,348	95,031	99,550	85,218	93,267	5,983	6,415
60	2,385	2,479	2,437	2,471	2,444	2,472	2,231	2,262	2,231	45,154	45,798	41,586	100,342	101,773	92,413	98,176	4,117	4,193
90	2,337	2,392	2,374	2,429	2,431	2,431	2,316	2,320	2,316	44,193	45,459	43,194	98,208	101,021	95,988	98,405	2,060	2,093
120	2,378	2,393	2,452	2,420	2,398	2,399	2,369	2,348	2,353	45,168	45,261	44,141	100,374	100,581	98,092	99,682	1,128	1,131
180	2,379	2,409	2,383	2,341	2,351	2,388	2,414	2,244	2,320	45,084	44,669	43,820	100,187	99,263	97,378	98,943	1,169	1,182
240	2,316	2,361	2,348	2,363	2,368	2,371	2,372	2,395	2,391	44,452	45,041	45,142	98,783	100,091	100,316	99,730	0,676	0,678
360	2,397	2,431	2,363	2,426	2,420	2,421	2,415	2,409	2,400	45,689	46,279	45,790	101,531	102,843	101,756	102,043	0,573	0,561
inf	2,314	2,320	2,313	2,454	2,393	2,417	2,332	2,366	2,351	45,300	46,506	44,974	100,667	103,346	99,941	101,318	1,464	1,445

Table 60: Table containing the spectrophotometric values and dissolution data of formula 4B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,226	0,225	0,226	0,227	0,213	0,219	0,286	0,259	0,244	4,835	4,715	5,579	10,745	10,477	12,397	11,206	0,849	7,576
5	0,713	0,722	0,722	0,754	0,745	0,749	0,859	0,863	0,862	14,724	15,333	17,578	32,719	34,074	39,062	35,285	2,727	7,729
10	1,255	1,271	1,269	1,375	1,276	1,294	1,525	1,460	1,473	25,730	26,730	30,161	57,177	59,399	67,024	61,200	4,217	6,891
15	1,811	1,667	1,677	1,797	1,704	1,763	1,789	2,003	1,894	34,936	35,666	38,517	77,635	79,259	85,594	80,829	3,434	4,248
30	1,991	2,032	2,008	2,462	2,092	2,034	2,223	2,225	2,432	40,957	44,690	46,693	91,016	99,311	103,761	98,030	5,282	5,388
60	1,712	2,235	2,274	1,814	1,970	1,983	1,773	1,694	1,793	42,450	39,464	36,136	94,334	87,698	80,303	87,445	5,731	6,554
90	1,772	2,213	1,938	1,408	1,785	1,563	1,744	1,683	1,724	40,690	32,937	35,604	90,423	73,193	79,121	80,912	7,147	8,833
120	1,796	1,619	1,724	2,135	2,116	2,073	2,449	2,405	2,463	35,684	43,567	50,240	79,297	96,816	111,644	95,919	13,221	13,783
180	1,595	1,628	1,590	1,926	1,815	1,883	1,707	2,062	1,894	33,709	39,132	39,486	74,909	86,960	87,747	83,205	5,875	7,061
240	1,619	1,621	1,644	1,759	1,725	1,739	1,516	1,655	1,630	34,360	36,665	33,950	76,356	81,478	75,444	77,759	2,656	3,415
360	1,699	1,847	1,733	1,573	1,581	1,569	1,935	1,889	1,914	37,169	33,533	40,371	82,598	74,517	89,713	82,276	6,208	7,545
inf	1,799	1,755	1,763	1,623	1,610	1,619	1,902	1,935	1,917	37,558	34,558	40,691	83,461	76,795	90,424	83,560	5,565	6,659

Dissolution results Formulation 4C

Table 61: Table containing the spectrophotometric values and dissolution data of formula 4C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,010	0,008	0,009	0,008	0,008	0,008	0,010	0,011	0,011	0,680	0,657	0,715	1,511	1,460	1,589	1,520	0,053	3,486
5	0,039	0,040	0,039	0,034	0,035	0,038	0,034	0,033	0,033	1,322	1,241	1,191	2,939	2,758	2,647	2,782	0,120	4,319
10	0,139	0,139	0,139	0,109	0,108	0,108	0,103	0,105	0,105	3,407	2,767	2,690	7,572	6,150	5,978	6,567	0,715	10,881
15	0,274	0,273	0,274	0,228	0,227	0,227	0,241	0,243	0,242	6,245	5,269	5,586	13,879	11,709	12,414	12,667	0,904	7,133
30	0,422	0,423	0,423	0,385	0,386	0,385	0,397	0,401	0,402	9,410	8,612	8,920	20,911	19,138	19,823	19,958	0,730	3,658
60	0,598	0,598	0,598	0,565	0,564	0,564	0,563	0,564	0,543	13,127	12,408	12,255	29,172	27,574	27,233	27,993	0,845	3,019
90	0,738	0,737	0,738	0,716	0,717	0,716	0,720	0,721	0,721	16,124	15,664	15,760	35,832	34,809	35,022	35,221	0,441	1,251
120	0,830	0,828	0,830	0,818	0,820	0,821	0,810	0,812	0,812	18,137	17,910	17,740	40,304	39,801	39,423	39,843	0,361	0,905
180	0,930	0,930	0,930	0,915	0,912	0,913	0,907	0,908	0,908	20,343	19,979	19,855	45,207	44,398	44,123	44,576	0,460	1,032
240	0,990	0,994	0,996	1,000	1,001	1,007	0,997	0,988	0,990	21,785	21,952	21,717	48,411	48,783	48,260	48,484	0,220	0,453
360	1,044	1,065	1,065	1,042	1,046	1,049	1,053	1,050	1,052	23,251	22,977	23,095	51,668	51,061	51,323	51,351	0,249	0,484
inf	1,142	1,143	1,143	1,131	1,132	1,133	1,120	1,119	1,121	24,914	24,900	24,649	55,364	55,334	54,775	55,158	0,271	0,491

Table 62: Table containing the spectrophotometric values and dissolution data of formula 4C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,033	0,035	0,033	0,117	0,118	0,118	0,036	0,037	0,037	0,829	2,361	0,885	1,842	5,246	1,966	3,018	1,576	52,216
5	0,227	0,225	0,225	0,602	0,602	0,602	0,213	0,210	0,212	4,324	11,172	4,069	9,609	24,826	9,041	14,492	7,311	50,449
10	0,737	0,741	0,742	1,369	1,365	1,367	0,787	0,790	0,789	13,696	25,146	14,587	30,437	55,880	32,415	39,577	11,556	29,199
15	1,295	1,294	1,296	1,979	1,975	1,976	1,360	1,358	1,364	23,859	36,371	25,062	53,020	80,825	55,694	63,180	12,525	19,824
30	1,813	1,789	1,796	2,141	2,321	2,196	1,774	1,775	1,769	33,163	40,984	32,690	73,696	91,075	72,645	79,139	8,451	10,679
60	2,056	2,018	2,043	2,231	2,282	2,273	1,890	1,940	1,924	37,705	41,978	35,507	83,789	93,285	78,905	85,326	5,970	6,997
90	2,019	2,102	2,104	2,445	2,414	2,483	1,968	1,968	1,968	38,556	45,581	36,612	85,681	101,292	81,360	89,444	8,561	9,572
120	2,129	2,077	2,083	2,405	2,460	2,432	2,057	2,063	2,061	39,162	45,556	38,496	87,027	101,236	85,547	91,270	7,073	7,750
180	2,075	2,118	2,093	2,377	2,316	2,343	2,133	2,092	2,114	39,356	44,215	39,658	87,459	98,257	88,129	91,282	4,940	5,411
240	2,118	2,118	2,124	2,315	2,325	2,319	2,067	1,960	1,983	40,012	43,985	37,880	88,915	97,745	84,178	90,279	5,622	6,227
360	2,162	2,081	2,092	2,338	2,334	2,340	2,013	2,014	2,014	40,078	44,541	38,268	89,062	98,980	85,040	91,028	5,858	6,436
inf	2,012	2,027	2,019	2,397	2,384	2,391	2,335	2,310	2,293	42,638	45,743	43,900	94,751	101,651	97,557	97,986	2,833	2,891

Table 63: Table containing the spectrophotometric values and dissolution data of formula 4C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,026	0,026	0,027	0,044	0,056	0,053	0,040	0,027	0,029	0,846	1,339	0,963	1,880	2,975	2,139	2,331	0,467	20,037
5	0,315	0,310	0,314	0,398	0,406	0,393	0,285	0,303	0,333	6,581	8,306	6,462	14,624	18,457	14,361	15,814	1,872	11,838
10	0,825	0,937	0,922	1,109	0,990	1,003	0,876	0,833	0,848	18,250	21,045	17,400	40,555	46,766	38,667	41,996	3,460	8,238
15	1,269	1,345	1,298	1,925	1,647	1,731	1,477	1,531	1,493	26,535	35,834	30,456	58,967	79,632	67,679	68,759	8,471	12,320
30	1,402	2,063	1,733	1,784	1,829	1,802	1,905	1,511	1,633	35,254	36,779	34,283	78,342	81,732	76,185	78,753	2,283	2,899
60	1,893	1,877	1,890	1,937	1,907	1,913	1,853	1,865	1,885	38,520	39,257	38,167	85,601	87,238	84,815	85,885	1,009	1,175
90	2,314	2,456	2,440	1,997	1,983	1,998	1,895	1,884	1,888	49,075	40,945	38,795	109,055	90,989	86,211	95,418	9,838	10,310
120	1,995	1,746	1,794	1,652	1,760	1,735	2,029	1,901	1,943	38,167	35,628	40,376	84,816	79,173	89,723	84,571	4,311	5,097
180	1,988	1,828	1,814	2,148	2,130	2,093	1,955	1,701	1,821	39,014	43,982	37,953	86,698	97,737	84,340	89,592	5,839	6,518
240	1,872	2,363	1,902	1,991	2,245	2,019	1,952	2,160	2,073	42,599	43,441	42,878	94,665	96,535	95,284	95,495	0,778	0,815
360	2,011	2,274	2,187	2,295	2,208	2,313	1,861	2,186	2,073	45,059	47,411	42,672	100,132	105,357	94,826	100,105	4,299	4,295
inf	1,934	1,977	2,074	2,009	2,013	1,998	1,681	1,743	1,795	40,423	42,356	36,895	89,830	94,125	81,989	88,648	5,025	5,668

Dissolution results Formulation 4D

Table 64: Table containing the spectrophotometric values and dissolution data of formula 4D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,015	0,014	0,015	0,009	0,009	0,009	0,010	0,009	0,010	0,795	0,679	0,691	1,766	1,509	1,536	1,604	0,115	7,176
5	0,072	0,073	0,079	0,048	0,049	0,049	0,061	0,059	0,059	2,062	1,515	1,743	4,582	3,367	3,874	3,941	0,498	12,636
10	0,240	0,231	0,233	0,185	0,184	0,184	0,204	0,205	0,204	5,418	4,359	4,779	12,041	9,686	10,620	10,782	0,968	8,979
15	0,472	0,475	0,473	0,397	0,403	0,403	0,415	0,416	0,416	10,451	8,925	9,239	23,225	19,833	20,530	21,196	1,463	6,901
30	0,741	0,743	0,741	0,647	0,646	0,646	0,660	0,660	0,659	16,135	14,118	14,402	35,857	31,374	32,004	33,078	1,981	5,990
60	0,982	0,986	0,984	0,922	0,923	0,922	0,936	0,932	0,934	21,301	19,977	20,226	47,337	44,393	44,947	45,559	1,277	2,804
90	1,217	1,216	1,216	1,198	1,198	1,198	1,186	1,193	1,191	26,283	25,859	25,697	58,406	57,463	57,104	57,658	0,549	0,952
120	1,360	1,360	1,361	1,346	1,345	1,347	1,366	1,366	1,368	29,452	29,106	29,548	65,449	64,681	65,663	65,264	0,422	0,646
180	1,502	1,502	1,504	1,514	1,508	1,507	1,510	1,503	1,504	32,595	32,697	32,615	72,434	72,660	72,478	72,524	0,098	0,135
240	1,648	1,649	1,642	1,640	1,604	1,607	1,559	1,576	1,566	35,773	35,121	34,080	79,496	78,047	75,733	77,759	1,550	1,993
360	1,665	1,663	1,663	1,657	1,664	1,664	1,636	1,658	1,648	36,332	36,248	35,953	80,737	80,551	79,895	80,394	0,361	0,449
inf	1,759	1,761	1,761	1,761	1,761	1,762	1,743	1,743	1,744	38,439	38,531	38,154	85,419	85,624	84,786	85,276	0,357	0,418

Table 65: Table containing the spectrophotometric values and dissolution data of formula 4D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,289	0,292	0,291	0,165	0,165	0,166	0,095	0,094	0,096	5,505	3,224	1,944	12,233	7,164	4,321	7,906	3,273	41,395
5	1,100	1,095	1,099	0,673	0,666	0,669	0,455	0,459	0,455	20,213	12,406	8,523	44,918	27,568	18,940	30,475	10,803	35,448
10	1,744	1,715	1,733	1,371	1,368	1,369	1,131	1,126	1,131	31,822	25,200	20,804	70,714	56,000	46,230	57,648	10,063	17,457
15	2,093	2,087	2,089	1,875	1,878	1,876	1,639	1,635	1,638	38,531	34,549	30,159	85,624	76,775	67,020	76,473	7,598	9,936
30	2,220	2,165	2,187	2,144	2,088	2,091	1,924	1,896	1,888	40,578	38,950	35,143	90,174	86,556	78,096	84,942	5,061	5,959
60	2,210	2,214	2,236	2,151	2,194	2,173	1,946	1,981	1,962	41,326	40,342	36,439	91,836	89,649	80,975	87,487	4,690	5,361
90	2,367	2,380	2,371	2,313	2,321	2,320	1,976	2,000	1,982	44,327	43,207	37,052	98,505	96,015	82,338	92,286	7,107	7,701
120	2,363	2,197	2,244	2,219	2,222	2,221	1,995	1,997	1,988	42,667	41,668	37,387	94,814	92,595	83,082	90,164	5,089	5,644
180	2,169	2,106	2,125	2,467	2,231	2,296	2,039	2,065	2,087	40,444	43,911	38,866	89,876	97,579	86,368	91,274	4,683	5,130
240	2,260	2,400	2,436	2,305	2,378	2,356	2,021	2,029	2,068	44,881	44,422	38,632	99,735	98,716	85,850	94,767	6,319	6,668
360	2,156	2,237	2,240	2,255	2,109	2,174	2,027	1,976	1,984	42,314	41,618	38,040	94,030	92,484	84,534	90,349	4,160	4,605
inf	2,482	2,463	2,441	2,126	2,131	2,129	1,991	2,018	2,013	42,322	40,916	38,452	94,048	90,923	85,449	90,140	3,554	3,943

Table 66: Table containing the spectrophotometric values and dissolution data of formula 4D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,163	0,172	0,167	0,068	0,067	0,068	0,071	0,070	0,069	3,667	1,672	1,721	8,148	3,716	3,825	5,230	2,064	39,471
5	0,748	0,679	0,684	0,515	0,488	0,484	0,493	0,479	0,484	14,413	10,240	10,034	32,029	22,754	22,297	25,694	4,484	17,451
10	1,319	1,314	1,316	1,181	1,116	1,163	1,108	1,137	1,113	26,744	23,447	22,765	59,431	52,105	50,589	54,042	3,861	7,144
15	2,004	1,636	1,874	1,620	1,457	1,497	1,378	1,409	1,413	37,324	31,002	28,507	82,943	68,893	63,348	71,728	8,247	11,497
30	1,836	1,982	2,076	2,167	2,425	2,363	2,047	2,168	2,143	40,066	47,048	43,048	89,035	104,551	95,663	96,417	6,357	6,593
60	2,339	2,350	2,357	2,327	2,112	2,364	2,170	2,155	2,166	47,957	46,291	44,164	106,571	102,869	98,142	102,527	3,450	3,365
90	2,061	2,094	2,086	2,122	1,850	1,993	1,929	1,935	1,983	42,844	40,952	40,114	95,209	91,005	89,143	91,785	2,537	2,764
120	2,118	1,926	1,894	1,930	1,859	1,893	1,878	1,905	1,906	41,064	39,293	39,279	91,253	87,318	87,287	88,619	1,862	2,101
180	2,001	2,082	2,003	2,135	1,984	1,963	2,092	1,922	1,845	42,269	42,162	40,623	93,931	93,693	90,274	92,633	1,670	1,803
240	2,435	1,972	1,943	1,799	1,832	1,807	1,843	1,894	1,897	44,262	38,095	39,345	98,361	84,655	87,433	90,150	5,916	6,562
360	1,995	2,188	2,014	2,073	2,349	2,165	2,212	2,318	2,308	43,470	45,959	47,576	96,600	102,131	105,724	101,485	3,753	3,698
inf	2,130	2,074	2,109	2,407	2,390	2,396	1,834	1,965	1,947	45,167	50,244	40,551	100,372	111,652	90,113	100,712	8,797	8,734

Dissolution results Formulation 4E

Table 67: Table containing the spectrophotometric values and dissolution data of formula 4E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,006	0,007	0,007	0,007	0,007	0,007	0,009	0,009	0,008	0,634	0,635	0,675	1,408	1,412	1,500	1,440	0,042	2,950
5	0,027	0,027	0,027	0,030	0,029	0,029	0,051	0,050	0,050	1,055	1,106	1,550	2,344	2,458	3,445	2,749	0,494	17,985
10	0,125	0,129	0,123	0,128	0,127	0,127	0,183	0,192	0,191	3,125	3,163	4,451	6,946	7,029	9,892	7,955	1,370	17,218
15	0,295	0,293	0,293	0,306	0,309	0,306	0,376	0,373	0,375	6,665	6,944	8,377	14,811	15,430	18,615	16,285	1,667	10,234
30	0,484	0,489	0,487	0,485	0,484	0,486	0,555	0,551	0,553	10,747	10,719	12,159	23,883	23,821	27,020	24,908	1,494	5,997
60	0,681	0,678	0,678	0,705	0,701	0,702	0,734	0,727	0,727	14,840	15,328	15,919	32,979	34,062	35,375	34,139	0,980	2,871
90	0,867	0,867	0,867	0,878	0,873	0,874	0,898	0,894	0,895	18,854	19,030	19,487	41,897	42,288	43,304	42,496	0,593	1,395
120	1,012	1,010	0,997	1,028	1,022	1,022	1,035	1,029	1,030	21,885	22,251	22,441	48,633	49,447	49,870	49,316	0,513	1,041
180	1,087	1,088	1,088	1,107	1,101	1,111	1,123	1,126	1,125	23,699	24,104	24,512	52,665	53,564	54,471	53,567	0,737	1,376
240	1,185	1,164	1,155	1,208	1,209	1,206	1,207	1,198	1,206	25,505	26,354	26,300	56,677	58,565	58,446	57,896	0,863	1,491
360	1,244	1,236	1,241	1,271	1,277	1,276	1,286	1,282	1,280	27,161	27,899	28,095	60,357	61,998	62,434	61,596	0,894	1,452
inf	1,299	1,284	1,289	1,303	1,308	1,300	1,336	1,332	1,337	28,759	28,645	29,345	63,909	63,655	65,211	64,258	0,681	1,060

Table 68: Table containing the spectrophotometric values and dissolution data of formula 4E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,031	0,028	0,028	0,025	0,023	0,024	0,094	0,099	0,098	0,748	0,652	1,982	1,662	1,449	4,405	2,505	1,346	53,731
5	0,233	0,226	0,228	0,266	0,266	0,254	0,662	0,604	0,644	4,386	4,984	11,804	9,747	11,075	26,231	15,684	7,477	47,674
10	0,804	0,817	0,800	0,750	0,769	0,768	1,418	1,409	1,410	14,919	14,108	25,967	33,154	31,352	57,704	40,737	12,020	29,507
15	1,389	1,353	1,371	1,305	1,324	1,304	1,910	1,997	1,982	25,250	24,160	36,130	56,111	53,690	80,289	63,363	12,009	18,953
30	1,842	1,928	1,916	1,828	1,917	1,902	2,321	2,283	2,290	34,927	34,683	42,414	77,616	77,072	94,254	82,981	7,975	9,610
60	2,038	2,125	2,118	1,986	2,056	2,010	2,235	2,163	2,242	38,722	37,321	41,107	86,048	82,935	91,349	86,777	3,474	4,003
90	2,039	2,163	2,094	2,019	2,166	2,035	2,381	2,400	2,401	39,024	38,552	44,619	86,719	85,670	99,154	90,514	6,124	6,766
120	2,181	2,153	2,170	2,316	2,315	2,144	2,463	2,427	2,490	40,497	42,116	46,054	89,993	93,592	102,343	95,309	5,186	5,441
180	2,155	2,197	2,186	2,231	2,175	2,181	2,358	2,368	2,410	40,924	41,207	44,824	90,943	91,570	99,609	94,041	3,946	4,196
240	2,248	2,217	2,220	2,232	2,231	2,237	2,483	2,406	2,486	42,029	42,113	46,520	93,397	93,584	103,378	96,786	4,662	4,816
360	2,179	2,215	2,216	2,146	2,183	2,191	2,506	2,351	2,384	41,803	41,248	45,951	92,895	91,662	102,114	95,557	4,664	4,881
inf	2,116	2,140	2,119	2,010	2,003	2,011	2,147	2,151	2,172	40,083	38,464	41,521	89,074	85,475	92,270	88,940	2,775	3,121

Table 69: Table containing the spectrophotometric values and dissolution data of formula 4E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,033	0,034	0,034	0,120	0,127	0,127	0,061	0,065	0,065	0,993	2,814	1,593	2,206	6,253	3,541	4,000	1,684	42,099
5	0,317	0,325	0,320	0,648	0,631	0,638	0,431	0,413	0,427	6,734	13,116	8,803	14,965	29,146	19,562	21,225	5,907	27,833
10	0,901	0,924	0,918	1,472	1,373	1,392	1,095	1,116	1,109	18,643	28,646	22,508	41,430	63,658	50,018	51,702	9,153	17,702
15	1,420	1,473	1,440	1,758	1,791	1,774	1,770	1,673	1,694	29,340	36,047	34,742	65,199	80,105	77,204	74,169	6,452	8,700
30	1,675	1,688	1,671	1,758	1,764	1,804	1,816	1,739	1,777	34,175	36,264	36,229	75,945	80,587	80,510	79,014	2,170	2,747
60	1,699	1,556	1,622	1,765	1,611	1,679	1,706	1,771	1,743	33,320	34,656	35,682	74,044	77,014	79,292	76,783	2,149	2,799
90	1,689	1,660	1,673	2,012	1,959	1,940	1,784	1,725	1,744	34,471	40,548	36,093	76,602	90,107	80,208	82,306	5,709	6,937
120	1,741	1,834	1,803	1,991	2,089	1,991	2,073	2,021	2,093	37,023	41,833	42,525	82,274	92,962	94,499	89,912	5,437	6,047
180	1,994	2,204	2,105	2,085	2,085	2,110	2,238	1,789	1,899	43,394	43,455	41,006	96,432	96,567	91,124	94,708	2,534	2,676
240	2,225	2,104	2,174	1,843	1,851	1,871	2,231	1,946	1,994	44,960	38,922	42,855	99,912	86,494	95,234	93,880	5,561	5,923
360	1,797	1,602	1,774	2,102	2,045	2,100	1,807	1,905	1,886	36,337	43,671	39,271	80,748	97,047	87,268	88,354	6,698	7,581
inf	1,851	1,843	1,841	2,225	2,186	2,209	1,822	1,885	1,830	41,353	46,391	39,066	91,895	103,092	86,813	93,933	6,800	7,239

Dissolution results Formulation 4F

Table 70: Table containing the spectrophotometric values and dissolution data of formula 4F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,023	0,022	0,023	0,017	0,017	0,017	0,007	0,006	0,007	0,965	0,850	0,633	2,145	1,888	1,407	1,813	0,306	16,863
5	0,096	0,095	0,095	0,070	0,072	0,071	0,033	0,032	0,032	2,488	1,980	1,167	5,530	4,399	2,594	4,174	1,209	28,968
10	0,286	0,284	0,286	0,241	0,242	0,241	0,138	0,138	0,139	6,489	5,557	3,402	14,420	12,350	7,560	11,443	2,873	25,104
15	0,518	0,519	0,518	0,484	0,478	0,480	0,353	0,352	0,353	11,410	10,602	7,902	25,355	23,561	17,560	22,158	3,333	15,043
30	0,772	0,770	0,771	0,734	0,730	0,731	0,596	0,602	0,599	16,767	15,929	13,107	37,260	35,397	29,127	33,928	3,479	10,254
60	1,013	1,010	1,010	1,012	1,009	1,010	0,912	0,908	0,910	21,881	21,854	19,695	48,625	48,564	43,766	46,985	2,276	4,845
90	1,205	1,204	1,200	1,203	1,204	1,203	1,118	1,103	1,110	26,024	26,016	24,004	57,831	57,812	53,342	56,329	2,112	3,749
120	1,300	1,293	1,296	1,302	1,311	1,311	1,263	1,260	1,260	28,124	28,351	27,292	62,499	63,003	60,649	62,050	1,012	1,631
180	1,370	1,369	1,370	1,403	1,393	1,397	1,353	1,351	1,351	29,813	30,379	29,342	66,251	67,510	65,205	66,322	0,942	1,421
240	1,502	1,475	1,437	1,471	1,477	1,458	1,383	1,384	1,446	32,105	32,031	30,611	71,345	71,179	68,024	70,183	1,528	2,177
360	1,435	1,439	1,432	1,497	1,497	1,506	1,435	1,440	1,438	31,521	32,858	31,466	70,047	73,019	69,924	70,996	1,431	2,016
inf	1,522	1,526	1,521	1,533	1,538	1,541	1,467	1,457	1,453	33,177	33,819	32,079	73,726	75,152	71,286	73,388	1,596	2,175

Table 71: Table containing the spectrophotometric values and dissolution data of formula 4F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,261	0,240	0,240	0,175	0,171	0,152	0,044	0,037	0,039	4,704	3,232	0,947	10,454	7,182	2,104	6,580	3,435	52,210
5	0,902	0,884	0,876	0,736	0,738	0,741	0,387	0,353	0,364	16,382	13,662	6,906	36,406	30,359	15,346	27,370	8,853	32,346
10	1,735	1,698	1,724	1,570	1,563	1,503	1,026	1,023	1,018	31,589	28,403	18,844	70,198	63,117	41,876	58,397	12,035	20,608
15	2,092	2,139	2,127	2,021	2,032	2,027	1,579	1,586	1,600	39,038	37,312	29,242	86,751	82,916	64,982	78,216	9,488	12,131
30	2,354	2,430	2,387	2,338	2,369	2,403	2,028	2,002	2,016	44,176	43,762	37,170	98,169	97,250	82,599	92,673	7,133	7,697
60	2,291	2,234	2,279	2,409	2,494	2,407	2,228	2,213	2,218	42,197	45,218	41,084	93,771	100,485	91,297	95,184	3,882	4,078
90	2,481	2,265	2,293	2,412	2,449	2,429	2,223	2,209	2,216	43,851	45,338	41,242	97,447	100,752	91,648	96,616	3,763	3,894
120	2,199	2,296	2,263	2,463	2,473	2,489	2,344	2,305	2,324	42,385	46,403	43,430	94,189	103,118	96,512	97,940	3,783	3,862
180	2,487	2,445	2,463	2,468	2,465	2,494	2,172	2,192	2,201	46,476	46,658	41,200	103,280	103,684	91,556	99,507	5,624	5,652
240	2,472	2,421	2,474	2,472	2,467	2,489	2,233	2,336	2,330	46,555	46,923	43,440	103,455	104,272	96,534	101,420	3,471	3,423
360	2,493	2,417	2,393	2,308	2,194	2,264	2,379	2,254	2,288	46,415	43,155	43,804	103,144	95,899	97,342	98,795	3,131	3,170
inf	2,461	2,421	2,490	2,289	2,243	2,290	2,138	2,163	2,130	44,063	43,725	41,069	97,917	97,167	91,265	95,450	2,975	3,117

Table 72: Table containing the spectrophotometric values and dissolution data of formula 4F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,112	0,110	0,112	0,073	0,074	0,078	0,020	0,019	0,021	2,549	1,822	0,721	5,664	4,049	1,601	3,771	1,670	44,280
5	0,631	0,637	0,633	0,486	0,490	0,485	0,263	0,263	0,265	13,004	10,064	5,599	28,899	22,364	12,442	21,235	6,766	31,861
10	1,457	1,423	1,447	1,135	1,116	1,130	0,776	0,801	0,794	29,251	22,921	16,159	65,002	50,936	35,909	50,615	11,879	23,470
15	1,660	2,156	2,214	1,812	1,825	1,819	1,209	1,282	1,264	40,766	36,882	25,468	90,590	81,959	56,596	76,382	14,428	18,889
30	2,316	1,889	1,878	1,885	2,012	1,940	1,717	1,716	1,719	41,332	39,619	34,923	91,848	88,042	77,607	85,832	6,020	7,014
60	1,659	1,967	1,904	1,701	1,929	1,902	1,641	1,783	1,764	37,876	37,805	35,355	84,168	84,012	78,567	82,249	2,604	3,166
90	1,876	2,132	2,085	2,148	1,970	1,993	1,827	1,838	1,829	41,833	41,870	37,591	92,962	93,045	83,535	89,847	4,464	4,968
120	1,933	1,825	1,874	1,745	1,595	1,672	1,671	1,955	1,908	38,990	34,772	38,054	86,645	77,272	84,565	82,827	4,019	4,852
180	2,145	2,437	2,193	2,269	2,310	2,296	1,820	2,477	1,827	46,814	47,381	42,192	104,031	105,292	93,761	101,028	5,164	5,112
240	2,152	2,276	2,193	1,913	2,023	2,012	1,849	1,739	1,825	46,044	41,447	37,679	102,319	92,105	83,730	92,718	7,601	8,198
360	2,186	2,170	2,244	2,407	2,397	2,385	2,097	2,114	2,086	46,142	49,940	43,780	102,538	110,977	97,290	103,602	5,638	5,442
inf	2,208	2,196	2,220	2,218	2,224	2,119	2,114	2,109	2,010	45,542	46,023	43,579	101,204	102,272	96,842	100,106	2,349	2,346

Dissolution results Formulation 5A

Table 73: Table containing the spectrophotometric values and dissolution data of formula 5A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,018	0,017	0,017	0,026	0,025	0,025	0,022	0,018	0,020	0,847	1,023	0,912	1,882	2,273	2,027	2,061	0,162	7,841
5	0,059	0,060	0,060	0,054	0,052	0,052	0,049	0,050	0,049	1,746	1,596	1,522	3,880	3,547	3,381	3,603	0,208	5,762
10	0,133	0,141	0,138	0,257	0,253	0,254	0,137	0,136	0,141	3,381	5,834	3,395	7,513	12,964	7,545	9,340	2,562	27,430
15	0,330	0,326	0,327	0,393	0,395	0,395	0,270	0,272	0,272	7,388	8,799	6,207	16,418	19,553	13,794	16,589	2,354	14,193
30	0,477	0,483	0,481	0,582	0,573	0,576	0,421	0,419	0,421	10,628	12,677	9,360	23,617	28,172	20,799	24,196	3,037	12,553
60	0,628	0,631	0,631	0,773	0,771	0,771	0,600	0,601	0,601	13,817	16,822	13,194	30,705	37,382	29,320	32,469	3,520	10,840
90	0,783	0,781	0,783	0,923	0,929	0,928	0,755	0,758	0,759	17,088	20,158	16,548	37,972	44,795	36,773	39,847	3,533	8,867
120	0,903	0,907	0,905	1,055	1,054	1,054	0,868	0,866	0,869	19,745	22,938	18,946	43,879	50,973	42,101	45,651	3,833	8,396
180	1,003	1,003	1,003	1,130	1,131	1,132	0,974	0,978	0,977	21,903	24,672	21,323	48,674	54,827	47,384	50,295	3,248	6,457
240	1,060	1,065	1,065	1,199	1,186	1,188	1,055	1,058	1,050	23,295	26,061	23,074	51,767	57,914	51,277	53,653	3,020	5,628
360	1,136	1,115	1,120	1,259	1,255	1,256	1,120	1,123	1,122	24,676	27,579	24,602	54,835	61,286	54,671	56,930	3,080	5,411
inf	1,159	1,159	1,158	1,175	1,176	1,180	1,060	1,061	1,061	24,989	26,062	23,461	55,531	57,915	52,136	55,194	2,371	4,296

Table 74: Table containing the spectrophotometric values and dissolution data of formula 5A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,343	0,340	0,340	0,099	0,096	0,090	0,280	0,281	0,272	6,419	1,944	5,264	14,265	4,321	11,698	10,095	4,215	41,758
5	0,525	0,526	0,525	0,432	0,444	0,454	0,589	0,581	0,586	9,804	8,290	10,881	21,786	18,423	24,181	21,463	2,362	11,004
10	1,044	1,047	1,049	1,033	1,022	1,026	1,054	1,096	1,094	19,338	18,947	19,968	42,974	42,105	44,374	43,151	0,935	2,166
15	1,044	1,047	1,049	1,033	1,022	1,026	1,054	1,096	1,094	19,444	19,051	20,078	43,209	42,335	44,617	43,387	0,940	2,166
30	1,987	1,979	1,981	1,880	1,866	1,871	1,910	1,915	1,912	36,560	34,519	35,295	81,245	76,710	78,433	78,796	1,869	2,372
60	2,071	2,070	2,072	2,021	2,003	2,010	2,064	2,093	2,093	38,374	37,237	38,596	85,275	82,749	85,770	84,598	1,323	1,564
90	2,064	2,061	2,071	2,038	2,061	2,043	2,202	2,213	2,209	38,478	38,097	41,075	85,507	84,660	91,277	87,148	2,940	3,374
120	2,220	2,181	2,192	2,105	2,049	2,051	2,088	2,024	2,064	41,093	38,682	38,586	91,317	85,959	85,747	87,674	2,577	2,940
180	2,374	2,277	2,294	2,012	2,127	2,117	2,167	2,074	2,090	43,447	39,201	39,728	96,549	87,113	88,285	90,649	4,199	4,632
240	2,013	1,996	1,998	1,924	1,913	1,918	2,195	2,087	2,091	37,998	36,382	40,193	84,441	80,848	89,319	84,869	3,471	4,090
360	2,318	2,291	2,298	2,175	2,084	2,124	2,228	2,147	2,189	43,652	40,378	41,570	97,005	89,729	92,377	93,037	3,007	3,232
inf	2,288	2,279	2,281	2,235	2,230	2,240	2,195	2,188	2,182	42,666	42,539	41,794	94,813	94,532	92,875	94,074	0,855	0,909

Table 75: Table containing the spectrophotometric values and dissolution data of formula 5A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,154	0,150	0,150	0,110	0,106	0,106	0,163	0,147	0,149	3,343	2,466	3,385	7,430	5,480	7,523	6,811	0,942	13,828
5	0,603	0,612	0,607	0,414	0,403	0,409	0,334	0,332	0,329	12,482	8,501	6,969	27,738	18,892	15,487	20,705	5,163	24,937
10	1,227	1,245	1,246	0,790	0,785	0,784	0,746	0,743	0,744	25,194	16,105	15,265	55,986	35,788	33,921	41,898	9,990	23,844
15	1,499	1,557	1,524	1,031	1,046	1,037	1,067	1,053	1,058	31,078	21,227	21,641	69,062	47,170	48,092	54,775	10,110	18,457
30	2,038	2,019	2,027	1,312	1,343	1,383	1,278	1,479	1,409	41,273	27,497	28,341	91,718	61,105	62,980	71,934	14,010	19,476
60	1,855	1,853	1,859	1,667	1,566	1,565	1,522	1,403	1,483	38,053	32,711	30,111	84,562	72,691	66,914	74,722	7,347	9,832
90	2,135	2,365	2,225	1,817	1,742	1,779	1,814	1,751	1,759	45,970	36,494	36,389	102,155	81,098	80,865	88,039	9,982	11,338
120	1,823	2,181	2,025	1,915	2,059	2,004	1,997	1,823	1,822	41,581	40,960	38,705	92,402	91,021	86,011	89,811	2,746	3,057
180	1,910	1,963	1,863	2,055	1,800	1,890	1,987	1,674	1,873	39,858	39,630	38,185	88,574	88,067	84,855	87,165	1,647	1,889
240	2,016	2,004	2,010	2,036	2,086	2,063	1,723	1,969	1,903	42,025	42,768	38,805	93,388	95,041	86,233	91,554	3,823	4,175
360	1,918	1,677	1,723	2,334	1,953	2,037	2,072	1,999	1,986	37,509	43,927	42,089	83,352	97,615	93,532	91,500	5,997	6,555
inf	1,687	1,696	1,706	1,963	1,936	1,997	1,957	1,987	1,973	39,804	41,302	41,378	88,454	91,783	91,951	90,729	1,610	1,775

Dissolution results Formulation 5B

Table 76: Table containing the spectrophotometric values and dissolution data of formula 5B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,013	0,013	0,013	0,014	0,013	0,014	0,025	0,025	0,025	0,768	0,779	1,014	1,707	1,732	2,253	1,897	0,252	13,285
5	0,041	0,040	0,039	0,104	0,104	0,104	0,088	0,089	0,089	1,330	2,667	2,358	2,955	5,926	5,240	4,707	1,270	26,979
10	0,128	0,128	0,129	0,254	0,259	0,259	0,218	0,217	0,216	3,189	5,906	5,054	7,086	13,125	11,232	10,481	2,522	24,063
15	0,293	0,296	0,298	0,462	0,465	0,461	0,380	0,390	0,381	6,714	10,233	8,572	14,919	22,740	19,048	18,903	3,195	16,900
30	0,507	0,511	0,510	0,650	0,646	0,648	0,560	0,558	0,559	11,227	14,178	12,292	24,950	31,506	27,316	27,924	2,711	9,709
60	0,745	0,751	0,748	0,863	0,861	0,822	0,781	0,781	0,781	16,285	18,461	17,015	36,190	41,024	37,811	38,342	2,009	5,240
90	0,976	0,978	0,978	1,085	1,076	1,078	0,985	0,984	0,984	21,186	23,396	21,362	47,080	51,990	47,472	48,847	2,228	4,561
120	1,156	1,153	1,154	1,221	1,231	1,229	1,163	1,165	1,165	25,009	26,614	25,257	55,576	59,143	56,126	56,948	1,568	2,753
180	1,283	1,295	1,293	1,381	1,399	1,398	1,329	1,317	1,319	28,000	30,230	28,693	62,223	67,178	63,762	64,388	2,071	3,216
240	1,373	1,368	1,369	1,490	1,486	1,488	1,421	1,419	1,419	29,809	32,390	30,896	66,242	71,977	68,659	68,959	2,351	3,409
360	1,421	1,446	1,443	1,566	1,574	1,575	1,484	1,486	1,487	31,372	34,316	32,443	69,716	76,258	72,096	72,690	2,704	3,719
inf	1,343	1,348	1,344	1,422	1,424	1,422	1,385	1,386	1,389	30,449	31,378	30,546	67,664	69,730	67,879	68,424	0,927	1,355

Table 77: Table containing the spectrophotometric values and dissolution data of formula 5B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,301	0,298	0,299	0,212	0,218	0,215	0,331	0,331	0,332	5,656	4,124	6,242	12,568	9,165	13,872	11,868	1,984	16,720
5	0,638	0,637	0,639	0,620	0,617	0,619	0,843	0,846	0,849	11,846	11,486	15,632	26,324	25,524	34,737	28,862	4,167	14,438
10	1,159	0,184	1,164	1,119	1,163	1,143	1,567	1,583	1,570	15,503	21,059	28,940	34,451	46,799	64,310	48,520	12,250	25,248
15	1,599	1,587	1,589	1,610	1,547	1,550	1,983	1,990	1,988	29,334	28,940	36,620	65,186	64,311	81,377	70,291	7,847	11,163
30	1,818	1,799	1,809	1,786	1,775	1,787	2,193	2,119	2,183	33,439	32,986	40,057	74,309	73,302	89,016	78,876	7,182	9,106
60	1,818	1,799	1,809	1,786	1,775	1,787	2,193	2,119	2,183	33,622	33,166	40,276	74,715	73,702	89,502	79,306	7,221	9,106
90	1,985	1,979	1,972	1,946	1,970	1,953	2,378	2,372	2,377	36,900	36,502	44,326	81,999	81,116	98,503	87,206	7,996	9,169
120	2,083	1,963	1,984	2,040	1,994	1,997	2,240	2,256	2,243	37,668	37,679	42,218	83,707	83,732	93,817	87,085	4,760	5,466
180	2,031	1,935	1,986	2,102	2,033	2,061	2,448	2,184	2,193	37,405	38,886	42,963	83,122	86,413	95,473	88,336	5,222	5,912
240	1,997	2,028	2,019	2,063	2,001	2,044	2,187	2,209	2,206	38,161	38,558	41,848	84,803	85,685	92,995	87,827	3,672	4,180
360	2,153	2,101	2,136	2,200	2,163	2,144	2,227	2,194	2,250	40,453	41,187	42,483	89,895	91,528	94,407	91,943	1,866	2,029
inf	2,295	2,264	2,242	2,162	2,160	2,143	2,293	2,301	2,263	42,596	41,156	43,830	94,659	91,457	97,399	94,505	2,428	2,570

Table 78: Table containing the spectrophotometric values and dissolution data of formula 5B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,342	0,338	0,393	0,381	0,363	0,372	0,398	0,386	0,386	7,471	7,759	8,121	16,601	17,241	18,046	17,296	0,591	3,417
5	0,828	0,863	0,819	0,840	0,904	0,882	0,974	1,020	1,002	17,092	17,870	20,338	37,982	39,711	45,196	40,963	3,075	7,507
10	1,333	1,435	1,419	1,601	1,321	1,383	1,820	1,759	1,893	28,365	29,155	36,955	63,034	64,789	82,122	69,982	8,614	12,309
15	1,492	1,651	1,633	1,488	1,634	1,613	2,445	2,469	2,435	32,446	32,187	49,666	72,103	71,526	110,368	84,666	18,176	21,468
30	1,800	2,033	1,943	1,770	1,758	1,754	2,435	2,430	2,440	39,286	36,002	49,644	87,302	80,005	110,320	92,542	12,919	13,960
60	1,964	1,998	1,973	1,936	1,848	1,873	2,443	2,445	2,444	40,566	38,706	50,090	90,146	86,014	111,312	95,824	11,081	11,564
90	2,068	2,160	2,133	1,930	1,930	1,912	2,336	2,462	2,293	43,617	39,677	48,767	96,927	88,172	108,371	97,823	8,271	8,455
120	2,383	2,390	2,383	2,182	2,239	2,239	2,285	2,224	2,265	49,162	45,817	46,906	109,249	101,816	104,235	105,100	3,096	2,945
180	2,094	1,946	1,994	2,063	1,988	1,893	2,154	2,099	2,135	41,946	41,288	44,589	93,212	91,752	99,087	94,684	3,170	3,348
240	1,850	1,807	1,829	2,440	2,412	2,440	1,938	2,359	2,438	38,519	50,491	47,140	85,598	112,203	104,755	100,852	11,207	11,112
360	2,205	2,292	2,001	2,226	1,939	2,044	2,329	2,179	2,322	45,465	43,542	48,018	101,033	96,760	106,707	101,500	4,074	4,014
inf	2,288	2,264	2,281	2,240	2,243	2,237	2,191	2,234	2,116	47,045	47,183	46,358	104,543	104,850	103,017	104,137	0,802	0,770

Dissolution results Formulation 5C

Table 79: Table containing the spectrophotometric values and dissolution data of formula 5C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,012	0,011	0,012	0,020	0,021	0,019	0,019	0,018	0,019	0,737	0,913	0,881	1,638	2,030	1,957	1,875	0,170	9,062
5	0,038	0,040	0,039	0,072	0,072	0,072	0,081	0,084	0,083	1,315	1,999	2,224	2,923	4,442	4,943	4,102	0,859	20,941
10	0,120	0,128	0,128	0,188	0,187	0,188	0,217	0,217	0,218	3,121	4,440	5,061	6,935	9,868	11,246	9,349	1,798	19,230
15	0,260	0,260	0,260	0,338	0,335	0,335	0,358	0,352	0,353	5,965	7,566	7,956	13,256	16,814	17,680	15,917	1,914	12,027
30	0,432	0,428	0,429	0,485	0,501	0,492	0,528	0,524	0,526	9,554	10,889	11,603	21,231	24,197	25,785	23,738	1,887	7,950
60	0,617	0,619	0,620	0,657	0,659	0,657	0,693	0,688	0,689	13,570	14,411	15,097	30,157	32,024	33,549	31,910	1,387	4,347
90	0,763	0,765	0,765	0,827	0,828	0,828	0,859	0,851	0,858	16,686	18,051	18,652	37,080	40,114	41,449	39,547	1,828	4,622
120	0,872	0,873	0,873	0,931	0,932	0,934	1,015	1,006	1,010	19,049	20,337	21,991	42,332	45,193	48,868	45,464	2,675	5,884
180	0,899	0,894	0,895	1,043	1,041	1,047	0,970	0,978	0,976	19,637	22,787	21,367	43,637	50,637	47,483	47,252	2,862	6,057
240	1,073	1,075	1,073	1,108	1,111	1,111	1,089	1,086	1,086	23,469	24,299	23,832	52,152	53,997	52,959	53,036	0,755	1,424
360	1,135	1,127	1,129	1,203	1,185	1,193	1,168	1,163	1,162	24,782	26,177	25,579	55,070	58,172	56,842	56,695	1,270	2,241
inf	1,148	1,149	1,147	1,139	1,148	1,185	1,121	1,127	1,129	25,193	25,557	24,900	55,985	56,794	55,333	56,037	0,598	1,067

Table 80: Table containing the spectrophotometric values and dissolution data of formula 5C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,104	0,107	0,107	0,196	0,199	0,201	0,200	0,171	0,179	2,148	3,832	3,553	4,774	8,514	7,896	7,062	1,637	23,181
5	0,479	0,477	0,476	0,600	0,615	0,607	0,590	0,611	0,611	8,908	11,282	11,219	19,796	25,072	24,930	23,266	2,454	10,549
10	0,956	0,953	0,959	1,223	1,225	1,231	1,244	1,244	1,247	17,655	22,594	22,929	39,234	50,209	50,953	46,799	5,358	11,448
15	1,598	1,608	1,608	1,683	1,694	1,688	1,703	1,704	1,730	29,546	31,115	31,557	65,659	69,144	70,126	68,310	1,917	2,806
30	1,942	1,942	1,941	1,991	1,942	1,963	2,131	2,236	2,217	35,836	36,323	40,499	79,635	80,718	89,997	83,450	4,651	5,573
60	1,941	1,987	1,963	2,184	2,090	2,163	2,059	2,065	2,060	36,435	39,806	38,299	80,968	88,459	85,110	84,845	3,064	3,611
90	2,000	2,010	2,010	2,234	2,184	2,197	2,088	2,051	2,073	37,417	41,098	38,671	83,150	91,330	85,936	86,805	3,395	3,912
120	2,073	2,004	2,034	2,203	2,139	2,163	2,195	2,187	2,181	38,169	40,654	41,008	84,819	90,343	91,128	88,763	2,807	3,163
180	2,041	2,101	2,086	2,207	2,273	2,264	2,175	2,084	2,088	39,082	42,315	39,925	86,848	94,034	88,722	89,868	3,043	3,386
240	2,098	2,069	2,069	2,369	2,162	2,379	2,202	2,125	2,194	39,339	43,557	41,191	87,419	96,793	91,535	91,916	3,836	4,174
360	2,171	2,040	2,063	2,033	2,181	2,091	2,070	2,099	2,071	39,780	40,119	39,707	88,400	89,152	88,238	88,597	0,398	0,449
inf	2,067	2,061	2,069	2,125	2,096	2,137	2,046	2,049	2,056	39,761	40,655	39,385	88,358	90,344	87,521	88,741	1,184	1,334

Table 81: Table containing the spectrophotometric values and dissolution data of formula 5C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,134	0,136	0,136	0,175	0,165	0,168	0,213	0,220	0,217	3,028	3,703	4,657	6,729	8,228	10,350	8,436	1,485	17,609
5	0,534	0,536	0,533	0,689	0,703	0,693	0,768	0,800	0,800	11,020	14,240	16,137	24,490	31,645	35,859	30,665	4,693	15,305
10	1,093	1,120	1,101	1,304	1,416	1,402	1,439	1,435	1,441	22,490	27,897	29,201	49,977	61,994	64,890	58,954	6,457	10,952
15	1,472	1,428	1,470	1,786	1,905	1,763	1,807	1,767	1,729	29,651	36,924	35,946	65,891	82,053	79,879	75,941	7,162	9,430
30	1,840	1,761	1,793	1,923	1,905	1,914	2,023	1,763	1,893	36,646	39,050	38,647	81,435	86,778	85,882	84,698	2,336	2,758
60	1,675	1,592	1,610	1,691	1,882	1,893	1,732	1,935	1,922	33,389	37,422	38,254	74,199	83,160	85,008	80,789	4,721	5,843
90	1,877	1,587	1,693	1,935	1,978	1,921	1,809	1,731	1,793	35,440	40,076	36,756	78,756	89,059	81,680	83,165	4,335	5,213
120	1,651	1,585	1,613	2,235	2,270	2,280	2,127	2,257	2,254	33,574	46,634	45,652	74,610	103,632	101,448	93,230	13,197	14,155
180	1,894	1,860	1,872	2,395	2,343	2,340	2,045	1,873	1,817	38,933	48,834	39,880	86,517	108,521	88,622	94,553	9,914	10,485
240	1,624	1,674	1,653	1,708	1,685	1,693	1,816	1,743	1,762	34,643	35,821	37,327	76,985	79,603	82,949	79,845	2,441	3,057
360	1,851	1,699	1,703	1,925	1,771	1,793	1,874	2,147	1,903	36,840	38,697	41,549	81,868	85,993	92,332	86,731	4,304	4,962
inf	1,788	1,806	1,795	1,527	1,584	1,610	2,113	2,003	2,105	38,311	33,787	43,752	85,135	75,082	97,227	85,815	9,053	10,550

Dissolution results Formulation 5D

Table 82: Table containing the spectrophotometric values and dissolution data of formula 5D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,014	0,015	0,015	0,015	0,015	0,016	0,008	0,008	0,009	0,797	0,813	0,663	1,772	1,806	1,474	1,684	0,149	8,864
5	0,036	0,038	0,037	0,036	0,037	0,037	0,028	0,027	0,026	1,269	1,257	1,058	2,819	2,793	2,350	2,654	0,215	8,109
10	0,092	0,093	0,093	0,095	0,094	0,095	0,094	0,093	0,093	2,438	2,481	2,450	5,417	5,514	5,444	5,459	0,041	0,744
15	0,200	0,203	0,202	0,200	0,200	0,199	0,200	0,204	0,203	4,737	4,694	4,749	10,526	10,432	10,553	10,503	0,052	0,494
30	0,407	0,409	0,406	0,422	0,422	0,422	0,410	0,407	0,409	9,065	9,379	9,101	20,144	20,843	20,225	20,404	0,312	1,529
60	0,742	0,736	0,741	0,781	0,777	0,779	0,719	0,718	0,719	16,084	16,913	15,642	35,743	37,585	34,761	36,030	1,171	3,249
90	1,008	1,006	1,007	1,079	1,072	1,077	0,990	0,987	0,987	21,775	23,224	21,369	48,388	51,609	47,487	49,161	1,770	3,600
120	1,174	1,164	1,170	1,244	1,244	1,245	1,227	1,221	1,227	25,298	26,886	26,457	56,218	59,747	58,794	58,253	1,491	2,559
180	1,314	1,328	1,324	1,405	1,405	1,406	1,344	1,347	1,332	28,638	30,397	29,029	63,641	67,548	64,509	65,233	1,675	2,568
240	1,440	1,429	1,432	1,453	1,444	1,448	1,423	1,426	1,429	31,127	31,473	30,963	69,171	69,940	68,807	69,306	0,472	0,681
360	1,508	1,504	1,505	1,548	1,546	1,548	1,475	1,513	1,508	32,802	33,721	32,667	72,893	74,936	72,594	73,474	1,041	1,416
inf	1,384	1,387	1,381	1,407	1,403	1,411	1,373	1,376	1,371	30,517	30,955	30,208	67,815	68,789	67,129	67,911	0,681	1,003

Table 83: Table containing the spectrophotometric values and dissolution data of formula 5D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,149	0,151	0,151	0,061	0,061	0,059	0,042	0,041	0,042	2,950	1,315	0,976	6,555	2,923	2,168	3,882	1,915	49,331
5	0,545	0,534	0,544	0,311	0,327	0,321	0,320	0,323	0,321	10,069	6,036	6,061	22,376	13,413	13,468	16,419	4,212	25,655
10	1,298	1,300	1,294	0,785	0,785	0,782	0,876	0,879	0,874	23,873	14,510	16,184	53,052	32,244	35,964	40,420	9,060	22,415
15	1,857	1,815	1,844	1,163	1,202	1,204	1,361	1,361	1,361	33,846	21,962	25,088	75,213	48,804	55,750	59,922	11,178	18,654
30	1,914	1,905	1,914	1,635	1,648	1,636	1,794	1,785	1,786	35,345	30,270	32,995	78,545	67,266	73,322	73,044	4,609	6,310
60	2,335	2,246	2,263	1,874	1,947	1,931	2,018	2,061	2,040	42,276	35,485	37,746	93,946	78,855	83,881	85,561	6,275	7,334
90	2,244	2,204	2,236	2,059	2,015	2,043	2,142	2,252	2,202	41,538	37,887	40,846	92,308	84,194	90,769	89,090	3,519	3,950
120	2,273	2,360	2,329	2,092	2,293	2,174	2,401	2,205	2,206	43,447	40,773	42,371	96,549	90,606	94,157	93,771	2,442	2,604
180	2,275	2,279	2,283	2,324	2,275	2,174	2,465	2,391	2,413	42,923	42,294	45,372	95,385	93,986	100,826	96,732	2,950	3,050
240	2,409	2,446	2,457	2,163	2,171	2,169	2,332	2,193	2,207	46,028	40,874	42,362	102,283	90,832	94,137	95,751	4,812	5,026
360	2,112	2,249	2,259	2,031	2,026	2,030	2,243	2,207	2,040	42,086	38,580	41,120	93,525	85,733	91,378	90,212	3,286	3,643
inf	2,324	2,316	2,310	2,060	2,073	2,101	2,124	2,264	2,195	42,120	39,677	41,903	93,601	88,171	93,117	91,630	2,454	2,678

Table 84: Table containing the spectrophotometric values and dissolution data of formula 5D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,054	0,051	0,052	0,044	0,048	0,043	0,035	0,040	0,036	1,363	1,220	1,060	3,030	2,711	2,356	2,699	0,275	10,202
5	0,314	0,317	0,314	0,322	0,329	0,319	0,319	0,317	0,320	6,621	6,792	6,689	14,714	15,093	14,864	14,890	0,156	1,046
10	0,859	0,863	0,861	0,910	0,894	0,903	0,779	0,789	0,788	17,581	18,410	16,068	39,068	40,910	35,707	38,562	2,154	5,586
15	1,379	1,601	1,392	1,466	1,442	1,461	1,225	1,183	1,193	29,608	29,588	24,453	65,795	65,751	54,341	61,962	5,389	8,697
30	2,300	1,934	1,983	1,903	2,191	2,213	1,815	1,893	1,874	42,066	42,669	37,791	93,481	94,820	83,980	90,760	4,826	5,317
60	2,155	2,157	2,149	2,048	2,177	2,135	1,954	1,927	1,947	43,914	43,252	39,642	97,587	96,115	88,092	93,931	4,172	4,442
90	2,113	2,095	2,144	1,741	1,751	1,773	1,809	1,850	1,873	43,433	36,191	37,879	96,518	80,425	84,176	87,040	6,875	7,898
120	2,204	2,215	2,185	2,098	2,154	2,129	2,090	1,986	1,993	45,342	43,832	41,664	100,761	97,405	92,587	96,918	3,355	3,461
180	2,085	2,080	2,075	2,196	2,203	2,186	2,268	1,964	1,983	43,165	45,429	42,865	95,922	100,953	95,256	97,377	2,543	2,612
240	1,906	2,006	2,008	1,786	1,647	1,792	1,577	1,629	1,614	41,263	36,597	33,799	91,697	81,328	75,108	82,711	6,843	8,273
360	1,607	1,779	1,903	1,752	1,743	1,825	1,525	1,544	1,524	37,280	37,428	32,458	82,845	83,172	72,130	79,382	5,130	6,462
inf	1,913	1,925	1,911	1,915	1,921	1,911	1,748	1,703	1,685	39,171	40,465	36,248	87,047	89,923	80,552	85,841	3,919	4,566

Dissolution results Formulation 5E

Table 85: Table containing the spectrophotometric values and dissolution data of formula 5E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,011	0,011	0,011	0,011	0,011	0,011	0,014	0,014	0,013	0,723	0,721	0,775	1,606	1,603	1,722	1,644	0,056	3,386
5	0,053	0,054	0,054	0,061	0,060	0,061	0,067	0,068	0,068	1,619	1,766	1,916	3,598	3,925	4,258	3,927	0,270	6,868
10	0,189	0,188	0,188	0,209	0,199	0,199	0,198	0,197	0,197	4,446	4,737	4,637	9,881	10,527	10,304	10,237	0,268	2,618
15	0,374	0,374	0,375	0,372	0,373	0,373	0,360	0,360	0,361	8,371	8,339	8,076	18,603	18,532	17,946	18,360	0,294	1,602
30	0,566	0,564	0,564	0,555	0,552	0,554	0,533	0,528	0,528	12,401	12,170	11,674	27,559	27,045	25,942	26,849	0,674	2,512
60	0,662	0,664	0,663	0,703	0,703	0,704	0,671	0,670	0,671	14,527	15,379	14,690	32,283	34,175	32,645	33,034	0,820	2,482
90	0,807	0,804	0,805	0,819	0,820	0,819	0,801	0,798	0,800	17,591	17,881	17,472	39,090	39,736	38,827	39,218	0,382	0,974
120	0,931	0,937	0,933	0,911	0,903	0,906	0,900	0,895	0,896	20,375	19,822	19,604	45,279	44,050	43,564	44,297	0,722	1,629
180	1,045	1,028	1,036	0,985	0,984	0,987	0,983	0,969	0,974	22,638	21,575	21,350	50,307	47,944	47,444	48,565	1,248	2,571
240	1,082	1,089	1,086	1,070	1,048	1,050	1,055	1,052	1,052	23,793	23,166	23,094	52,873	51,481	51,321	51,891	0,697	1,344
360	1,135	1,133	1,135	1,139	1,117	1,119	1,122	1,114	1,173	24,940	24,734	24,959	55,423	54,964	55,464	55,284	0,227	0,410
inf	1,144	1,144	1,141	1,105	1,113	1,109	1,098	1,096	1,100	24,699	24,531	24,292	54,886	54,514	53,982	54,461	0,371	0,681

Table 86: Table containing the spectrophotometric values and dissolution data of formula 5E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,042	0,041	0,042	0,032	0,036	0,033	0,056	0,055	0,056	0,976	0,833	1,225	2,168	1,851	2,723	2,247	0,361	16,047
5	0,251	0,259	0,252	0,263	0,263	0,263	0,299	0,300	0,299	4,839	4,999	5,666	10,754	11,109	12,590	11,485	0,795	6,924
10	0,737	0,739	0,737	0,768	0,756	0,761	0,801	0,810	0,802	13,663	14,097	14,879	30,361	31,327	33,065	31,585	1,119	3,543
15	1,273	1,280	1,258	1,238	1,242	1,238	1,306	1,308	1,308	23,422	22,853	24,103	52,049	50,784	53,563	52,132	1,136	2,179
30	1,681	1,667	1,679	1,678	1,671	1,673	1,734	1,736	1,730	30,919	30,884	31,983	68,708	68,631	71,073	69,471	1,133	1,632
60	1,877	1,886	1,880	1,889	1,867	1,873	1,978	1,865	1,883	34,821	34,733	35,345	77,381	77,185	78,545	77,704	0,600	0,773
90	1,966	1,947	1,952	2,017	1,970	1,993	1,948	1,943	1,941	36,356	37,049	36,179	80,790	82,332	80,399	81,174	0,835	1,028
120	2,079	2,043	2,064	2,094	2,089	2,090	2,048	2,010	2,021	38,494	39,029	37,877	85,542	86,731	84,171	85,481	1,046	1,224
180	2,199	2,173	2,179	2,246	2,150	2,194	2,142	2,076	2,094	40,918	41,162	39,488	90,930	91,471	87,752	90,051	1,641	1,822
240	2,139	2,181	2,174	2,166	2,134	2,150	2,115	1,997	1,999	40,793	40,532	38,484	90,651	90,072	85,520	88,747	2,295	2,585
360	2,271	2,117	2,193	2,294	2,216	2,274	2,085	1,994	2,035	41,542	42,773	38,708	92,315	95,051	86,019	91,128	3,782	4,150
inf	2,179	2,150	2,169	2,084	2,125	2,109	2,056	2,003	2,044	40,095	40,181	38,842	89,101	89,291	86,316	88,236	1,360	1,541

Table 87: Table containing the spectrophotometric values and dissolution data of formula 5E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,049	0,052	0,050	0,062	0,057	0,057	0,032	0,038	0,035	1,325	1,489	1,014	2,944	3,310	2,253	2,836	0,438	15,445
5	0,360	0,382	0,367	0,274	0,252	0,274	0,316	0,320	0,318	7,722	5,658	6,689	17,161	12,574	14,863	14,866	1,872	12,594
10	0,923	0,907	0,913	0,659	0,672	0,663	0,824	0,792	0,799	18,652	13,649	16,463	41,449	30,331	36,585	36,121	4,551	12,599
15	1,178	1,293	1,235	1,016	0,971	0,993	1,310	1,449	1,414	25,174	20,296	28,263	55,941	45,102	62,807	54,617	7,289	13,345
30	1,848	1,948	1,950	1,389	1,379	1,377	1,874	1,847	1,781	38,917	28,179	37,283	86,482	62,620	82,850	77,317	10,498	13,578
60	2,086	1,745	1,716	1,548	1,662	1,573	1,995	2,013	2,144	37,796	32,583	41,816	83,992	72,407	92,925	83,108	8,400	10,107
90	1,786	1,742	1,773	1,927	1,715	1,783	2,002	2,123	2,213	36,364	37,036	43,294	80,810	82,303	96,209	86,441	6,934	8,022
120	1,945	2,007	2,013	2,232	2,236	2,193	1,878	1,877	1,932	40,986	45,481	39,184	91,080	101,070	87,075	93,075	5,885	6,323
180	1,829	1,527	1,631	1,938	1,488	1,493	2,062	1,515	1,935	34,681	34,108	38,227	77,069	75,796	84,949	79,271	4,048	5,107
240	2,269	2,067	2,009	2,015	2,048	2,009	1,961	1,933	1,941	43,924	41,980	40,582	97,610	93,288	90,182	93,693	3,046	3,251
360	2,106	2,114	2,157	2,023	1,929	1,935	2,095	1,985	1,973	44,377	40,970	42,252	98,616	91,044	93,894	94,518	3,123	3,304
inf	2,138	2,115	2,141	1,848	1,904	1,885	2,015	1,995	2,003	42,191	39,517	42,209	93,757	87,816	93,798	91,790	2,811	3,062

Dissolution results Formulation 5F

Table 88: Table containing the spectrophotometric values and dissolution data of formula 5F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,010	0,010	0,010	0,023	0,020	0,022	0,019	0,019	0,020	0,697	0,945	0,898	1,548	2,101	1,995	1,882	0,240	12,735
5	0,024	0,024	0,025	0,075	0,075	0,075	0,067	0,065	0,068	1,002	2,069	1,895	2,226	4,598	4,210	3,678	1,039	28,239
10	0,079	0,080	0,080	0,247	0,247	0,247	0,276	0,276	0,276	2,170	5,679	6,293	4,821	12,619	13,985	10,475	4,036	38,534
15	0,229	0,231	0,231	0,506	0,505	0,505	0,597	0,595	0,598	5,329	11,121	13,039	11,842	24,713	28,976	21,844	7,283	33,342
30	0,489	0,489	0,490	0,802	0,808	0,806	0,827	0,827	0,828	10,793	17,475	17,949	23,985	38,834	39,886	34,235	7,261	21,208
60	0,859	0,854	0,854	1,066	1,057	1,059	1,061	1,056	1,058	18,525	22,919	22,882	41,168	50,932	50,850	47,650	4,584	9,620
90	1,125	1,125	1,126	1,280	1,279	1,279	1,350	1,334	1,343	24,276	27,619	28,969	53,947	61,377	64,375	59,900	4,383	7,317
120	1,179	1,186	1,183	1,384	1,387	1,387	1,456	1,435	1,437	25,610	30,013	31,223	56,911	66,695	69,385	64,331	5,360	8,332
180	1,444	1,451	1,449	1,489	1,484	1,486	1,528	1,543	1,541	31,308	32,281	33,382	69,572	71,735	74,182	71,830	1,883	2,621
240	1,463	1,469	1,470	1,544	1,530	1,533	1,583	1,587	1,588	31,882	33,493	34,568	70,849	74,429	76,817	74,032	2,453	3,313
360	1,606	1,608	1,606	1,629	1,626	1,625	1,646	1,646	1,646	34,976	35,573	36,019	77,725	79,050	80,042	78,939	0,949	1,202
inf	1,504	1,511	1,508	1,561	1,567	1,561	1,576	1,577	1,577	33,960	34,427	34,759	75,467	76,503	77,242	76,404	0,728	0,953

Table 89: Table containing the spectrophotometric values and dissolution data of formula 5F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,024	0,026	0,025	0,097	0,089	0,090	0,017	0,017	0,017	0,671	1,890	0,523	1,491	4,201	1,162	2,285	1,361	59,593
5	0,123	0,126	0,124	0,393	0,413	0,396	0,142	0,141	0,140	2,474	7,516	2,782	5,498	16,702	6,183	9,461	5,128	54,201
10	0,429	0,441	0,429	0,991	1,020	1,008	0,459	0,464	0,459	8,100	18,563	8,612	18,001	41,250	19,138	26,130	10,702	40,956
15	0,800	0,822	0,824	1,530	1,532	1,526	0,869	0,889	0,875	15,100	28,176	16,235	33,555	62,614	36,078	44,083	13,144	29,817
30	1,340	1,358	1,351	1,881	1,908	1,903	1,448	1,429	1,431	24,894	35,016	26,478	55,321	77,812	58,841	63,991	9,878	15,436
60	1,776	1,751	1,763	2,146	2,314	2,273	1,896	1,847	1,863	32,553	41,522	34,489	72,339	92,271	76,643	80,418	8,564	10,649
90	1,892	1,965	1,943	2,363	2,255	2,274	1,997	2,132	2,033	35,825	42,712	38,040	79,610	94,916	84,533	86,353	6,380	7,388
120	1,962	1,691	1,958	2,407	2,409	2,397	2,168	2,198	2,174	34,873	44,888	40,547	77,495	99,752	90,104	89,117	9,113	10,226
180	2,002	2,176	2,193	3,157	2,417	2,439	2,206	2,206	2,210	39,674	49,980	41,261	88,164	111,067	91,691	96,974	10,069	10,383
240	2,032	2,028	2,031	2,389	2,296	2,343	2,190	2,215	2,204	38,182	44,276	41,406	84,849	98,390	92,014	91,751	5,531	6,029
360	2,140	2,049	2,044	2,339	2,345	2,394	2,208	2,219	2,215	39,247	44,813	41,823	87,215	99,584	92,941	93,247	5,054	5,421
inf	2,143	2,143	2,151	2,353	2,328	2,299	2,139	2,174	2,150	41,848	44,467	40,967	92,996	98,815	91,038	94,283	3,303	3,503

Table 90: Table containing the spectrophotometric values and dissolution data of formula 5F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,000	0,000	0,000	0,013	0,010	0,018	0,000	0,000	0,000	0,320	0,598	0,320	0,711	1,329	0,711	0,917	0,291	31,757
5	0,105	0,110	0,107	0,360	0,288	0,302	0,096	0,090	0,094	2,471	6,652	2,184	5,492	14,781	4,853	8,375	4,537	54,171
10	0,428	0,427	0,421	0,768	0,777	0,754	0,384	0,383	0,387	8,845	15,687	8,028	19,656	34,859	17,839	24,118	7,631	31,641
15	0,807	0,799	0,813	1,091	1,171	1,163	0,716	0,740	0,722	16,507	23,277	14,892	36,683	51,727	33,093	40,501	8,072	19,931
30	1,302	1,460	1,414	1,489	1,504	1,493	1,334	1,437	1,403	28,305	30,473	28,278	62,900	67,719	62,840	64,486	2,286	3,545
60	1,781	1,501	1,624	1,965	1,910	1,734	1,709	1,661	1,679	33,328	38,133	34,266	74,063	84,740	76,146	78,316	4,621	5,901
90	1,708	1,645	1,693	1,779	1,860	1,823	1,980	2,137	1,937	34,443	37,363	41,156	76,540	83,030	91,458	83,676	6,107	7,299
120	2,011	1,736	1,694	1,908	1,839	1,860	1,910	1,669	1,909	37,263	38,519	37,607	82,808	85,598	83,571	83,992	1,177	1,402
180	1,613	1,487	1,502	1,763	1,927	1,893	1,518	1,758	1,703	31,874	38,579	34,412	70,832	85,730	76,471	77,678	6,142	7,907
240	2,006	2,013	1,997	2,274	2,237	2,280	1,989	1,914	1,937	41,478	46,828	40,345	92,173	104,062	89,655	95,297	6,283	6,593
360	2,217	2,062	2,003	2,439	2,420	2,417	2,003	2,085	2,065	43,469	50,317	42,641	96,597	111,815	94,757	101,057	7,644	7,565
inf	2,044	2,064	2,112	2,082	2,115	2,046	2,194	2,086	2,257	44,043	43,700	45,433	97,873	97,111	100,963	98,649	1,666	1,689

Dissolution results Formulation 6A

Table 91: Table containing the spectrophotometric values and dissolution data of formula 6A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,014	0,013	0,013	0,010	0,010	0,010	0,012	0,012	0,012	0,770	0,695	0,746	1,711	1,544	1,657	1,637	0,070	4,267
5	0,046	0,045	0,045	0,036	0,035	0,035	0,055	0,053	0,055	1,441	1,230	1,634	3,202	2,734	3,631	3,189	0,366	11,482
10	0,125	0,125	0,125	0,086	0,086	0,087	0,161	0,160	0,160	3,117	2,302	3,860	6,926	5,114	8,577	6,872	1,414	20,576
15	0,231	0,234	0,232	0,152	0,151	0,151	0,302	0,304	0,304	5,379	3,678	6,876	11,954	8,174	15,280	11,803	2,903	24,596
30	0,417	0,409	0,411	0,256	0,257	0,257	0,524	0,522	0,524	9,179	5,903	11,524	20,398	13,117	25,610	19,708	5,123	25,995
60	0,677	0,675	0,678	0,394	0,419	0,409	0,790	0,795	0,793	14,779	9,091	17,231	32,842	20,203	38,291	30,446	7,576	24,885
90	0,916	0,911	0,912	0,602	0,594	0,599	1,031	1,033	1,031	19,804	13,141	22,338	44,009	29,202	49,640	40,950	8,620	21,049
120	1,068	1,077	1,081	0,762	0,764	0,761	1,189	1,182	1,186	23,322	16,656	25,681	51,827	37,013	57,069	48,636	8,493	17,463
180	1,209	1,204	1,208	0,919	0,919	0,920	1,297	1,299	1,298	26,201	20,034	28,173	58,225	44,521	62,608	55,118	7,704	13,977
240	1,310	1,309	1,310	1,052	1,058	1,056	1,380	1,368	1,370	28,494	22,993	29,890	63,319	51,095	66,422	60,279	6,616	10,976
360	1,397	1,389	1,379	1,216	1,210	1,214	1,444	1,452	1,450	30,294	26,420	31,643	67,320	58,712	70,318	65,450	4,919	7,516
inf	1,342	1,344	1,347	1,262	1,250	1,250	1,431	1,413	1,420	29,443	27,418	31,245	65,429	60,928	69,433	65,264	3,474	5,323

Table 92: Table containing the spectrophotometric values and dissolution data of formula 6A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,175	0,188	0,179	0,898	0,091	0,090	0,046	0,046	0,046	3,505	6,758	1,052	7,789	15,018	2,338	8,382	5,194	61,964
5	0,542	0,518	0,526	0,317	0,358	0,326	0,311	0,303	0,307	9,852	6,324	5,808	21,892	14,054	12,906	16,284	3,993	24,523
10	1,074	1,079	1,073	0,870	0,843	0,853	0,751	0,740	0,740	19,833	15,842	13,772	44,074	35,203	30,604	36,627	5,591	15,263
15	1,479	1,508	1,479	1,314	1,280	1,280	1,227	1,235	1,235	27,465	23,853	22,729	61,034	53,006	50,509	54,850	4,490	8,186
30	1,877	1,925	1,903	1,720	1,683	1,689	1,684	1,635	1,633	35,125	31,362	30,466	78,055	69,693	67,702	71,817	4,485	6,245
60	2,100	2,119	2,107	1,948	2,038	2,002	1,896	1,895	1,893	39,082	36,966	35,070	86,849	82,146	77,933	82,309	3,642	4,425
90	2,305	2,109	2,194	1,921	2,031	1,963	1,913	1,877	1,896	40,996	36,725	35,276	91,103	81,612	78,392	83,702	5,396	6,446
120	2,355	2,214	2,212	1,979	1,963	1,979	1,855	1,885	1,863	42,273	36,956	34,960	93,941	82,125	77,689	84,585	6,859	8,109
180	2,277	2,179	2,181	2,025	2,027	2,031	1,947	1,935	1,893	41,631	38,138	36,190	92,514	84,751	80,422	85,896	5,003	5,824
240	2,160	2,208	2,209	2,039	2,015	2,022	1,940	1,951	1,943	41,486	38,308	36,745	92,191	85,129	81,655	86,325	4,383	5,078
360	2,143	2,186	2,164	1,978	1,991	1,983	1,971	1,961	1,971	41,200	37,754	37,359	91,555	83,897	83,021	86,158	3,833	4,449
inf	2,249	2,249	2,211	2,034	2,041	2,040	1,976	1,982	1,979	39,967	38,942	37,763	88,815	86,538	83,918	86,424	2,001	2,315

Table 93: Table containing the spectrophotometric values and dissolution data of formula 6A read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,089	0,091	0,090	0,212	0,194	0,198	0,154	0,148	0,149	2,119	4,337	3,329	4,708	9,639	7,399	7,248	2,016	27,808
5	0,459	0,428	0,436	0,733	0,724	0,736	0,510	0,496	0,491	9,155	14,963	10,313	20,345	33,251	22,917	25,504	5,577	21,868
10	1,005	1,169	1,035	1,407	1,356	1,403	1,034	0,814	0,929	21,768	28,200	18,902	48,374	62,666	42,005	51,015	8,639	16,934
15	1,469	1,189	1,235	2,150	2,154	2,074	1,138	1,232	1,274	26,451	43,092	24,785	58,780	95,760	55,078	69,873	18,367	26,287
30	1,705	1,615	1,673	2,062	2,376	2,300	1,399	1,401	1,389	33,929	45,733	28,553	75,399	101,628	63,452	80,160	15,945	19,892
60	1,849	2,046	1,935	2,275	2,197	2,204	1,726	2,069	1,844	39,691	45,566	38,373	88,202	101,258	85,273	91,578	6,949	7,588
90	1,918	1,942	1,903	2,146	2,256	2,296	1,699	1,744	2,001	39,468	45,967	37,285	87,706	102,149	82,855	90,903	8,195	9,015
120	2,185	2,207	2,077	2,246	2,197	2,205	1,523	1,507	1,512	44,376	45,876	31,476	98,614	101,946	69,947	90,169	14,364	15,930
180	2,158	2,147	2,104	2,246	2,186	2,195	1,410	1,382	1,395	44,217	45,987	29,275	98,259	102,194	65,056	88,503	16,657	18,821
240	2,065	2,358	2,035	2,458	2,424	2,039	1,774	1,779	1,780	44,785	48,191	37,073	99,521	107,090	82,385	96,332	10,335	10,728
360	2,086	2,121	2,074	2,481	2,204	2,002	1,909	1,963	1,906	43,846	46,881	40,239	97,436	104,180	89,420	97,012	6,033	6,219
inf	2,347	2,295	2,286	2,361	2,295	2,293	1,956	1,933	1,995	46,115	48,881	41,156	102,478	108,625	91,457	100,853	7,102	7,042

Dissolution results Formulation 6B

Table 94: Table containing the spectrophotometric values and dissolution data of formula 6B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,009	0,009	0,009	0,014	0,015	0,015	0,009	0,009	0,010	0,676	0,797	0,686	1,503	1,770	1,525	1,600	0,121	7,572
5	0,017	0,015	0,016	0,047	0,044	0,046	0,019	0,018	0,019	0,825	1,448	0,884	1,833	3,217	1,964	2,338	0,624	26,680
10	0,045	0,045	0,045	0,135	0,135	0,135	0,068	0,068	0,069	1,437	3,332	1,931	3,193	7,404	4,292	4,963	1,784	35,938
15	0,117	0,117	0,117	0,271	0,270	0,271	0,160	0,160	0,161	2,951	6,188	3,865	6,559	13,752	8,589	9,633	3,028	31,432
30	0,259	0,256	0,258	0,477	0,475	0,477	0,318	0,315	0,316	5,918	10,534	7,154	13,150	23,408	15,897	17,485	4,336	24,797
60	0,480	0,475	0,477	0,756	0,766	0,761	0,537	0,537	0,537	10,558	16,552	11,816	23,461	36,782	26,257	28,834	5,735	19,891
90	0,703	0,693	0,674	1,018	1,022	1,020	0,737	0,737	0,737	15,063	22,077	16,068	33,474	49,059	35,708	39,414	6,881	17,459
120	0,858	0,852	0,857	1,181	1,182	1,181	0,924	1,029	1,030	18,617	25,572	21,550	41,372	56,826	47,888	48,695	6,335	13,009
180	0,977	0,970	0,973	1,298	1,292	1,292	1,037	1,029	1,030	21,180	28,077	22,455	47,066	62,393	49,899	53,119	6,658	12,535
240	1,139	1,132	1,137	1,378	1,383	1,381	1,164	1,151	1,158	24,709	30,044	25,209	54,909	66,765	56,021	59,231	5,346	9,026
360	1,289	1,283	1,287	1,425	1,426	1,426	1,297	1,283	1,290	27,995	31,141	28,125	62,211	69,203	62,501	64,638	3,230	4,997
inf	1,272	1,282	1,279	1,418	1,415	1,419	1,379	1,370	1,378	29,622	31,137	30,073	65,827	69,193	66,829	67,283	1,411	2,097

Table 95: Table containing the spectrophotometric values and dissolution data of formula 6B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,045	0,039	0,039	0,047	0,043	0,043	0,083	0,079	0,079	0,961	1,022	1,674	2,135	2,272	3,720	2,709	0,717	26,472
5	0,211	0,222	0,218	0,290	0,290	0,283	0,402	0,406	0,406	4,167	5,449	7,586	9,259	12,110	16,857	12,742	3,134	24,596
10	0,592	0,589	0,589	0,782	0,789	0,786	1,069	1,088	1,083	10,975	14,533	19,904	24,388	32,295	44,230	33,638	8,156	24,247
15	1,144	1,139	1,140	1,324	1,338	1,329	1,649	1,653	1,640	21,048	24,518	30,327	46,773	54,484	67,394	56,217	8,507	15,132
30	1,689	1,701	1,686	1,794	1,854	1,837	1,988	1,950	1,963	31,186	33,711	36,305	69,303	74,914	80,678	74,965	4,644	6,195
60	1,967	1,957	1,969	2,051	2,031	2,041	2,240	2,268	2,271	36,303	37,759	41,821	80,673	83,909	92,936	85,839	5,189	6,045
90	2,021	2,008	2,011	2,100	2,115	2,103	2,174	2,211	2,213	37,391	39,144	40,951	83,092	86,986	91,003	87,027	3,230	3,711
120	2,037	2,023	2,029	2,104	2,132	2,107	2,202	2,081	2,101	37,893	39,510	39,878	84,207	87,800	88,619	86,875	1,916	2,206
180	2,063	1,933	1,983	2,157	2,161	2,164	2,069	2,136	2,103	37,429	40,568	39,631	83,177	90,151	88,069	87,132	2,923	3,355
240	2,042	2,041	2,040	2,062	2,103	2,093	2,215	2,143	2,143	38,512	39,429	41,013	85,582	87,619	91,141	88,114	2,296	2,606
360	2,168	2,136	2,156	2,137	2,187	2,143	2,238	2,284	2,281	40,757	40,905	43,069	90,571	90,900	95,708	92,393	2,348	2,541
inf	2,135	2,162	2,123	2,238	2,222	2,202	2,241	2,230	2,220	41,767	42,307	42,615	92,816	94,016	94,701	93,844	0,779	0,830

Table 96: Table containing the spectrophotometric values and dissolution data of formula 6B read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,110	0,109	0,109	0,072	0,062	0,068	0,099	0,098	0,094	2,505	1,666	2,258	5,566	3,702	5,018	4,762	0,782	16,423
5	0,417	0,388	0,399	0,387	0,386	0,387	0,499	0,497	0,490	8,357	8,056	10,233	18,572	17,903	22,739	19,738	2,140	10,841
10	0,821	0,845	0,829	0,936	0,902	0,914	1,145	1,183	1,133	17,013	18,716	23,454	37,808	41,592	52,120	43,840	6,055	13,812
15	1,242	1,180	1,193	1,334	1,396	1,373	1,538	1,563	1,541	24,574	27,828	31,457	54,608	61,839	69,904	62,117	6,247	10,057
30	1,674	1,633	1,683	1,647	1,509	1,543	1,853	1,720	1,773	33,869	31,952	36,330	75,265	71,005	80,733	75,668	3,982	5,262
60	1,727	1,805	1,794	1,782	1,799	1,789	1,945	1,876	1,964	36,299	36,599	39,448	80,663	81,331	87,662	83,219	3,154	3,789
90	1,992	1,762	1,794	1,703	1,792	1,739	1,957	1,948	1,950	37,972	35,893	40,131	84,382	79,763	89,181	84,442	3,845	4,554
120	1,655	1,641	1,649	1,666	1,537	1,536	1,802	1,910	1,904	34,160	32,782	38,749	75,911	72,850	86,109	78,290	5,668	7,240
180	1,739	1,843	1,865	1,664	1,689	1,693	1,876	1,742	1,794	37,680	35,008	37,601	83,733	77,795	83,558	81,695	2,759	3,377
240	1,795	2,107	1,894	1,698	1,650	1,639	1,932	2,136	1,973	40,212	34,805	41,993	89,360	77,344	93,319	86,674	6,792	7,837
360	2,255	1,884	1,922	1,746	1,794	1,763	2,109	2,009	1,999	42,196	37,094	42,730	93,769	82,430	94,956	90,385	5,646	6,247
inf	1,870	1,903	1,897	1,899	1,866	1,896	2,197	2,007	2,047	41,082	39,677	43,837	91,292	88,172	97,416	92,293	3,840	4,160

Dissolution results Formulation 6C

Table 97: Table containing the spectrophotometric values and dissolution data of formula 6C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,018	0,018	0,015	0,009	0,010	0,011	0,013	0,012	0,012	0,846	0,706	0,753	1,881	1,568	1,674	1,708	0,130	7,591
5	0,020	0,022	0,021	0,032	0,035	0,034	0,032	0,033	0,032	0,933	1,201	1,171	2,074	2,669	2,603	2,449	0,266	10,865
10	0,054	0,053	0,054	0,103	0,100	0,100	0,089	0,087	0,088	1,624	2,614	2,341	3,608	5,808	5,201	4,873	0,928	19,045
15	0,144	0,142	0,143	0,227	0,224	0,225	0,198	0,195	0,197	3,498	5,231	4,626	7,773	11,624	10,279	9,892	1,596	16,133
30	0,320	0,315	0,393	0,419	0,417	0,418	0,366	0,365	0,368	7,707	9,301	8,212	17,126	20,669	18,248	18,681	1,479	7,915
60	0,552	0,550	0,551	0,663	0,669	0,675	0,619	0,608	0,609	12,104	14,615	13,407	26,898	32,477	29,793	29,723	2,278	7,664
90	0,776	0,773	0,774	0,865	0,865	0,865	0,799	0,798	0,799	16,859	18,798	17,388	37,464	41,773	38,640	39,292	1,819	4,629
120	0,910	0,910	0,909	1,019	1,011	1,017	0,947	0,933	0,938	19,782	22,054	20,422	43,960	49,009	45,382	46,117	2,126	4,609
180	1,070	1,069	1,069	1,121	1,123	1,124	1,031	1,029	1,030	23,235	24,422	22,441	51,632	54,270	49,870	51,924	1,808	3,483
240	1,152	1,156	1,154	1,228	1,225	1,229	1,140	1,131	1,138	25,144	26,740	24,788	55,875	59,423	55,084	56,794	1,887	3,322
360	1,250	1,253	1,251	1,329	1,342	1,341	1,212	1,222	1,221	27,312	29,189	26,638	60,693	64,865	59,195	61,584	2,399	3,896
inf	1,361	1,350	1,353	1,421	1,419	1,420	1,319	1,333	1,329	29,888	31,080	29,068	66,418	69,067	64,596	66,694	1,836	2,753

Table 98: Table containing the spectrophotometric values and dissolution data of formula 6C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,019	0,020	0,020	0,020	0,023	0,024	0,024	0,024	0,024	0,575	0,627	0,648	1,277	1,394	1,441	1,371	0,069	5,040
5	0,221	0,204	0,214	0,199	0,195	0,199	0,127	0,136	0,139	4,090	3,816	2,655	9,089	8,480	5,899	7,823	1,383	17,676
10	0,659	0,663	0,660	0,663	0,663	0,665	0,543	0,562	0,559	12,256	12,307	10,320	27,235	27,349	22,932	25,839	2,056	7,956
15	1,134	1,124	1,131	1,162	1,164	1,164	1,164	1,168	1,164	20,847	21,457	21,476	46,326	47,683	47,725	47,244	0,650	1,375
30	1,606	1,657	1,641	1,656	1,667	1,659	1,628	1,626	1,626	30,147	30,619	29,984	66,994	68,042	66,630	67,222	0,598	0,890
60	1,949	1,964	1,953	2,024	2,027	2,023	2,031	2,099	2,064	36,144	37,404	38,110	80,320	83,121	84,690	82,710	1,807	2,185
90	1,988	1,991	1,991	2,154	2,058	2,049	2,094	2,095	2,093	36,963	38,745	38,852	82,139	86,100	86,338	84,859	1,926	2,269
120	2,223	2,211	2,219	2,487	2,336	2,365	2,269	2,194	2,295	41,307	44,568	41,950	91,793	99,040	93,223	94,685	3,134	3,310
180	2,543	2,290	2,346	2,396	2,393	2,463	2,393	2,320	2,320	44,720	45,197	43,846	99,377	100,437	97,436	99,084	1,243	1,254
240	2,295	2,227	2,249	2,375	2,257	2,295	2,334	2,397	2,347	42,492	43,475	44,354	94,428	96,611	98,565	96,534	1,690	1,750
360	2,060	2,095	2,094	2,415	2,396	2,307	2,233	2,241	2,206	39,550	44,871	42,179	87,888	99,713	93,731	93,778	4,828	5,148
inf	1,973	1,946	1,991	2,066	2,144	2,096	2,011	2,050	2,135	39,084	40,186	39,465	86,854	89,302	87,701	87,952	1,015	1,154

Table 99: Table containing the spectrophotometric values and dissolution data of formula 6C read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,016	0,022	0,019	0,027	0,028	0,028	0,022	0,011	0,019	0,705	0,867	0,668	1,567	1,927	1,484	1,660	0,192	11,584
5	0,228	0,225	0,229	0,212	0,205	0,210	0,205	0,209	0,204	4,871	4,501	4,439	10,824	10,002	9,864	10,230	0,424	4,143
10	0,612	0,630	0,629	0,618	0,855	0,694	0,654	0,627	0,644	12,823	14,792	13,179	28,496	32,870	29,286	30,218	1,903	6,298
15	0,997	0,965	0,974	1,033	0,993	0,994	1,032	1,059	1,414	19,984	20,557	23,776	44,409	45,683	52,836	47,642	3,709	7,785
30	1,252	1,387	1,329	1,523	1,453	1,497	1,797	1,611	1,703	26,978	30,356	34,623	59,951	67,459	76,939	68,116	6,951	10,204
60	1,625	1,853	1,738	1,537	1,619	1,604	1,938	1,689	1,793	35,450	32,431	36,870	78,779	72,068	81,933	77,593	4,114	5,302
90	1,683	1,620	1,663	2,010	2,070	2,261	1,941	2,132	1,955	33,976	43,155	41,121	75,503	95,900	91,379	87,594	8,747	9,985
120	1,800	1,973	1,932	1,729	1,726	1,712	2,423	2,371	2,416	39,088	35,566	49,229	86,861	79,037	109,398	91,765	12,871	14,026
180	2,369	2,024	2,197	1,723	1,917	1,829	2,430	2,434	2,429	45,194	37,767	50,044	100,430	83,926	111,209	98,522	11,220	11,388
240	2,006	2,014	2,101	2,400	2,002	1,994	2,387	2,401	2,377	42,308	44,144	49,458	94,017	98,099	109,906	100,674	6,737	6,692
360	2,106	2,005	2,001	2,263	2,225	2,257	2,297	2,355	2,335	42,474	46,707	48,534	94,386	103,794	107,854	102,011	5,641	5,530
inf	2,009	1,995	1,985	2,185	2,194	2,188	2,277	2,242	2,207	44,804	45,772	47,056	99,564	101,715	104,570	101,950	2,050	2,011

Dissolution results Formulation 6D

Table 100: Table containing the spectrophotometric values and dissolution data of formula 6D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,012	0,013	0,013	0,017	0,015	0,014	0,013	0,013	0,012	0,753	0,815	0,757	1,674	1,811	1,682	1,722	0,063	3,639
5	0,025	0,025	0,025	0,028	0,035	0,035	0,026	0,026	0,026	1,014	1,178	1,032	2,253	2,618	2,292	2,388	0,163	6,838
10	0,103	0,095	0,099	0,102	0,994	0,102	0,098	0,099	0,098	2,572	8,869	2,562	5,717	19,710	5,694	10,373	6,602	63,642
15	0,276	0,275	0,276	0,281	0,281	0,282	0,295	0,291	0,291	6,286	6,442	6,636	13,968	14,316	14,748	14,344	0,319	2,223
30	0,586	0,582	0,584	0,571	0,568	0,571	0,566	0,567	0,566	12,782	12,526	12,410	28,404	27,835	27,577	27,939	0,345	1,236
60	0,959	0,963	0,960	0,955	0,954	0,955	0,975	0,964	0,968	20,749	20,658	20,913	46,109	45,906	46,472	46,163	0,234	0,507
90	1,230	1,228	1,229	1,245	1,249	1,241	1,215	1,203	1,209	26,482	26,853	26,069	58,849	59,673	57,930	58,818	0,712	1,210
120	1,390	1,375	1,378	1,390	1,392	1,391	1,417	1,393	1,408	29,820	30,059	30,338	66,267	66,799	67,418	66,828	0,470	0,704
180	1,495	1,495	1,496	1,468	1,482	1,477	1,491	1,490	1,491	32,368	31,998	32,274	71,928	71,106	71,720	71,585	0,349	0,487
240	1,550	1,544	1,548	1,544	1,517	1,523	1,545	1,544	1,545	33,628	33,259	33,583	74,730	73,909	74,629	74,423	0,366	0,491
360	1,610	1,607	1,604	1,587	1,580	1,586	1,576	1,579	1,583	35,064	34,629	34,486	77,919	76,954	76,636	77,170	0,546	0,707
inf	1,654	1,644	1,648	1,610	1,630	1,649	1,647	1,647	1,649	35,990	35,759	36,110	79,979	79,463	80,244	79,895	0,324	0,406

Table 101: Table containing the spectrophotometric values and dissolution data of formula 6D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,028	0,026	0,027	0,027	0,027	0,027	0,021	0,022	0,024	0,705	0,713	0,618	1,568	1,584	1,372	1,508	0,096	6,372
5	0,187	0,185	0,187	0,181	0,174	0,181	0,094	0,100	0,099	3,605	3,469	1,992	8,011	7,710	4,426	6,716	1,624	24,175
10	0,546	0,596	0,603	0,575	0,601	0,600	0,370	0,371	0,369	10,815	11,009	6,954	24,034	24,465	15,453	21,317	4,150	19,470
15	1,063	1,086	1,073	1,099	1,094	1,099	0,706	0,791	0,786	19,828	20,252	14,109	44,063	45,005	31,354	40,141	6,225	15,507
30	1,553	1,611	1,606	1,628	1,623	1,616	1,372	1,368	1,360	29,317	29,904	25,191	65,148	66,454	55,979	62,527	4,661	7,454
60	2,002	2,032	2,009	1,936	1,941	1,939	1,754	1,770	1,764	37,188	35,820	32,529	82,639	79,599	72,287	78,175	4,344	5,557
90	2,047	2,053	2,046	1,989	2,044	2,036	1,879	1,881	1,880	38,025	37,552	34,839	84,500	83,448	77,421	81,790	3,119	3,813
120	2,277	2,226	2,250	2,147	2,276	2,202	1,983	2,070	1,994	41,903	41,120	37,497	93,117	91,377	83,326	89,273	4,265	4,778
180	2,155	2,168	2,160	2,099	2,143	2,129	2,078	1,956	1,963	40,493	39,809	37,396	89,984	88,465	83,102	87,184	2,952	3,386
240	2,170	2,117	2,165	2,109	2,069	2,044	2,067	2,020	2,040	40,525	39,122	38,394	90,056	86,937	85,319	87,437	1,966	2,249
360	2,079	2,085	2,080	2,241	2,102	2,209	2,012	2,027	2,001	39,482	41,328	38,071	87,738	91,840	84,603	88,060	2,963	3,365
inf	1,871	1,880	1,879	1,897	1,904	1,890	1,805	1,863	1,850	35,870	36,335	35,101	79,710	80,744	78,003	79,486	1,130	1,422

Table 102: Table containing the spectrophotometric values and dissolution data of formula 6D read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,016	0,022	0,019	0,027	0,028	0,028	0,022	0,011	0,019	0,705	0,867	0,668	1,567	1,927	1,484	1,660	0,192	11,584
5	0,228	0,225	0,229	0,212	0,205	0,210	0,205	0,209	0,204	4,871	4,501	4,439	10,824	10,002	9,864	10,230	0,424	4,143
10	0,612	0,630	0,629	0,618	0,855	0,694	0,653	0,627	0,644	12,823	14,792	13,176	28,496	32,870	29,280	30,216	1,904	6,302
15	0,997	0,965	0,974	1,033	0,993	0,994	1,032	1,059	1,414	19,984	20,557	23,776	44,409	45,683	52,836	47,642	3,709	7,785
30	1,252	1,387	1,329	1,523	1,453	1,497	1,797	1,611	1,703	26,978	30,356	34,623	59,951	67,459	76,939	68,116	6,951	10,204
60	1,625	1,853	1,738	1,537	1,619	1,604	1,938	1,689	1,793	35,450	32,431	36,870	78,779	72,068	81,933	77,593	4,114	5,302
90	1,683	1,620	1,663	2,010	2,070	2,261	1,941	2,132	1,955	33,976	43,155	41,121	75,503	95,900	91,379	87,594	8,747	9,985
120	1,800	1,973	1,932	1,729	1,726	1,712	2,423	2,371	2,416	39,088	35,566	49,229	86,861	79,037	109,398	91,765	12,871	14,026
180	2,369	2,024	2,197	1,723	1,917	1,829	2,430	2,434	2,429	45,194	37,767	50,044	100,430	83,926	111,209	98,522	11,220	11,388
240	2,006	2,014	2,101	2,400	2,002	1,994	2,446	2,459	2,422	42,308	44,144	50,540	94,017	98,099	112,310	101,475	7,841	7,727
360	2,124	2,101	2,009	2,263	2,243	2,302	2,433	2,387	2,420	43,286	47,129	50,228	96,190	104,732	111,617	104,180	6,310	6,057
inf	2,130	2,085	2,180	2,306	2,287	2,311	2,256	2,223	2,270	46,510	48,020	47,232	103,356	106,711	104,960	105,009	1,370	1,305

Dissolution results Formulation 6E

Table 103: Table containing the spectrophotometric values and dissolution data of formula 6E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,013	0,013	0,014	0,016	0,017	0,016	0,014	0,013	0,016	0,773	0,829	0,795	1,718	1,843	1,766	1,776	0,052	2,919
5	0,071	0,072	0,071	0,058	0,058	0,058	0,050	0,049	0,050	1,990	1,713	1,533	4,423	3,806	3,408	3,879	0,418	10,769
10	0,229	0,227	0,229	0,179	0,179	0,179	0,156	0,156	0,156	5,287	4,251	3,768	11,748	9,447	8,373	9,856	1,408	14,285
15	0,420	0,422	0,421	0,342	0,342	0,341	0,305	0,307	0,305	9,355	7,677	6,926	20,789	17,059	15,392	17,747	2,256	12,715
30	0,580	0,581	0,581	0,501	0,497	0,499	0,472	0,470	0,471	12,748	11,029	10,431	28,329	24,508	23,180	25,339	2,183	8,614
60	0,757	0,756	0,757	0,676	0,678	0,678	0,674	0,679	0,678	16,507	14,812	14,799	36,682	32,916	32,886	34,161	1,782	5,217
90	0,930	0,931	0,931	0,862	0,857	0,859	0,839	0,841	0,840	20,240	18,707	18,300	44,977	41,572	40,666	42,405	1,856	4,377
120	1,062	1,060	1,061	0,972	0,963	0,969	0,959	0,957	0,958	23,079	21,098	20,864	51,287	46,884	46,364	48,178	2,208	4,584
180	1,169	1,170	1,170	1,055	1,053	1,054	1,063	1,061	1,062	25,483	23,008	23,161	56,629	51,129	51,469	53,076	2,516	4,741
240	1,255	1,258	1,256	1,136	1,133	1,134	1,154	1,158	1,157	27,444	24,819	25,264	60,988	55,154	56,142	57,428	2,549	4,439
360	1,322	1,317	1,319	1,213	1,205	1,208	1,222	1,220	1,221	28,905	26,503	26,749	64,234	58,895	59,441	60,857	2,398	3,941
inf	1,359	1,361	1,361	1,246	1,242	1,243	1,242	1,241	1,241	28,274	27,379	27,321	62,830	60,843	60,714	61,462	0,969	1,576

Table 104: Table containing the spectrophotometric values and dissolution data of formula 6E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,177	0,176	0,176	0,091	0,093	0,092	0,122	0,116	0,115	3,425	1,882	2,353	7,611	4,183	5,228	5,674	1,434	25,280
5	0,631	0,634	0,633	0,386	0,381	0,379	0,391	0,397	0,394	11,735	7,175	7,393	26,079	15,944	16,429	19,484	4,667	23,956
10	1,249	1,261	1,295	0,865	0,857	0,856	0,841	0,858	0,851	23,364	15,894	15,723	51,920	35,320	34,939	40,726	7,917	19,439
15	1,735	1,716	1,719	1,307	1,295	1,291	1,299	1,329	1,308	31,764	23,943	24,207	70,586	53,207	53,794	59,196	8,058	13,612
30	1,996	2,012	2,006	1,704	1,710	1,709	1,700	1,695	1,692	37,051	31,532	31,318	82,335	70,072	69,595	74,001	5,896	7,968
60	2,169	2,132	2,147	1,956	2,022	2,009	2,015	2,015	1,958	39,880	36,939	36,945	88,623	82,088	82,100	84,270	3,078	3,652
90	2,228	2,204	2,210	2,090	2,134	2,111	2,066	2,151	2,064	41,270	39,251	38,927	91,710	87,225	86,503	88,480	2,303	2,603
120	2,255	2,318	2,305	2,151	2,153	2,140	2,125	2,105	2,174	42,925	40,124	39,880	95,390	89,164	88,623	91,059	3,070	3,372
180	2,226	2,379	2,287	2,103	2,142	2,140	2,238	2,187	2,190	43,247	39,984	41,379	96,103	88,853	91,953	92,303	2,970	3,218
240	2,286	2,358	2,341	2,124	2,154	2,143	2,148	2,079	2,094	44,039	40,423	39,816	97,864	89,828	88,481	92,057	4,142	4,500
360	2,265	2,291	2,240	2,201	2,200	2,201	2,236	2,171	2,164	43,132	41,733	41,541	95,849	92,741	92,313	93,634	1,576	1,683
inf	2,020	2,064	2,042	1,914	1,906	1,925	1,935	1,963	1,931	37,930	36,763	37,265	84,289	81,695	82,812	82,932	1,062	1,281

Table 105: Table containing the spectrophotometric values and dissolution data of formula 6E read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,093	0,087	0,091	0,233	0,252	0,242	0,145	0,412	0,144	2,129	5,163	4,999	4,732	11,474	11,108	9,105	3,096	34,001
5	0,416	0,434	0,420	0,760	0,779	0,763	0,581	0,593	0,591	8,793	15,695	12,113	19,539	34,878	26,919	27,112	6,263	23,102
10	0,971	0,944	0,963	1,226	1,393	1,286	1,100	1,361	1,285	19,570	26,465	25,387	43,488	58,811	56,416	52,905	6,730	12,721
15	1,422	1,285	1,330	1,926	2,178	2,035	1,827	1,831	1,925	27,391	41,505	37,767	60,869	92,234	83,926	79,010	13,268	16,793
30	1,867	1,723	1,774	2,273	1,704	1,837	2,188	2,207	2,437	36,397	39,560	46,302	80,883	87,912	102,894	90,563	9,179	10,136
60	2,010	1,900	1,994	1,697	2,036	2,055	1,789	1,673	1,793	40,189	39,605	36,041	89,308	88,012	80,090	85,803	4,074	4,748
90	2,231	2,166	2,230	1,770	2,462	2,094	2,392	2,440	2,270	45,231	43,407	48,551	100,514	96,459	107,892	101,621	4,733	4,657
120	1,849	1,863	1,880	2,344	2,296	2,287	2,406	2,397	2,366	38,573	47,645	49,256	85,718	105,877	109,457	100,351	10,449	10,413
180	1,958	1,893	1,924	1,812	1,665	1,693	2,266	2,224	2,230	39,998	36,192	46,532	88,885	80,427	103,404	90,905	9,488	10,438
240	2,134	2,042	2,130	1,614	1,643	1,650	2,118	2,135	2,013	43,756	34,631	43,751	97,235	76,957	97,225	90,472	9,557	10,563
360	2,325	2,301	2,287	1,607	1,624	1,617	2,196	2,223	2,187	48,033	34,416	46,256	106,740	76,480	102,791	95,337	13,431	14,088
inf	2,266	2,246	2,245	1,665	1,653	1,659	2,226	2,197	2,214	43,030	35,460	46,700	95,622	78,800	103,778	92,733	10,400	11,215

Dissolution results Formulation 6F

Table 106: Table containing the spectrophotometric values and dissolution data of formula 6F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,010	0,010	0,010	0,010	0,010	0,011	0,009	0,009	0,009	0,702	0,704	0,681	1,559	1,564	1,514	1,546	0,022	1,450
5	0,035	0,038	0,036	0,031	0,032	0,032	0,020	0,020	0,020	1,260	1,158	0,914	2,799	2,574	2,032	2,469	0,322	13,047
10	0,132	0,134	0,132	0,103	0,103	0,103	0,085	0,085	0,085	3,279	2,656	2,274	7,286	5,903	5,053	6,080	0,920	15,134
15	0,296	0,298	0,298	0,229	0,228	0,229	0,202	0,201	0,201	6,742	5,302	4,723	14,982	11,782	10,496	12,420	1,886	15,187
30	0,534	0,534	0,533	0,446	0,440	0,443	0,388	0,383	0,344	11,734	9,823	8,323	26,076	21,830	18,496	22,134	3,102	14,014
60	0,871	0,862	0,863	0,790	0,782	0,786	0,665	0,662	0,663	18,750	17,069	14,471	41,667	37,932	32,159	37,252	3,911	10,500
90	1,133	1,136	1,135	1,053	1,060	1,056	0,931	0,933	0,934	24,498	22,823	20,201	54,440	50,718	44,890	50,016	3,930	7,858
120	1,304	1,305	1,305	1,247	1,249	1,250	1,135	1,128	1,133	28,190	26,979	24,486	62,644	59,954	54,413	59,004	3,427	5,808
180	1,372	1,359	1,363	1,347	1,348	1,350	1,245	1,242	1,251	29,600	29,205	27,004	65,778	64,900	60,008	63,562	2,539	3,994
240	1,462	1,451	1,456	1,425	1,425	1,425	1,373	1,380	1,375	31,687	30,975	29,879	70,416	68,834	66,397	68,549	1,653	2,411
360	1,518	1,514	1,512	1,479	1,501	1,501	1,420	1,423	1,419	33,080	32,581	30,980	73,512	72,402	68,844	71,586	1,991	2,782
inf	1,519	1,496	1,510	1,472	1,476	1,481	1,424	1,425	1,423	32,307	32,393	31,216	71,794	71,984	69,368	71,049	1,191	1,676

Table 107: Table containing the spectrophotometric values and dissolution data of formula 6F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,051	0,053	0,052	0,129	0,129	0,130	0,207	0,208	0,207	1,162	2,569	3,991	2,583	5,709	8,869	5,720	2,566	44,859
5	0,348	0,350	0,346	0,550	0,540	0,543	0,676	0,679	0,674	6,546	10,128	12,537	14,546	22,506	27,861	21,638	5,470	25,281
10	1,017	1,021	1,019	1,193	1,190	1,191	1,313	1,321	1,320	18,788	21,944	24,264	41,750	48,765	53,921	48,146	4,988	10,360
15	1,578	1,629	1,618	1,720	1,689	1,691	1,786	1,790	1,785	29,603	31,315	32,931	65,784	69,589	73,181	69,518	3,020	4,345
30	2,021	1,950	1,963	2,052	2,027	2,044	2,232	2,133	2,139	36,487	37,685	40,043	81,082	83,744	88,986	84,604	3,283	3,881
60	2,233	2,222	2,252	2,356	2,217	2,250	2,343	2,334	2,335	41,372	42,132	43,338	91,937	93,627	96,306	93,957	1,799	1,914
90	2,297	2,171	2,191	2,249	2,264	2,270	2,387	2,437	2,396	41,302	42,121	44,838	91,783	93,602	99,640	95,008	3,358	3,535
120	2,223	2,223	2,225	2,268	2,235	2,250	2,181	2,169	2,160	41,605	42,169	40,778	92,456	93,708	90,618	92,261	1,269	1,375
180	2,272	2,124	2,195	2,246	2,237	2,277	2,282	2,367	2,195	41,337	42,433	43,017	91,859	94,297	95,594	93,917	1,548	1,649
240	2,344	2,327	2,366	2,180	2,285	2,292	2,200	2,285	2,241	44,269	42,648	42,528	98,376	94,773	94,507	95,885	1,765	1,840
360	2,154	2,180	2,204	2,185	2,194	2,150	2,267	2,249	2,296	41,478	41,489	43,286	92,173	92,197	96,192	93,520	1,889	2,020
inf	2,102	2,010	2,105	2,040	2,092	2,064	2,311	2,288	2,240	40,970	39,696	43,673	91,044	88,214	97,052	92,103	3,685	4,001

Table 108: Table containing the spectrophotometric values and dissolution data of formula 6F read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	**1**	**2**	**3**	**1**	**2**	**3**	**1**	**2**	**3**	**Sample 1**	**Sample 2**	**Sample 3**	**Sample 1**	**Sample 2**	**Sample 3**			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,072	0,069	0,069	0,072	0,072	0,081	0,450	0,464	0,400	1,722	1,819	9,077	3,827	4,043	20,170	9,347	7,654	81,890
5	0,383	0,380	0,383	0,471	0,474	0,470	1,013	1,051	1,020	7,968	9,761	20,931	17,708	21,691	46,513	28,637	12,744	44,502
10	0,939	0,930	0,935	1,290	1,310	1,305	1,467	1,423	1,449	19,065	26,407	29,412	42,366	58,683	65,360	55,470	9,658	17,412
15	1,309	1,369	1,346	2,035	2,038	2,003	1,543	1,694	1,623	27,304	41,030	33,044	60,676	91,178	73,432	75,095	12,508	16,656
30	1,906	1,832	1,865	2,318	2,400	2,402	1,958	1,996	1,985	37,979	48,218	40,416	84,398	107,150	89,812	93,787	9,704	10,347
60	2,147	2,291	2,064	2,150	2,040	2,206	1,578	1,703	1,642	44,177	43,653	33,864	98,172	97,008	75,252	90,144	10,541	11,693
90	1,770	1,748	1,773	2,196	2,299	2,182	1,606	1,583	1,497	36,340	45,768	32,465	80,756	101,707	72,145	84,869	12,414	14,628
120	1,662	1,875	1,694	2,430	2,298	2,365	1,695	1,637	1,702	36,139	48,781	34,959	80,310	108,402	77,686	88,799	13,903	15,656
180	1,769	2,219	2,040	2,313	2,269	2,199	1,770	1,703	1,763	41,647	46,975	36,497	92,548	104,389	81,105	92,680	9,506	10,257
240	1,563	2,000	1,913	2,278	2,319	2,198	1,535	1,633	1,696	38,192	47,311	34,208	84,871	105,137	76,017	88,675	12,188	13,745
360	2,113	2,126	2,200	2,347	2,306	2,323	1,947	1,957	1,995	44,815	48,768	41,279	99,589	108,374	91,730	99,898	6,798	6,805
inf	2,246	2,249	2,246	2,401	2,399	2,375	2,005	2,020	1,999	46,433	50,347	42,338	103,185	111,883	94,084	103,051	7,267	7,052

Dissolution results of control formulations

Table 109: Table containing the spectrophotometric values and dissolution data of the control formulation (0.5mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,013	0,008	0,009	0,014	0,015	0,014	0,004	0,005	0,004	0,704	0,790	0,584	1,565	1,756	1,298	1,540	0,188	12,200
5	0,007	0,007	0,007	0,017	0,017	0,017	0,008	0,008	0,007	0,632	0,850	0,655	1,403	1,889	1,455	1,582	0,218	13,766
10	0,011	0,012	0,012	0,025	0,025	0,025	0,009	0,009	0,009	0,739	1,019	0,683	1,643	2,264	1,519	1,809	0,326	18,039
15	0,023	0,022	0,022	0,031	0,030	0,031	0,017	0,017	0,017	0,962	1,147	0,854	2,138	2,549	1,897	2,195	0,269	12,265
30	0,029	0,029	0,029	0,041	0,040	0,040	0,025	0,025	0,025	1,102	1,349	1,016	2,448	2,998	2,259	2,568	0,314	12,210
60	0,044	0,044	0,044	0,054	0,054	0,054	0,042	0,038	0,038	1,427	1,640	1,324	3,171	3,643	2,942	3,252	0,292	8,980
90	0,066	0,066	0,066	0,083	0,080	0,079	0,064	0,064	0,063	1,890	2,206	1,839	4,200	4,903	4,086	4,396	0,361	8,218
120	0,090	0,089	0,089	0,098	0,095	0,098	0,086	0,087	0,086	2,388	2,555	2,319	5,306	5,677	5,154	5,379	0,220	4,087
180	0,123	0,123	0,123	0,123	0,122	0,122	0,113	0,114	0,109	3,105	3,102	2,876	6,900	6,893	6,390	6,728	0,239	3,549
240	0,150	0,151	0,149	0,153	0,154	0,151	0,162	0,160	0,165	3,683	3,752	3,938	8,184	8,338	8,750	8,424	0,239	2,838
360	0,200	0,200	0,199	0,200	0,199	0,199	0,168	0,167	0,165	4,739	4,745	4,045	10,530	10,544	8,988	10,021	0,730	7,288
inf	0,234	0,235	0,234	0,231	0,231	0,232	0,218	0,218	0,218	5,491	5,433	5,144	12,202	12,072	11,432	11,902	0,337	2,828

Table 110: Table containing the spectrophotometric values and dissolution data of the control formulation (0.5 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,011	0,010	0,010	0,017	0,017	0,017	0,018	0,019	0,019	0,401	0,525	0,555	0,890	1,166	1,232	1,096	0,148	13,516
5	0,024	0,024	0,024	0,032	0,033	0,032	0,035	0,036	0,035	0,657	0,805	0,858	1,461	1,790	1,907	1,719	0,189	10,988
10	0,061	0,057	0,060	0,061	0,060	0,060	0,071	0,072	0,072	1,302	1,323	1,525	2,894	2,939	3,388	3,074	0,223	7,264
15	0,092	0,091	0,090	0,095	0,094	0,094	0,114	0,113	0,112	1,885	1,938	2,283	4,189	4,307	5,073	4,523	0,392	8,662
30	0,142	0,142	0,142	0,140	0,140	0,140	0,175	0,174	0,174	2,816	2,782	3,413	6,258	6,183	7,583	6,675	0,643	9,635
60	0,232	0,231	0,230	0,222	0,221	0,220	0,286	0,286	0,283	4,447	4,273	5,440	9,882	9,497	12,090	10,490	1,143	10,892
90	0,340	0,338	0,337	0,310	0,310	0,310	0,406	0,404	0,405	6,423	5,908	7,649	14,273	13,129	16,998	14,800	1,623	10,967
120	0,418	0,419	0,417	0,390	0,389	0,389	0,496	0,495	0,492	7,903	7,384	9,316	17,563	16,409	20,701	18,224	1,814	9,952
180	0,525	0,519	0,524	0,476	0,474	0,473	0,634	0,632	0,631	9,853	8,967	11,879	21,896	19,927	26,399	22,741	2,709	11,912
240	0,649	0,649	0,649	0,573	0,576	0,570	0,779	0,778	0,778	12,202	10,815	14,595	27,115	24,033	32,434	27,861	3,470	12,455
360	0,824	0,821	0,821	0,715	0,711	0,718	0,962	0,956	0,952	15,413	13,447	17,918	34,251	29,882	39,817	34,650	4,066	11,734
inf	1,024	1,025	1,025	0,885	0,905	0,901	1,155	1,159	1,158	19,211	16,829	21,658	42,690	37,398	48,129	42,739	4,381	10,250

Table 111: Table containing the spectrophotometric values and dissolution data of the control formulation (0.5 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,071	0,072	0,072	0,024	0,024	0,025	0,108	0,109	0,110	1,753	0,808	2,497	3,895	1,796	5,548	3,746	1,536	40,991
5	0,568	0,565	0,561	0,340	0,338	0,337	0,437	0,438	0,438	11,614	7,093	9,092	25,809	15,762	20,205	20,592	4,111	19,964
10	0,884	0,887	0,886	0,855	0,853	0,857	0,879	0,880	0,881	18,105	17,460	17,981	40,233	38,799	39,957	39,663	0,621	1,566
15	1,143	1,145	1,136	1,243	1,237	1,241	1,158	1,162	1,159	23,313	25,263	23,673	51,807	56,139	52,607	53,518	1,882	3,517
30	1,416	1,415	1,403	1,583	1,590	1,582	1,412	1,416	1,417	28,844	32,294	28,901	64,097	71,765	64,225	66,696	3,585	5,375
60	1,619	1,613	1,613	1,933	1,923	1,902	1,634	1,622	1,614	33,071	39,146	33,233	73,490	86,991	73,852	78,111	6,281	8,041
90	1,749	1,755	1,733	2,143	2,075	2,083	1,787	1,798	1,790	35,865	42,990	36,777	79,700	95,534	81,727	85,653	7,036	8,214
120	1,846	1,839	1,829	2,248	2,275	2,264	1,920	1,919	1,929	37,908	46,463	39,595	84,240	103,251	87,988	91,827	8,222	8,954
180	2,007	2,009	2,001	2,296	2,299	2,288	2,130	2,123	2,122	41,467	47,347	43,856	92,149	105,216	97,458	98,274	5,366	5,460
240	2,124	2,134	2,127	2,418	2,412	2,400	2,169	2,143	2,160	44,134	49,920	44,740	98,075	110,934	99,423	102,811	5,770	5,612
360	2,184	2,248	2,206	2,407	2,314	2,357	2,139	1,971	1,987	46,056	49,174	42,470	102,346	109,275	94,378	102,000	6,087	5,967
inf	2,180	2,236	2,201	2,386	2,306	2,349	2,126	1,969	1,982	45,903	49,183	42,564	102,007	109,296	94,586	101,963	6,005	5,890

Table 112: Table containing the spectrophotometric values and dissolution data of the control formulation (0.75 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,007	0,006	0,007	0,012	0,011	0,011	0,006	0,007	0,006	0,631	0,730	0,626	1,402	1,623	1,391	1,472	0,107	7,241
5	0,009	0,008	0,010	0,015	0,015	0,014	0,010	0,009	0,009	0,679	0,799	0,682	1,508	1,775	1,516	1,600	0,124	7,751
10	0,017	0,015	0,016	0,023	0,023	0,022	0,018	0,018	0,019	0,825	0,970	0,879	1,833	2,156	1,953	1,981	0,133	6,723
15	0,025	0,024	0,024	0,029	0,028	0,027	0,029	0,028	0,027	1,003	1,085	1,081	2,229	2,412	2,402	2,347	0,084	3,580
30	0,046	0,040	0,040	0,039	0,038	0,038	0,031	0,031	0,031	1,382	1,305	1,146	3,070	2,900	2,547	2,839	0,218	7,676
60	0,053	0,053	0,053	0,054	0,054	0,054	0,048	0,049	0,048	1,621	1,641	1,515	3,602	3,646	3,366	3,538	0,123	3,480
90	0,081	0,081	0,081	0,079	0,078	0,077	0,073	0,073	0,074	2,215	2,150	2,046	4,921	4,779	4,548	4,749	0,154	3,243
120	0,107	0,107	0,107	0,103	0,107	0,106	0,100	0,101	0,100	2,756	2,727	2,625	6,124	6,060	5,832	6,005	0,125	2,085
180	0,148	0,140	0,138	0,132	0,132	0,132	0,135	0,134	0,135	3,509	3,299	3,353	7,798	7,331	7,452	7,527	0,198	2,630
240	0,183	0,182	0,182	0,164	0,164	0,163	0,159	0,160	0,162	4,368	3,980	3,906	9,707	8,845	8,681	9,078	0,450	4,961
360	0,225	0,230	0,227	0,214	0,213	0,213	0,203	0,210	0,211	5,333	5,041	4,916	11,851	11,201	10,924	11,325	0,388	3,430
inf	0,271	0,269	0,270	0,250	0,248	0,250	0,246	0,251	0,245	5,953	5,819	5,773	13,229	12,932	12,829	12,997	0,170	1,304

Table 113: Table containing the spectrophotometric values and dissolution data of the control formulation (0.75 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,014	0,014	0,015	0,019	0,019	0,020	0,012	0,012	0,012	0,478	0,568	0,436	1,061	1,263	0,970	1,098	0,123	11,170
5	0,034	0,034	0,033	0,036	0,036	0,036	0,027	0,028	0,027	0,824	0,875	0,715	1,831	1,945	1,588	1,788	0,149	8,330
10	0,069	0,069	0,069	0,071	0,071	0,071	0,062	0,063	0,063	1,475	1,509	1,355	3,278	3,352	3,012	3,214	0,146	4,544
15	0,102	0,103	0,161	0,105	0,104	0,104	0,088	0,087	0,087	2,451	2,125	1,815	5,446	4,722	4,034	4,734	0,577	12,179
30	0,161	0,161	0,162	0,158	0,156	0,157	0,134	0,134	0,135	3,175	3,098	2,676	7,056	6,884	5,947	6,629	0,487	7,351
60	0,254	0,257	0,255	0,249	0,248	0,247	0,216	0,216	0,211	4,900	4,766	4,147	10,888	10,592	9,215	10,232	0,729	7,128
90	0,347	0,354	0,353	0,335	0,336	0,333	0,298	0,296	0,297	6,673	6,364	5,671	14,829	14,141	12,603	13,858	0,931	6,715
120	0,422	0,422	0,421	0,405	0,404	0,403	0,361	0,358	0,359	7,982	7,659	6,833	17,738	17,020	15,184	16,648	1,076	6,461
180	0,525	0,524	0,524	0,515	0,514	0,512	0,449	0,447	0,446	9,896	9,696	8,473	21,992	21,546	18,829	20,789	1,398	6,723
240	0,636	0,636	0,632	0,626	0,619	0,621	0,538	0,536	0,537	11,958	11,720	10,144	26,574	26,045	22,542	25,054	1,789	7,141
360	0,769	0,773	0,770	0,778	0,774	0,777	0,659	0,669	0,666	14,489	14,589	12,521	32,197	32,419	27,823	30,813	2,116	6,867
inf	0,903	0,904	0,905	0,927	0,924	0,924	0,805	0,804	0,808	16,525	17,371	15,151	36,722	38,602	33,668	36,331	2,033	5,596

Table 114: Table containing the spectrophotometric values and dissolution data of the control formulation (0.75 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,108	0,108	0,107	0,172	0,172	0,172	0,131	0,131	0,131	2,173	3,348	2,601	4,828	7,441	5,780	6,017	1,080	17,945
5	0,459	0,460	0,457	0,550	0,549	0,552	0,440	0,441	0,440	8,568	10,242	8,231	19,040	22,761	18,292	20,031	1,954	9,756
10	0,899	0,901	0,906	1,035	1,035	1,029	0,817	0,818	0,811	16,677	19,072	15,101	37,060	42,383	33,558	37,667	3,628	9,632
15	1,184	1,181	1,180	1,356	1,363	1,358	1,082	1,083	1,081	21,845	25,105	20,036	48,544	55,789	44,524	49,619	4,661	9,395
30	1,466	1,469	1,472	1,750	1,701	1,716	1,377	1,364	1,367	27,191	31,851	25,366	60,425	70,780	56,368	62,524	6,068	9,705
60	1,703	1,702	1,680	2,008	2,047	1,991	1,627	1,670	1,648	31,455	37,352	30,573	69,900	83,004	67,940	73,614	6,687	9,084
90	1,893	1,891	1,895	2,245	2,234	2,035	1,886	1,888	1,884	35,216	40,390	35,066	78,257	89,755	77,925	81,979	5,500	6,709
120	1,991	1,994	1,995	2,232	2,235	2,230	1,969	1,989	2,081	37,235	41,716	37,563	82,745	92,703	83,474	86,308	4,532	5,251
180	2,123	2,207	2,188	2,303	2,291	2,291	2,152	2,140	2,163	40,700	43,082	40,284	90,444	95,739	89,521	91,901	2,740	2,981
240	2,164	2,178	2,176	2,382	2,381	2,380	2,227	2,267	2,244	40,918	44,875	42,220	90,929	99,722	93,822	94,824	3,659	3,859
360	2,121	2,170	2,165	2,317	2,327	2,357	2,060	2,037	2,150	40,765	44,258	39,473	90,588	98,352	87,717	92,219	4,492	4,871
inf	2,121	2,166	2,161	2,310	2,319	2,346	2,060	2,036	2,146	41,577	44,330	39,649	92,394	98,512	88,108	93,005	4,269	4,590

Table 115: Table containing the spectrophotometric values and dissolution data of the control formulation (1 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,006	0,006	0,006	0,008	0,006	0,006	0,007	0,007	0,007	0,614	0,630	0,636	1,363	1,399	1,413	1,392	0,021	1,503
5	0,009	0,008	0,009	0,008	0,008	0,008	0,017	0,016	0,017	0,674	0,664	0,838	1,499	1,475	1,862	1,612	0,177	10,988
10	0,017	0,018	0,018	0,018	0,018	0,018	0,020	0,022	0,022	0,866	0,870	0,939	1,925	1,934	2,087	1,982	0,074	3,752
15	0,025	0,025	0,024	0,026	0,027	0,025	0,032	0,033	0,033	1,016	1,044	1,185	2,257	2,321	2,633	2,403	0,164	6,833
30	0,037	0,035	0,034	0,039	0,038	0,039	0,048	0,049	0,048	1,241	1,313	1,518	2,759	2,918	3,374	3,017	0,261	8,649
60	0,058	0,058	0,056	0,066	0,066	0,073	0,076	0,078	0,076	1,703	1,937	2,115	3,783	4,305	4,699	4,263	0,375	8,797
90	0,086	0,085	0,084	0,094	0,097	0,094	0,111	0,110	0,110	2,291	2,501	2,832	5,092	5,557	6,294	5,648	0,495	8,760
120	0,101	0,101	0,101	0,123	0,124	0,123	0,153	0,151	0,159	2,640	3,107	3,758	5,867	6,905	8,350	7,041	1,018	14,463
180	0,139	0,130	0,132	0,157	0,156	0,155	0,192	0,187	0,185	3,332	3,800	4,493	7,404	8,445	9,985	8,611	1,060	12,311
240	0,157	0,161	0,161	0,186	0,191	0,193	0,225	0,221	0,223	3,889	4,538	5,247	8,642	10,085	11,660	10,129	1,232	12,165
360	0,209	0,207	0,210	0,249	0,245	0,254	0,291	0,291	0,288	4,933	5,801	6,677	10,963	12,892	14,839	12,898	1,582	12,267
inf	0,242	0,240	0,239	0,278	0,271	0,274	0,327	0,326	0,327	6,471	6,356	7,480	14,379	14,126	16,622	15,042	1,122	7,458

Table 116: Table containing the spectrophotometric values and dissolution data of the control formulation (1 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,014	0,015	0,014	0,016	0,016	0,016	0,018	0,018	0,018	0,475	0,502	0,543	1,055	1,116	1,207	1,126	0,062	5,550
5	0,037	0,037	0,037	0,038	0,038	0,038	0,049	0,050	0,050	0,889	0,909	1,117	1,976	2,020	2,482	2,159	0,229	10,602
10	0,070	0,071	0,071	0,086	0,086	0,086	0,107	0,108	0,108	1,504	1,779	2,187	3,342	3,953	4,860	4,051	0,623	15,388
15	0,113	0,112	0,112	0,134	0,135	0,135	0,167	0,167	0,167	2,275	2,678	3,272	5,055	5,952	7,272	6,093	0,910	14,944
30	0,174	0,173	0,174	0,207	0,206	0,206	0,251	0,253	0,252	3,399	4,003	4,839	7,554	8,895	10,753	9,067	1,312	14,464
60	0,273	0,274	0,273	0,311	0,312	0,310	0,380	0,380	0,381	5,228	5,919	7,195	11,619	13,154	15,989	13,587	1,810	13,324
90	0,374	0,373	0,371	0,417	0,417	0,414	0,501	0,500	0,499	7,067	7,858	9,408	15,704	17,462	20,907	18,025	2,161	11,988
120	0,450	0,449	0,449	0,463	0,462	0,461	0,524	0,524	0,522	8,495	8,741	9,887	18,878	19,425	21,970	20,091	1,347	6,707
180	0,555	0,561	0,558	0,657	0,660	0,658	0,762	0,763	0,760	10,513	12,356	14,270	23,362	27,457	31,712	27,511	3,409	12,391
240	0,667	0,667	0,667	0,750	0,750	0,750	0,859	0,858	0,858	12,553	14,087	16,101	27,896	31,304	35,779	31,659	3,228	10,197
360	0,798	0,816	0,822	0,914	0,911	0,910	1,037	1,030	1,029	15,256	17,104	19,344	33,901	38,008	42,986	38,298	3,715	9,699
inf	0,940	0,950	0,952	1,019	1,020	1,040	1,148	1,148	1,148	19,495	19,284	21,562	43,322	42,852	47,915	44,696	2,284	5,110

Table 117: Table containing the spectrophotometric values and dissolution data of the control formulation (1 mm bead size) read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,132	0,131	0,131	0,137	0,138	0,135	0,103	0,102	0,102	2,605	2,700	2,080	5,790	6,000	4,622	5,471	0,606	11,078
5	0,553	0,551	0,549	0,615	0,615	0,613	0,527	0,527	0,520	10,253	11,403	9,765	22,785	25,340	21,701	23,275	1,525	6,554
10	1,145	1,137	1,135	1,241	1,238	1,234	1,166	1,154	1,151	20,995	22,796	21,312	46,656	50,659	47,360	48,225	1,745	3,619
15	1,619	1,612	1,613	1,652	1,658	1,652	1,678	1,670	1,668	29,755	30,495	30,804	66,122	67,768	68,453	67,447	0,978	1,450
30	2,014	2,014	2,012	2,022	2,022	2,012	2,094	2,103	2,093	37,168	37,286	38,689	82,595	82,858	85,976	83,810	1,535	1,832
60	2,302	2,220	2,265	2,307	2,309	2,298	2,254	2,286	2,264	41,902	42,686	42,011	93,115	94,857	93,358	93,777	0,770	0,821
90	2,275	2,272	2,279	2,351	2,346	2,346	2,303	2,306	2,317	42,368	43,705	42,984	94,151	97,123	95,521	95,598	1,214	1,270
120	2,380	2,289	2,284	2,351	2,345	2,329	2,344	2,290	2,289	43,362	43,837	43,198	96,360	97,415	95,996	96,591	0,602	0,623
180	2,338	2,339	2,337	2,413	2,409	2,405	2,298	2,286	2,294	43,974	45,296	43,158	97,721	100,657	95,907	98,095	1,957	1,995
240	2,386	2,156	2,247	2,412	2,396	2,400	2,406	2,270	2,347	42,840	45,424	44,268	95,201	100,942	98,374	98,172	2,348	2,392
360	2,309	2,325	2,320	2,389	2,378	2,380	2,344	2,244	2,334	44,070	45,292	43,892	97,933	100,649	97,537	98,706	1,383	1,401
inf	2,309	2,308	2,312	2,376	2,375	2,379	2,338	2,230	2,325	44,483	45,431	43,947	98,851	100,958	97,660	99,156	1,363	1,375

Dissolution results of the commercial product Lasix®

Table 118: Table containing the spectrophotometric values and dissolution data of the commercial product read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in an acidic media with a pH value of 1.2 using a 0.1M HCl buffer solution.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,020	0,019	0,020	0,013	0,014	0,012	0,028	0,020	0,020	0,904	0,767	0,972	2,008	1,704	2,160	1,957	0,190	9,698
5	0,082	0,067	0,067	0,058	0,058	0,057	0,065	0,067	0,067	2,008	1,703	1,877	4,462	3,785	4,171	4,139	0,277	6,701
10	0,162	0,157	0,157	0,160	0,160	0,164	0,167	0,174	0,175	3,828	3,882	4,112	8,506	8,626	9,137	8,756	0,274	3,125
15	0,255	0,254	0,254	0,255	0,257	0,257	0,280	0,276	0,276	5,852	5,894	6,345	13,005	13,097	14,100	13,401	0,496	3,700
30	0,370	0,373	0,369	0,363	0,363	0,363	0,460	0,448	0,447	8,325	8,154	10,022	18,500	18,120	22,272	19,631	1,874	9,546
60	0,489	0,487	0,487	0,408	0,417	0,423	0,476	0,480	0,477	10,819	9,310	10,623	24,042	20,689	23,607	22,780	1,489	6,535
90	0,577	0,576	0,576	0,545	0,552	0,551	0,560	0,564	0,571	12,739	12,157	12,511	28,310	27,016	27,801	27,709	0,532	1,920
120	0,617	0,597	0,617	0,609	0,615	0,609	0,621	0,616	0,624	13,508	13,516	13,732	30,017	30,036	30,516	30,190	0,231	0,765
180	0,686	0,681	0,680	0,663	0,663	0,668	0,690	0,684	0,688	15,087	14,712	15,210	33,527	32,693	33,800	33,340	0,471	1,412
240	0,737	0,737	0,735	0,720	0,728	0,730	0,748	0,739	0,741	16,302	16,072	16,449	36,227	35,715	36,554	36,165	0,345	0,955
360	0,772	0,786	0,787	0,774	0,805	0,801	0,783	0,803	0,777	17,343	17,566	17,478	38,539	39,035	38,839	38,804	0,204	0,525
inf	0,779	0,789	0,788	0,777	0,813	0,811	0,789	0,844	0,783	17,752	17,807	17,940	39,448	39,571	39,866	39,628	0,175	0,443

Table 119: Table containing the spectrophotometric values and dissolution data of the commercial product read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 4.6.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	0,174	0,170	0,171	0,082	0,080	0,079	0,222	0,217	0,215	3,338	1,679	4,182	7,418	3,731	9,294	6,814	2,311	33,916
5	0,465	0,469	0,468	0,252	0,240	0,238	0,539	0,536	0,538	8,734	4,649	10,012	19,410	10,330	22,250	17,330	5,083	29,333
10	0,798	0,793	0,791	0,446	0,447	0,448	1,057	1,073	1,095	14,722	8,373	19,841	32,716	18,607	44,091	31,805	10,424	32,774
15	1,026	1,026	1,025	0,796	0,793	0,789	1,392	1,391	1,392	19,014	14,703	25,710	42,254	32,673	57,134	44,020	10,064	22,863
30	1,117	1,116	1,123	1,129	1,128	1,132	1,630	1,631	1,625	20,809	20,910	30,156	46,242	46,467	67,013	53,241	9,739	18,292
60	1,611	1,618	1,636	1,536	1,539	1,513	1,686	1,685	1,707	30,063	28,297	31,485	66,807	62,883	69,967	66,552	2,898	4,354
90	1,867	1,850	1,853	1,799	1,853	1,833	1,991	2,027	2,018	34,493	33,889	37,460	76,651	75,310	83,244	78,402	3,468	4,423
120	1,987	1,982	1,948	1,907	1,909	1,947	2,139	2,063	2,106	36,788	35,762	39,310	81,751	79,471	87,356	82,859	3,313	3,998
180	2,144	2,080	2,130	2,067	2,087	2,077	2,255	2,246	2,131	39,635	38,787	41,489	88,078	86,193	92,199	88,823	2,508	2,823
240	2,205	2,143	2,115	2,145	2,108	2,068	2,359	2,295	2,315	40,516	39,538	43,756	90,034	87,862	97,235	91,711	4,006	4,368
360	2,371	2,288	2,268	2,239	2,363	2,285	2,290	2,300	2,372	43,546	43,184	43,947	96,769	95,965	97,659	96,798	0,692	0,715
inf	2,374	2,291	2,283	2,256	2,375	2,295	2,302	2,323	2,385	43,983	43,651	44,468	97,740	97,001	98,817	97,853	0,746	0,762

Table 120: Table containing the spectrophotometric values and dissolution data of the commercial product read at a wavelength of 273 nm after withdrawal from the dissolution vessels. This dissolution test was performed in a citric acid buffer solution with a pH value of 7.4.

Volume of sample withdrawn	5ml
Volume of dissolution medium	900ml
Furosemide ug/ml 100%	45
y=0.0477x - 0.0235	
c	-0,0235
m	0,0477

	Sample 1			Sample 2			Sample 3			Average concentration (µg/ml)			Percentage dissolution			Average % Dissolution	Standard deviation	%RSD
Withdrawal times (min)	1	2	3	1	2	3	1	2	3	Sample 1	Sample 2	Sample 3	Sample 1	Sample 2	Sample 3			
0	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000	0,000
2	1,759	1,741	1,748	1,813	1,833	1,839	1,750	1,732	1,770	35,309	36,885	35,335	78,465	81,967	78,521	79,651	1,638	2,056
5	2,265	2,115	2,195	2,179	2,227	2,171	2,141	2,166	2,078	44,343	44,366	43,081	98,540	98,591	95,735	97,622	1,335	1,367
10	2,268	2,174	2,230	2,399	2,224	2,226	2,414	2,357	2,439	45,239	46,426	48,821	100,532	103,169	108,491	104,064	3,311	3,181
15	2,338	2,315	2,464	2,408	2,408	2,297	2,272	2,266	2,320	48,452	48,438	46,737	107,672	107,639	103,859	106,390	1,790	1,682
30	2,314	2,285	2,285	2,264	2,372	2,319	2,280	2,240	2,323	47,163	47,646	46,889	104,807	105,881	104,197	104,962	0,696	0,663
60	2,327	2,374	2,342	2,446	2,253	2,204	2,213	2,271	2,255	48,471	47,563	46,455	107,713	105,695	103,234	105,547	1,831	1,735
90	2,261	2,189	2,149	2,147	2,235	2,169	2,256	2,220	2,135	45,778	45,464	45,850	101,728	101,030	101,888	101,549	0,372	0,367
120	2,240	2,170	2,171	2,189	2,226	2,280	2,273	2,270	2,219	45,908	46,670	47,096	102,018	103,712	104,658	103,463	1,092	1,055
180	2,173	2,161	2,173	2,161	2,172	2,234	2,214	2,222	2,299	45,657	46,073	47,176	101,459	102,384	104,836	102,893	1,425	1,385
240	2,162	2,206	2,180	2,266	2,170	2,218	2,211	2,257	2,206	46,164	46,894	47,011	102,587	104,208	104,468	103,754	0,832	0,802
360	2,098	2,209	2,132	2,185	2,234	2,251	2,182	2,226	2,168	45,680	47,247	46,611	101,511	104,993	103,580	103,361	1,430	1,383
inf	2,098	2,207	2,130	2,181	2,231	2,249	2,180	2,215	2,159	46,657	47,424	46,699	103,682	105,386	103,776	104,281	0,782	0,750

Annexure H

MDT, DRi and AUC results

In this Annexure the MDT, DRi and AUC results are given for all formulations evaluated in three different pH environments (1.2, 4.6 and 7.4).

Table 1: Table containing the AUC, DRi and MDT values and information regarding formula 1A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,289	1727,341	3,430	936,949	16,076	4881,572
3	5	15,840	6379,295	10,787	2946,303	29,092	8833,983
4	10	32,253	12988,898	17,685	4830,224	31,980	9711,016
5	15	50,375	20287,325	21,749	5940,274	40,023	12153,518
6	30	67,519	27191,264	36,137	9870,169	50,325	15281,744
7	60	84,567	34057,276	45,363	12390,215	52,224	15858,410
8	90	87,739	35334,561	51,711	14124,019	62,399	18947,930
9	120	93,120	37501,599	58,542	15989,666	66,307	20134,900
10	180	94,528	38068,600	61,797	16878,681	68,899	20921,889
11	240	97,679	39337,446	62,526	17077,825	70,011	21259,485
12	360	99,437	40045,601	65,987	18023,232	73,048	22181,657

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40272,3	27313,2	30366

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1727,341	936,949	4881,572
3	5	2-5	6379,295	2946,303	8833,983
4	10	5-10	12988,898	4830,224	9711,016
5	15	10-15	20287,325	5940,274	12153,518
6	30	15-30	27191,264	9870,169	15281,744
7	60	30-60	34057,276	12390,215	15858,410
8	90	60-90	35334,561	14124,019	18947,930
9	120	90-120	37501,599	15989,666	20134,900
10	180	120-180	38068,600	16878,681	20921,889
11	240	180-240	39337,446	17077,825	21259,485
12	360	240-360	40045,601	18023,232	22181,657

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1727,341	936,949	4881,572
3	2-5	3,5	4651,954	2009,354	3952,411
4	5-10	7,5	6609,603	1883,921	877,033
5	10-15	12,5	7298,427	1110,050	2442,502
6	15-30	22,5	6903,939	3929,895	3128,226
7	30-60	45	6866,012	2520,046	576,666
8	60-90	75	1277,286	1733,804	3089,519
9	90-120	105	2167,038	1865,647	1186,970
10	120-180	150	567,000	889,016	786,989
11	180-240	210	1268,846	199,144	337,596
12	240-360	300	708,155	945,407	922,172
		sum	40045,601	18023,232	22181,657

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1727,341	936,949	4881,572
3	2-5	3,5	16281,840	7032,738	13833,438
4	5-10	7,5	49572,025	14129,405	6577,748
5	10-15	12,5	91230,339	13875,627	30531,275
6	15-30	22,5	155338,616	88422,641	70385,094
7	30-60	45	308970,530	113402,057	25949,974
8	60-90	75	95796,416	130035,313	231713,949
9	90-120	105	227539,016	195892,911	124631,850
10	120-180	150	85050,049	133352,350	118048,346
11	180-240	210	266457,701	41820,152	70895,261
12	240-360	300	212446,623	283621,960	276651,495
		sum	1510410,497	1022522,102	974100,003

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
37,717	56,734	43,915	46,122	7,919

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,930	1,544	7,234
13,587	9,597	30,488
54,105	32,031	68,706
92,957	44,362	81,004
397,892	195,364	304,927
1026,581	550,128	692,209
1163,070	655,255	773,703
1220,800	744,209	868,765
2533,249	1624,572	1825,287
2594,790	1678,356	1875,283
5322,125	3469,855	3862,579

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14421,085	9005,274	10390,184

Average AUC0-360 (µg/ml.min)		11272,181
	STDEV	2813,573

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,289	3,430	16,076
5	15,840	10,787	29,092
10	32,253	17,685	31,980
15	50,375	21,749	40,023

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,407	1,478	2,332	2,405	0,789

Table 2: Table containing the AUC, DRi and MDT values and information regarding formula 1B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,676	1828,419	7,949	2452,970	6,407	1946,976
3	5	13,396	4315,365	13,371	4126,071	10,360	3147,913
4	10	21,074	6788,567	20,934	6459,619	14,976	4550,830
5	15	27,198	8761,628	29,269	9031,713	26,478	8045,747
6	30	37,585	12107,639	34,383	10609,695	29,907	9087,773
7	60	42,133	13572,526	44,944	13868,547	40,214	12219,645
8	90	52,074	16775,061	56,352	17388,619	54,116	16444,062
9	120	63,376	20415,697	55,208	17035,859	62,442	18973,944
10	180	66,719	21492,761	65,716	20278,373	64,557	19616,657
11	240	70,210	22617,221	69,506	21447,694	70,421	21398,661
12	360	70,764	22795,811	76,190	23510,367	75,029	22798,794

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
32213,7	30857,4	30386,7

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1828,419	2452,970	1946,976
3	5	2-5	4315,365	4126,071	3147,913
4	10	5-10	6788,567	6459,619	4550,830
5	15	10-15	8761,628	9031,713	8045,747
6	30	15-30	12107,639	10609,695	9087,773
7	60	30-60	13572,526	13868,547	12219,645
8	90	60-90	16775,061	17388,619	16444,062
9	120	90-120	20415,697	17035,859	18973,944
10	180	120-180	21492,761	20278,373	19616,657
11	240	180-240	22617,221	21447,694	21398,661
12	360	240-360	22795,811	23510,367	22798,794

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1828,419	2452,970	1946,976
3	2-5	3,5	2486,945	1673,100	1200,937
4	5-10	7,5	2473,202	2333,548	1402,917
5	10-15	12,5	1973,062	2572,094	3494,917
6	15-30	22,5	3346,010	1577,981	1042,026
7	30-60	45	1464,887	3258,852	3131,872
8	60-90	75	3202,536	3520,072	4224,417
9	90-120	105	3640,636	-352,761	2529,881
10	120-180	150	1077,064	3242,515	642,713
11	180-240	210	1124,460	1169,321	1782,004
12	240-360	300	178,590	2062,673	1400,133
		sum	22795,811	23510,367	22798,794

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1828,419	2452,970	1946,976
3	2-5	3,5	8704,308	5855,851	4203,279
4	5-10	7,5	18549,016	17501,613	10521,878
5	10-15	12,5	24663,271	32151,178	43686,468
6	15-30	22,5	75285,235	35504,579	23445,584
7	30-60	45	65919,901	146648,362	140934,218
8	60-90	75	240190,165	264005,395	316831,308
9	90-120	105	382266,822	-37039,861	265637,540
10	120-180	150	161559,580	486377,219	96407,010
11	180-240	210	236136,584	245557,322	374220,897
12	240-360	300	53576,943	618802,002	420039,875
		sum	1268680,245	1817816,630	1697875,032

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
55,654	77,320	74,472	69,149	9,613

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,554157932	3,577218728	2,883298393
12,87357326	14,39153273	11,31761589
38,77829218	38,59333993	28,5028826
54,30599231	56,47834653	46,6360257
218,6454111	214,8261123	190,2991498
538,0974843	535,4570813	473,315863
635,8977987	683,7448171	636,7260075
779,2883764	753,0291754	786,7637433
1756,284416	1632,484044	1714,477405
1848,545073	1825,500233	1822,201141
3806,305614	3933,797577	3927,150012

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9691,57619	9691,879478	9640,273144

Average AUC0-360 (µg/ml.min)		9674,576271
	STDEV	29,70776605

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 %Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,675906514	7,949374951	6,407329762
5	13,39605387	13,37141427	10,35950859
10	21,07353918	20,93377678	14,97638706
15	27,19845399	29,26919792	26,47785801

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,783129901	1,832302069	1,601400867	1,738944279	0,099308

Table 3: Table containing the AUC, DRi and MDT values and information regarding formula 1C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,978	468,754	1,584	389,368	1,318	328,066
3	5	6,967	1650,631	3,478	854,987	4,441	1105,070
4	10	8,815	2088,474	9,594	2358,449	12,254	3049,111
5	15	14,424	3417,646	18,516	4551,639	22,420	5578,913
6	30	21,905	5190,153	29,715	7304,354	31,761	7903,200
7	60	30,226	7161,531	36,900	9070,563	39,667	9870,437
8	90	36,761	8709,910	42,243	10384,089	43,732	10881,945
9	120	41,333	9793,143	47,185	11598,904	49,589	12339,292
10	180	45,772	10844,975	48,282	11868,498	52,824	13144,416
11	240	48,036	11381,360	54,216	13327,200	57,998	14431,642
12	360	52,723	12491,813	57,031	14019,119	59,370	14773,117

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
23693,4	24581,7	24883,2

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	468,754	389,368	328,066
3	5	2-5	1650,631	854,987	1105,070
4	10	5-10	2088,474	2358,449	3049,111
5	15	10-15	3417,646	4551,639	5578,913
6	30	15-30	5190,153	7304,354	7903,200
7	60	30-60	7161,531	9070,563	9870,437
8	90	60-90	8709,910	10384,089	10881,945
9	120	90-120	9793,143	11598,904	12339,292
10	180	120-180	10844,975	11868,498	13144,416
11	240	180-240	11381,360	13327,200	14431,642
12	360	240-360	12491,813	14019,119	14773,117

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	468,754	389,368	328,066
3	2-5	3,5	1181,878	465,619	777,003
4	5-10	7,5	437,843	1503,462	1944,041
5	10-15	12,5	1329,172	2193,190	2529,802
6	15-30	22,5	1772,507	2752,715	2324,287
7	30-60	45	1971,378	1766,209	1967,237
8	60-90	75	1548,379	1313,526	1011,508
9	90-120	105	1083,233	1214,815	1457,347
10	120-180	150	1051,832	269,595	805,124
11	180-240	210	536,385	1458,702	1287,226
12	240-360	300	1110,453	691,919	341,475
		sum	12491,813	14019,119	14773,117

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	468,754	389,368	328,066
3	2-5	3,5	4136,572	1629,666	2719,512
4	5-10	7,5	3283,820	11275,965	14580,311
5	10-15	12,5	16614,646	27414,875	31622,521
6	15-30	22,5	39881,406	61936,093	52296,453
7	30-60	45	88711,997	79479,399	88525,669
8	60-90	75	116128,444	98514,485	75863,104
9	90-120	105	113739,511	127555,527	153021,472
10	120-180	150	157774,790	40439,209	120768,564
11	180-240	210	112640,816	306327,351	270317,452
12	240-360	300	333135,815	207575,619	102442,506
		sum	986516,573	962537,557	912485,630

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
78,973	68,659	61,767	69,800	7,071

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,890	0,713	0,593
6,038	3,417	3,888
17,754	14,707	18,782
26,144	31,625	39,008
122,614	162,780	182,863
351,886	449,646	482,141
452,161	534,214	562,944
527,132	603,641	629,916
1175,916	1288,804	1382,580
1266,410	1383,720	1496,097
2720,486	3003,660	3168,919

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6667,431	7476,925	7967,731

Average AUC0-360 (µg/ml.min)	7370,696
STDEV	656,626

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 %Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,978	1,584	1,318
5	6,967	3,478	4,441
10	8,815	9,594	12,254
15	14,424	18,516	22,420

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,920	1,219	1,507	1,216	0,240

Table 4: Table containing the AUC, DRi and MDT values and information regarding formula 1D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,193	367,534	1,221	371,348	2,059	635,053
3	5	2,395	738,108	3,335	1014,569	4,692	1447,044
4	10	6,982	2151,608	7,723	2349,726	9,225	2844,951
5	15	15,046	4636,788	16,219	4934,358	17,396	5365,046
6	30	26,677	8221,094	27,678	8420,553	27,931	8614,097
7	60	36,611	11282,493	40,667	12372,442	35,116	10829,806
8	90	47,529	14646,837	51,343	15620,351	43,897	13537,931
9	120	55,695	17163,342	61,323	18656,795	58,546	18055,788
10	180	63,106	19447,410	67,581	20560,635	64,716	19958,512
11	240	69,177	21318,214	74,940	22799,542	72,101	22236,207
12	360	73,205	22559,475	74,294	22602,968	75,556	23301,831

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
30816,9	30423,6	30840,3

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	367,534	371,348	635,053
3	5	2-5	738,108	1014,569	1447,044
4	10	5-10	2151,608	2349,726	2844,951
5	15	10-15	4636,788	4934,358	5365,046
6	30	15-30	8221,094	8420,553	8614,097
7	60	30-60	11282,493	12372,442	10829,806
8	90	60-90	14646,837	15620,351	13537,931
9	120	90-120	17163,342	18656,795	18055,788
10	180	120-180	19447,410	20560,635	19958,512
11	240	180-240	21318,214	22799,542	22236,207
12	360	240-360	22559,475	22602,968	23301,831

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	367,534	371,348	635,053
3	2-5	3,5	370,573	643,221	811,991
4	5-10	7,5	1413,500	1335,157	1397,907
5	10-15	12,5	2485,180	2584,632	2520,095
6	15-30	22,5	3584,306	3486,195	3249,051
7	30-60	45	3061,399	3951,889	2215,709
8	60-90	75	3364,344	3247,908	2708,125
9	90-120	105	2516,505	3036,444	4517,856
10	120-180	150	2284,068	1903,841	1902,724
11	180-240	210	1870,804	2238,907	2277,695
12	240-360	300	1241,261	-196,574	1065,624
		sum	22559,475	22602,968	23301,831

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	367,534	371,348	635,053
3	2-5	3,5	1297,006	2251,273	2841,970
4	5-10	7,5	10601,250	10013,677	10484,301
5	10-15	12,5	31064,754	32307,899	31501,182
6	15-30	22,5	80646,887	78439,395	73103,652
7	30-60	45	137762,957	177835,025	99706,913
8	60-90	75	252325,781	243593,136	203109,401
9	90-120	105	264233,003	318826,603	474374,891
10	120-180	150	342610,198	285576,082	285408,670
11	180-240	210	392868,935	470170,411	478315,995
12	240-360	300	372378,253	-58972,350	319687,244
		sum	1886156,560	1560412,499	1979169,271

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
83,608	69,036	84,936	79,193	7,203

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,537	0,549	0,927
2,422	3,075	4,557
10,549	12,440	15,656
24,782	26,935	29,949
140,817	148,151	152,980
427,198	461,328	425,568
567,945	621,068	533,335
696,756	760,498	691,490
1603,812	1740,213	1664,034
1785,825	1924,041	1847,027
3844,311	4029,332	3986,754

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9104,954	9727,630	9352,278

Average AUC0-360 (µg/ml.min)		9394,954
	STDEV	313,524

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 %Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,193	1,221	2,059
5	2,395	3,335	4,692
10	6,982	7,723	9,225
15	15,046	16,219	17,396

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,978	1,054	1,121	1,051	0,058

Table 5: Table containing the AUC, DRi and MDT values and information regarding formula 1E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,839	908,957	3,367	815,113	3,149	768,231
3	5	7,434	1760,117	8,585	2078,437	11,123	2713,184
4	10	12,395	2934,782	16,296	3945,434	19,169	4676,125
5	15	22,188	5253,594	26,836	6497,246	26,809	6539,661
6	30	30,303	7175,220	35,260	8536,757	34,526	8422,128
7	60	34,946	8274,525	42,037	10177,595	40,892	9975,065
8	90	41,421	9807,729	46,034	11145,277	46,119	11249,999
9	120	46,663	11048,795	49,403	11960,875	49,930	12179,804
10	180	47,851	11330,148	50,843	12309,577	52,684	12851,545
11	240	50,181	11881,893	53,343	12914,773	55,563	13553,932
12	360	53,680	12710,307	56,551	13691,406	58,249	14209,081

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
23678,1	24210,9	24393,6

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	908,957	815,113	768,231
3	5	2-5	1760,117	2078,437	2713,184
4	10	5-10	2934,782	3945,434	4676,125
5	15	10-15	5253,594	6497,246	6539,661
6	30	15-30	7175,220	8536,757	8422,128
7	60	30-60	8274,525	10177,595	9975,065
8	90	60-90	9807,729	11145,277	11249,999
9	120	90-120	11048,795	11960,875	12179,804
10	180	120-180	11330,148	12309,577	12851,545
11	240	180-240	11881,893	12914,773	13553,932
12	360	240-360	12710,307	13691,406	14209,081

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	908,957	815,113	768,231
3	2-5	3,5	851,160	1263,324	1944,953
4	5-10	7,5	1174,665	1866,997	1962,941
5	10-15	12,5	2318,812	2551,812	1863,536
6	15-30	22,5	1921,625	2039,511	1882,466
7	30-60	45	1099,305	1640,838	1552,938
8	60-90	75	1533,205	967,682	1274,934
9	90-120	105	1241,066	815,598	929,805
10	120-180	150	281,352	348,702	671,741
11	180-240	210	551,745	605,196	702,387
12	240-360	300	828,414	776,632	655,149
		sum	12710,307	13691,406	14209,081

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	908,957	815,113	768,231
3	2-5	3,5	2979,061	4421,632	6807,337
4	5-10	7,5	8809,991	14002,478	14722,056
5	10-15	12,5	28985,148	31897,653	23294,203
6	15-30	22,5	43236,571	45888,998	42355,493
7	30-60	45	49468,734	73837,699	69882,200
8	60-90	75	114990,339	72576,147	95620,046
9	90-120	105	130311,946	85637,795	97629,486
10	120-180	150	42202,872	52305,307	100761,156
11	180-240	210	115866,540	127091,215	147501,256
12	240-360	300	248524,141	232989,730	196544,722
		sum	786284,298	741463,769	795886,185

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
61,862	54,155	56,013	57,343	3,284

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,727	1,515	1,417
7,609	8,067	9,633
22,307	27,991	34,078
38,905	48,524	51,726
177,156	209,574	207,005
440,431	521,756	509,072
515,477	594,482	587,323
594,564	644,200	648,331
1275,929	1353,321	1385,295
1323,428	1406,510	1461,342
2804,234	2967,122	3072,943

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7201,768	7783,061	7968,165

Average AUC0-360 (µg/ml.min)		7650,998
	STDEV	399,902

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 %Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,839	3,367	3,149
5	7,434	8,585	11,123
10	12,395	16,296	19,169
15	22,188	26,836	26,809

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,395	1,760	1,811	1,655	0,185

Table 6: Table containing the AUC, DRi and MDT values and information regarding formula 1F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,169	679,015	1,565	488,573	1,756	573,576
3	5	2,449	766,429	3,146	981,840	5,544	1810,677
4	10	5,759	1802,607	6,199	1934,910	12,335	4028,355
5	15	12,666	3964,394	15,862	4950,789	24,422	7975,485
6	30	26,251	8216,506	29,990	9360,393	34,575	11291,234
7	60	40,837	12781,817	46,204	14421,065	45,692	14921,847
8	90	52,643	16476,940	58,391	18225,131	56,564	18472,388
9	120	63,518	19880,650	69,439	21673,291	65,241	21305,841
10	180	60,379	18898,168	68,683	21437,470	70,035	22871,417
11	240	66,876	20931,906	70,838	22109,948	73,516	24008,407
12	360	70,860	22178,769	73,807	23036,594	76,490	24979,617

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
31299,357	31211,974	32657,310

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	679,015	488,573	573,576
3	5	2-5	766,429	981,840	1810,677
4	10	5-10	1802,607	1934,910	4028,355
5	15	10-15	3964,394	4950,789	7975,485
6	30	15-30	8216,506	9360,393	11291,234
7	60	30-60	12781,817	14421,065	14921,847
8	90	60-90	16476,940	18225,131	18472,388
9	120	90-120	19880,650	21673,291	21305,841
10	180	120-180	18898,168	21437,470	22871,417
11	240	180-240	20931,906	22109,948	24008,407
12	360	240-360	22178,769	23036,594	24979,617

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0,000	0,000	0,000
2	0-2	1	679,015	488,573	573,576
3	2-5	3,5	87,414	493,267	1237,102
4	5-10	7,5	1036,178	953,070	2217,677
5	10-15	12,5	2161,786	3015,878	3947,131
6	15-30	22,5	4252,112	4409,605	3315,749
7	30-60	45	4565,311	5060,672	3630,613
8	60-90	75	3695,123	3804,066	3550,541
9	90-120	105	3403,710	3448,160	2833,453
10	120-180	150	-982,482	-235,821	1565,576
11	180-240	210	2033,739	672,477	1136,989
12	240-360	300	1246,863	926,646	971,211
		sum	22178,769	23036,594	24979,617

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	679,015	488,573	573,576
3	2-5	3,5	305,949	1726,433	4329,855
4	5-10	7,5	7771,333	7148,028	16632,580
5	10-15	12,5	27022,330	37698,481	49339,131
6	15-30	22,5	95672,528	99216,102	74604,355
7	30-60	45	205439,001	227730,236	163377,580
8	60-90	75	277134,230	285304,966	266290,578
9	90-120	105	357389,575	362056,759	297512,553
10	120-180	150	-147372,363	-35373,086	234836,459
11	180-240	210	427085,102	141220,268	238767,727
12	240-360	300	374058,789	277993,939	291363,179
		sum	1625185,490	1405210,700	1637627,573

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
73,277	60,999	65,559	66,611	5,067

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,976	0,704	0,790
3,117	3,180	4,928
9,234	10,513	20,115
20,728	24,819	41,352
131,346	154,749	199,114
452,849	514,305	541,803
630,993	706,017	690,232
784,086	862,856	822,184
1672,603	1864,654	1826,216
1717,946	1883,540	1937,936
3718,889	3905,413	4050,170

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9142,766	9930,751	10134,839

Average AUC0-360 (µg/ml.min)		9736,118696
	STDEV	523,892

Dri			
Withdrawal times	Vessel 1 %Dissolution	Vessel 2 %Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,169	1,565	1,756
5	2,449	3,146	5,544
10	5,759	6,199	12,335
15	12,666	15,862	24,422

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,782	0,988	1,601	1,124	0,348

Table 7: Table containing the AUC, DRi and MDT values and information regarding formula 2A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,517	404,625	5,590	1442,145	3,089	809,586
3	5	9,618	2565,047	6,395	1649,688	4,014	1052,232
4	10	10,019	2672,098	8,373	2159,996	8,633	2262,910
5	15	14,252	3800,969	14,127	3644,141	15,294	4008,617
6	30	20,381	5435,504	22,070	5693,303	22,854	5990,272
7	60	40,848	10893,754	39,286	10134,488	30,029	7870,888
8	90	33,591	8958,520	48,280	12454,588	42,542	11150,570
9	120	47,452	12655,013	53,745	13864,303	54,549	14297,639
10	180	55,220	14726,772	42,919	11071,615	55,390	14518,205
11	240	61,521	16407,110	46,817	12077,073	58,876	15431,931
12	360	65,850	17561,677	60,032	15486,161	63,203	16566,028

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
26669,231	25796,377	26210,818

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	404,625	1442,145	809,586
3	5	2-5	2565,047	1649,688	1052,232
4	10	5-10	2672,098	2159,996	2262,910
5	15	10-15	3800,969	3644,141	4008,617
6	30	15-30	5435,504	5693,303	5990,272
7	60	30-60	10893,754	10134,488	7870,888
8	90	60-90	8958,520	12454,588	11150,570
9	120	90-120	12655,013	13864,303	14297,639
10	180	120-180	14726,772	11071,615	14518,205
11	240	180-240	16407,110	12077,073	15431,931
12	360	240-360	17561,677	15486,161	16566,028

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	404,625	1442,145	809,586
3	2-5	3,5	2160,421	207,542	242,645
4	5-10	7,5	107,051	510,308	1210,678
5	10-15	12,5	1128,871	1484,146	1745,708
6	15-30	22,5	1634,535	2049,162	1981,655
7	30-60	45	5458,250	4441,185	1880,616
8	60-90	75	-1935,234	2320,100	3279,682
9	90-120	105	3696,492	1409,715	3147,069
10	120-180	150	2071,759	-2792,688	220,566
11	180-240	210	1680,338	1005,458	913,726
12	240-360	300	1154,567	3409,087	1134,097
		sum	17561,677	15486,161	16566,028

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	404,625	1442,145	809,586
3	2-5	3,5	7561,475	726,397	849,258
4	5-10	7,5	802,883	3827,310	9080,084
5	10-15	12,5	14110,889	18551,821	21821,346
6	15-30	22,5	36777,044	46106,141	44587,238
7	30-60	45	245621,260	199853,317	84627,727
8	60-90	75	-145142,548	174007,534	245976,146
9	90-120	105	388131,707	148020,073	330442,214
10	120-180	150	310763,810	-418903,192	33084,908
11	180-240	210	352870,990	211146,184	191882,356
12	240-360	300	346370,067	1022726,152	340229,126
		sum	1558272,202	1407503,882	1303389,990

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
88,731	90,888	78,678	86,099	5,321

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,683	2,516	1,390
7,516	8,090	4,795
22,092	16,614	14,229
27,306	25,312	26,918
116,888	122,164	128,749
413,295	414,157	356,963
502,462	591,076	489,854
547,040	688,672	655,361
1386,070	1304,970	1484,173
1576,001	1211,439	1542,595
3439,009	2884,930	3296,139

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8038,361	7269,941	8001,166

Average AUC0-360 (µg/ml.min)		7769,823
	STDEV	433,310

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,517	5,590	3,089
5	9,618	6,395	4,014
10	10,019	8,373	8,633
15	14,252	14,127	15,294

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,928	0,791	0,961	0,894	0,073

Table 8: Table containing the AUC, DRi and MDT values and information regarding formula 2B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,764345058	1388,311672	4,214612936	1305,101725	4,691358025	1449,670773
3	5	7,446428725	2169,86045	9,614350666	2977,19051	8,377772601	2588,805208
4	10	10,43058899	3039,433177	12,52826738	3879,517196	12,48054973	3856,599323
5	15	18,43307365	5371,326171	22,29559748	6904,07949	21,03946994	6501,380729
6	30	30,46917031	8878,598057	30,87606008	9561,115071	40,61849177	12551,47019
7	60	45,19913554	13170,8528	45,39530329	14057,16006	46,56081821	14387,70117
8	90	41,67165325	12142,95814	55,89460017	17308,38399	58,40807171	18048,6064
9	120	62,36113052	18171,79157	64,35288282	19927,5852	53,75790909	16611,66537
10	180	67,20034337	19581,91943	68,87480912	21327,84992	59,66794351	18437,91784
11	240	71,94965965	20965,85177	72,74286306	22525,6358	68,77871815	21253,22711
12	360	49,1963748	14335,63281	76,45953361	23676,54413	76,29846175	23576,89383

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
29139,61216	30966,11111	30900,87701

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1388,311672	1305,101725	1449,670773
3	5	2-5	2169,86045	2977,19051	2588,805208
4	10	5-10	3039,433177	3879,517196	3856,599323
5	15	10-15	5371,326171	6904,07949	6501,380729
6	30	15-30	8878,598057	9561,115071	12551,47019
7	60	30-60	13170,8528	14057,16006	14387,70117
8	90	60-90	12142,95814	17308,38399	18048,6064
9	120	90-120	18171,79157	19927,5852	16611,66537
10	180	120-180	19581,91943	21327,84992	18437,91784
11	240	180-240	20965,85177	22525,6358	21253,22711
12	360	240-360	14335,63281	23676,54413	23576,89383

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1388,311672	1305,101725	1449,670773
3	2-5	3,5	781,5487785	1672,088785	1139,134434
4	5-10	7,5	869,5727262	902,3266867	1267,794115
5	10-15	12,5	2331,892994	3024,562293	2644,781406
6	15-30	22,5	3507,271886	2657,035581	6050,089457
7	30-60	45	4292,25474	4496,044986	1836,230985
8	60-90	75	-1027,894659	3251,223936	3660,905232
9	90-120	105	6028,833435	2619,201203	-1436,941033
10	120-180	150	1410,127854	1400,264724	1826,252468
11	180-240	210	1383,932346	1197,78588	2815,309268
12	240-360	300	-6630,218958	1150,908332	2323,66672
		sum	14335,63281	23676,54413	23576,89383

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1388,311672	1305,101725	1449,670773
3	2-5	3,5	2735,420725	5852,310748	3986,97052
4	5-10	7,5	6521,795447	6767,45015	9508,455863
5	10-15	12,5	29148,66243	37807,02867	33059,76758
6	15-30	22,5	78913,61743	59783,30058	136127,0128
7	30-60	45	193151,4633	202322,0244	82630,39431
8	60-90	75	-77092,09943	243841,7952	274567,8924
9	90-120	105	633027,5106	275016,1263	-150878,8085
10	120-180	150	211519,1782	210039,7086	273937,8702
11	180-240	210	290625,7926	251535,0349	591214,9463
12	240-360	300	-1989065,687	345272,4995	697100,016
		sum	-619126,0344	1639542,381	1952704,188

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-43,18791102	69,24753763	82,82279263	36,29413975	56,47488635

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,143955276	1,896575821	2,111111111
8,242272304	9,334550431	8,821663173
20,11164493	24,9104453	23,46561263
32,47162047	39,17684797	37,71002213
165,0450734	179,4543443	208,0956208
510,7610645	514,8317028	588,4603424
586,3778244	683,7068484	708,540007
702,2212905	811,6705101	757,1203704
1749,079898	1798,573841	1531,24901
1878,525041	1911,838574	1734,029932
3270,94293	4028,46471	3917,083857

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8925,922614	10003,85895	9516,687549

Average AUC0-360 (µg/ml.min)		9482,156371
	STDEV	539,797173

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,764345058	4,214612936	4,691358025
5	7,446428725	9,614350666	8,377772601
10	10,43058899	12,52826738	12,48054973
15	18,43307365	22,29559748	21,03946994

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,103796483	1,372918988	1,296907262	1,257874245	0,113282576

Table 9: Table containing the AUC, DRi and MDT values and information regarding formula 2C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,882	543,151	2,381	703,522	1,727	493,544
3	5	4,581	1321,944	6,255	1848,340	4,693	1341,383
4	10	10,768	3107,557	13,237	3911,836	11,335	3239,601
5	15	18,293	5279,051	20,699	6117,082	19,647	5615,246
6	30	25,159	7260,410	28,176	8326,668	26,009	7433,672
7	60	32,812	9469,078	35,352	10447,388	34,469	9851,450
8	90	40,550	11701,904	45,372	13408,453	43,596	12459,975
9	120	49,402	14256,522	52,903	15633,950	51,165	14623,331
10	180	55,622	16051,488	59,095	17463,892	56,826	16241,324
11	240	60,983	17598,767	63,289	18703,270	62,850	17962,852
12	360	65,184	18810,886	68,831	20340,931	66,513	19009,955

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
28858,270	29552,055	28580,709

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	543,151	703,522	493,544
3	5	2-5	1321,944	1848,340	1341,383
4	10	5-10	3107,557	3911,836	3239,601
5	15	10-15	5279,051	6117,082	5615,246
6	30	15-30	7260,410	8326,668	7433,672
7	60	30-60	9469,078	10447,388	9851,450
8	90	60-90	11701,904	13408,453	12459,975
9	120	90-120	14256,522	15633,950	14623,331
10	180	120-180	16051,488	17463,892	16241,324
11	240	180-240	17598,767	18703,270	17962,852
12	360	240-360	18810,886	20340,931	19009,955

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	543,151	703,522	493,544
3	2-5	3,5	778,793	1144,818	847,839
4	5-10	7,5	1785,612	2063,496	1898,218
5	10-15	12,5	2171,495	2205,246	2375,645
6	15-30	22,5	1981,359	2209,585	1818,426
7	30-60	45	2208,668	2120,721	2417,777
8	60-90	75	2232,826	2961,064	2608,525
9	90-120	105	2554,618	2225,497	2163,357
10	120-180	150	1794,966	1829,942	1617,993
11	180-240	210	1547,279	1239,378	1721,527
12	240-360	300	1212,119	1637,661	1047,104
		sum	18810,886	20340,931	19009,955

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	543,151	703,522	493,544
3	2-5	3,5	2725,776	4006,863	2967,438
4	5-10	7,5	13392,091	15476,222	14236,632
5	10-15	12,5	27143,682	27565,575	29695,566
6	15-30	22,5	44580,583	49715,670	40914,587
7	30-60	45	99390,066	95432,439	108799,985
8	60-90	75	167461,921	222079,823	195639,382
9	90-120	105	268234,924	233677,190	227152,468
10	120-180	150	269244,892	274491,371	242698,948
11	180-240	210	324928,575	260269,412	361520,711
12	240-360	300	363635,718	491298,221	314131,118
		sum	1581281,379	1674716,308	1538250,378

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
84,062	82,332	80,918	82,438	1,286

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,847	1,071	0,777
4,362	5,829	4,334
17,268	21,928	18,032
32,694	38,179	34,855
146,650	164,955	154,090
391,306	428,819	408,228
495,193	544,892	526,936
607,172	663,359	639,635
1417,819	1511,979	1457,881
1574,171	1652,192	1615,623
3406,513	3567,242	3492,796

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8093,995	8600,446	8353,187

Average AUC0-360 (µg/ml.min)		8349,209
	STDEV	253,249

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,882	2,381	1,727
5	4,581	6,255	4,693
10	10,768	13,237	11,335
15	18,293	20,699	19,647

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,216	1,384	1,311	1,303	0,069

Table 10: Table containing the AUC, DRi and MDT values and information regarding formula 2D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,547	498,932	1,896	599,142	1,759	579,365
3	5	3,209	1035,241	3,657	1155,528	4,271	1406,419
4	10	7,923	2555,858	7,858	2482,940	10,861	3576,278
5	15	15,410	4971,057	14,626	4621,464	19,714	6491,441
6	30	26,273	8475,113	23,832	7530,422	28,623	9425,258
7	60	40,676	13121,090	38,638	12209,165	43,230	14234,983
8	90	54,656	17630,827	52,566	16609,937	55,930	18417,128
9	120	64,338	20754,092	61,112	19310,483	66,237	21811,074
10	180	69,043	22271,650	66,234	20928,823	71,048	23395,229
11	240	73,139	23593,137	71,362	22549,198	74,367	24487,938
12	360	77,226	24911,282	74,477	23533,663	77,145	25402,953

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
32257,729	31598,494	32928,704

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	498,932	599,142	579,365
3	5	2-5	1035,241	1155,528	1406,419
4	10	5-10	2555,858	2482,940	3576,278
5	15	10-15	4971,057	4621,464	6491,441
6	30	15-30	8475,113	7530,422	9425,258
7	60	30-60	13121,090	12209,165	14234,983
8	90	60-90	17630,827	16609,937	18417,128
9	120	90-120	20754,092	19310,483	21811,074
10	180	120-180	22271,650	20928,823	23395,229
11	240	180-240	23593,137	22549,198	24487,938
12	360	240-360	24911,282	23533,663	25402,953

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	498,932	599,142	579,365
3	2-5	3,5	536,310	556,386	827,054
4	5-10	7,5	1520,617	1327,412	2169,858
5	10-15	12,5	2415,198	2138,524	2915,164
6	15-30	22,5	3504,056	2908,958	2933,817
7	30-60	45	4645,977	4678,742	4809,725
8	60-90	75	4509,737	4400,773	4182,145
9	90-120	105	3123,265	2700,545	3393,945
10	120-180	150	1517,558	1618,341	1584,155
11	180-240	210	1321,487	1620,375	1092,709
12	240-360	300	1318,144	984,465	915,016
		sum	24911,282	23533,663	25402,953

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	498,932	599,142	579,365
3	2-5	3,5	1877,084	1947,351	2894,690
4	5-10	7,5	11404,627	9955,587	16273,936
5	10-15	12,5	30189,979	26731,554	36439,546
6	15-30	22,5	78841,268	65451,561	66010,878
7	30-60	45	209068,981	210543,399	216437,641
8	60-90	75	338230,265	330057,953	313660,881
9	90-120	105	327942,807	283557,249	356364,263
10	120-180	150	227633,768	242751,135	237623,248
11	180-240	210	277512,230	340278,660	229468,841
12	240-360	300	395443,338	295339,642	274504,726
		sum	1898643,278	1807213,233	1750258,016

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
76,216	76,793	68,900	73,970	3,593

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,696	0,853	0,792
3,210	3,748	4,071
12,524	12,954	17,023
26,250	25,294	34,396
140,682	129,793	163,137
451,905	421,673	485,007
643,491	615,627	669,330
803,213	767,324	824,631
1800,646	1719,166	1853,353
1919,461	1857,536	1963,098
4059,862	3937,647	4090,820

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9861,941	9491,615	10105,658

Average AUC0-360 (µg/ml.min)		9819,738
	STDEV	309,189

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,547	1,896	1,759
5	3,209	3,657	4,271
10	7,923	7,858	10,861
15	15,410	14,626	19,714

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,004	0,942	1,306	1,084	0,159

Table 11: Table containing the AUC, DRi and MDT values and information regarding formula 2E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,537	332,917	1,631	333,548	1,474	321,569
3	5	2,007	434,670	2,109	431,362	1,836	400,642
4	10	4,168	902,522	4,414	902,973	4,010	874,912
5	15	9,174	1986,679	8,764	1792,702	8,428	1839,080
6	30	16,147	3496,515	15,552	3181,322	15,566	3396,489
7	60	25,182	5453,196	25,085	5131,298	25,699	5607,674
8	90	34,754	7525,902	33,064	6763,552	34,546	7537,940
9	120	40,625	8797,175	37,778	7727,779	40,691	8879,000
10	180	45,980	9956,916	42,173	8626,959	43,788	9554,668
11	240	48,482	10498,702	44,331	9068,386	47,772	10423,921
12	360	53,290	11539,890	47,643	9745,811	50,885	11103,220

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
21654,769	20456,020	21820,283

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	332,917	333,548	321,569
3	5	2-5	434,670	431,362	400,642
4	10	5-10	902,522	902,973	874,912
5	15	10-15	1986,679	1792,702	1839,080
6	30	15-30	3496,515	3181,322	3396,489
7	60	30-60	5453,196	5131,298	5607,674
8	90	60-90	7525,902	6763,552	7537,940
9	120	90-120	8797,175	7727,779	8879,000
10	180	120-180	9956,916	8626,959	9554,668
11	240	180-240	10498,702	9068,386	10423,921
12	360	240-360	11539,890	9745,811	11103,220

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	332,917	333,548	321,569
3	2-5	3,5	101,753	97,814	79,073
4	5-10	7,5	467,852	471,610	474,270
5	10-15	12,5	1084,156	889,729	964,167
6	15-30	22,5	1509,837	1388,620	1557,410
7	30-60	45	1956,681	1949,976	2211,185
8	60-90	75	2072,707	1632,253	1930,266
9	90-120	105	1271,272	964,227	1341,060
10	120-180	150	1159,741	899,180	675,668
11	180-240	210	541,787	441,427	869,253
12	240-360	300	1041,187	677,425	679,299
		sum	11539,890	9745,811	11103,220

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	332,917	333,548	321,569
3	2-5	3,5	356,135	342,350	276,754
4	5-10	7,5	3508,889	3537,078	3557,027
5	10-15	12,5	13551,956	11121,619	12052,091
6	15-30	22,5	33971,329	31243,954	35041,724
7	30-60	45	88050,623	87748,925	99503,303
8	60-90	75	155452,991	122418,986	144769,957
9	90-120	105	133483,575	101243,853	140811,250
10	120-180	150	173961,158	134877,003	101350,208
11	180-240	210	113775,224	92699,651	182543,212
12	240-360	300	312356,191	203227,599	203789,821
		sum	1028800,988	788794,565	924016,917

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
89,152	80,937	83,221	84,436	3,462

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,692	0,734	0,663
2,393	2,524	2,234
6,947	7,338	6,576
15,010	14,825	13,993
85,458	82,065	80,980
278,971	274,297	278,539
404,571	392,502	406,653
508,806	478,179	507,850
1169,166	1079,335	1140,473
1275,243	1167,809	1236,056
2747,857	2483,295	2663,727

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6495,113	5982,903	6337,746

Average AUC0-360 (µg/ml.min)		6271,921
	STDEV	262,373

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,537	1,631	1,474
5	2,007	2,109	1,836
10	4,168	4,414	4,010
15	9,174	8,764	8,428

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,565	0,544	0,522	0,544	0,018

Table 12: Table containing the AUC, DRi and MDT values and information regarding formula 2F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,387	423,097	1,635	524,433	1,463	433,824
3	5	2,101	641,062	3,345	1072,739	2,432	721,343
4	10	5,382	1641,994	8,320	2668,471	6,074	1801,194
5	15	12,620	3850,488	16,846	5402,594	13,481	3997,842
6	30	22,561	6883,292	27,881	8941,723	23,705	7030,084
7	60	37,967	11583,530	44,501	14271,877	38,554	11433,492
8	90	52,862	16128,217	57,336	18388,279	50,695	15034,036
9	120	59,192	18059,256	63,742	20442,835	61,187	18145,812
10	180	64,907	19802,967	69,036	22140,703	64,803	19218,139
11	240	68,361	20856,982	73,064	23432,526	69,737	20681,347
12	360	73,256	22350,255	76,679	24591,913	72,847	21603,614

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
30509,871	32071,122	29656,129

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	423,097	524,433	433,824
3	5	2-5	641,062	1072,739	721,343
4	10	5-10	1641,994	2668,471	1801,194
5	15	10-15	3850,488	5402,594	3997,842
6	30	15-30	6883,292	8941,723	7030,084
7	60	30-60	11583,530	14271,877	11433,492
8	90	60-90	16128,217	18388,279	15034,036
9	120	90-120	18059,256	20442,835	18145,812
10	180	120-180	19802,967	22140,703	19218,139
11	240	180-240	20856,982	23432,526	20681,347
12	360	240-360	22350,255	24591,913	21603,614

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	423,097	524,433	433,824
3	2-5	3,5	217,966	548,306	287,519
4	5-10	7,5	1000,931	1595,731	1079,851
5	10-15	12,5	2208,494	2734,123	2196,648
6	15-30	22,5	3032,804	3539,129	3032,242
7	30-60	45	4700,238	5330,155	4403,407
8	60-90	75	4544,686	4116,401	3600,544
9	90-120	105	1931,039	2054,557	3111,776
10	120-180	150	1743,712	1697,868	1072,327
11	180-240	210	1054,015	1291,823	1463,208
12	240-360	300	1493,273	1159,387	922,267
		sum	22350,255	24591,913	21603,614

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	423,097	524,433	433,824
3	2-5	3,5	762,880	1919,071	1006,318
4	5-10	7,5	7506,986	11967,985	8098,886
5	10-15	12,5	27606,180	34176,540	27458,099
6	15-30	22,5	68238,089	79630,399	68225,445
7	30-60	45	211510,703	239856,953	198153,321
8	60-90	75	340851,487	308730,095	270040,823
9	90-120	105	202759,084	215728,449	326736,514
10	120-180	150	261556,778	254680,166	160849,017
11	180-240	210	221343,083	271282,908	307273,705
12	240-360	300	447981,903	347816,074	276680,005
		sum	1790540,271	1766313,073	1644955,956

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
80,113	71,825	76,143	76,027	3,384

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,624	0,736	0,658
2,354	3,362	2,629
8,418	13,124	9,569
20,253	28,312	21,999
118,737	150,952	125,503
408,560	488,576	420,247
613,094	687,397	602,425
756,363	817,277	755,203
1675,327	1792,509	1700,874
1799,120	1918,357	1816,296
3823,666	4043,076	3849,774

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9226,516	9943,678	9305,177

Average AUC0-360 (µg/ml.min)		9491,790
	STDEV	393,318

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,387	1,635	1,463
5	2,101	3,345	2,432
10	5,382	8,320	6,074
15	12,620	16,846	13,481

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,797	1,092	0,858	0,915	0,127

Table 13: Table containing the AUC, DRi and MDT values and information regarding formula 3A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,041	494,664	2,848	683,425	3,061	727,845
3	5	6,236	1511,619	8,189	1965,042	8,768	2084,950
4	10	14,265	3458,042	18,785	4507,706	18,518	4403,423
5	15	24,095	5841,012	29,448	7066,307	27,821	6615,813
6	30	32,718	7931,440	51,882	12449,829	35,645	8476,260
7	60	39,593	9598,126	43,397	10413,567	41,458	9858,663
8	90	46,922	11374,727	48,202	11566,612	47,719	11347,461
9	120	50,709	12292,803	52,068	12494,343	50,781	12075,402
10	180	54,631	13243,499	54,996	13196,966	53,814	12796,711
11	240	57,857	14025,565	56,817	13634,075	56,765	13498,405
12	360	59,857	14510,419	59,250	14217,808	58,330	13870,532

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
24241,946	23996,275	23779,595

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	494,664	683,425	727,845
3	5	2-5	1511,619	1965,042	2084,950
4	10	5-10	3458,042	4507,706	4403,423
5	15	10-15	5841,012	7066,307	6615,813
6	30	15-30	7931,440	12449,829	8476,260
7	60	30-60	9598,126	10413,567	9858,663
8	90	60-90	11374,727	11566,612	11347,461
9	120	90-120	12292,803	12494,343	12075,402
10	180	120-180	13243,499	13196,966	12796,711
11	240	180-240	14025,565	13634,075	13498,405
12	360	240-360	14510,419	14217,808	13870,532

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	494,664	683,425	727,845
3	2-5	3,5	1016,955	1281,617	1357,105
4	5-10	7,5	1946,423	2542,664	2318,473
5	10-15	12,5	2382,970	2558,601	2212,390
6	15-30	22,5	2090,428	5383,522	1860,446
7	30-60	45	1666,686	-2036,262	1382,403
8	60-90	75	1776,601	1153,045	1488,798
9	90-120	105	918,076	927,731	727,941
10	120-180	150	950,696	702,623	721,309
11	180-240	210	782,066	437,109	701,694
12	240-360	300	484,854	583,733	372,127
		sum	14510,419	14217,808	13870,532

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	494,664	683,425	727,845
3	2-5	3,5	3559,341	4485,659	4749,869
4	5-10	7,5	14598,170	19069,980	17388,548
5	10-15	12,5	29787,131	31982,509	27654,875
6	15-30	22,5	47034,627	121129,253	41860,045
7	30-60	45	75000,862	-91631,805	62208,132
8	60-90	75	133245,060	86478,385	111659,836
9	90-120	105	96397,986	97411,792	76433,853
10	120-180	150	142604,408	105393,378	108196,325
11	180-240	210	164233,931	91792,880	147355,754
12	240-360	300	145456,069	175119,957	111637,987
		sum	852412,249	641915,414	709873,069

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
58,745	45,149	51,179	51,691	5,562

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,918	1,282	1,377
5,586	7,450	7,984
23,063	30,346	30,696
43,154	54,262	52,131
191,742	274,488	214,199
488,098	643,133	520,449
583,974	618,288	601,950
659,006	676,819	664,874
1422,081	1445,360	1412,024
1518,576	1509,480	1492,810
3178,258	3133,823	3107,544

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8114,457	8394,732	8106,039

Average AUC0-360 (µg/ml.min)		8205,076
	STDEV	164,301

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,041	2,848	3,061
5	6,236	8,189	8,768
10	14,265	18,785	18,518
15	24,095	29,448	27,821

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,614	1,990	1,878	1,827	0,157

Table 14: Table containing the AUC, DRi and MDT values and information regarding formula 3B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,682	1169,792	2,621	811,718	2,544	810,477
3	5	10,753	3416,254	8,500	2632,055	7,783	2480,013
4	10	20,357	6467,531	17,757	5498,778	16,893	5382,442
5	15	28,494	9052,651	27,226	8430,887	26,734	8518,147
6	30	36,377	11557,217	35,039	10850,163	32,664	10407,405
7	60	45,187	14356,160	41,379	12813,296	41,270	13149,548
8	90	52,789	16771,663	52,056	16119,521	52,847	16838,319
9	120	59,621	18942,124	57,554	17822,219	63,781	20322,061
10	180	64,750	20571,563	62,839	19458,881	68,669	21879,608
11	240	72,477	23026,519	70,738	21904,762	74,247	23656,973
12	360	78,447	24923,176	75,706	23443,258	78,087	24880,482

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
31770,877	30966,003	31862,449

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1169,792	811,718	810,477
3	5	2-5	3416,254	2632,055	2480,013
4	10	5-10	6467,531	5498,778	5382,442
5	15	10-15	9052,651	8430,887	8518,147
6	30	15-30	11557,217	10850,163	10407,405
7	60	30-60	14356,160	12813,296	13149,548
8	90	60-90	16771,663	16119,521	16838,319
9	120	90-120	18942,124	17822,219	20322,061
10	180	120-180	20571,563	19458,881	21879,608
11	240	180-240	23026,519	21904,762	23656,973
12	360	240-360	24923,176	23443,258	24880,482

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1169,792	811,718	810,477
3	2-5	3,5	2246,462	1820,337	1669,536
4	5-10	7,5	3051,277	2866,723	2902,429
5	10-15	12,5	2585,120	2932,109	3135,704
6	15-30	22,5	2504,566	2419,276	1889,258
7	30-60	45	2798,943	1963,133	2742,143
8	60-90	75	2415,503	3306,225	3688,772
9	90-120	105	2170,460	1702,699	3483,742
10	120-180	150	1629,439	1636,661	1557,547
11	180-240	210	2454,957	2445,882	1777,366
12	240-360	300	1896,656	1538,496	1223,509
		sum	24923,176	23443,258	24880,482

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1169,792	811,718	810,477
3	2-5	3,5	7862,617	6371,179	5843,375
4	5-10	7,5	22884,578	21500,422	21768,221
5	10-15	12,5	32314,001	36651,358	39196,302
6	15-30	22,5	56352,727	54433,708	42508,315
7	30-60	45	125952,446	88340,988	123396,421
8	60-90	75	181162,743	247966,857	276657,878
9	90-120	105	227898,338	178783,364	365792,868
10	120-180	150	244415,872	245499,163	233631,985
11	180-240	210	515540,924	513635,157	373246,778
12	240-360	300	568996,944	461548,684	367052,744
		sum	1984550,981	1855542,599	1849905,363

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
79,627	79,150	74,352	77,710	2,382

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,657	1,180	1,145
9,743	7,507	6,971
34,998	29,539	27,761
54,957	50,607	49,080
218,937	210,145	200,467
550,552	515,818	499,050
661,338	630,680	635,287
758,771	739,865	787,236
1679,005	1625,314	1788,069
1852,559	1803,298	1929,368
4074,932	3954,003	4113,027

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9897,450	9567,956	10037,460

Average AUC0-360 (µg/ml.min)		9834,289
	STDEV	241,040

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,682	2,621	2,544
5	10,753	8,500	7,783
10	20,357	17,757	16,893
15	28,494	27,226	26,734

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,924	1,841	1,801	1,855	0,051

Table 15: Table containing the AUC, DRi and MDT values and information regarding formula 3C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,255	867,448	2,578	624,819	3,188	785,696
3	5	10,432	2780,191	8,167	1979,586	11,607	2860,534
4	10	23,643	6301,037	19,763	4790,244	25,032	6168,864
5	15	34,264	9131,599	30,076	7289,752	34,904	8601,874
6	30	41,706	11114,805	38,019	9215,074	40,310	9934,162
7	60	46,517	12396,922	43,780	10611,501	45,590	11235,325
8	90	52,810	14074,029	48,290	11704,507	52,395	12912,351
9	120	51,729	13785,979	53,000	12846,179	53,521	13190,000
10	180	52,124	13891,145	53,851	13052,478	55,570	13694,987
11	240	64,189	17106,637	56,895	13790,262	57,069	14064,233
12	360	65,804	17536,933	59,847	14505,789	60,850	14996,173

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
26650,437	24238,078	24644,371

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	867,448	624,819	785,696
3	5	2-5	2780,191	1979,586	2860,534
4	10	5-10	6301,037	4790,244	6168,864
5	15	10-15	9131,599	7289,752	8601,874
6	30	15-30	11114,805	9215,074	9934,162
7	60	30-60	12396,922	10611,501	11235,325
8	90	60-90	14074,029	11704,507	12912,351
9	120	90-120	13785,979	12846,179	13190,000
10	180	120-180	13891,145	13052,478	13694,987
11	240	180-240	17106,637	13790,262	14064,233
12	360	240-360	17536,933	14505,789	14996,173

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	867,448	624,819	785,696
3	2-5	3,5	1912,743	1354,767	2074,838
4	5-10	7,5	3520,846	2810,658	3308,330
5	10-15	12,5	2830,562	2499,508	2433,011
6	15-30	22,5	1983,207	1925,322	1332,288
7	30-60	45	1282,116	1396,426	1301,163
8	60-90	75	1677,108	1093,006	1677,025
9	90-120	105	-288,050	1141,672	277,649
10	120-180	150	105,166	206,299	504,987
11	180-240	210	3215,492	737,784	369,246
12	240-360	300	430,296	715,526	931,941
		sum	17536,933	14505,789	14996,173

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	867,448	624,819	785,696
3	2-5	3,5	6694,599	4741,686	7261,933
4	5-10	7,5	26406,346	21079,936	24812,475
5	10-15	12,5	35382,024	31243,844	30412,632
6	15-30	22,5	44622,151	43319,754	29976,474
7	30-60	45	57695,226	62839,180	58552,339
8	60-90	75	125783,067	81975,480	125776,898
9	90-120	105	-30245,283	119875,606	29153,161
10	120-180	150	15774,918	30944,844	75748,098
11	180-240	210	675253,312	154934,624	77541,587
12	240-360	300	129088,764	214657,896	279582,248
		sum	1087322,572	766237,669	739603,540

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
62,002	52,823	49,319	54,715	5,348

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,465	1,160	1,435
9,239	7,253	9,987
38,335	31,422	41,219
65,146	56,069	67,427
256,400	229,819	253,848
595,503	552,145	579,824
670,454	621,473	661,396
705,636	683,706	714,933
1402,008	1442,490	1472,739
1570,218	1495,073	1520,629
3509,798	3152,038	3183,814

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8824,200	8272,648	8507,251

Average AUC0-360 (µg/ml.min)		8534,700
	STDEV	276,799

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,255	2,578	3,188
5	10,432	8,167	11,607
10	23,643	19,763	25,032
15	34,264	30,076	34,904

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,352	2,058	2,413	2,274	0,155

Table 16: Table containing the AUC, DRi and MDT values and information regarding formula 3D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,735	523,215	2,027	640,511	1,613	470,149
3	5	3,748	1130,412	5,471	1729,298	3,053	889,552
4	10	9,449	2850,174	13,312	4207,236	8,235	2399,547
5	15	17,737	5350,002	23,014	7273,639	15,770	4595,307
6	30	25,996	7841,156	30,679	9696,325	22,678	6608,174
7	60	36,069	10879,517	42,500	13432,421	31,036	9043,416
8	90	45,104	13604,765	55,657	17590,963	40,103	11685,664
9	120	54,158	16335,931	62,821	19855,091	52,072	15173,118
10	180	61,873	18663,105	69,454	21951,635	60,323	17577,305
11	240	66,883	20174,101	73,225	23143,375	67,281	19604,793
12	360	74,477	22464,877	78,039	24665,018	71,948	20964,721

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
30163,347	31605,905	29138,826

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	523,215	640,511	470,149
3	5	2-5	1130,412	1729,298	889,552
4	10	5-10	2850,174	4207,236	2399,547
5	15	10-15	5350,002	7273,639	4595,307
6	30	15-30	7841,156	9696,325	6608,174
7	60	30-60	10879,517	13432,421	9043,416
8	90	60-90	13604,765	17590,963	11685,664
9	120	90-120	16335,931	19855,091	15173,118
10	180	120-180	18663,105	21951,635	17577,305
11	240	180-240	20174,101	23143,375	19604,793
12	360	240-360	22464,877	24665,018	20964,721

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	523,215	640,511	470,149
3	2-5	3,5	607,196	1088,787	419,403
4	5-10	7,5	1719,762	2477,938	1509,995
5	10-15	12,5	2499,828	3066,403	2195,760
6	15-30	22,5	2491,155	2422,686	2012,867
7	30-60	45	3038,360	3736,096	2435,242
8	60-90	75	2725,248	4158,542	2642,249
9	90-120	105	2731,166	2264,129	3487,453
10	120-180	150	2327,174	2096,543	2404,188
11	180-240	210	1510,996	1191,740	2027,488
12	240-360	300	2290,776	1521,643	1359,928
		sum	22464,877	24665,018	20964,721

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	523,215	640,511	470,149
3	2-5	3,5	2125,187	3810,754	1467,912
4	5-10	7,5	12898,213	18584,533	11324,959
5	10-15	12,5	31247,850	38330,043	27447,005
6	15-30	22,5	56050,977	54510,431	45289,505
7	30-60	45	136726,221	168124,322	109585,878
8	60-90	75	204393,624	311890,615	198168,640
9	90-120	105	286772,421	237733,511	366182,589
10	120-180	150	349076,124	314481,495	360628,135
11	180-240	210	317309,170	250265,481	425772,420
12	240-360	300	687232,799	456492,927	407978,256
		sum	2084355,803	1854864,625	1954315,448

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
92,783	75,202	93,219	87,068	8,392

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,781	0,912	0,726
3,701	5,061	3,150
14,846	21,131	12,699
30,584	40,866	27,006
147,597	181,212	129,764
418,934	493,955	362,569
547,913	662,559	480,189
670,017	799,727	622,183
1566,428	1785,713	1517,325
1738,210	1926,167	1722,644
3816,726	4084,131	3759,166

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8955,737	10001,434	8637,420

Average AUC0-360 (µg/ml.min)		9198,197
	STDEV	713,599

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,735	2,027	1,613
5	3,748	5,471	3,053
10	9,449	13,312	8,235
15	17,737	23,014	15,770

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,164	1,537	1,031	1,244	0,214

Table 17: Table containing the AUC, DRi and MDT values and information regarding formula 3E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,503	285,161	1,494	271,779	1,404	288,604
3	5	2,523	478,547	3,231	587,752	2,288	470,293
4	10	6,604	1252,754	8,344	1517,969	6,246	1284,151
5	15	14,399	2731,491	16,355	2975,430	14,394	2959,077
6	30	23,234	4407,535	23,993	4364,951	25,696	5282,738
7	60	30,340	5755,510	29,949	5448,514	37,063	7619,544
8	90	35,929	6815,668	34,158	6214,208	43,366	8915,324
9	120	38,707	7342,743	37,236	6774,086	46,841	9629,694
10	180	41,053	7787,704	39,896	7258,070	49,202	10115,032
11	240	42,637	8088,215	41,248	7504,123	50,205	10321,200
12	360	43,975	8342,149	44,042	8012,374	50,611	10404,664

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
18970,007	18192,540	20558,263

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	285,161	271,779	288,604
3	5	2-5	478,547	587,752	470,293
4	10	5-10	1252,754	1517,969	1284,151
5	15	10-15	2731,491	2975,430	2959,077
6	30	15-30	4407,535	4364,951	5282,738
7	60	30-60	5755,510	5448,514	7619,544
8	90	60-90	6815,668	6214,208	8915,324
9	120	90-120	7342,743	6774,086	9629,694
10	180	120-180	7787,704	7258,070	10115,032
11	240	180-240	8088,215	7504,123	10321,200
12	360	240-360	8342,149	8012,374	10404,664

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	285,161	271,779	288,604
3	2-5	3,5	193,386	315,972	181,688
4	5-10	7,5	774,207	930,218	813,858
5	10-15	12,5	1478,736	1457,461	1674,926
6	15-30	22,5	1676,045	1389,521	2323,661
7	30-60	45	1347,975	1083,564	2336,806
8	60-90	75	1060,157	765,694	1295,780
9	90-120	105	527,076	559,878	714,370
10	120-180	150	444,961	483,984	485,338
11	180-240	210	300,511	246,053	206,168
12	240-360	300	253,933	508,250	83,463
		sum	8342,149	8012,374	10404,664

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	285,161	271,779	288,604
3	2-5	3,5	676,850	1105,903	635,909
4	5-10	7,5	5806,554	6976,632	6103,934
5	10-15	12,5	18484,202	18218,261	20936,578
6	15-30	22,5	37711,008	31264,217	52282,382
7	30-60	45	60658,877	48760,358	105156,260
8	60-90	75	79511,809	57427,018	97183,514
9	90-120	105	55342,934	58787,232	75008,849
10	120-180	150	66744,111	72597,591	72800,739
11	180-240	210	63107,322	51671,155	43295,265
12	240-360	300	76180,017	152475,118	25038,972
		sum	464508,848	499555,266	498731,008

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
55,682	62,348	47,933	55,321	5,890

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,676	0,672	0,632
2,717	3,189	2,492
10,267	13,021	9,601
23,628	27,787	23,220
127,012	136,176	135,304
361,626	364,110	423,627
447,314	432,723	542,898
503,791	481,906	608,898
1076,758	1041,274	1296,577
1129,809	1095,447	1341,987
2338,533	2302,842	2722,012

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6022,133	5899,147	7107,247

Average AUC0-360 (µg/ml.min)		6342,842
	STDEV	664,844

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,503	1,494	1,404
5	2,523	3,231	2,288
10	6,604	8,344	6,246
15	14,399	16,355	14,394

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,921	1,070	0,918	0,970	0,071

Table 18: Table containing the AUC, DRi and MDT values and information regarding formula 3F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,452	405,099	2,514	746,459	2,763	798,911
3	5	2,243	625,749	7,690	2283,214	5,962	1723,998
4	10	5,683	1585,465	17,158	5094,109	14,377	4157,724
5	15	11,966	3338,604	26,626	7905,344	23,759	6870,783
6	30	20,037	5590,161	35,530	10549,009	31,955	9240,880
7	60	30,154	8413,040	43,558	12932,335	39,450	11408,386
8	90	38,618	10774,420	42,268	12549,308	46,654	13491,556
9	120	44,022	12282,148	59,089	17543,438	56,513	16342,659
10	180	50,194	14004,164	62,098	18437,056	59,900	17322,172
11	240	57,100	15930,783	67,501	20041,000	65,534	18951,517
12	360	62,385	17405,401	72,414	21499,774	70,911	20506,319

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
27899,825	29690,080	28918,417

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	405,099	746,459	798,911
3	5	2-5	625,749	2283,214	1723,998
4	10	5-10	1585,465	5094,109	4157,724
5	15	10-15	3338,604	7905,344	6870,783
6	30	15-30	5590,161	10549,009	9240,880
7	60	30-60	8413,040	12932,335	11408,386
8	90	60-90	10774,420	12549,308	13491,556
9	120	90-120	12282,148	17543,438	16342,659
10	180	120-180	14004,164	18437,056	17322,172
11	240	180-240	15930,783	20041,000	18951,517
12	360	240-360	17405,401	21499,774	20506,319

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	405,099	746,459	798,911
3	2-5	3,5	220,650	1536,755	925,087
4	5-10	7,5	959,716	2810,895	2433,727
5	10-15	12,5	1753,139	2811,235	2713,059
6	15-30	22,5	2251,557	2643,665	2370,097
7	30-60	45	2822,879	2383,326	2167,505
8	60-90	75	2361,379	-383,027	2083,171
9	90-120	105	1507,728	4994,130	2851,103
10	120-180	150	1722,016	893,617	979,513
11	180-240	210	1926,619	1603,945	1629,345
12	240-360	300	1474,617	1458,774	1554,802
		sum	17405,401	21499,774	20506,319

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	405,099	746,459	798,911
3	2-5	3,5	772,275	5378,643	3237,804
4	5-10	7,5	7197,869	21081,709	18252,950
5	10-15	12,5	21914,238	35140,440	33913,232
6	15-30	22,5	50660,041	59482,459	53327,187
7	30-60	45	127029,557	107249,681	97537,741
8	60-90	75	177103,451	-28727,037	156237,817
9	90-120	105	158311,452	524383,668	299365,794
10	120-180	150	258302,471	134042,602	146926,921
11	180-240	210	404589,999	336828,379	342162,350
12	240-360	300	442385,210	437632,261	466440,739
		sum	1648671,662	1633239,264	1618201,446

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
94,722	75,965	78,912	83,200	8,236

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,653	1,131	1,243
2,494	6,888	5,889
8,916	27,954	22,881
19,855	49,257	42,904
108,010	209,779	188,035
338,789	533,845	481,985
464,216	579,322	581,203
557,824	684,155	696,376
1271,926	1636,023	1571,577
1448,474	1749,587	1693,367
3226,102	3777,696	3684,024

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7447,260	9255,636	8969,485

Average AUC0-360 (µg/ml.min)		8557,460
	STDEV	972,049

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,452	2,514	2,763
5	2,243	7,690	5,962
10	5,683	17,158	14,377
15	11,966	26,626	23,759

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,763	1,802	1,579	1,381	0,447

Table 19: Table containing the AUC, DRi and MDT values and information regarding formula 4A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,828	406,862	1,921	416,505	2,008	434,642
3	5	4,458	992,309	4,527	981,483	4,586	992,741
4	10	10,648	2370,184	10,090	2187,651	10,718	2320,021
5	15	18,215	4054,702	17,162	3721,042	18,216	3943,068
6	30	25,862	5756,809	24,832	5384,105	25,971	5621,793
7	60	31,993	7121,540	32,448	7035,425	32,373	7007,532
8	90	40,014	8907,115	39,149	8488,350	39,045	8451,898
9	120	43,009	9573,763	41,405	8977,406	41,171	8912,103
10	180	47,184	10503,109	45,651	9898,228	45,012	9743,370
11	240	51,566	11478,469	49,068	10639,048	48,352	10466,383
12	360	54,000	12020,274	50,474	10943,954	49,678	10753,440

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
22259,885	21682,177	21646,394

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	406,862	416,505	434,642
3	5	2-5	992,309	981,483	992,741
4	10	5-10	2370,184	2187,651	2320,021
5	15	10-15	4054,702	3721,042	3943,068
6	30	15-30	5756,809	5384,105	5621,793
7	60	30-60	7121,540	7035,425	7007,532
8	90	60-90	8907,115	8488,350	8451,898
9	120	90-120	9573,763	8977,406	8912,103
10	180	120-180	10503,109	9898,228	9743,370
11	240	180-240	11478,469	10639,048	10466,383
12	360	240-360	12020,274	10943,954	10753,440

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	406,862	416,505	434,642
3	2-5	3,5	585,447	564,978	558,099
4	5-10	7,5	1377,875	1206,168	1327,280
5	10-15	12,5	1684,518	1533,390	1623,047
6	15-30	22,5	1702,107	1663,063	1678,725
7	30-60	45	1364,732	1651,320	1385,738
8	60-90	75	1785,575	1452,925	1444,367
9	90-120	105	666,648	489,056	460,205
10	120-180	150	929,346	920,821	831,268
11	180-240	210	975,361	740,820	723,012
12	240-360	300	541,805	304,906	287,057
		sum	12020,274	10943,954	10753,440

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	406,862	416,505	434,642
3	2-5	3,5	2049,063	1977,421	1953,347
4	5-10	7,5	10334,064	9046,264	9954,599
5	10-15	12,5	21056,472	19167,381	20288,090
6	15-30	22,5	38297,407	37418,927	37771,311
7	30-60	45	61412,929	74309,394	62358,221
8	60-90	75	133918,092	108969,395	108327,493
9	90-120	105	69998,053	51350,877	48321,484
10	120-180	150	139401,829	138123,216	124690,166
11	180-240	210	204825,795	155572,270	151832,616
12	240-360	300	162541,463	91471,771	86117,207
		sum	844242,029	687823,422	652049,176

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
70,235	62,850	60,636	64,574	4,104

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,823	0,864	0,904
4,243	4,352	4,451
16,994	16,443	17,217
32,471	30,658	32,550
148,760	141,729	149,131
390,518	386,639	393,821
486,047	483,279	482,072
560,407	543,736	541,462
1217,606	1175,256	1163,468
1333,121	1278,715	1260,402
2850,267	2687,650	2646,793

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7041,256	6749,322	6692,270

Average AUC0-360 (µg/ml.min)		6827,616
	STDEV	187,204

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,828	1,921	2,008
5	4,458	4,527	4,586
10	10,648	10,090	10,718
15	18,215	17,162	18,216

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,211	1,134	1,206	1,184	0,035

Table 20: Table containing the AUC, DRi and MDT values and information regarding formula 4B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,084	651,822	1,868	588,001	2,263	707,112
3	5	4,366	1365,590	4,474	1408,059	6,405	2001,547
4	10	11,073	3463,213	11,676	3675,053	15,220	4756,697
5	15	20,638	6454,992	22,023	6931,677	27,118	8474,932
6	30	32,331	10112,203	33,599	10575,320	37,362	11676,439
7	60	40,849	12776,355	47,404	14920,362	50,857	15893,785
8	90	57,811	18081,722	57,602	18130,333	63,930	19979,397
9	120	61,825	19337,199	62,514	19676,290	68,134	21293,243
10	180	64,279	20104,657	66,108	20807,499	76,015	23756,232
11	240	71,313	22304,757	71,550	22520,187	75,576	23619,305
12	360	73,990	23141,925	74,555	23466,078	77,061	24083,190

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
31277,233	31474,941	31252,198

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	651,822	588,001	707,112
3	5	2-5	1365,590	1408,059	2001,547
4	10	5-10	3463,213	3675,053	4756,697
5	15	10-15	6454,992	6931,677	8474,932
6	30	15-30	10112,203	10575,320	11676,439
7	60	30-60	12776,355	14920,362	15893,785
8	90	60-90	18081,722	18130,333	19979,397
9	120	90-120	19337,199	19676,290	21293,243
10	180	120-180	20104,657	20807,499	23756,232
11	240	180-240	22304,757	22520,187	23619,305
12	360	240-360	23141,925	23466,078	24083,190

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	651,822	588,001	707,112
3	2-5	3,5	713,768	820,058	1294,435
4	5-10	7,5	2097,623	2266,994	2755,150
5	10-15	12,5	2991,779	3256,625	3718,235
6	15-30	22,5	3657,211	3643,643	3201,507
7	30-60	45	2664,152	4345,041	4217,347
8	60-90	75	5305,367	3209,971	4085,612
9	90-120	105	1255,477	1545,957	1313,846
10	120-180	150	767,458	1131,209	2462,990
11	180-240	210	2200,100	1712,688	-136,928
12	240-360	300	837,168	945,891	463,885
		sum	23141,925	23466,078	24083,190

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	651,822	588,001	707,112
3	2-5	3,5	2498,189	2870,201	4530,524
4	5-10	7,5	15732,176	17002,451	20663,622
5	10-15	12,5	37397,234	40707,811	46477,941
6	15-30	22,5	82287,245	81981,968	72033,901
7	30-60	45	119886,830	195526,857	189780,603
8	60-90	75	397902,548	240747,818	306420,895
9	90-120	105	131825,072	162325,507	137953,779
10	120-180	150	115118,706	169681,350	369448,426
11	180-240	210	462020,996	359664,473	-28754,821
12	240-360	300	251150,423	283767,318	139165,583
		sum	1616471,241	1554863,757	1258427,565

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
69,850	66,260	52,253	62,788	7,592

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,938	0,841	1,018
4,354	4,281	5,850
17,369	18,168	24,328
35,674	37,911	47,631
178,770	187,724	217,619
493,962	546,771	595,475
665,954	708,793	774,806
807,545	810,787	891,426
1702,405	1736,401	1946,000
1830,491	1858,379	2046,479
3923,174	3944,818	4121,206

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9660,637	9854,875	10671,839

Average AUC0-360 (µg/ml.min)		10062,450
	STDEV	536,608

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,084	1,868	2,263
5	4,366	4,474	6,405
10	11,073	11,676	15,220
15	20,638	22,023	27,118

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,354	1,454	1,804	1,537	0,193

Table 21: Table containing the AUC, DRi and MDT values and information regarding formula 4C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,511	338,802	1,460	327,129	1,589	352,423
3	5	2,939	658,971	2,758	618,171	2,647	587,291
4	10	7,572	1697,867	6,150	1378,205	5,978	1326,085
5	15	13,879	3111,966	11,709	2624,094	12,414	2753,837
6	30	20,911	4688,827	19,138	4288,913	19,823	4397,565
7	60	29,172	6541,084	27,574	6179,370	27,233	6041,391
8	90	35,832	8034,399	34,809	7800,754	35,022	7769,323
9	120	40,304	9037,191	39,801	8919,390	39,423	8745,678
10	180	45,207	10136,544	44,398	9949,699	44,123	9788,203
11	240	48,411	10854,884	48,783	10932,223	48,260	10706,041
12	360	51,668	11585,272	51,061	11442,789	51,323	11385,472

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
22422,565	22410,070	22184,029

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	338,802	327,129	352,423
3	5	2-5	658,971	618,171	587,291
4	10	5-10	1697,867	1378,205	1326,085
5	15	10-15	3111,966	2624,094	2753,837
6	30	15-30	4688,827	4288,913	4397,565
7	60	30-60	6541,084	6179,370	6041,391
8	90	60-90	8034,399	7800,754	7769,323
9	120	90-120	9037,191	8919,390	8745,678
10	180	120-180	10136,544	9949,699	9788,203
11	240	180-240	10854,884	10932,223	10706,041
12	360	240-360	11585,272	11442,789	11385,472

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	338,802	327,129	352,423
3	2-5	3,5	320,169	291,042	234,868
4	5-10	7,5	1038,896	760,033	738,794
5	10-15	12,5	1414,099	1245,889	1427,752
6	15-30	22,5	1576,861	1664,819	1643,728
7	30-60	45	1852,257	1890,457	1643,826
8	60-90	75	1493,315	1621,384	1727,932
9	90-120	105	1002,791	1118,636	976,355
10	120-180	150	1099,354	1030,309	1042,526
11	180-240	210	718,340	982,524	917,838
12	240-360	300	730,388	510,567	679,431
		sum	11585,272	11442,789	11385,472

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	338,802	327,129	352,423
3	2-5	3,5	1120,592	1018,648	822,038
4	5-10	7,5	7791,721	5700,250	5540,955
5	10-15	12,5	17676,237	15573,617	17846,903
6	15-30	22,5	35479,369	37458,434	36983,888
7	30-60	45	83351,562	85070,567	73972,169
8	60-90	75	111998,641	121603,789	129594,873
9	90-120	105	105293,083	117456,764	102517,261
10	120-180	150	164903,086	154546,366	156378,828
11	180-240	210	150851,392	206329,943	192745,948
12	240-360	300	219116,340	153169,988	203829,292
		sum	897920,826	898255,496	920584,577

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
77,505	78,500	80,856	78,954	1,405

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,680	0,657	0,715
3,004	2,847	2,859
11,825	10,022	9,703
24,132	20,092	20,690
117,416	104,111	108,799
338,061	315,309	317,629
438,775	421,087	420,223
513,916	503,617	502,507
1154,397	1136,689	1127,872
1263,835	1257,943	1247,169
2702,118	2695,776	2688,740

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6568,159	6468,150	6446,906

Average AUC0-360 (µg/ml.min)		6494,405
	STDEV	64,750

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,511	1,460	1,589
5	2,939	2,758	2,647
10	7,572	6,150	5,978
15	13,879	11,709	12,414

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,911	0,754	0,788	0,818	0,067

Table 22: Table containing the AUC, DRi and MDT values and information regarding formula 4D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,766	610,828	1,509	523,437	1,536	527,380
3	5	4,582	1585,037	3,367	1167,762	3,874	1330,224
4	10	12,041	4165,590	9,686	3359,046	10,620	3646,610
5	15	23,225	8034,747	19,833	6877,535	20,530	7049,793
6	30	35,857	12404,489	31,374	10879,680	32,004	10989,563
7	60	47,337	16376,012	44,393	15394,446	44,947	15434,137
8	90	58,406	20205,375	57,463	19926,972	57,104	19608,726
9	120	65,449	22642,076	64,681	22429,782	65,663	22547,585
10	180	72,434	25058,402	72,660	25196,847	72,478	24887,883
11	240	79,496	27501,442	78,047	27064,753	75,733	26005,511
12	360	80,737	27930,884	80,551	27933,107	79,895	27434,688

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
34594,787	34677,697	34338,386

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	610,828	523,437	527,380
3	5	2-5	1585,037	1167,762	1330,224
4	10	5-10	4165,590	3359,046	3646,610
5	15	10-15	8034,747	6877,535	7049,793
6	30	15-30	12404,489	10879,680	10989,563
7	60	30-60	16376,012	15394,446	15434,137
8	90	60-90	20205,375	19926,972	19608,726
9	120	90-120	22642,076	22429,782	22547,585
10	180	120-180	25058,402	25196,847	24887,883
11	240	180-240	27501,442	27064,753	26005,511
12	360	240-360	27930,884	27933,107	27434,688

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	610,828	523,437	527,380
3	2-5	3,5	974,209	644,325	802,844
4	5-10	7,5	2580,553	2191,285	2316,386
5	10-15	12,5	3869,157	3518,489	3403,183
6	15-30	22,5	4369,743	4002,145	3939,771
7	30-60	45	3971,522	4514,766	4444,574
8	60-90	75	3829,363	4532,525	4174,589
9	90-120	105	2436,701	2502,810	2938,859
10	120-180	150	2416,325	2767,066	2340,299
11	180-240	210	2443,041	1867,906	1117,628
12	240-360	300	429,442	868,353	1429,177
		sum	27930,884	27933,107	27434,688

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	610,828	523,437	527,380
3	2-5	3,5	3409,731	2255,136	2809,952
4	5-10	7,5	19354,148	16434,637	17372,893
5	10-15	12,5	48364,459	43981,111	42539,786
6	15-30	22,5	98319,209	90048,252	88644,840
7	30-60	45	178718,512	203164,483	200005,833
8	60-90	75	287202,228	339939,400	313094,143
9	90-120	105	255853,640	262795,053	308580,170
10	120-180	150	362448,822	415059,826	351044,827
11	180-240	210	513038,531	392260,342	234701,805
12	240-360	300	128832,609	260505,914	428753,011
		sum	1896152,717	2026967,590	1988074,640

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
67,887	72,565	72,466	70,973	2,182

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,795	0,679	0,691
4,284	3,292	3,652
18,701	14,686	16,305
39,675	33,209	35,044
199,401	172,822	177,303
561,554	511,425	519,419
713,762	687,530	688,848
836,023	824,473	828,679
1861,426	1854,101	1864,907
2051,054	2034,540	2000,854
4326,296	4282,125	4201,960

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
10612,971	10418,880	10337,661

Average AUC0-360 (µg/ml.min)		10456,504
	STDEV	141,459

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,766	1,509	1,536
5	4,582	3,367	3,874
10	12,041	9,686	10,620
15	23,225	19,833	20,530

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,534	1,301	1,358	1,398	0,099

Table 23: Table containing the AUC, DRi and MDT values and information regarding formula 4E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,408	364,565	1,412	363,916	1,500	396,185
3	5	2,344	606,586	2,458	633,805	3,445	909,851
4	10	6,946	1797,738	7,029	1811,978	9,892	2612,460
5	15	14,811	3833,556	15,430	3977,939	18,615	4916,325
6	30	23,883	6181,695	23,821	6141,074	27,020	7136,128
7	60	32,979	8535,938	34,062	8781,316	35,375	9342,692
8	90	41,897	10844,393	42,288	10901,983	43,304	11436,626
9	120	48,633	12587,824	49,447	12747,521	49,870	13170,750
10	180	52,665	13631,585	53,564	13809,098	54,471	14385,921
11	240	56,677	14669,917	58,565	15098,385	58,446	15435,607
12	360	60,357	15622,372	61,998	15983,268	62,434	16489,058

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
25883,333	25780,419	26410,255

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	364,565	363,916	396,185
3	5	2-5	606,586	633,805	909,851
4	10	5-10	1797,738	1811,978	2612,460
5	15	10-15	3833,556	3977,939	4916,325
6	30	15-30	6181,695	6141,074	7136,128
7	60	30-60	8535,938	8781,316	9342,692
8	90	60-90	10844,393	10901,983	11436,626
9	120	90-120	12587,824	12747,521	13170,750
10	180	120-180	13631,585	13809,098	14385,921
11	240	180-240	14669,917	15098,385	15435,607
12	360	240-360	15622,372	15983,268	16489,058

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	364,565	363,916	396,185
3	2-5	3,5	242,021	269,888	513,666
4	5-10	7,5	1191,152	1178,173	1702,609
5	10-15	12,5	2035,818	2165,961	2303,865
6	15-30	22,5	2348,139	2163,134	2219,803
7	30-60	45	2354,242	2640,243	2206,564
8	60-90	75	2308,456	2120,666	2093,934
9	90-120	105	1743,431	1845,538	1734,123
10	120-180	150	1043,761	1061,577	1215,171
11	180-240	210	1038,332	1289,288	1049,686
12	240-360	300	952,454	884,883	1053,450
		sum	15622,372	15983,268	16489,058

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	364,565	363,916	396,185
3	2-5	3,5	847,073	944,608	1797,831
4	5-10	7,5	8933,642	8836,301	12769,571
5	10-15	12,5	25447,724	27074,517	28798,316
6	15-30	22,5	52833,131	48670,525	49945,557
7	30-60	45	105940,891	118810,921	99295,402
8	60-90	75	173134,191	159049,980	157045,047
9	90-120	105	183060,255	193781,517	182082,943
10	120-180	150	156564,121	159236,476	182275,669
11	180-240	210	218049,783	270750,451	220434,137
12	240-360	300	285736,271	265464,855	316035,132
		sum	1210911,647	1252984,068	1250875,790

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
77,511	78,393	75,861	77,255	1,050

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,634	0,635	0,675
2,533	2,612	3,338
10,450	10,673	15,004
24,476	25,266	32,070
130,592	132,471	154,020
383,815	390,708	421,170
505,411	515,361	531,083
611,078	619,207	628,922
1367,529	1390,646	1408,601
1476,125	1513,750	1524,372
3159,917	3255,202	3263,755

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7672,559	7856,531	7983,010

Average AUC0-360 (µg/ml.min)		7837,367
	STDEV	156,110

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,408	1,412	1,500
5	2,344	2,458	3,445
10	6,946	7,029	9,892
15	14,811	15,430	18,615

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,958	0,994	1,235	1,062	0,123

Table 24: Table containing the AUC, DRi and MDT values and information regarding formula 4F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,145	640,350	1,888	574,751	1,407	406,198
3	5	5,530	1651,070	4,399	1338,961	2,594	748,783
4	10	14,420	4305,597	12,350	3758,873	7,560	2182,740
5	15	25,355	7570,666	23,561	7171,070	17,560	5069,656
6	30	37,260	11125,472	35,397	10773,692	29,127	8409,238
7	60	48,625	14518,966	48,564	14781,335	43,766	12635,665
8	90	57,831	17267,912	57,812	17596,193	53,342	15400,416
9	120	62,499	18661,506	63,003	19176,070	60,649	17509,877
10	180	66,251	19781,796	67,510	20547,721	65,205	18825,374
11	240	71,345	21302,813	71,179	21664,567	68,024	19639,237
12	360	70,047	20915,280	73,019	22224,545	69,924	20187,606

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
29859,022	30436,744	28870,978

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	640,350	574,751	406,198
3	5	2-5	1651,070	1338,961	748,783
4	10	5-10	4305,597	3758,873	2182,740
5	15	10-15	7570,666	7171,070	5069,656
6	30	15-30	11125,472	10773,692	8409,238
7	60	30-60	14518,966	14781,335	12635,665
8	90	60-90	17267,912	17596,193	15400,416
9	120	90-120	18661,506	19176,070	17509,877
10	180	120-180	19781,796	20547,721	18825,374
11	240	180-240	21302,813	21664,567	19639,237
12	360	240-360	20915,280	22224,545	20187,606

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	640,350	574,751	406,198
3	2-5	3,5	1010,721	764,210	342,586
4	5-10	7,5	2654,527	2419,912	1433,957
5	10-15	12,5	3265,069	3412,197	2886,916
6	15-30	22,5	3554,806	3602,623	3339,582
7	30-60	45	3393,495	4007,642	4226,427
8	60-90	75	2748,946	2814,859	2764,750
9	90-120	105	1393,594	1579,877	2109,461
10	120-180	150	1120,290	1371,650	1315,497
11	180-240	210	1521,017	1116,846	813,863
12	240-360	300	-387,533	559,978	548,370
		sum	20915,280	22224,545	20187,606

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	640,350	574,751	406,198
3	2-5	3,5	3537,523	2674,735	1199,049
4	5-10	7,5	19908,951	18149,337	10754,677
5	10-15	12,5	40813,364	42652,464	36086,450
6	15-30	22,5	79983,124	81059,011	75140,594
7	30-60	45	152707,253	180343,909	190189,223
8	60-90	75	206170,953	211114,388	207356,273
9	90-120	105	146327,329	165887,066	221493,428
10	120-180	150	168043,455	205747,565	197324,622
11	180-240	210	319413,555	234537,730	170911,155
12	240-360	300	-116259,842	167993,305	164510,850
		sum	1021286,015	1310734,260	1275372,519

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
48,830	58,977	63,176	56,994	6,022

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,965	0,850	0,633
5,180	4,244	2,700
22,443	18,843	11,423
44,746	40,399	28,260
211,325	198,982	157,567
579,724	566,737	492,027
718,582	718,041	655,480
812,229	815,504	769,439
1738,116	1761,920	1699,028
1857,536	1872,296	1798,596
3817,568	3893,340	3724,587

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9808,415	9891,156	9339,741

Average AUC0-360 (µg/ml.min)		9679,771
	STDEV	297,366

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,145	1,888	1,407
5	5,530	4,399	2,594
10	14,420	12,350	7,560
15	25,355	23,561	17,560

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,694	1,559	1,129	1,461	0,241

Table 25: Table containing the AUC, DRi and MDT values and information regarding formula 5A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,882	423,297	2,273	564,291	2,027	448,713
3	5	3,880	872,723	3,547	880,439	3,381	748,657
4	10	7,513	1689,613	12,964	3217,677	7,545	1670,551
5	15	16,418	3692,549	19,553	4853,268	13,794	3054,172
6	30	23,617	5311,562	28,172	6992,380	20,799	4605,322
7	60	30,705	6905,586	37,382	9278,526	29,320	6491,996
8	90	37,972	8540,092	44,795	11118,488	36,773	8142,139
9	120	43,879	9868,447	50,973	12651,946	42,101	9321,945
10	180	48,674	10946,878	54,827	13608,489	47,384	10491,559
11	240	51,767	11642,636	57,914	14374,549	51,277	11353,467
12	360	54,835	12332,505	61,286	15211,529	54,671	12105,011

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
22490,255	24820,695	22141,656

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	423,297	564,291	448,713
3	5	2-5	872,723	880,439	748,657
4	10	5-10	1689,613	3217,677	1670,551
5	15	10-15	3692,549	4853,268	3054,172
6	30	15-30	5311,562	6992,380	4605,322
7	60	30-60	6905,586	9278,526	6491,996
8	90	60-90	8540,092	11118,488	8142,139
9	120	90-120	9868,447	12651,946	9321,945
10	180	120-180	10946,878	13608,489	10491,559
11	240	180-240	11642,636	14374,549	11353,467
12	360	240-360	12332,505	15211,529	12105,011

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	423,297	564,291	448,713
3	2-5	3,5	449,427	316,148	299,944
4	5-10	7,5	816,889	2337,239	921,894
5	10-15	12,5	2002,937	1635,591	1383,621
6	15-30	22,5	1619,013	2139,112	1551,150
7	30-60	45	1594,024	2286,146	1886,674
8	60-90	75	1634,506	1839,962	1650,144
9	90-120	105	1328,355	1533,459	1179,805
10	120-180	150	1078,431	956,543	1169,614
11	180-240	210	695,758	766,060	861,909
12	240-360	300	689,869	836,980	751,543
		sum	12332,505	15211,529	12105,011

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	423,297	564,291	448,713
3	2-5	3,5	1572,994	1106,518	1049,805
4	5-10	7,5	6126,669	17529,291	6914,203
5	10-15	12,5	25036,710	20444,884	17295,262
6	15-30	22,5	36427,787	48130,015	34900,874
7	30-60	45	71731,061	102876,569	84900,332
8	60-90	75	122587,956	137997,143	123760,781
9	90-120	105	139477,301	161013,155	123879,549
10	120-180	150	161764,581	143481,375	175442,124
11	180-240	210	146109,182	160872,629	181000,833
12	240-360	300	206960,756	251093,932	225463,000
		sum	918218,292	1045109,801	975055,474

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
74,455	68,705	80,550	74,570	4,836

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,847	1,023	0,912
3,890	3,929	3,650
12,817	18,575	12,292
26,922	36,582	24,006
135,120	161,071	116,752
366,673	442,488	338,308
463,571	554,698	446,129
552,495	646,438	532,402
1249,461	1428,308	1208,050
1355,958	1522,000	1331,914
2878,263	3218,379	2860,576

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7046,019	8033,491	6874,991

Average AUC0-360 (µg/ml.min)		7318,167
	STDEV	625,363

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,882	2,273	2,027
5	3,880	3,547	3,381
10	7,513	12,964	7,545
15	16,418	19,553	13,794

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,036	1,340	0,886	1,087	0,189

Table 26: Table containing the AUC, DRi and MDT values and information regarding formula 5B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,707	481,875	1,732	534,768	2,253	657,934
3	5	2,955	834,485	5,926	1830,335	5,240	1529,955
4	10	7,086	2000,650	13,125	4053,470	11,232	3279,672
5	15	14,919	4212,444	22,740	7023,196	19,048	5561,883
6	30	24,950	7044,626	31,506	9730,651	27,316	7975,935
7	60	36,190	10218,203	41,024	12670,207	37,811	11040,314
8	90	47,080	13293,011	51,990	16056,978	47,472	13861,211
9	120	55,576	15691,820	59,143	18266,034	56,126	16388,208
10	180	62,223	17568,630	67,178	20747,791	63,762	18617,776
11	240	66,242	18703,428	71,977	22229,850	68,659	20047,592
12	360	69,716	19684,404	76,258	23552,139	72,096	21051,313

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
28235,056	30884,651	29198,941

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	481,875	534,768	657,934
3	5	2-5	834,485	1830,335	1529,955
4	10	5-10	2000,650	4053,470	3279,672
5	15	10-15	4212,444	7023,196	5561,883
6	30	15-30	7044,626	9730,651	7975,935
7	60	30-60	10218,203	12670,207	11040,314
8	90	60-90	13293,011	16056,978	13861,211
9	120	90-120	15691,820	18266,034	16388,208
10	180	120-180	17568,630	20747,791	18617,776
11	240	180-240	18703,428	22229,850	20047,592
12	360	240-360	19684,404	23552,139	21051,313

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	481,875	534,768	657,934
3	2-5	3,5	352,610	1295,567	872,021
4	5-10	7,5	1166,165	2223,135	1749,717
5	10-15	12,5	2211,794	2969,726	2282,211
6	15-30	22,5	2832,182	2707,456	2414,052
7	30-60	45	3173,577	2939,556	3064,379
8	60-90	75	3074,808	3386,771	2820,897
9	90-120	105	2398,809	2209,055	2526,998
10	120-180	150	1876,810	2481,758	2229,567
11	180-240	210	1134,798	1482,059	1429,816
12	240-360	300	980,976	1322,289	1003,721
		sum	19684,404	23552,139	21051,313

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	481,875	534,768	657,934
3	2-5	3,5	1234,135	4534,484	3052,073
4	5-10	7,5	8746,239	16673,511	13122,879
5	10-15	12,5	27647,419	37121,579	28527,637
6	15-30	22,5	63724,103	60917,749	54316,175
7	30-60	45	142810,979	132280,021	137897,039
8	60-90	75	230610,588	254007,806	211567,252
9	90-120	105	251874,975	231950,824	265334,771
10	120-180	150	281521,492	372263,676	334435,077
11	180-240	210	238307,540	311232,339	300261,426
12	240-360	300	294292,927	396686,746	301116,302
		sum	1541252,273	1818203,502	1650288,565

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
78,298	77,199	78,394	77,964	0,542

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,768	0,779	1,014
3,147	5,169	5,058
11,296	21,432	18,531
24,756	40,348	34,065
134,558	183,082	156,479
412,693	489,582	439,604
562,070	627,847	575,655
692,924	750,147	699,284
1590,279	1705,335	1618,486
1734,272	1878,597	1787,676
3670,867	4002,356	3800,379

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8837,631	9704,675	9136,231

Average AUC0-360 (µg/ml.min)		9226,179
	STDEV	440,465

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,707	1,732	2,253
5	2,955	5,926	5,240
10	7,086	13,125	11,232
15	14,919	22,740	19,048

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,953	1,521	1,253	1,242	0,232

Table 27: Table containing the AUC, DRi and MDT values and information regarding formula 5C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,638	371,473	2,030	478,178	1,957	450,446
3	5	2,923	662,646	4,442	1046,483	4,943	1137,943
4	10	6,935	1572,325	9,868	2324,778	11,246	2588,934
5	15	13,256	3005,698	16,814	3961,375	17,680	4070,123
6	30	21,231	4813,889	24,197	5700,661	25,785	5935,914
7	60	30,157	6837,672	32,024	7544,619	33,549	7723,294
8	90	37,080	8407,424	40,114	9450,607	41,449	9541,879
9	120	42,332	9598,377	45,193	10647,315	48,868	11249,863
10	180	43,637	9894,304	50,637	11929,783	47,483	10931,107
11	240	52,152	11825,015	53,997	12721,492	52,959	12191,812
12	360	55,070	12486,603	58,172	13704,932	56,842	13085,614

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
22673,938	23559,493	23021,020

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	371,473	478,178	450,446
3	5	2-5	662,646	1046,483	1137,943
4	10	5-10	1572,325	2324,778	2588,934
5	15	10-15	3005,698	3961,375	4070,123
6	30	15-30	4813,889	5700,661	5935,914
7	60	30-60	6837,672	7544,619	7723,294
8	90	60-90	8407,424	9450,607	9541,879
9	120	90-120	9598,377	10647,315	11249,863
10	180	120-180	9894,304	11929,783	10931,107
11	240	180-240	11825,015	12721,492	12191,812
12	360	240-360	12486,603	13704,932	13085,614

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	371,473	478,178	450,446
3	2-5	3,5	291,173	568,305	687,497
4	5-10	7,5	909,679	1278,295	1450,991
5	10-15	12,5	1433,373	1636,597	1481,190

6	15-30	22,5	1808,191	1739,286	1865,791
7	30-60	45	2023,783	1843,958	1787,380
8	60-90	75	1569,752	1905,987	1818,585
9	90-120	105	1190,953	1196,709	1707,984
10	120-180	150	295,926	1282,468	-318,756
11	180-240	210	1930,711	791,709	1260,705
12	240-360	300	661,588	983,439	893,802
		sum	12486,603	13704,932	13085,614

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	371,473	478,178	450,446
3	2-5	3,5	1019,106	1989,068	2406,238
4	5-10	7,5	6822,589	9587,214	10882,433
5	10-15	12,5	17917,166	20457,466	18514,870
6	15-30	22,5	40684,305	39133,930	41980,294
7	30-60	45	91070,217	82978,112	80432,091
8	60-90	75	117731,416	142949,057	136393,900
9	90-120	105	125050,109	125654,412	179338,288
10	120-180	150	44388,971	192370,212	-47813,438
11	180-240	210	405449,291	166258,851	264748,108
12	240-360	300	198476,327	295031,785	268140,636
		sum	1048980,969	1076888,285	955473,865

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
84,009	78,577	73,017	78,534	4,487

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,737	0,913	0,881
3,079	4,368	4,657
11,089	16,098	18,213
22,715	30,017	32,542
116,394	138,413	146,694
346,865	379,489	400,502
453,844	486,928	506,233
536,030	575,823	609,635
1160,589	1293,707	1300,738
1293,162	1412,561	1355,976
2895,014	3028,560	2964,641

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6839,519	7366,878	7340,710

Average AUC0-360 (µg/ml.min)		7182,369
	STDEV	297,205

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,638	2,030	1,957
5	2,923	4,442	4,943
10	6,935	9,868	11,246
15	13,256	16,814	17,680

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,856	1,106	1,186	1,049	0,141

Table 28: Table containing the AUC, DRi and MDT values and information regarding formula 5D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,772	523,090	1,806	548,117	1,474	433,280
3	5	2,819	832,278	2,793	847,646	2,350	690,945
4	10	5,417	1599,334	5,514	1673,385	5,444	1600,644
5	15	10,526	3107,363	10,432	3165,866	10,553	3102,527
6	30	20,144	5946,813	20,843	6325,558	20,225	5946,342
7	60	35,743	10551,851	37,585	11406,751	34,761	10219,852
8	90	48,388	14285,116	51,609	15662,943	47,487	13961,292
9	120	56,218	16596,527	59,747	18132,666	58,794	17285,824
10	180	63,641	18787,861	67,548	20500,173	64,509	18966,054
11	240	69,171	20420,563	69,940	21226,041	68,807	20229,583
12	360	72,893	21519,428	74,936	22742,393	72,594	21342,963

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
29521,803	30349,085	29400,510

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	523,090	548,117	433,280
3	5	2-5	832,278	847,646	690,945
4	10	5-10	1599,334	1673,385	1600,644
5	15	10-15	3107,363	3165,866	3102,527
6	30	15-30	5946,813	6325,558	5946,342
7	60	30-60	10551,851	11406,751	10219,852
8	90	60-90	14285,116	15662,943	13961,292
9	120	90-120	16596,527	18132,666	17285,824
10	180	120-180	18787,861	20500,173	18966,054
11	240	180-240	20420,563	21226,041	20229,583
12	360	240-360	21519,428	22742,393	21342,963

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	523,090	548,117	433,280
3	2-5	3,5	309,188	299,529	257,665
4	5-10	7,5	767,056	825,739	909,698
5	10-15	12,5	1508,029	1492,481	1501,884
6	15-30	22,5	2839,450	3159,692	2843,815
7	30-60	45	4605,038	5081,193	4273,510
8	60-90	75	3733,265	4256,193	3741,439
9	90-120	105	2311,412	2469,723	3324,532
10	120-180	150	2191,334	2367,507	1680,231
11	180-240	210	1632,701	725,869	1263,529
12	240-360	300	1098,866	1516,352	1113,380
		sum	21519,428	22742,393	21342,963

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	523,090	548,117	433,280
3	2-5	3,5	1082,158	1048,353	901,828
4	5-10	7,5	5752,920	6193,041	6822,738
5	10-15	12,5	18850,359	18656,010	18773,545
6	15-30	22,5	63887,632	71093,066	63985,831
7	30-60	45	207226,713	228653,689	192307,963
8	60-90	75	279994,859	319214,447	280607,959
9	90-120	105	242698,225	259320,898	349075,871
10	120-180	150	328700,065	355125,999	252034,593
11	180-240	210	342867,275	152432,415	265341,031
12	240-360	300	329659,751	454905,576	334013,902
		sum	1821243,046	1867191,610	1764298,539

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
84,633	82,102	82,664	83,133	1,085

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,797	0,813	0,663
3,099	3,104	2,581
9,266	9,345	8,769
17,936	17,938	17,997
103,509	105,550	103,876
377,233	394,388	371,156
567,884	602,062	555,170
706,092	751,655	717,396
1618,090	1718,481	1664,598
1792,959	1856,082	1799,768
3835,741	3911,643	3817,821

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9032,606	9371,062	9059,794

Average AUC0-360 (µg/ml.min)	9154,487
STDEV	188,051

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,772	1,806	1,474
5	2,819	2,793	2,350
10	5,417	5,514	5,444
15	10,526	10,432	10,553

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,659	0,655	0,674	0,663	0,008

Table 29: Table containing the AUC, DRi and MDT values and information regarding formula 5E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,606	360,423	1,603	356,747	1,722	386,856
3	5	3,598	807,581	3,925	873,830	4,258	956,586
4	10	9,881	2217,884	10,527	2343,379	10,304	2314,700
5	15	18,603	4175,594	18,532	4125,277	17,946	4031,264
6	30	27,559	6185,948	27,045	6020,369	25,942	5827,416
7	60	32,283	7246,337	34,175	7607,494	32,645	7333,085
8	90	39,090	8774,293	39,736	8845,474	38,827	8721,717
9	120	45,279	10163,426	44,050	9805,608	43,564	9785,757
10	180	50,307	11291,964	47,944	10672,639	47,444	10657,313
11	240	52,873	11868,059	51,481	11459,850	51,321	11528,189
12	360	55,423	12440,397	54,964	12235,216	55,464	12459,052

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
22446,293	22260,419	22463,117

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	360,423	356,747	386,856
3	5	2-5	807,581	873,830	956,586
4	10	5-10	2217,884	2343,379	2314,700
5	15	10-15	4175,594	4125,277	4031,264
6	30	15-30	6185,948	6020,369	5827,416
7	60	30-60	7246,337	7607,494	7333,085
8	90	60-90	8774,293	8845,474	8721,717
9	120	90-120	10163,426	9805,608	9785,757
10	180	120-180	11291,964	10672,639	10657,313
11	240	180-240	11868,059	11459,850	11528,189
12	360	240-360	12440,397	12235,216	12459,052

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	360,423	356,747	386,856
3	2-5	3,5	447,158	517,082	569,730
4	5-10	7,5	1410,303	1469,549	1358,114
5	10-15	12,5	1957,710	1781,897	1716,564
6	15-30	22,5	2010,354	1895,092	1796,152
7	30-60	45	1060,389	1587,125	1505,669
8	60-90	75	1527,956	1237,981	1388,631
9	90-120	105	1389,133	960,134	1064,040
10	120-180	150	1128,539	867,031	871,556
11	180-240	210	576,095	787,210	870,876
12	240-360	300	572,338	775,367	930,863
		sum	12440,397	12235,216	12459,052

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	360,423	356,747	386,856
3	2-5	3,5	1565,052	1809,788	1994,055
4	5-10	7,5	10577,272	11021,621	10185,858
5	10-15	12,5	24471,375	22273,719	21457,048
6	15-30	22,5	45232,966	42639,575	40413,421
7	30-60	45	47717,500	71420,617	67755,102
8	60-90	75	114596,670	92848,539	104147,362
9	90-120	105	145858,958	100814,055	111724,224
10	120-180	150	169280,788	130054,672	130733,397
11	180-240	210	120979,866	165314,192	182883,909
12	240-360	300	171701,330	232610,060	279259,034
		sum	852342,201	871163,585	950940,267

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
68,514	71,201	76,325	72,014	3,240

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,723	0,721	0,775
3,512	3,731	4,037
15,164	16,259	16,383
32,044	32,691	31,782
155,795	153,823	148,123
403,933	413,236	395,463
481,769	498,901	482,435
569,491	565,555	556,136
1290,404	1241,919	1228,598
1392,926	1342,242	1333,316
2923,994	2874,010	2883,195

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7269,754	7143,089	7080,243

Average AUC0-360 (µg/ml.min)		7164,362
	STDEV	96,530

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,606	1,603	1,722
5	3,598	3,925	4,258
10	9,881	10,527	10,304
15	18,603	18,532	17,946

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,230	1,238	1,192	1,220	0,020

Table 30: Table containing the AUC, DRi and MDT values and information regarding formula 5F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,548	487,368	2,101	672,671	1,995	646,876
3	5	2,226	700,804	4,598	1471,922	4,210	1364,845
4	10	4,821	1517,666	12,619	4040,060	13,985	4533,345
5	15	11,842	3727,835	24,713	7912,089	28,976	9393,240
6	30	23,985	7550,203	38,834	12432,946	39,886	12929,872
7	60	41,168	12958,951	50,932	16306,014	50,850	16483,860
8	90	53,947	16981,861	61,377	19649,861	64,375	20868,194
9	120	56,911	17914,810	66,695	21352,741	69,385	22492,558
10	180	69,572	21900,319	71,735	22966,052	74,182	24047,293
11	240	70,849	22302,277	74,429	23828,510	76,817	24901,701
12	360	77,725	24466,596	79,050	25308,085	80,042	25946,903

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
31478,519	32015,269	32416,810

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	487,368	672,671	646,876
3	5	2-5	700,804	1471,922	1364,845
4	10	5-10	1517,666	4040,060	4533,345
5	15	10-15	3727,835	7912,089	9393,240
6	30	15-30	7550,203	12432,946	12929,872
7	60	30-60	12958,951	16306,014	16483,860
8	90	60-90	16981,861	19649,861	20868,194
9	120	90-120	17914,810	21352,741	22492,558
10	180	120-180	21900,319	22966,052	24047,293
11	240	180-240	22302,277	23828,510	24901,701
12	360	240-360	24466,596	25308,085	25946,903

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	487,368	672,671	646,876
3	2-5	3,5	213,436	799,251	717,968
4	5-10	7,5	816,862	2568,138	3168,500
5	10-15	12,5	2210,169	3872,030	4859,895
6	15-30	22,5	3822,368	4520,856	3536,632
7	30-60	45	5408,748	3873,068	3553,988
8	60-90	75	4022,910	3343,847	4384,334
9	90-120	105	932,949	1702,879	1624,364
10	120-180	150	3985,508	1613,311	1554,735
11	180-240	210	401,958	862,458	854,408
12	240-360	300	2164,319	1479,575	1045,202
		sum	24466,596	25308,085	25946,903

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	487,368	672,671	646,876
3	2-5	3,5	747,027	2797,377	2512,889
4	5-10	7,5	6126,465	19261,033	23763,748
5	10-15	12,5	27627,111	48400,373	60748,692
6	15-30	22,5	86003,277	101719,264	79574,220
7	30-60	45	243393,670	174288,077	159929,473
8	60-90	75	301718,223	250788,553	328825,021
9	90-120	105	97959,688	178802,340	170558,255
10	120-180	150	597826,252	241996,721	233210,241
11	180-240	210	84411,183	181116,087	179425,705
12	240-360	300	649295,670	443872,643	313560,502
		sum	2095595,934	1643715,139	1552755,624

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
85,651	64,948	59,844	70,148	11,159

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,697	0,945	0,898
2,548	4,522	4,189
7,929	19,369	20,469
18,747	41,999	48,331
120,919	214,474	232,412
439,782	605,923	612,468
642,027	758,083	777,764
748,296	864,486	902,881
1707,527	1868,807	1938,155
1895,690	1973,204	2038,484
4011,496	4143,923	4235,186

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9595,656	10495,736	10811,237

Average AUC0-360 (µg/ml.min)		10300,876
	STDEV	630,783

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,548	2,101	1,995
5	2,226	4,598	4,210
10	4,821	12,619	13,985
15	11,842	24,713	28,976

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,732	1,624	1,909	1,422	0,501

Table 31: Table containing the AUC, DRi and MDT values and information regarding formula 6A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,711	466,580	1,544	380,896	1,657	471,882
3	5	3,202	873,126	2,734	674,656	3,631	1033,988
4	10	6,926	1888,225	5,114	1262,039	8,577	2442,584
5	15	11,954	3259,092	8,174	2017,064	15,280	4351,651
6	30	20,398	5561,373	13,117	3236,854	25,610	7293,300
7	60	32,842	8954,314	20,203	4985,279	38,291	10904,815
8	90	44,009	11998,861	29,202	7205,843	49,640	14136,826
9	120	51,827	14130,284	37,013	9133,193	57,069	16252,538
10	180	58,225	15874,775	44,521	10985,968	62,608	17829,863
11	240	63,319	17263,571	51,095	12608,120	66,422	18916,163
12	360	67,320	18354,343	58,712	14487,651	70,318	20025,658

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
27264,462	24675,870	28478,749

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	466,580	380,896	471,882
3	5	2-5	873,126	674,656	1033,988
4	10	5-10	1888,225	1262,039	2442,584
5	15	10-15	3259,092	2017,064	4351,651
6	30	15-30	5561,373	3236,854	7293,300
7	60	30-60	8954,314	4985,279	10904,815
8	90	60-90	11998,861	7205,843	14136,826
9	120	90-120	14130,284	9133,193	16252,538
10	180	120-180	15874,775	10985,968	17829,863
11	240	180-240	17263,571	12608,120	18916,163
12	360	240-360	18354,343	14487,651	20025,658

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	466,580	380,896	471,882
3	2-5	3,5	406,545	293,760	562,106
4	5-10	7,5	1015,099	587,383	1408,596
5	10-15	12,5	1370,868	755,025	1909,067
6	15-30	22,5	2302,281	1219,790	2941,649
7	30-60	45	3392,941	1748,425	3611,515
8	60-90	75	3044,547	2220,564	3232,012
9	90-120	105	2131,422	1927,350	2115,711
10	120-180	150	1744,492	1852,775	1577,325
11	180-240	210	1388,796	1622,151	1086,301
12	240-360	300	1090,771	1879,531	1109,495
		sum	18354,343	14487,651	20025,658

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	466,580	380,896	471,882
3	2-5	3,5	1422,909	1028,159	1967,370
4	5-10	7,5	7613,243	4405,374	10564,472
5	10-15	12,5	17135,846	9437,811	23863,338
6	15-30	22,5	51801,313	27445,271	66187,109
7	30-60	45	152682,363	78679,124	162518,153
8	60-90	75	228341,015	166542,324	242400,872
9	90-120	105	223799,337	202371,704	222149,685
10	120-180	150	261673,773	277916,321	236598,723
11	180-240	210	291647,181	340651,800	228123,205
12	240-360	300	327231,407	563859,309	332848,375
		sum	1563814,967	1672718,094	1527693,186

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
85,201	115,458	76,287	92,315	16,764

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,770	0,695	0,746
3,317	2,887	3,569
11,394	8,830	13,734
21,239	14,950	26,839
109,186	71,860	138,004
359,372	224,914	431,330
518,748	333,484	593,534
646,892	446,949	720,285
1485,701	1100,706	1615,634
1640,845	1290,816	1741,900
3527,242	2964,782	3691,978

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8324,708	6460,872	8977,553

Average AUC0-360 (µg/ml.min)		7921,044
	STDEV	1305,997

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,711	1,544	1,657
5	3,202	2,734	3,631
10	6,926	5,114	8,577
15	11,954	8,174	15,280

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,776	0,523	1,005	0,768	0,197

Table 32: Table containing the AUC, DRi and MDT values and information regarding formula 6B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,503	400,760	1,770	496,175	1,525	412,741
3	5	1,833	488,720	3,217	901,565	1,964	531,494
4	10	3,193	851,239	7,404	2075,227	4,292	1161,576
5	15	6,559	1748,594	13,752	3854,282	8,589	2324,737
6	30	13,150	3505,844	23,408	6560,654	15,897	4302,583
7	60	23,461	6254,837	36,782	10309,121	26,257	7106,749
8	90	33,474	8924,197	49,059	13750,049	35,708	9664,520
9	120	41,372	11029,834	56,826	15926,697	47,888	12961,321
10	180	47,066	12547,835	62,393	17486,973	49,899	13505,490
11	240	54,909	14638,648	66,765	18712,471	56,021	15162,324
12	360	62,211	16585,451	69,203	19395,853	62,501	16916,226

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
26660,035	28027,345	27065,643

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	400,760	496,175	412,741
3	5	2-5	488,720	901,565	531,494
4	10	5-10	851,239	2075,227	1161,576
5	15	10-15	1748,594	3854,282	2324,737
6	30	15-30	3505,844	6560,654	4302,583
7	60	30-60	6254,837	10309,121	7106,749
8	90	60-90	8924,197	13750,049	9664,520
9	120	90-120	11029,834	15926,697	12961,321
10	180	120-180	12547,835	17486,973	13505,490
11	240	180-240	14638,648	18712,471	15162,324
12	360	240-360	16585,451	19395,853	16916,226

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	400,760	496,175	412,741
3	2-5	3,5	87,961	405,391	118,753
4	5-10	7,5	362,519	1173,661	630,082
5	10-15	12,5	897,355	1779,055	1163,161
6	15-30	22,5	1757,249	2706,372	1977,846
7	30-60	45	2748,994	3748,467	2804,166
8	60-90	75	2669,359	3440,928	2557,771
9	90-120	105	2105,637	2176,648	3296,801
10	120-180	150	1518,001	1560,276	544,169
11	180-240	210	2090,813	1225,498	1656,835
12	240-360	300	1946,803	683,382	1753,902
		sum	16585,451	19395,853	16916,226

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	400,760	496,175	412,741
3	2-5	3,5	307,862	1418,868	415,635
4	5-10	7,5	2718,893	8802,459	4725,612
5	10-15	12,5	11216,939	22238,186	14539,514
6	15-30	22,5	39538,111	60893,372	44501,536
7	30-60	45	123704,715	168681,025	126187,492
8	60-90	75	200201,944	258069,625	191832,832
9	90-120	105	221091,883	228547,990	346164,088
10	120-180	150	227700,173	234041,420	81625,291
11	180-240	210	439070,772	257354,669	347935,260
12	240-360	300	584040,862	205014,472	526170,613
		sum	1849992,913	1445558,261	1684510,614

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
111,543	74,529	99,580	95,217	15,422

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,676	0,797	0,686
2,252	3,366	2,355
5,654	11,949	7,037
10,971	23,801	14,491
66,518	125,415	82,641
247,129	406,285	284,542
384,315	579,432	418,265
505,212	714,724	564,274
1193,916	1609,444	1320,131
1376,658	1743,628	1429,914
3162,226	3671,146	3200,075

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
6955,528	8889,986	7324,411

Average AUC0-360 (µg/ml.min)		7723,308
	STDEV	1027,069

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,503	1,770	1,525
5	1,833	3,217	1,964
10	3,193	7,404	4,292
15	6,559	13,752	8,589

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,394	0,889	0,535	0,606	0,208

Table 33: Table containing the AUC, DRi and MDT values and information regarding formula 6C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,881	505,862	1,568	438,729	1,674	437,953
3	5	2,074	557,998	2,669	746,576	2,603	680,928
4	10	3,608	970,494	5,808	1624,739	5,201	1360,764
5	15	7,773	2090,806	11,624	3251,436	10,279	2689,105
6	30	17,126	4606,665	20,669	5781,529	18,248	4773,944
7	60	26,898	7235,446	32,477	9084,459	29,793	7794,136
8	90	37,464	10077,535	41,773	11684,925	38,640	10108,632
9	120	43,960	11824,895	49,009	13708,805	45,382	11872,673
10	180	51,632	13888,688	54,270	15180,616	49,870	13046,569
11	240	55,875	15029,986	59,423	16621,970	55,084	14410,671
12	360	60,693	16325,920	64,865	18144,291	59,195	15486,203

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
26899,217	27972,257	26161,377

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	505,862	438,729	437,953
3	5	2-5	557,998	746,576	680,928
4	10	5-10	970,494	1624,739	1360,764
5	15	10-15	2090,806	3251,436	2689,105
6	30	15-30	4606,665	5781,529	4773,944
7	60	30-60	7235,446	9084,459	7794,136
8	90	60-90	10077,535	11684,925	10108,632
9	120	90-120	11824,895	13708,805	11872,673
10	180	120-180	13888,688	15180,616	13046,569
11	240	180-240	15029,986	16621,970	14410,671
12	360	240-360	16325,920	18144,291	15486,203

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	505,862	438,729	437,953
3	2-5	3,5	52,136	307,847	242,975
4	5-10	7,5	412,496	878,163	679,836
5	10-15	12,5	1120,312	1626,697	1328,341
6	15-30	22,5	2515,859	2530,093	2084,839
7	30-60	45	2628,781	3302,930	3020,192
8	60-90	75	2842,089	2600,466	2314,496
9	90-120	105	1747,360	2023,879	1764,042
10	120-180	150	2063,793	1471,812	1173,896
11	180-240	210	1141,298	1441,354	1364,102
12	240-360	300	1295,934	1522,321	1075,532
		sum	16325,920	18144,291	15486,203

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	505,862	438,729	437,953
3	2-5	3,5	182,477	1077,463	850,413
4	5-10	7,5	3093,720	6586,226	5098,767
5	10-15	12,5	14003,903	20333,708	16604,268
6	15-30	22,5	56606,833	56927,094	46908,878
7	30-60	45	118295,151	148631,856	135908,646
8	60-90	75	213156,647	195034,947	173587,170
9	90-120	105	183472,755	212507,345	185224,368
10	120-180	150	309569,006	220771,747	176084,340
11	180-240	210	239672,604	302684,336	286461,353
12	240-360	300	388780,263	456696,310	322659,687
		sum	1527339,220	1621689,763	1349825,843

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
93,553	89,377	87,163	90,031	2,649

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,846	0,706	0,753
2,670	2,860	2,887
6,393	9,537	8,780
12,803	19,611	17,415
84,032	108,987	96,279
297,162	358,732	324,274
434,446	501,187	461,916
549,612	612,777	567,148
1290,496	1394,264	1285,902
1451,351	1534,860	1416,870
3147,339	3355,786	3085,524

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
7277,150	7899,308	7267,749

Average AUC0-360 (µg/ml.min)		7481,403
	STDEV	361,947

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,881	1,568	1,674
5	2,074	2,669	2,603
10	3,608	5,808	5,201
15	7,773	11,624	10,279

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,460	0,739	0,644	0,614	0,116

Table 34: Table containing the AUC, DRi and MDT values and information regarding formula 6D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,674	542,245	1,811	582,731	1,682	546,568
3	5	2,253	729,904	2,618	842,392	2,292	744,958
4	10	5,717	1851,683	19,710	6343,073	5,694	1850,344
5	15	13,968	4524,426	14,316	4607,149	14,748	4792,838
6	30	28,404	9200,369	27,835	8958,085	27,577	8962,360
7	60	46,109	14935,344	45,906	14773,899	46,472	15102,973
8	90	58,849	19062,096	59,673	19204,412	57,930	18826,711
9	120	66,267	21464,876	66,799	21497,594	67,418	21910,058
10	180	71,928	23298,450	71,106	22883,863	71,720	23308,189
11	240	74,730	24205,970	73,909	23785,917	74,629	24253,668
12	360	77,919	25239,060	76,954	24765,765	76,636	24905,941

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
32391,321	32182,666	32498,857

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	542,245	582,731	546,568
3	5	2-5	729,904	842,392	744,958
4	10	5-10	1851,683	6343,073	1850,344
5	15	10-15	4524,426	4607,149	4792,838
6	30	15-30	9200,369	8958,085	8962,360
7	60	30-60	14935,344	14773,899	15102,973
8	90	60-90	19062,096	19204,412	18826,711
9	120	90-120	21464,876	21497,594	21910,058
10	180	120-180	23298,450	22883,863	23308,189
11	240	180-240	24205,970	23785,917	24253,668
12	360	240-360	25239,060	24765,765	24905,941

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	542,245	582,731	546,568
3	2-5	3,5	187,659	259,661	198,390
4	5-10	7,5	1121,779	5500,681	1105,386
5	10-15	12,5	2672,743	-1735,925	2942,494
6	15-30	22,5	4675,943	4350,936	4169,522
7	30-60	45	5734,975	5815,814	6140,613
8	60-90	75	4126,752	4430,513	3723,738
9	90-120	105	2402,780	2293,182	3083,347
10	120-180	150	1833,574	1386,269	1398,131
11	180-240	210	907,519	902,054	945,478
12	240-360	300	1033,090	979,848	652,273
		sum	25239,060	24765,765	24905,941

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	542,245	582,731	546,568
3	2-5	3,5	656,807	908,813	694,364
4	5-10	7,5	8413,343	41255,109	8290,397
5	10-15	12,5	33409,287	-21699,061	36781,171
6	15-30	22,5	105208,728	97896,064	93814,239
7	30-60	45	258073,868	261711,619	276327,598
8	60-90	75	309506,376	332288,504	279280,353
9	90-120	105	252291,937	240784,098	323751,436
10	120-180	150	275036,157	207940,404	209719,702
11	180-240	210	190579,039	189431,268	198550,465
12	240-360	300	309927,018	293954,507	195682,033
		sum	1743644,805	1645054,057	1623438,325

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
69,085	66,425	65,183	66,897	1,628

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,753	0,815	0,757
2,651	2,989	2,682
8,966	25,118	8,984
22,145	38,278	22,996
143,005	142,259	142,847
502,962	497,755	499,836
708,470	712,662	704,718
844,538	853,685	846,101
1865,638	1861,715	1878,362
1979,881	1957,706	1975,716
4121,523	4073,297	4084,173

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
10200,533	10166,279	10167,173

Average AUC0-360 (µg/ml.min)		10177,995
	STDEV	19,524

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,674	1,811	1,682
5	2,253	2,618	2,292
10	5,717	19,710	5,694
15	13,968	14,316	14,748

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,873	1,223	0,916	1,004	0,156

Table 35: Table containing the AUC, DRi and MDT values and information regarding formula 6E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,718	446,809	1,843	454,217	1,766	434,162
3	5	4,423	1150,645	3,806	937,776	3,408	837,929
4	10	11,748	3056,205	9,447	2327,859	8,373	2058,799
5	15	20,789	5408,226	17,059	4203,586	15,392	3784,748
6	30	28,329	7369,646	24,508	6039,159	23,180	5699,698
7	60	36,682	9542,586	32,916	8110,961	32,886	8086,453
8	90	44,977	11700,719	41,572	10243,842	40,666	9999,443
9	120	51,287	13342,144	46,884	11552,986	46,364	11400,453
10	180	56,629	14731,768	51,129	12598,940	51,469	12655,827
11	240	60,988	15865,722	55,154	13590,667	56,142	13804,810
12	360	64,234	16710,223	58,895	14512,529	59,441	14616,137

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
26014,689	24641,391	24589,154

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	446,809	454,217	434,162
3	5	2-5	1150,645	937,776	837,929
4	10	5-10	3056,205	2327,859	2058,799
5	15	10-15	5408,226	4203,586	3784,748
6	30	15-30	7369,646	6039,159	5699,698
7	60	30-60	9542,586	8110,961	8086,453
8	90	60-90	11700,719	10243,842	9999,443
9	120	90-120	13342,144	11552,986	11400,453
10	180	120-180	14731,768	12598,940	12655,827
11	240	180-240	15865,722	13590,667	13804,810
12	360	240-360	16710,223	14512,529	14616,137

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	446,809	454,217	434,162
3	2-5	3,5	703,836	483,559	403,767
4	5-10	7,5	1905,560	1390,083	1220,870
5	10-15	12,5	2352,021	1875,727	1725,948
6	15-30	22,5	1961,420	1835,573	1914,951
7	30-60	45	2172,941	2071,802	2386,755
8	60-90	75	2158,132	2132,881	1912,990
9	90-120	105	1641,425	1309,144	1401,010
10	120-180	150	1389,625	1045,954	1255,375
11	180-240	210	1133,953	991,727	1148,983
12	240-360	300	844,502	921,862	811,327
		sum	16710,223	14512,529	14616,137

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	446,809	454,217	434,162
3	2-5	3,5	2463,426	1692,456	1413,184
4	5-10	7,5	14291,701	10425,620	9156,528
5	10-15	12,5	29400,261	23446,588	21574,352
6	15-30	22,5	44131,954	41300,398	43086,388
7	30-60	45	97782,326	93231,091	107403,953
8	60-90	75	161859,918	159966,070	143474,283
9	90-120	105	172349,621	137460,081	147106,015
10	120-180	150	208443,731	156893,151	188306,197
11	180-240	210	238130,183	208262,704	241286,448
12	240-360	300	253350,496	276558,586	243398,072
		sum	1222650,426	1109690,962	1146639,581

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
73,168	76,464	78,450	76,027	2,179

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,773	0,829	0,795
4,145	3,813	3,492
18,192	14,909	13,253
36,604	29,819	26,735
165,773	140,289	130,179
438,820	387,613	378,445
551,197	502,792	496,478
649,784	597,079	587,451
1456,861	1323,184	1320,744
1587,819	1434,820	1452,749
3380,976	3079,316	3120,748

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
8290,945	7514,466	7531,070

Average AUC0-360 (µg/ml.min)		7778,827
	STDEV	443,585

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,718	1,843	1,766
5	4,423	3,806	3,408
10	11,748	9,447	8,373
15	20,789	17,059	15,392

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
1,390	1,121	1,005	1,172	0,161

Table 36: Table containing the AUC, DRi and MDT values and information regarding formula 6F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,559	464,190	1,564	458,547	1,514	425,372
3	5	2,799	833,444	2,574	754,839	2,032	570,870
4	10	7,286	2169,187	5,903	1730,803	5,053	1419,583
5	15	14,982	4460,597	11,782	3454,867	10,496	2948,797
6	30	26,076	7763,336	21,830	6401,087	18,496	5196,298
7	60	41,667	12405,205	37,932	11122,631	32,159	9034,660
8	90	54,440	16208,055	50,718	14872,072	44,890	12611,487
9	120	62,644	18650,650	59,954	17580,114	54,413	15286,934
10	180	65,778	19583,842	64,900	19030,482	60,008	16858,686
11	240	70,416	20964,581	68,834	20184,200	66,397	18653,798
12	360	73,512	21886,368	72,402	21230,376	68,844	19341,070

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
29772,435	29322,862	28094,158

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	464,190	458,547	425,372
3	5	2-5	833,444	754,839	570,870
4	10	5-10	2169,187	1730,803	1419,583
5	15	10-15	4460,597	3454,867	2948,797
6	30	15-30	7763,336	6401,087	5196,298
7	60	30-60	12405,205	11122,631	9034,660
8	90	60-90	16208,055	14872,072	12611,487
9	120	90-120	18650,650	17580,114	15286,934
10	180	120-180	19583,842	19030,482	16858,686
11	240	180-240	20964,581	20184,200	18653,798
12	360	240-360	21886,368	21230,376	19341,070

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	464,190	458,547	425,372
3	2-5	3,5	369,254	296,292	145,499
4	5-10	7,5	1335,744	975,964	848,712
5	10-15	12,5	2291,410	1724,064	1529,215
6	15-30	22,5	3302,739	2946,220	2247,501
7	30-60	45	4641,868	4721,545	3838,362
8	60-90	75	3802,851	3749,441	3576,827
9	90-120	105	2442,595	2708,042	2675,447
10	120-180	150	933,191	1450,367	1571,752
11	180-240	210	1380,740	1153,719	1795,112
12	240-360	300	921,787	1046,175	687,272
		sum	21886,368	21230,376	19341,070

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	464,190	458,547	425,372
3	2-5	3,5	1292,388	1037,023	509,246
4	5-10	7,5	10018,077	7319,730	6365,341
5	10-15	12,5	28642,622	21550,796	19115,182
6	15-30	22,5	74311,631	66289,954	50568,775
7	30-60	45	208884,068	212469,507	172726,282
8	60-90	75	285213,797	281208,080	268262,052
9	90-120	105	256472,497	284344,405	280921,910
10	120-180	150	139978,684	217555,112	235762,753
11	180-240	210	289955,333	242280,894	376973,471
12	240-360	300	276536,046	313852,598	206181,612
		sum	1571769,333	1648366,643	1617811,995

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
71,815	77,642	83,646	77,701	4,830

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,702	0,704	0,681
2,942	2,793	2,394
11,346	9,536	7,971
25,052	19,895	17,493
138,570	113,440	97,848
457,261	403,389	341,918
648,719	598,387	520,078
790,316	747,036	670,297
1733,703	1685,521	1544,684
1838,626	1805,411	1706,471
3886,063	3813,385	3651,512

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
9533,299	9199,497	8561,345

Average AUC0-360 (µg/ml.min)		9098,047
	STDEV	493,855

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,559	1,564	1,514
5	2,799	2,574	2,032
10	7,286	5,903	5,053
15	14,982	11,782	10,496

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,967	0,751	0,663	0,794	0,128

Table 37: Table containing the AUC, DRi and MDT values and information regarding formula 1A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	15,383	6212,460	15,360	5822,633	17,930	7416,551
3	5	45,417	18341,746	43,673	16555,249	47,613	19694,813
4	10	73,351	29622,842	1,000	379,071	73,869	30555,304
5	15	84,824	34255,919	87,254	33075,475	83,594	34577,630
6	30	87,923	35507,368	90,616	34349,718	89,994	37225,300
7	60	91,996	37152,529	93,496	35441,647	98,354	40683,269
8	90	97,134	39227,281	91,376	34637,886	98,196	40617,894
9	120	96,910	39136,827	93,354	35387,760	98,573	40773,765
10	180	94,740	38260,384	91,448	34665,321	99,505	41159,362
11	240	95,947	38747,996	92,508	35067,114	97,904	40496,882
12	360	99,715	40269,511	93,597	35479,812	101,026	41788,231

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40384,800	37907,100	41364,000

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	6212,460	5822,633	7416,551
3	5	2-5	18341,746	16555,249	19694,813
4	10	5-10	29622,842	379,071	30555,304
5	15	10-15	34255,919	33075,475	34577,630
6	30	15-30	35507,368	34349,718	37225,300
7	60	30-60	37152,529	35441,647	40683,269
8	90	60-90	39227,281	34637,886	40617,894
9	120	90-120	39136,827	35387,760	40773,765
10	180	120-180	38260,384	34665,321	41159,362
11	240	180-240	38747,996	35067,114	40496,882
12	360	240-360	40269,511	35479,812	41788,231

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	6212,460	5822,633	7416,551
3	2-5	3,5	12129,285	10732,616	12278,262
4	5-10	7,5	11281,096	-16176,178	10860,490
5	10-15	12,5	4633,078	32696,404	4022,326
6	15-30	22,5	1251,448	1274,243	2647,670
7	30-60	45	1645,162	1091,929	3457,969
8	60-90	75	2074,751	-803,761	-65,375
9	90-120	105	-90,454	749,874	155,871
10	120-180	150	-876,442	-722,439	385,597
11	180-240	210	487,612	401,793	-662,480
12	240-360	300	1521,514	412,698	1291,349
		sum	40269,511	35479,812	41788,231

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	6212,460	5822,633	7416,551
3	2-5	3,5	42452,499	37564,156	42973,917
4	5-10	7,5	84608,218	-121321,333	81453,678
5	10-15	12,5	57913,473	408705,049	50279,079
6	15-30	22,5	28157,588	28670,467	59572,586
7	30-60	45	74032,273	49136,791	155608,583
8	60-90	75	155606,351	-60282,074	-4903,096
9	90-120	105	-9497,680	78736,791	16366,449
10	120-180	150	-131466,348	-108365,805	57839,499
11	180-240	210	102398,539	84376,440	-139120,827
12	240-360	300	456454,301	123809,439	387404,732
		sum	866871,674	526852,553	714891,151

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
21,527	14,849	17,107	17,828	2,773

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
6,922	6,912	8,068
41,040	39,848	44,242
133,615	132,936	136,668
177,947	181,964	177,146
583,019	600,310	585,859
1214,453	1242,753	1271,354
1276,628	1247,885	1326,716
1309,794	1246,925	1328,193
2587,266	2494,827	2674,058
2574,268	2483,408	2665,021
5282,861	5024,829	5371,091

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15187,814	14702,596	15588,416

Average AUC0-360 (µg/ml.min)		15159,609
	STDEV	443,583

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	15,383	15,360	17,930
5	45,417	43,673	47,613
10	73,351	74,492	73,869
15	84,824	87,254	83,594

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,779	5,964	5,625	5,790	0,138

Table 38: Table containing the AUC, DRi and MDT values and information regarding formula 1B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	21,092	8902,472	11,246	4753,528	20,455	8841,441
3	5	58,862	24844,044	48,213	20379,480	60,491	26146,156
4	10	87,866	37085,772	83,002	35084,469	94,045	40649,465
5	15	96,742	40832,210	97,542	41230,493	99,700	43093,904
6	30	93,736	39563,582	94,835	40086,310	100,696	43524,276
7	60	96,948	40919,148	101,582	42938,294	104,908	45344,697
8	90	96,281	40637,665	98,569	41664,500	100,850	43590,885
9	120	96,699	40813,831	97,902	41382,568	102,224	44184,767
10	180	96,278	40636,184	96,051	40600,266	104,967	45370,347
11	240	97,170	41012,848	103,848	43895,866	102,354	44240,814
12	360	103,426	43653,395	104,220	44053,026	97,689	42224,640

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42207,300	42269,400	43223,400

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	8902,472	4753,528	8841,441
3	5	2-5	24844,044	20379,480	26146,156
4	10	5-10	37085,772	35084,469	40649,465
5	15	10-15	40832,210	41230,493	43093,904
6	30	15-30	39563,582	40086,310	43524,276
7	60	30-60	40919,148	42938,294	45344,697
8	90	60-90	40637,665	41664,500	43590,885
9	120	90-120	40813,831	41382,568	44184,767
10	180	120-180	40636,184	40600,266	45370,347
11	240	180-240	41012,848	43895,866	44240,814
12	360	240-360	43653,395	44053,026	42224,640

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	8902,472	4753,528	8841,441
3	2-5	3,5	15941,572	15625,952	17304,715
4	5-10	7,5	12241,728	14704,988	14503,309
5	10-15	12,5	3746,439	6146,025	2444,439
6	15-30	22,5	-1268,629	-1144,183	430,371
7	30-60	45	1355,566	2851,984	1820,421
8	60-90	75	-281,483	-1273,794	-1753,812
9	90-120	105	176,165	-281,932	593,883
10	120-180	150	-177,646	-782,302	1185,579
11	180-240	210	376,663	3295,599	-1129,533
12	240-360	300	2640,547	157,161	-2016,174
		sum	43653,395	44053,026	42224,640

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	8902,472	4753,528	8841,441
3	2-5	3,5	55795,504	54690,832	60566,504
4	5-10	7,5	91812,957	110287,411	108774,815
5	10-15	12,5	46830,484	76825,307	30555,491
6	15-30	22,5	-28544,143	-25744,128	9683,351
7	30-60	45	61000,491	128339,292	81918,967
8	60-90	75	-21111,229	-95534,537	-131535,937
9	90-120	105	18497,361	-29602,860	62357,686
10	120-180	150	-26646,970	-117345,263	177836,882
11	180-240	210	79099,322	692075,890	-237201,869
12	240-360	300	792164,228	47148,171	-604852,057
		sum	1077800,476	845893,644	-433054,726

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
24,690	19,202	-10,256	11,212	15,345

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
9,492	5,061	9,205
53,969	40,135	54,639
165,069	147,617	173,853
207,684	203,112	217,964
642,865	649,274	676,338
1287,120	1325,820	1387,826
1304,297	1351,022	1388,866
1302,613	1326,179	1370,752
2605,178	2618,368	2797,082
2611,543	2698,637	2798,833
5416,098	5617,823	5401,165

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15605,925	15983,047	16276,522

Average AUC0-360 (µg/ml.min)		15955,165
	STDEV	336,167

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	21,092	11,246	20,455
5	58,862	48,213	60,491
10	87,866	83,002	94,045
15	96,742	97,542	99,700

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,522	6,841	6,845	6,736	0,151

Table 39: Table containing the AUC, DRi and MDT values and information regarding formula 1C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	12,776	5793,244	11,791	5324,207	10,874	4531,227
3	5	36,018	16332,783	33,206	14993,916	37,119	15467,486
4	10	69,655	31585,574	66,033	29816,385	74,047	30855,293
5	15	93,237	42278,728	87,757	39625,806	93,017	38760,171
6	30	106,505	48295,449	99,886	45102,347	95,655	39859,552
7	60	103,853	47092,676	107,287	48444,368	98,313	40967,225
8	90	101,786	46155,354	101,201	45696,102	94,772	39491,534
9	120	111,965	50771,353	111,492	50343,031	102,889	42873,800
10	180	105,670	47916,914	105,272	47534,364	101,830	42432,737
11	240	103,860	47095,879	102,530	46296,420	96,908	40381,753
12	360	101,854	46186,412	105,066	47441,367	97,477	40618,522

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
45345,600	45153,900	41670,000

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	5793,244	5324,207	4531,227
3	5	2-5	16332,783	14993,916	15467,486
4	10	5-10	31585,574	29816,385	30855,293
5	15	10-15	42278,728	39625,806	38760,171
6	30	15-30	48295,449	45102,347	39859,552
7	60	30-60	47092,676	48444,368	40967,225
8	90	60-90	46155,354	45696,102	39491,534
9	120	90-120	50771,353	50343,031	42873,800
10	180	120-180	47916,914	47534,364	42432,737
11	240	180-240	47095,879	46296,420	40381,753
12	360	240-360	46186,412	47441,367	40618,522

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	5793,244	5324,207	4531,227
3	2-5	3,5	10539,539	9669,709	10936,260
4	5-10	7,5	15252,791	14822,470	15387,807
5	10-15	12,5	10693,154	9809,420	7904,879
6	15-30	22,5	6016,722	5476,541	1099,380
7	30-60	45	-1202,773	3342,020	1107,674
8	60-90	75	-937,322	-2748,266	-1475,692
9	90-120	105	4615,999	4646,929	3382,266
10	120-180	150	-2854,439	-2808,667	-441,063
11	180-240	210	-821,035	-1237,943	-2050,984
12	240-360	300	-909,467	1144,946	236,769
		sum	46186,412	47441,367	40618,522

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	5793,244	5324,207	4531,227
3	2-5	3,5	36888,386	33843,980	38276,908
4	5-10	7,5	114395,930	111168,522	115408,549
5	10-15	12,5	133664,426	122617,755	98810,981
6	15-30	22,5	135376,235	123222,180	24736,056
7	30-60	45	-54124,783	150390,917	49845,317
8	60-90	75	-70299,167	-206119,952	-110676,876
9	90-120	105	484679,881	487927,570	355137,977
10	120-180	150	-428165,777	-421300,077	-66159,426
11	180-240	210	-172417,407	-259968,081	-430706,639
12	240-360	300	-272840,048	343483,842	71030,747
		sum	-87049,078	490590,865	150234,821

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-1,885	10,341	3,699	4,052	4,997

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
5,749	5,306	4,893
32,936	30,373	32,395
118,883	111,644	125,061
183,253	173,014	187,947
674,129	633,295	636,769
1419,917	1398,418	1309,289
1388,060	1407,294	1303,328
1442,820	1435,677	1334,212
2938,084	2926,314	2763,711
2828,660	2805,329	2682,975
5554,281	5605,098	5248,398

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16586,771	16531,762	15628,978

Average AUC0-360 (µg/ml.min)		16249,170
	STDEV	537,806

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	12,776	11,791	10,874
5	36,018	33,206	37,119
10	69,655	66,033	74,047
15	93,237	87,757	93,017

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,340	5,992	6,479	6,271	0,205

Table 40: Table containing the AUC, DRi and MDT values and information regarding formula 1D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,2	2028,546	9,239057239	3697,997333	6,898316498	2799,778327
3	5	22,6416835	8832,633942	30,09577254	12046,04363	28,66728021	11635,01701
4	10	53,19156753	20750,29645	62,46876169	25003,55915	63,60479611	25814,89697
5	15	76,8209278	29968,22804	83,93381968	33595,09886	85,25675271	34602,64668
6	30	96,32270108	37575,96731	93,23608679	37318,39639	94,91931163	38524,3315
7	60	89,98838758	35104,91994	98,82989899	39557,35888	91,38581369	37090,21189
8	90	93,03278713	36292,55542	95,72468388	38314,47479	95,81498691	38887,85385
9	120	94,64626263	36921,98028	96,39316872	38582,04053	99,29631126	40300,79807
10	180	94,00866442	36673,25003	97,10154882	38865,57463	100,2122783	40672,55614
11	240	93,61789001	36520,80698	97,9968425	39223,92219	96,11622147	39010,11411
12	360	92,51507669	36090,59399	96,75684998	38727,6065	94,28398803	38266,47652

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39010,5	40025,7	40586,4

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2028,546	3697,997333	2799,778327
3	5	2-5	8832,633942	12046,04363	11635,01701
4	10	5-10	20750,29645	25003,55915	25814,89697
5	15	10-15	29968,22804	33595,09886	34602,64668
6	30	15-30	37575,96731	37318,39639	38524,3315
7	60	30-60	35104,91994	39557,35888	37090,21189
8	90	60-90	36292,55542	38314,47479	38887,85385
9	120	90-120	36921,98028	38582,04053	40300,79807
10	180	120-180	36673,25003	38865,57463	40672,55614
11	240	180-240	36520,80698	39223,92219	39010,11411
12	360	240-360	36090,59399	38727,6065	38266,47652

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2028,546	3697,997333	2799,778327
3	2-5	3,5	6804,087942	8348,046296	8835,238688
4	5-10	7,5	11917,66251	12957,51552	14179,87995
5	10-15	12,5	9217,931588	8591,539715	8787,749715
6	15-30	22,5	7607,739269	3723,297529	3921,684815
7	30-60	45	-2471,04737	2238,962488	-1434,119609
8	60-90	75	1187,635487	-1242,884086	1797,641957
9	90-120	105	629,4248582	267,56574	1412,944228
10	120-180	150	-248,7302475	283,5340926	371,7580622
11	180-240	210	-152,4430515	358,3475615	-1662,442023
12	240-360	300	-430,2129896	-496,3156852	-743,6375952
		sum	36090,59399	38727,6065	38266,47652

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2028,546	3697,997333	2799,778327
3	2-5	3,5	23814,3078	29218,16204	30923,33541
4	5-10	7,5	89382,46881	97181,36639	106349,0996
5	10-15	12,5	115224,1448	107394,2464	109846,8714
6	15-30	22,5	171174,1335	83774,1944	88237,90833
7	30-60	45	-111197,1317	100753,312	-64535,3824
8	60-90	75	89072,66152	-93216,30644	134823,1468
9	90-120	105	66089,61012	28094,4027	148359,1439
10	120-180	150	-37309,53712	42530,11389	55763,70933
11	180-240	210	-32013,04082	75252,98791	-349112,8249
12	240-360	300	-129063,8969	-148894,7056	-223091,2785
		sum	247202,2662	325785,7711	40363,50733

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
6,849492868	8,412236141	1,054800729	5,438843246	3,164955316

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,34	4,157575758	3,104242424
18,79313636	26,5510101	24,00677778
85,31240741	104,135101	103,8060859
146,2640572	164,702904	167,4692424
584,3597475	597,9484343	608,0942172
1257,599848	1296,445404	1257,559596
1235,392929	1313,243434	1263,605404
1266,833586	1296,795505	1317,001263
2546,841515	2612,178687	2693,36596
2532,958485	2633,828283	2650,434747
5025,590101	5258,349697	5140,805657

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14702,28581	15308,33604	15229,25319

Average AUC0-360 (µg/ml.min)		15079,95835
	STDEV	329,4555069

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,2	9,239057239	6,898316498
5	22,6416835	30,09577254	28,66728021
10	53,19156753	62,46876169	63,60479611
15	76,8209278	83,93381968	85,25675271

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,345651912	5,790432024	5,976531866	5,704205267	0,264674227

Table 41: Table containing the AUC, DRi and MDT values and information regarding formula 1E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,152	65,987	0,111	38,310	0,715	296,574
3	5	51,178	22163,513	18,340	6306,770	44,709	18555,565
4	10	87,439	37867,068	44,190	15195,864	80,089	33238,855
5	15	98,908	42834,210	64,812	22287,195	91,104	37810,582
6	30	96,704	41879,701	76,457	26291,340	94,557	39243,557
7	60	96,416	41754,981	81,627	28069,487	93,773	38918,158
8	90	103,058	44631,507	81,813	28133,411	98,562	40905,518
9	120	104,883	45421,854	84,216	28959,615	102,426	42509,242
10	180	105,680	45766,726	84,907	29197,221	102,475	42529,858
11	240	106,931	46308,718	83,641	28761,890	99,014	41093,238
12	360	96,709	41881,817	82,013	28201,931	95,914	39806,675

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
43307,079	34387,315	41502,521

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	65,987	38,310	296,574
3	5	2-5	22163,513	6306,770	18555,565
4	10	5-10	37867,068	15195,864	33238,855
5	15	10-15	42834,210	22287,195	37810,582
6	30	15-30	41879,701	26291,340	39243,557
7	60	30-60	41754,981	28069,487	38918,158
8	90	60-90	44631,507	28133,411	40905,518
9	120	90-120	45421,854	28959,615	42509,242
10	180	120-180	45766,726	29197,221	42529,858
11	240	180-240	46308,718	28761,890	41093,238
12	360	240-360	41881,817	28201,931	39806,675

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	65,987	38,310	296,574
3	2-5	3,5	22097,526	6268,460	18258,991
4	5-10	7,5	15703,555	8889,094	14683,291
5	10-15	12,5	4967,142	7091,331	4571,727
6	15-30	22,5	-954,509	4004,145	1432,975
7	30-60	45	-124,720	1778,147	-325,400
8	60-90	75	2876,526	63,925	1987,361
9	90-120	105	790,347	826,204	1603,724
10	120-180	150	344,872	237,606	20,616
11	180-240	210	541,991	-435,331	-1436,621
12	240-360	300	-4426,900	-559,959	-1286,563
		sum	41881,817	28201,931	39806,675

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	65,987	38,310	296,574
3	2-5	3,5	77341,341	21939,610	63906,467
4	5-10	7,5	117776,663	66668,205	110124,681
5	10-15	12,5	62089,276	88641,635	57146,588
6	15-30	22,5	-21476,447	90093,261	32241,939
7	30-60	45	-5612,422	80016,619	-14642,984
8	60-90	75	215739,487	4794,348	149052,043
9	90-120	105	82986,424	86751,400	168391,007
10	120-180	150	51730,816	35640,851	3092,427
11	180-240	210	113818,197	-91419,469	-301690,351
12	240-360	300	-1328070,140	-167987,631	-385968,789
		sum	-633610,819	215177,139	-118050,398

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-15,129	7,630	-2,966	-3,488	9,298

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,069	0,050	0,322
34,648	12,455	30,661
155,943	70,347	140,398
209,640	122,628	192,592
660,191	476,782	626,607
1303,561	1067,067	1271,228
1346,451	1103,225	1298,258
1403,605	1120,698	1356,664
2842,597	2283,160	2766,164
2870,243	2275,397	2720,104
5498,280	4472,647	5263,048

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16325,228	13004,456	15666,046

Average AUC0-360 (µg/ml.min)		14998,576
	STDEV	1758,129

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,152	0,111	0,715
5	51,178	18,340	44,709
10	87,439	44,190	80,089
15	98,908	64,812	91,104

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
7,326	4,627	6,743	6,232	1,160

Table 42: Table containing the AUC, DRi and MDT values and information regarding formula 1F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,129	793,510	1,643	539,834	6,652	2816,522
3	5	12,253	4566,210	6,594	2166,318	32,379	13709,910
4	10	34,928	13016,512	22,617	7430,662	69,220	29309,086
5	15	55,156	20554,487	42,177	13856,956	88,178	37336,466
6	30	77,133	28744,761	65,258	21440,433	95,076	40256,943
7	60	84,212	31382,683	75,805	24905,357	101,939	43162,854
8	90	85,385	31819,986	77,587	25491,030	96,964	41056,260
9	120	90,588	33758,956	79,310	26057,077	101,392	42931,340
10	180	92,016	34290,865	78,417	25763,533	102,573	43431,580
11	240	87,564	32631,899	81,123	26652,556	99,582	42164,934
12	360	84,364	31439,498	76,532	25144,371	104,548	44267,618

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37266,339	32854,658	42341,924

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	793,510	539,834	2816,522
3	5	2-5	4566,210	2166,318	13709,910
4	10	5-10	13016,512	7430,662	29309,086
5	15	10-15	20554,487	13856,956	37336,466
6	30	15-30	28744,761	21440,433	40256,943
7	60	30-60	31382,683	24905,357	43162,854
8	90	60-90	31819,986	25491,030	41056,260
9	120	90-120	33758,956	26057,077	42931,340
10	180	120-180	34290,865	25763,533	43431,580
11	240	180-240	32631,899	26652,556	42164,934
12	360	240-360	31439,498	25144,371	44267,618

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	793,510	539,834	2816,522
3	2-5	3,5	3772,700	1626,484	10893,387
4	5-10	7,5	8450,302	5264,344	15599,177
5	10-15	12,5	7537,975	6426,295	8027,379
6	15-30	22,5	8190,274	7583,477	2920,478
7	30-60	45	2637,921	3464,924	2905,911
8	60-90	75	437,303	585,673	-2106,594
9	90-120	105	1938,971	566,047	1875,080
10	120-180	150	531,909	-293,543	500,240
11	180-240	210	-1658,967	889,023	-1266,646
12	240-360	300	-1192,400	-1508,185	2102,684
		sum	31439,498	25144,371	44267,618

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	793,510	539,834	2816,522
3	2-5	3,5	13204,451	5692,693	38126,856
4	5-10	7,5	63377,266	39482,578	116993,826
5	10-15	12,5	94224,691	80328,685	100342,242
6	15-30	22,5	184281,170	170628,230	65710,746
7	30-60	45	118706,466	155921,568	130765,976
8	60-90	75	32797,725	43925,497	-157994,542
9	90-120	105	203591,909	59434,887	196883,437
10	120-180	150	79786,354	-44031,510	75035,973
11	180-240	210	-348383,056	186694,766	-265995,675
12	240-360	300	-357720,052	-452455,465	630805,330
		sum	84660,433	246161,764	933490,691

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
2,693	9,790	21,087	11,190	7,575

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,958	0,739	2,993
9,708	5,560	26,346
53,079	32,862	114,299
101,344	72,892	177,073
446,475	362,593	618,483
1089,080	952,176	1329,849
1144,781	1035,395	1342,591
1187,822	1059,058	1338,901
2465,154	2129,312	2753,534
2424,325	2153,781	2729,099
4642,065	4256,678	5511,509

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13564,792	12061,046	15944,678

Average AUC0-360 (µg/ml.min)		13856,839
	STDEV	1958,218

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,129	1,643	6,652
5	12,253	6,594	32,379
10	34,928	22,617	69,220
15	55,156	42,177	88,178

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,844	2,866	6,253	4,321	1,423

Table 43: Table containing the AUC, DRi and MDT values and information regarding formula 2A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	6,493	2421,501	5,684	2159,467	6,601	2665,986
3	5	23,820	8883,080	20,598	7824,988	23,880	9643,910
4	10	41,748	15568,885	39,428	14978,454	43,376	17517,280
5	15	56,987	21251,809	61,206	23251,444	61,664	24902,820
6	30	73,209	27301,187	68,249	25927,300	68,166	27528,770
7	60	73,344	27351,600	70,139	26645,262	75,786	30605,905
8	90	75,759	28252,280	79,706	30279,487	79,772	32215,541
9	120	90,946	33915,612	93,380	35474,050	87,740	35433,627
10	180	83,293	31061,658	81,320	30892,568	80,995	32709,643
11	240	86,961	32429,425	92,796	35252,241	99,715	40269,648
12	360	87,925	32788,970	89,132	33860,315	95,574	38597,168

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37292,103	37989,067	40384,660

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2421,501	2159,467	2665,986
3	5	2-5	8883,080	7824,988	9643,910
4	10	5-10	15568,885	14978,454	17517,280
5	15	10-15	21251,809	23251,444	24902,820
6	30	15-30	27301,187	25927,300	27528,770
7	60	30-60	27351,600	26645,262	30605,905
8	90	60-90	28252,280	30279,487	32215,541
9	120	90-120	33915,612	35474,050	35433,627
10	180	120-180	31061,658	30892,568	32709,643
11	240	180-240	32429,425	35252,241	40269,648
12	360	240-360	32788,970	33860,315	38597,168

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2421,501	2159,467	2665,986
3	2-5	3,5	6461,580	5665,521	6977,924
4	5-10	7,5	6685,805	7153,466	7873,370
5	10-15	12,5	5682,924	8272,990	7385,540
6	15-30	22,5	6049,378	2675,856	2625,950
7	30-60	45	50,413	717,962	3077,135
8	60-90	75	900,679	3634,225	1609,636
9	90-120	105	5663,332	5194,562	3218,086
10	120-180	150	-2853,954	-4581,481	-2723,984
11	180-240	210	1367,767	4359,672	7560,005
12	240-360	300	359,545	-1391,926	-1672,480
		sum	32788,970	33860,315	38597,168

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2421,501	2159,467	2665,986
3	2-5	3,5	22615,529	19829,322	24422,734
4	5-10	7,5	50143,538	53650,997	59050,275
5	10-15	12,5	71036,546	103412,376	92319,250
6	15-30	22,5	136110,998	60206,761	59083,879
7	30-60	45	2268,603	32308,294	138471,072
8	60-90	75	67550,962	272566,863	120722,712
9	90-120	105	594649,889	545429,056	337898,999
10	120-180	150	-428093,089	-687222,216	-408597,531
11	180-240	210	287231,054	915531,160	1587601,056
12	240-360	300	107863,496	-417577,697	-501744,002
		sum	913799,026	900294,385	1511894,430

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
27,869	26,588	39,171	31,210	5,654

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,922	2,558	2,971
20,462	17,741	20,575
73,765	67,530	75,663
111,078	113,213	118,170
439,413	436,911	438,178
989,234	934,124	971,679
1006,450	1011,454	1050,014
1125,260	1168,327	1130,706
2352,222	2358,440	2277,930
2298,421	2350,558	2439,591
4721,902	4912,042	5272,804

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13141,129	13372,896	13798,281

Average AUC0-360 (µg/ml.min)		13437,436
	STDEV	333,296

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	6,493	5,684	6,601
5	23,820	20,598	23,880
10	41,748	39,428	43,376
15	56,987	61,206	61,664

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,877	4,118	4,182	4,059	0,131

Table 44: Table containing the AUC, DRi and MDT values and information regarding formula 2B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	15,196	5823,581	15,475	5356,646	15,857	6251,221
3	5	39,221	15030,796	38,530	13337,457	44,054	17367,081
4	10	62,806	24069,114	60,559	20962,913	69,022	27209,740
5	15	80,178	30726,696	76,826	26593,495	85,049	33528,053
6	30	83,708	32079,539	79,901	27657,982	87,682	34565,986
7	60	85,185	32645,658	82,851	28679,088	93,753	36959,361
8	90	87,991	33720,799	83,295	28832,769	92,110	36311,583
9	120	86,972	33330,453	84,851	29371,520	92,241	36363,110
10	180	94,625	36263,433	84,524	29258,322	97,338	38372,452
11	240	87,311	33460,393	84,387	29210,751	93,599	36898,324
12	360	87,878	33677,656	85,470	29585,825	95,157	37512,589

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38323,218	34615,400	39421,876

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	5823,581	5356,646	6251,221
3	5	2-5	15030,796	13337,457	17367,081
4	10	5-10	24069,114	20962,913	27209,740
5	15	10-15	30726,696	26593,495	33528,053
6	30	15-30	32079,539	27657,982	34565,986
7	60	30-60	32645,658	28679,088	36959,361
8	90	60-90	33720,799	28832,769	36311,583
9	120	90-120	33330,453	29371,520	36363,110
10	180	120-180	36263,433	29258,322	38372,452
11	240	180-240	33460,393	29210,751	36898,324
12	360	240-360	33677,656	29585,825	37512,589

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	5823,581	5356,646	6251,221
3	2-5	3,5	9207,216	7980,812	11115,860
4	5-10	7,5	9038,318	7625,455	9842,659
5	10-15	12,5	6657,582	5630,583	6318,313
6	15-30	22,5	1352,843	1064,486	1037,932
7	30-60	45	566,120	1021,106	2393,375
8	60-90	75	1075,140	153,680	-647,778
9	90-120	105	-390,346	538,752	51,527
10	120-180	150	2932,981	-113,199	2009,342
11	180-240	210	-2803,040	-47,571	-1474,127
12	240-360	300	217,262	375,074	614,265
		sum	33677,656	29585,825	37512,589

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	5823,581	5356,646	6251,221
3	2-5	3,5	32225,254	27932,841	38905,510
4	5-10	7,5	67787,386	57190,915	73819,940
5	10-15	12,5	83219,772	70382,283	78978,919
6	15-30	22,5	30438,958	23950,943	23353,479
7	30-60	45	25475,392	45949,787	107701,892
8	60-90	75	80635,535	11526,035	-48583,369
9	90-120	105	-40986,359	56568,945	5410,354
10	120-180	150	439947,104	-16979,806	301401,256
11	180-240	210	-588638,438	-9989,826	-309566,761
12	240-360	300	65178,719	112522,195	184279,350
		sum	201106,903	384410,958	461951,790

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
5,972	12,993	12,315	10,426	3,162

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
6,838	6,964	7,136
36,732	36,453	40,440
114,780	111,476	127,211
160,856	154,558	173,330
553,114	528,952	582,969
1140,027	1098,572	1224,691
1168,935	1121,481	1254,580
1180,997	1134,983	1244,370
2451,562	2286,563	2559,315
2456,139	2280,293	2577,644
4730,102	4586,131	5096,395

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14000,082	13346,426	14888,082

Average AUC0-360 (µg/ml.min)		14078,197
	STDEV	773,791

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	15,196	15,475	15,857
5	39,221	38,530	44,054
10	62,806	60,559	69,022
15	80,178	76,826	85,049

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,321	5,072	5,687	5,360	0,253

Table 45: Table containing the AUC, DRi and MDT values and information regarding formula 2C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	10,920	4648,965	13,118	5557,349	14,482	6213,434
3	5	36,796	15665,341	42,290	17915,952	44,507	19095,484
4	10	67,136	28582,185	74,043	31368,362	74,660	32032,158
5	15	80,118	34108,919	87,215	36948,639	87,488	37535,809
6	30	88,150	37528,497	92,993	39396,291	96,223	41283,554
7	60	94,487	40226,374	95,387	40410,592	96,978	41607,673
8	90	94,171	40091,843	97,382	41255,882	97,982	42038,085
9	120	92,676	39455,362	94,928	40216,063	97,708	41920,691
10	180	98,239	41823,814	99,971	42352,438	100,210	42994,032
11	240	98,667	42005,906	103,219	43728,642	100,581	43153,330
12	360	102,795	43763,415	102,830	43563,849	100,410	43079,949

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42573,467	42364,800	42904,073

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4648,965	5557,349	6213,434
3	5	2-5	15665,341	17915,952	19095,484
4	10	5-10	28582,185	31368,362	32032,158
5	15	10-15	34108,919	36948,639	37535,809
6	30	15-30	37528,497	39396,291	41283,554
7	60	30-60	40226,374	40410,592	41607,673
8	90	60-90	40091,843	41255,882	42038,085
9	120	90-120	39455,362	40216,063	41920,691
10	180	120-180	41823,814	42352,438	42994,032
11	240	180-240	42005,906	43728,642	43153,330
12	360	240-360	43763,415	43563,849	43079,949

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4648,965	5557,349	6213,434
3	2-5	3,5	11016,376	12358,603	12882,050
4	5-10	7,5	12916,844	13452,411	12936,674
5	10-15	12,5	5526,734	5580,276	5503,650
6	15-30	22,5	3419,578	2447,652	3747,745
7	30-60	45	2697,877	1014,302	324,119
8	60-90	75	-134,531	845,289	430,411
9	90-120	105	-636,480	-1039,819	-117,393
10	120-180	150	2368,451	2136,375	1073,340
11	180-240	210	182,093	1376,205	159,299
12	240-360	300	1757,509	-164,793	-73,382
		sum	43763,415	43563,849	43079,949

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4648,965	5557,349	6213,434
3	2-5	3,5	38557,315	43255,111	45087,174
4	5-10	7,5	96876,330	100893,079	97025,057
5	10-15	12,5	69084,170	69753,453	68795,629
6	15-30	22,5	76940,503	55072,172	84324,271
7	30-60	45	121404,476	45643,579	14585,362
8	60-90	75	-10089,816	63396,712	32280,861
9	90-120	105	-66830,452	-109180,984	-12326,277
10	120-180	150	355267,695	320456,191	161001,024
11	180-240	210	38239,478	289002,966	33452,753
12	240-360	300	527252,555	-49437,962	-22014,460
		sum	1251351,220	834411,665	508424,828

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
28,594	19,154	11,802	19,850	6,873

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
4,914	5,903	6,517
32,208	37,400	39,818
116,924	130,875	134,063
165,661	181,416	182,416
567,904	608,203	620,024
1232,799	1271,566	1304,109
1273,441	1301,195	1315,980
1261,217	1298,096	1320,904
2577,354	2631,134	2671,888
2658,231	2743,066	2710,674
5439,472	5563,339	5426,754

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15330,124	15772,194	15733,146

Average AUC0-360 (µg/ml.min)	15611,821
STDEV	244,737

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	10,920	13,118	14,482
5	36,796	42,290	44,507
10	67,136	74,043	74,660
15	80,118	87,215	87,488

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,571	6,030	6,000	5,867	0,210

Table 46: Table containing the AUC, DRi and MDT values and information regarding formula 2D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	8,427	3380,427	3,931	1551,977	7,521	2900,945
3	5	31,093	12472,927	24,547	9690,535	26,001	10029,677
4	10	60,598	24308,515	56,938	22477,560	53,029	20455,259
5	15	79,580	31923,030	79,275	31295,618	72,288	27884,256
6	30	92,381	37058,237	90,128	35579,951	83,304	32133,458
7	60	95,522	38318,140	92,444	36494,475	89,252	34427,641
8	90	95,325	38239,202	93,413	36877,064	89,378	34476,322
9	120	93,900	37667,567	97,176	38362,318	95,244	36738,905
10	180	95,791	38426,058	90,836	35859,663	90,825	35034,611
11	240	96,143	38567,415	93,994	37106,257	90,532	34921,398
12	360	99,048	39732,753	97,475	38480,466	93,878	36212,309

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40114,542	39477,321	38573,639

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3380,427	1551,977	2900,945
3	5	2-5	12472,927	9690,535	10029,677
4	10	5-10	24308,515	22477,560	20455,259
5	15	10-15	31923,030	31295,618	27884,256
6	30	15-30	37058,237	35579,951	32133,458
7	60	30-60	38318,140	36494,475	34427,641
8	90	60-90	38239,202	36877,064	34476,322
9	120	90-120	37667,567	38362,318	36738,905
10	180	120-180	38426,058	35859,663	35034,611
11	240	180-240	38567,415	37106,257	34921,398
12	360	240-360	39732,753	38480,466	36212,309

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3380,427	1551,977	2900,945
3	2-5	3,5	9092,501	8138,558	7128,732
4	5-10	7,5	11835,588	12787,025	10425,582
5	10-15	12,5	7614,515	8818,058	7428,997
6	15-30	22,5	5135,208	4284,334	4249,202
7	30-60	45	1259,903	914,524	2294,183
8	60-90	75	-78,938	382,589	48,681
9	90-120	105	-571,634	1485,254	2262,583
10	120-180	150	758,491	-2502,655	-1704,294
11	180-240	210	141,357	1246,594	-113,213
12	240-360	300	1165,339	1374,210	1290,911
		sum	39732,753	38480,466	36212,309

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3380,427	1551,977	2900,945
3	2-5	3,5	31823,752	28484,952	24950,561
4	5-10	7,5	88766,909	95902,686	78191,862
5	10-15	12,5	95181,432	110225,724	92862,465
6	15-30	22,5	115542,173	96397,504	95607,038
7	30-60	45	56695,625	41153,579	103238,255
8	60-90	75	-5920,384	28694,164	3651,075
9	90-120	105	-60021,620	155951,679	237571,192
10	120-180	150	113773,577	-375398,310	-255644,089
11	180-240	210	29684,941	261784,795	-23774,696
12	240-360	300	349601,614	412262,862	387273,279
		sum	818508,445	857011,613	746827,888

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
20,600	22,271	20,624	21,165	0,782

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,792	1,769	3,384
26,676	19,223	22,627
103,152	91,671	88,909
157,700	153,239	140,982
580,368	571,733	525,125
1268,344	1232,359	1164,752
1288,216	1254,538	1205,750
1277,269	1286,475	1246,195
2560,827	2538,158	2511,929
2591,110	2495,205	2448,320
5270,170	5169,656	4979,074

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15127,624	14814,025	14337,049

Average AUC0-360 (µg/ml.min)		14759,566
	STDEV	398,091

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	8,427	3,931	7,521
5	31,093	24,547	26,001
10	60,598	56,938	53,029
15	79,580	79,275	72,288

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,509	5,597	4,981	5,362	0,272

Table 47: Table containing the AUC, DRi and MDT values and information regarding formula 2E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,655	590,459	1,987	716,006	2,583	962,753
3	5	7,450	2657,704	10,655	3840,312	13,011	4849,233
4	10	22,682	8091,323	28,599	10308,108	33,124	12345,267
5	15	39,999	14268,504	46,773	16858,325	52,459	19551,511
6	30	63,101	22509,611	68,350	24635,374	71,968	26822,513
7	60	70,634	25197,038	77,539	27947,435	79,753	29724,125
8	90	82,821	29544,212	84,037	30289,302	85,123	31725,472
9	120	79,246	28269,138	84,468	30444,831	86,461	32224,138
10	180	79,352	28306,813	86,346	31121,657	86,414	32206,598
11	240	80,455	28700,332	87,219	31436,287	88,567	33009,193
12	360	83,113	29648,657	88,995	32076,485	89,058	33192,358

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
35672,567	36042,997	37270,300

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	590,459	716,006	962,753
3	5	2-5	2657,704	3840,312	4849,233
4	10	5-10	8091,323	10308,108	12345,267
5	15	10-15	14268,504	16858,325	19551,511
6	30	15-30	22509,611	24635,374	26822,513
7	60	30-60	25197,038	27947,435	29724,125
8	90	60-90	29544,212	30289,302	31725,472
9	120	90-120	28269,138	30444,831	32224,138
10	180	120-180	28306,813	31121,657	32206,598
11	240	180-240	28700,332	31436,287	33009,193
12	360	240-360	29648,657	32076,485	33192,358

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	590,459	716,006	962,753
3	2-5	3,5	2067,245	3124,306	3886,479
4	5-10	7,5	5433,619	6467,796	7496,035
5	10-15	12,5	6177,181	6550,217	7206,244
6	15-30	22,5	8241,108	7777,049	7271,002
7	30-60	45	2687,427	3312,062	2901,612
8	60-90	75	4347,174	2341,867	2001,347
9	90-120	105	-1275,073	155,528	498,666
10	120-180	150	37,674	676,826	-17,541
11	180-240	210	393,519	314,630	802,596
12	240-360	300	948,324	640,198	183,164
		sum	29648,657	32076,485	33192,358

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	590,459	716,006	962,753
3	2-5	3,5	7235,356	10935,072	13602,678
4	5-10	7,5	40752,144	48508,474	56220,261
5	10-15	12,5	77214,759	81877,708	90078,048
6	15-30	22,5	185424,921	174983,593	163597,543
7	30-60	45	120934,205	149042,768	130572,543
8	60-90	75	326038,051	175640,032	150101,009
9	90-120	105	-133882,706	16330,471	52359,961
10	120-180	150	5651,159	101523,940	-2631,091
11	180-240	210	82639,044	66072,275	168545,081
12	240-360	300	284497,327	192059,418	54949,222
		sum	997094,718	1017689,755	878358,008

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
33,630	31,727	26,463	30,607	3,032

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,745	0,894	1,162
6,146	8,533	10,526
33,899	44,161	51,901
70,516	84,794	96,280
347,960	388,539	419,938
902,710	984,752	1024,113
1035,820	1090,636	1112,910
1093,950	1137,407	1158,187
2141,072	2305,989	2333,802
2157,390	2343,124	2362,238
4416,342	4757,775	4795,888

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12206,550	13146,604	13366,946

Average AUC0-360 (µg/ml.min)		12906,700
	STDEV	616,275

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,655	1,987	2,583
5	7,450	10,655	13,011
10	22,682	28,599	33,124
15	39,999	46,773	52,459

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,734	3,228	3,625	3,195	0,364

Table 48: Table containing the AUC, DRi and MDT values and information regarding formula 2F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,651	1896,756	5,088	1708,498	5,271	1775,646
3	5	20,745	6962,898	17,471	5866,231	18,190	6127,089
4	10	43,417	14572,276	38,676	12986,464	37,892	12763,725
5	15	64,610	21685,793	57,255	19224,900	56,080	18890,381
6	30	76,792	25774,466	72,537	24356,188	68,279	22999,665
7	60	78,870	26471,847	80,208	26931,849	80,393	27079,939
8	90	81,201	27254,138	79,089	26556,306	79,057	26630,105
9	120	81,736	27433,791	78,319	26297,700	80,273	27039,823
10	180	82,874	27815,683	81,258	27284,540	81,299	27385,233
11	240	82,143	27570,543	82,908	27838,325	83,172	28016,201
12	360	82,751	27774,347	81,653	27417,120	82,971	27948,492

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
33563,897	33577,555	33684,658

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1896,756	1708,498	1775,646
3	5	2-5	6962,898	5866,231	6127,089
4	10	5-10	14572,276	12986,464	12763,725
5	15	10-15	21685,793	19224,900	18890,381
6	30	15-30	25774,466	24356,188	22999,665
7	60	30-60	26471,847	26931,849	27079,939
8	90	60-90	27254,138	26556,306	26630,105
9	120	90-120	27433,791	26297,700	27039,823
10	180	120-180	27815,683	27284,540	27385,233
11	240	180-240	27570,543	27838,325	28016,201
12	360	240-360	27774,347	27417,120	27948,492

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1896,756	1708,498	1775,646
3	2-5	3,5	5066,142	4157,733	4351,443
4	5-10	7,5	7609,379	7120,233	6636,636
5	10-15	12,5	7113,517	6238,436	6126,656
6	15-30	22,5	4088,673	5131,288	4109,284
7	30-60	45	697,381	2575,661	4080,274
8	60-90	75	782,291	-375,544	-449,834
9	90-120	105	179,653	-258,606	409,718
10	120-180	150	381,893	986,841	345,411
11	180-240	210	-245,141	553,785	630,968
12	240-360	300	203,804	-421,205	-67,710
		sum	27774,347	27417,120	27948,492

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1896,756	1708,498	1775,646
3	2-5	3,5	17731,497	14552,065	15230,050
4	5-10	7,5	57070,340	53401,747	49774,771
5	10-15	12,5	88918,963	77980,447	76583,197
6	15-30	22,5	91995,138	115453,991	92458,884
7	30-60	45	31382,131	115904,744	183612,346
8	60-90	75	58671,839	-28165,765	-33737,585
9	90-120	105	18863,550	-27153,652	43020,374
10	120-180	150	57283,891	148026,140	51811,616
11	180-240	210	-51479,559	116294,786	132503,270
12	240-360	300	61141,291	-126361,646	-20312,869
		sum	433475,836	461641,355	592719,700

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
15,607	16,838	21,208	17,884	2,403

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,543	2,290	2,372
17,818	15,227	15,836
72,182	63,165	63,092
121,530	107,923	105,718
477,234	438,049	419,713
1050,720	1031,029	1003,535
1080,478	1075,257	1076,285
1099,823	1062,509	1075,481
2222,233	2154,297	2181,225
2227,733	2216,238	2220,356
4452,141	4443,138	4485,860

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12824,435	12609,122	12649,473

Average AUC0-360 (µg/ml.min)		12694,343
	STDEV	114,455

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,651	5,088	5,271
5	20,745	17,471	18,190
10	43,417	38,676	37,892
15	64,610	57,255	56,080

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,410	3,919	3,821	4,050	0,258

Table 49: Table containing the AUC, DRi and MDT values and information regarding formula 3A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	25,180	9719,063	18,513	6977,051	24,902	9786,067
3	5	60,555	23373,300	50,002	18844,213	61,456	24150,639
4	10	83,983	32416,158	79,501	29961,430	84,684	33278,803
5	15	90,583	34963,663	89,100	33579,079	93,728	36832,996
6	30	93,048	35915,405	92,812	34978,036	95,927	37697,152
7	60	91,136	35177,191	87,254	32883,545	90,996	35759,369
8	90	89,929	34711,387	90,002	33919,229	89,278	35084,144
9	120	91,996	35509,327	89,660	33790,239	91,549	35976,534
10	180	94,222	36368,366	90,756	34203,124	93,378	36695,532
11	240	93,805	36207,542	90,214	33999,078	94,492	37133,241
12	360	95,305	36786,571	91,248	34388,773	97,031	38131,198

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38598,655	37687,039	39297,755

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	9719,063	6977,051	9786,067
3	5	2-5	23373,300	18844,213	24150,639
4	10	5-10	32416,158	29961,430	33278,803
5	15	10-15	34963,663	33579,079	36832,996
6	30	15-30	35915,405	34978,036	37697,152
7	60	30-60	35177,191	32883,545	35759,369
8	90	60-90	34711,387	33919,229	35084,144
9	120	90-120	35509,327	33790,239	35976,534
10	180	120-180	36368,366	34203,124	36695,532
11	240	180-240	36207,542	33999,078	37133,241
12	360	240-360	36786,571	34388,773	38131,198

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	9719,063	6977,051	9786,067
3	2-5	3,5	13654,237	11867,162	14364,572
4	5-10	7,5	9042,858	11117,217	9128,164
5	10-15	12,5	2547,505	3617,648	3554,193
6	15-30	22,5	951,742	1398,958	864,157
7	30-60	45	-738,215	-2094,491	-1937,784
8	60-90	75	-465,803	1035,684	-675,225
9	90-120	105	797,939	-128,990	892,390
10	120-180	150	859,039	412,885	718,997
11	180-240	210	-160,823	-204,046	437,709
12	240-360	300	579,029	389,695	997,957
		sum	36786,571	34388,773	38131,198

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	9719,063	6977,051	9786,067
3	2-5	3,5	47789,830	41535,068	50276,001
4	5-10	7,5	67821,432	83379,127	68461,231
5	10-15	12,5	31843,818	45220,605	44427,413
6	15-30	22,5	21414,196	31476,545	19443,523
7	30-60	45	-33219,666	-94252,113	-87200,262
8	60-90	75	-34935,248	77676,330	-50641,839
9	90-120	105	83783,643	-13543,986	93700,931
10	120-180	150	128855,825	61932,791	107849,622
11	180-240	210	-33772,913	-42849,614	91918,903
12	240-360	300	173708,674	116908,495	299387,142
		sum	463008,654	314460,300	647408,733

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
12,586	9,144	16,978	12,903	3,206

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
11,331	8,331	11,206
57,871	46,248	58,292
162,604	145,690	164,407
196,386	189,675	200,713
619,754	613,952	640,086
1243,243	1215,446	1261,730
1222,187	1196,482	1216,847
1227,996	1212,722	1220,578
2513,945	2435,613	2496,511
2538,365	2443,094	2536,248
5105,984	4899,488	5171,135

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14899,666	14406,741	14977,752

Average AUC0-360 (µg/ml.min)		14761,386
	STDEV	309,603

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	25,180	18,513	24,902
5	60,555	50,002	61,456
10	83,983	79,501	84,684
15	90,583	89,100	93,728

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,937	6,039	6,135	6,037	0,081

Table 50: Table containing the AUC, DRi and MDT values and information regarding formula 3B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	41,468	17304,274	24,242	9028,170	34,613	14398,292
3	5	83,114	34682,765	51,569	19204,925	78,526	32665,511
4	10	97,920	40861,444	77,685	28930,861	97,558	40582,408
5	15	100,135	41785,441	87,251	32493,347	100,801	41931,400
6	30	101,511	42359,821	87,961	32757,892	99,224	41275,369
7	60	100,758	42045,339	87,869	32723,484	98,811	41103,514
8	90	103,035	42995,726	82,666	30785,961	99,001	41182,689
9	120	98,999	41311,495	89,369	33282,061	95,186	39595,462
10	180	101,003	42147,916	85,967	32015,327	100,236	41696,365
11	240	102,667	42842,197	87,769	32686,137	96,858	40291,109
12	360	101,633	42410,577	90,243	33607,501	101,540	42238,844

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41729,209	37241,203	41598,179

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	17304,274	9028,170	14398,292
3	5	2-5	34682,765	19204,925	32665,511
4	10	5-10	40861,444	28930,861	40582,408
5	15	10-15	41785,441	32493,347	41931,400
6	30	15-30	42359,821	32757,892	41275,369
7	60	30-60	42045,339	32723,484	41103,514
8	90	60-90	42995,726	30785,961	41182,689
9	120	90-120	41311,495	33282,061	39595,462
10	180	120-180	42147,916	32015,327	41696,365
11	240	180-240	42842,197	32686,137	40291,109
12	360	240-360	42410,577	33607,501	42238,844

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	17304,274	9028,170	14398,292
3	2-5	3,5	17378,491	10176,754	18267,218
4	5-10	7,5	6178,680	9725,937	7916,898
5	10-15	12,5	923,997	3562,485	1348,992
6	15-30	22,5	574,380	264,545	-656,031
7	30-60	45	-314,482	-34,407	-171,855
8	60-90	75	950,386	-1937,523	79,175
9	90-120	105	-1684,230	2496,100	-1587,227
10	120-180	150	836,420	-1266,733	2100,903
11	180-240	210	694,282	670,810	-1405,256
12	240-360	300	-431,620	921,364	1947,735
		sum	42410,577	33607,501	42238,844

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	17304,274	9028,170	14398,292
3	2-5	3,5	60824,717	35618,640	63935,265
4	5-10	7,5	46340,099	72944,524	59376,732
5	10-15	12,5	11549,960	44531,068	16862,397
6	15-30	22,5	12923,550	5952,260	-14760,701
7	30-60	45	-14151,681	-1548,331	-7733,480
8	60-90	75	71278,969	-145314,255	5938,128
9	90-120	105	-176844,173	262090,463	-166658,785
10	120-180	150	125463,012	-190009,968	315135,384
11	180-240	210	145799,140	140870,054	-295103,736
12	240-360	300	-129486,064	276409,141	584320,420
		sum	171001,803	510571,766	575709,916

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
4,032	15,192	13,630	10,951	4,934

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
18,661	10,909	15,576
84,093	51,173	76,369
203,664	145,411	198,095
222,812	185,553	223,154
680,555	591,342	675,084
1365,314	1186,856	1336,735
1375,600	1151,114	1335,231
1363,730	1161,238	1310,761
2700,032	2367,042	2638,192
2749,553	2345,439	2660,768
5516,100	4806,312	5356,746

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16280,114	14002,388	15826,710

Average AUC0-360 (µg/ml.min)		15369,737
	STDEV	1205,664

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	41,468	24,242	34,613
5	83,114	51,569	78,526
10	97,920	77,685	97,558
15	100,135	87,251	100,801

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,132	5,705	6,407	6,081	0,289

Table 51: Table containing the AUC, DRi and MDT values and information regarding formula 3C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	9,927	4074,850	2,928	1059,223	9,487	3852,208
3	5	38,754	15907,421	14,603	5282,998	32,808	13322,018
4	10	75,714	31078,314	39,292	14214,373	66,023	26809,190
5	15	83,716	34362,754	54,898	19860,167	75,280	30568,100
6	30	90,275	37055,282	61,101	22103,922	80,572	32716,832
7	60	97,500	40020,996	66,894	24199,728	84,172	34178,755
8	90	98,382	40382,793	75,077	27160,122	90,662	36813,752
9	120	99,394	40798,463	81,082	29332,314	93,520	37974,303
10	180	99,617	40889,617	86,227	31193,701	98,057	39816,683
11	240	101,351	41601,431	85,274	30849,145	92,618	37608,141
12	360	99,496	40839,950	89,324	32314,211	100,261	40711,639

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41047,021	36176,312	40605,682

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4074,850	1059,223	3852,208
3	5	2-5	15907,421	5282,998	13322,018
4	10	5-10	31078,314	14214,373	26809,190
5	15	10-15	34362,754	19860,167	30568,100
6	30	15-30	37055,282	22103,922	32716,832
7	60	30-60	40020,996	24199,728	34178,755
8	90	60-90	40382,793	27160,122	36813,752
9	120	90-120	40798,463	29332,314	37974,303
10	180	120-180	40889,617	31193,701	39816,683
11	240	180-240	41601,431	30849,145	37608,141
12	360	240-360	40839,950	32314,211	40711,639

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4074,850	1059,223	3852,208
3	2-5	3,5	11832,571	4223,775	9469,810
4	5-10	7,5	15170,893	8931,375	13487,172
5	10-15	12,5	3284,440	5645,795	3758,910
6	15-30	22,5	2692,528	2243,754	2148,732
7	30-60	45	2965,714	2095,806	1461,923
8	60-90	75	361,797	2960,394	2634,997
9	90-120	105	415,670	2172,192	1160,551
10	120-180	150	91,154	1861,387	1842,380
11	180-240	210	711,813	-344,556	-2208,542
12	240-360	300	-761,481	1465,066	3103,498
		sum	40839,950	32314,211	40711,639

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4074,850	1059,223	3852,208
3	2-5	3,5	41413,998	14783,211	33144,335
4	5-10	7,5	113781,698	66985,314	101153,789
5	10-15	12,5	41055,505	70572,433	46986,379
6	15-30	22,5	60581,879	50484,470	48346,465
7	30-60	45	133457,134	94311,280	65786,537
8	60-90	75	27134,799	222029,578	197624,800
9	90-120	105	43645,330	228080,158	121857,833
10	120-180	150	13673,127	279208,046	276356,984
11	180-240	210	149480,813	-72356,766	-463793,814
12	240-360	300	-228444,409	439519,861	931049,547
		sum	399854,723	1394676,809	1362365,063

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
9,791	43,160	33,464	28,805	14,016

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
4,467	1,318	4,269
32,860	11,834	28,549
128,777	60,632	111,185
179,358	105,964	158,967
587,219	391,496	526,002
1267,485	863,962	1112,025
1322,205	958,304	1180,129
1334,990	1054,071	1243,223
2686,648	2258,664	2586,284
2713,057	2315,268	2574,111
5422,847	4714,164	5207,729

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15679,913	12735,675	14732,473

Average AUC0-360 (µg/ml.min)	14382,687
STDEV	1502,963

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	9,927	2,928	9,487
5	38,754	14,603	32,808
10	75,714	39,292	66,023
15	83,716	54,898	75,280

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,996	3,889	5,345	5,077	0,881

Table 52: Table containing the AUC, DRi and MDT values and information regarding formula 3D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,288	3087,205	5,973	2545,371	10,325	4441,993
3	5	36,370	15407,531	30,975	13199,564	41,709	17944,464
4	10	73,731	31234,303	63,855	27211,239	73,809	31755,332
5	15	83,677	35447,850	83,708	35671,270	88,418	38040,697
6	30	90,239	38227,827	91,542	39009,822	94,057	40466,748
7	60	94,014	39826,883	95,314	40617,076	98,571	42408,538
8	90	97,101	41134,699	99,165	42258,475	106,231	45704,191
9	120	103,642	43905,744	105,220	44838,677	105,520	45398,265
10	180	104,599	44311,216	105,054	44767,768	104,927	45143,154
11	240	104,421	44235,518	101,181	43117,394	99,723	42904,159
12	360	104,185	44135,828	105,112	44792,760	104,718	45053,395

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42362,770	42614,158	43023,479

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3087,205	2545,371	4441,993
3	5	2-5	15407,531	13199,564	17944,464
4	10	5-10	31234,303	27211,239	31755,332
5	15	10-15	35447,850	35671,270	38040,697
6	30	15-30	38227,827	39009,822	40466,748
7	60	30-60	39826,883	40617,076	42408,538
8	90	60-90	41134,699	42258,475	45704,191
9	120	90-120	43905,744	44838,677	45398,265
10	180	120-180	44311,216	44767,768	45143,154
11	240	180-240	44235,518	43117,394	42904,159
12	360	240-360	44135,828	44792,760	45053,395

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3087,205	2545,371	4441,993
3	2-5	3,5	12320,326	10654,193	13502,471
4	5-10	7,5	15826,772	14011,675	13810,868
5	10-15	12,5	4213,547	8460,031	6285,365
6	15-30	22,5	2779,977	3338,552	2426,051
7	30-60	45	1599,056	1607,254	1941,790
8	60-90	75	1307,816	1641,399	3295,653
9	90-120	105	2771,045	2580,202	-305,925
10	120-180	150	405,472	-70,909	-255,112
11	180-240	210	-75,698	-1650,375	-2238,995
12	240-360	300	-99,690	1675,366	2149,236
		sum	44135,828	44792,760	45053,395

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3087,205	2545,371	4441,993
3	2-5	3,5	43121,143	37289,676	47258,647
4	5-10	7,5	118700,790	105087,565	103581,512
5	10-15	12,5	52669,340	105750,388	78567,061
6	15-30	22,5	62549,485	75117,425	54586,147
7	30-60	45	71957,515	72326,413	87380,541
8	60-90	75	98086,215	123104,936	247173,990
9	90-120	105	290959,721	270921,205	-32122,169
10	120-180	150	60820,766	-10636,322	-38266,753
11	180-240	210	-15896,641	-346578,696	-470188,872
12	240-360	300	-29906,879	502609,836	644770,810
		sum	756148,658	937537,796	727182,906

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
17,132	20,931	16,140	18,068	2,064

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,279	2,688	4,646
29,469	24,940	35,122
123,864	106,683	129,958
177,083	166,008	182,506
586,967	591,467	615,856
1243,708	1261,275	1300,239
1290,026	1312,733	1382,410
1355,018	1379,602	1429,316
2811,263	2838,697	2841,028
2821,772	2784,168	2762,768
5632,366	5569,919	5519,902

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16074,816	16038,179	16203,752

Average AUC0-360 (µg/ml.min)		16105,582
	STDEV	86,968

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,288	5,973	10,325
5	36,370	30,975	41,709
10	73,731	63,855	73,809
15	83,677	83,708	88,418

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,046	5,899	6,182	6,042	0,115

Table 53: Table containing the AUC, DRi and MDT values and information regarding formula 3E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,372	450,664	4,450	1886,685	1,491	536,364
3	5	6,480	2128,012	21,139	8962,529	8,140	2928,514
4	10	24,621	8085,144	56,141	23803,104	27,209	9788,623
5	15	42,264	13878,504	82,429	34949,060	49,759	17900,967
6	30	62,419	20497,223	95,900	40660,613	69,354	24950,469
7	60	71,425	23454,543	104,689	44387,093	88,829	31956,707
8	90	73,998	24299,508	95,183	40356,743	79,014	28425,966
9	120	77,087	25313,861	102,640	43518,200	81,705	29393,761
10	180	77,309	25386,677	100,082	42433,835	83,221	29939,212
11	240	81,081	26625,380	103,818	44017,991	82,936	29836,586
12	360	79,061	25961,848	102,731	43556,830	83,542	30054,701

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
32837,903	42399,024	35975,639

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	450,664	1886,685	536,364
3	5	2-5	2128,012	8962,529	2928,514
4	10	5-10	8085,144	23803,104	9788,623
5	15	10-15	13878,504	34949,060	17900,967
6	30	15-30	20497,223	40660,613	24950,469
7	60	30-60	23454,543	44387,093	31956,707
8	90	60-90	24299,508	40356,743	28425,966
9	120	90-120	25313,861	43518,200	29393,761
10	180	120-180	25386,677	42433,835	29939,212
11	240	180-240	26625,380	44017,991	29836,586
12	360	240-360	25961,848	43556,830	30054,701

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	450,664	1886,685	536,364
3	2-5	3,5	1677,347	7075,844	2392,150
4	5-10	7,5	5957,132	14840,575	6860,109
5	10-15	12,5	5793,360	11145,956	8112,344
6	15-30	22,5	6618,718	5711,553	7049,503
7	30-60	45	2957,320	3726,479	7006,238
8	60-90	75	844,965	-4030,350	-3530,741
9	90-120	105	1014,353	3161,457	967,794
10	120-180	150	72,816	-1084,365	545,452
11	180-240	210	1238,703	1584,156	-102,627
12	240-360	300	-663,532	-461,161	218,115
		sum	25961,848	43556,830	30054,701

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	450,664	1886,685	536,364
3	2-5	3,5	5870,716	24765,452	8372,525
4	5-10	7,5	44678,492	111304,315	51450,817
5	10-15	12,5	72417,005	139324,455	101404,298
6	15-30	22,5	148921,162	128509,944	158613,808
7	30-60	45	133079,417	167691,567	315280,692
8	60-90	75	63372,362	-302276,253	-264805,538
9	90-120	105	106507,103	331953,001	101618,422
10	120-180	150	10922,380	-162654,744	81817,729
11	180-240	210	260127,568	332672,832	-21551,629
12	240-360	300	-199059,609	-138348,349	65434,479
		sum	647287,259	634828,904	598171,968

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
24,932	14,575	19,903	19,803	4,229

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,618	2,002	0,671
5,301	17,272	6,501
34,989	86,939	39,768
75,246	155,891	86,589
353,305	601,860	402,004
903,451	1353,975	1067,732
981,609	1349,137	1132,942
1019,828	1335,304	1084,854
2084,351	2736,743	2226,493
2138,269	2752,657	2243,110
4323,830	5576,827	4494,888

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
11920,798	15968,607	12785,552

Average AUC0-360 (µg/ml.min)			13558,319
		STDEV	2131,681

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,372	4,450	1,491
5	6,480	21,139	8,140
10	24,621	56,141	27,209
15	42,264	82,429	49,759

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,929	5,776	3,404	4,036	1,245

Table 54: Table containing the AUC, DRi and MDT values and information regarding formula 3F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,941	2003,367	8,346	2822,405	7,938	3649,610
3	5	28,289	11468,925	29,729	10053,275	36,669	16859,009
4	10	66,986	27157,645	29,830	10087,639	75,415	34673,050
5	15	87,954	35658,483	51,573	17440,466	90,114	41431,137
6	30	90,168	36556,449	73,293	24785,560	94,865	43615,090
7	60	96,044	38938,590	77,841	26323,447	97,369	44766,548
8	90	100,105	40584,802	83,499	28236,671	98,410	45245,047
9	120	95,902	38880,927	81,868	27685,284	96,959	44578,081
10	180	95,303	38637,903	82,068	27753,035	101,146	46503,009
11	240	99,980	40534,425	81,321	27500,153	113,521	52192,795
12	360	96,151	38981,811	80,838	27337,040	98,714	45384,998

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40542,379	33816,936	45976,170

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2003,367	2822,405	3649,610
3	5	2-5	11468,925	10053,275	16859,009
4	10	5-10	27157,645	10087,639	34673,050
5	15	10-15	35658,483	17440,466	41431,137
6	30	15-30	36556,449	24785,560	43615,090
7	60	30-60	38938,590	26323,447	44766,548
8	90	60-90	40584,802	28236,671	45245,047
9	120	90-120	38880,927	27685,284	44578,081
10	180	120-180	38637,903	27753,035	46503,009
11	240	180-240	40534,425	27500,153	52192,795
12	360	240-360	38981,811	27337,040	45384,998

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2003,367	2822,405	3649,610
3	2-5	3,5	9465,558	7230,871	13209,399
4	5-10	7,5	15688,721	34,363	17814,041
5	10-15	12,5	8500,837	7352,827	6758,088
6	15-30	22,5	897,966	7345,094	2183,952
7	30-60	45	2382,142	1537,887	1151,458
8	60-90	75	1646,212	1913,224	478,500
9	90-120	105	-1703,875	-551,387	-666,966
10	120-180	150	-243,024	67,750	1924,927
11	180-240	210	1896,522	-252,882	5689,786
12	240-360	300	-1552,614	-163,113	-6807,796
		sum	38981,811	27337,040	45384,998

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2003,367	2822,405	3649,610
3	2-5	3,5	33129,453	25308,047	46232,897
4	5-10	7,5	117665,404	257,726	133605,304
5	10-15	12,5	106260,468	91910,334	84476,095
6	15-30	22,5	20204,233	165264,620	49138,928
7	30-60	45	107196,370	69204,937	51815,608
8	60-90	75	123465,877	143491,789	35887,471
9	90-120	105	-178906,874	-57895,620	-70031,407
10	120-180	150	-36453,559	10162,540	288739,118
11	180-240	210	398269,582	-53105,191	1194855,014
12	240-360	300	-465784,155	-48933,980	-2042338,859
		sum	227050,165	348487,608	-223970,222

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
5,825	12,748	-4,935	4,546	7,275

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,224	3,756	3,572
22,430	25,700	30,110
107,184	67,003	126,095
174,307	91,579	186,221
601,162	421,424	624,304
1256,935	1020,157	1297,577
1324,004	1089,042	1321,507
1323,044	1116,225	1318,740
2581,260	2213,143	2674,417
2636,319	2205,753	2898,009
5295,541	4378,292	5730,361

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15324,411	12632,076	16210,912

Average AUC0-360 (µg/ml.min)		14722,466
	STDEV	1863,805

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,941	8,346	7,938
5	28,289	29,729	36,669
10	66,986	29,830	75,415
15	87,954	51,573	90,114

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,275	3,167	6,436	5,293	1,504

Table 55: Table containing the AUC, DRi and MDT values and information regarding formula 4A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,120	765,375	3,460	1284,534	2,985	1141,240
3	5	8,416	3038,521	13,530	5023,270	14,992	5732,626
4	10	23,638	8534,574	36,871	13688,873	37,300	14262,975
5	15	41,830	15102,644	52,905	19641,395	55,897	21374,339
6	30	60,844	21967,581	71,837	26670,099	75,406	28834,293
7	60	75,206	27153,210	81,152	30128,657	87,725	33544,769
8	90	78,158	28218,686	83,836	31125,053	89,490	34219,763
9	120	82,645	29838,733	84,456	31355,051	91,478	34979,889
10	180	81,838	29547,654	86,986	32294,407	91,231	34885,729
11	240	81,960	29591,526	91,669	34033,061	94,417	36103,762
12	360	82,544	29802,517	89,786	33333,845	92,346	35311,809

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
36104,888	37125,988	38238,755

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	765,375	1284,534	1141,240
3	5	2-5	3038,521	5023,270	5732,626
4	10	5-10	8534,574	13688,873	14262,975
5	15	10-15	15102,644	19641,395	21374,339
6	30	15-30	21967,581	26670,099	28834,293
7	60	30-60	27153,210	30128,657	33544,769
8	90	60-90	28218,686	31125,053	34219,763
9	120	90-120	29838,733	31355,051	34979,889
10	180	120-180	29547,654	32294,407	34885,729
11	240	180-240	29591,526	34033,061	36103,762
12	360	240-360	29802,517	33333,845	35311,809

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	765,375	1284,534	1141,240
3	2-5	3,5	2273,146	3738,736	4591,386
4	5-10	7,5	5496,053	8665,603	8530,349
5	10-15	12,5	6568,069	5952,522	7111,364
6	15-30	22,5	6864,937	7028,704	7459,953
7	30-60	45	5185,629	3458,559	4710,477
8	60-90	75	1065,476	996,396	674,993
9	90-120	105	1620,046	229,998	760,126
10	120-180	150	-291,079	939,356	-94,159
11	180-240	210	43,872	1738,655	1218,032
12	240-360	300	210,991	-699,216	-791,953
		sum	29802,517	33333,845	35311,809

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	765,375	1284,534	1141,240
3	2-5	3,5	7956,013	13085,575	16069,850
4	5-10	7,5	41220,395	64992,021	63977,621
5	10-15	12,5	82100,867	74406,528	88892,050
6	15-30	22,5	154461,087	158145,833	167848,949
7	30-60	45	233353,306	155635,141	211971,450
8	60-90	75	79910,734	74729,697	50624,506
9	90-120	105	170104,877	24149,768	79813,207
10	120-180	150	-43661,791	140903,333	-14123,877
11	180-240	210	9213,027	365117,465	255786,797
12	240-360	300	63297,420	-209764,748	-237585,837
		sum	798721,309	862685,147	684415,958

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
26,800	25,880	19,382	24,021	3,302

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,954	1,557	1,343
7,112	11,468	12,134
36,061	56,702	58,828
73,652	100,998	104,846
346,524	421,002	443,148
918,339	1032,677	1101,131
1035,207	1113,674	1196,196
1085,414	1135,972	1221,529
2220,520	2314,464	2466,571
2211,277	2411,844	2506,248
4441,612	4899,281	5042,582

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12376,671	13499,640	14154,556

Average AUC0-360 (µg/ml.min)		13343,622
	STDEV	899,152

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,120	3,460	2,985
5	8,416	13,530	14,992
10	23,638	36,871	37,300
15	41,830	52,905	55,897

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,840	3,710	3,893	3,481	0,459

Table 56: Table containing the AUC, DRi and MDT values and information regarding formula 4B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	8,582	3528,846	12,517	5239,094	8,405	3463,969
3	5	31,277	12861,239	42,991	17993,890	28,261	11646,658
4	10	61,471	25276,904	79,888	33437,246	54,958	22648,767
5	15	81,961	33702,318	92,170	38577,855	73,845	30432,503
6	30	95,031	39076,889	99,550	41667,048	85,218	35119,518
7	60	100,342	41260,469	101,773	42597,447	92,413	38084,397
8	90	98,208	40383,036	101,021	42282,576	95,988	39557,763
9	120	100,374	41273,871	100,581	42098,269	98,092	40424,850
10	180	100,187	41197,068	99,263	41546,950	97,378	40130,547
11	240	98,783	40619,624	100,091	41893,245	100,316	41341,425
12	360	101,531	41749,559	102,843	43045,206	101,756	41935,086

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41120,033	41855,258	41211,297

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3528,846	5239,094	3463,969
3	5	2-5	12861,239	17993,890	11646,658
4	10	5-10	25276,904	33437,246	22648,767
5	15	10-15	33702,318	38577,855	30432,503
6	30	15-30	39076,889	41667,048	35119,518
7	60	30-60	41260,469	42597,447	38084,397
8	90	60-90	40383,036	42282,576	39557,763
9	120	90-120	41273,871	42098,269	40424,850
10	180	120-180	41197,068	41546,950	40130,547
11	240	180-240	40619,624	41893,245	41341,425
12	360	240-360	41749,559	43045,206	41935,086

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3528,846	5239,094	3463,969
3	2-5	3,5	9332,392	12754,796	8182,689
4	5-10	7,5	12415,666	15443,356	11002,109
5	10-15	12,5	8425,413	5140,609	7783,736
6	15-30	22,5	5374,571	3089,194	4687,015
7	30-60	45	2183,580	930,399	2964,879
8	60-90	75	-877,434	-314,871	1473,366
9	90-120	105	890,836	-184,307	867,087
10	120-180	150	-76,804	-551,318	-294,304
11	180-240	210	-577,443	346,295	1210,878
12	240-360	300	1129,935	1151,961	593,662
		sum	41749,559	43045,206	41935,086

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3528,846	5239,094	3463,969
3	2-5	3,5	32663,373	44641,784	28639,411
4	5-10	7,5	93117,492	115825,171	82515,817
5	10-15	12,5	105317,666	64257,607	97296,704
6	15-30	22,5	120927,857	69506,856	105457,836
7	30-60	45	98261,096	41867,941	133419,562
8	60-90	75	-65807,514	-23615,338	110502,473
9	90-120	105	93537,738	-19352,255	91044,127
10	120-180	150	-11520,532	-82697,721	-44145,578
11	180-240	210	-121263,117	72721,889	254284,433
12	240-360	300	338980,448	345588,198	178098,482
		sum	687743,355	633983,228	1040577,234

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
16,473	14,728	24,814	18,672	4,401

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,862	5,633	3,782
26,905	37,468	24,750
104,342	138,238	93,621
161,361	193,565	144,903
597,348	647,055	536,838
1318,766	1358,934	1199,007
1340,207	1368,861	1271,701
1340,427	1360,810	1310,036
2707,580	2697,894	2638,834
2686,100	2691,281	2668,859
5408,478	5479,212	5455,945

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15695,377	15978,951	15348,278

Average AUC0-360 (µg/ml.min)		15674,202
	STDEV	315,869

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	8,582	12,517	8,405
5	31,277	42,991	28,261
10	61,471	79,888	54,958
15	81,961	92,170	73,845

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,661	6,468	5,069	5,733	0,573

Table 57: Table containing the AUC, DRi and MDT values and information regarding formula 4C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,842	707,018	5,246	2159,612	1,966	776,905
3	5	9,609	3687,347	24,826	10220,667	9,041	3572,227
4	10	30,437	11679,859	55,880	23004,957	32,415	12807,429
5	15	53,020	20346,159	80,825	33274,528	55,694	22004,968
6	30	73,696	28280,361	91,075	37494,210	72,645	28702,199
7	60	83,789	32153,390	93,285	38404,032	78,905	31175,759
8	90	85,681	32879,447	101,292	41700,271	81,360	32145,625
9	120	87,027	33396,147	101,236	41677,493	85,547	33799,993
10	180	87,459	33561,732	98,257	40450,712	88,129	34820,305
11	240	88,915	34120,539	97,745	40239,951	84,178	33259,133
12	360	89,062	34177,025	98,980	40748,718	85,040	33599,647

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38374,336	41168,461	39510,424

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	707,018	2159,612	776,905
3	5	2-5	3687,347	10220,667	3572,227
4	10	5-10	11679,859	23004,957	12807,429
5	15	10-15	20346,159	33274,528	22004,968
6	30	15-30	28280,361	37494,210	28702,199
7	60	30-60	32153,390	38404,032	31175,759
8	90	60-90	32879,447	41700,271	32145,625
9	120	90-120	33396,147	41677,493	33799,993
10	180	120-180	33561,732	40450,712	34820,305
11	240	180-240	34120,539	40239,951	33259,133
12	360	240-360	34177,025	40748,718	33599,647

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	707,018	2159,612	776,905
3	2-5	3,5	2980,329	8061,056	2795,322
4	5-10	7,5	7992,511	12784,290	9235,202
5	10-15	12,5	8666,300	10269,570	9197,539
6	15-30	22,5	7934,202	4219,683	6697,231
7	30-60	45	3873,029	909,821	2473,559
8	60-90	75	726,057	3296,240	969,866
9	90-120	105	516,700	-22,779	1654,368
10	120-180	150	165,585	-1226,780	1020,312
11	180-240	210	558,807	-210,762	-1561,172
12	240-360	300	56,486	508,767	340,514
		sum	34177,025	40748,718	33599,647

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	707,018	2159,612	776,905
3	2-5	3,5	10431,152	28213,695	9783,627
4	5-10	7,5	59943,836	95882,176	69264,013
5	10-15	12,5	108328,756	128369,629	114969,237
6	15-30	22,5	178519,545	94942,856	150687,703
7	30-60	45	174286,287	40941,965	111310,177
8	60-90	75	54454,303	247217,992	72739,977
9	90-120	105	54253,473	-2391,791	173708,622
10	120-180	150	24837,800	-184017,012	153046,799
11	180-240	210	117349,410	-44259,930	-327846,060
12	240-360	300	16945,866	152630,104	102154,180
		sum	800057,446	559689,296	630595,181

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
23,409	13,735	18,768	18,637	3,951

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,829	2,361	0,885
7,730	20,299	7,430
45,051	90,795	46,639
93,889	153,794	99,123
427,667	580,164	433,143
1063,022	1244,431	1022,961
1143,920	1313,394	1081,789
1165,780	1367,066	1126,621
2355,562	2693,156	2344,632
2381,046	2646,016	2326,152
4805,384	5311,576	4568,888

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13489,881	15423,050	13058,263

Average AUC0-360 (µg/ml.min)		13990,398
	STDEV	1259,342

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,842	5,246	1,966
5	9,609	24,826	9,041
10	30,437	55,880	32,415
15	53,020	80,825	55,694

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,646	5,619	3,850	4,372	0,886

Table 58: Table containing the AUC, DRi and MDT values and information regarding formula 4D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	12,233	4941,238	7,164	2864,007	4,321	1511,287
3	5	44,918	18143,509	27,568	11021,798	18,940	6624,989
4	10	70,714	28563,475	56,000	22388,751	46,230	16170,898
5	15	85,624	34585,883	76,775	30694,441	67,020	23442,880
6	30	90,174	36423,716	86,556	34605,007	78,096	27317,156
7	60	91,836	37095,102	89,649	35841,429	80,975	28324,400
8	90	98,505	39789,022	96,015	38386,713	82,338	28801,242
9	120	94,814	38298,125	92,595	37019,228	83,082	29061,287
10	180	89,876	36303,245	97,579	39012,061	86,368	30210,874
11	240	99,735	40285,684	98,716	39466,282	85,850	30029,469
12	360	94,030	37981,384	92,484	36974,934	84,534	29569,150

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40392,700	39979,800	34979,142

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4941,238	2864,007	1511,287
3	5	2-5	18143,509	11021,798	6624,989
4	10	5-10	28563,475	22388,751	16170,898
5	15	10-15	34585,883	30694,441	23442,880
6	30	15-30	36423,716	34605,007	27317,156
7	60	30-60	37095,102	35841,429	28324,400
8	90	60-90	39789,022	38386,713	28801,242
9	120	90-120	38298,125	37019,228	29061,287
10	180	120-180	36303,245	39012,061	30210,874
11	240	180-240	40285,684	39466,282	30029,469
12	360	240-360	37981,384	36974,934	29569,150

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4941,238	2864,007	1511,287
3	2-5	3,5	13202,272	8157,791	5113,702
4	5-10	7,5	10419,966	11366,953	9545,909
5	10-15	12,5	6022,408	8305,691	7271,982
6	15-30	22,5	1837,833	3910,566	3874,276
7	30-60	45	671,386	1236,421	1007,245
8	60-90	75	2693,920	2545,285	476,842
9	90-120	105	-1490,897	-1367,486	260,044
10	120-180	150	-1994,880	1992,834	1149,588
11	180-240	210	3982,439	454,220	-181,405
12	240-360	300	-2304,300	-2491,347	-460,319
		sum	37981,384	36974,934	29569,150

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4941,238	2864,007	1511,287
3	2-5	3,5	46207,951	28552,267	17897,957
4	5-10	7,5	78149,742	85252,145	71594,315
5	10-15	12,5	75280,100	103821,132	90899,773
6	15-30	22,5	41351,245	87987,732	87171,203
7	30-60	45	30212,380	55638,959	45326,020
8	60-90	75	202043,968	190896,366	35763,131
9	90-120	105	-156544,198	-143585,993	27304,656
10	120-180	150	-299231,932	298925,061	172438,143
11	180-240	210	836312,221	95386,239	-38094,995
12	240-360	300	-691290,007	-747404,188	-138095,770
		sum	167432,707	58333,726	373715,719

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
4,408	1,578	12,639	6,208	4,692

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
5,505	3,224	1,944
38,577	23,444	15,701
130,086	94,015	73,316
175,881	149,372	127,406
593,319	551,242	489,764
1228,569	1189,384	1073,727
1284,806	1253,233	1102,366
1304,910	1273,118	1116,586
2493,318	2567,353	2287,575
2559,746	2649,982	2324,942
5231,665	5162,389	4600,349

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15046,381	14916,756	13213,675

Average AUC0-360 (µg/ml.min)		14392,271
	STDEV	1022,749

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	12,233	7,164	4,321
5	44,918	27,568	18,940
10	70,714	56,000	46,230
15	85,624	76,775	67,020

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,859	5,307	4,673	5,280	0,485

Table 59: Table containing the AUC, DRi and MDT values and information regarding formula 4E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,662	628,646	1,449	549,297	4,405	1844,450
3	5	9,747	3686,727	11,075	4197,824	26,231	10982,218
4	10	33,154	12540,846	31,352	11883,728	57,704	24159,585
5	15	56,111	21224,478	53,690	20350,900	80,289	33615,481
6	30	77,616	29358,911	77,072	29213,932	94,254	39462,465
7	60	86,048	32548,455	82,935	31436,002	91,349	38246,173
8	90	86,719	32802,124	85,670	32472,917	99,154	41513,790
9	120	89,993	34040,448	93,592	35475,467	102,343	42849,073
10	180	90,943	34399,769	91,570	34709,386	99,609	41704,379
11	240	93,397	35328,086	93,584	35472,543	103,378	43282,346
12	360	92,895	35138,241	91,662	34744,160	102,114	42753,289

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37825,752	37904,570	41868,067

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	628,646	549,297	1844,450
3	5	2-5	3686,727	4197,824	10982,218
4	10	5-10	12540,846	11883,728	24159,585
5	15	10-15	21224,478	20350,900	33615,481
6	30	15-30	29358,911	29213,932	39462,465
7	60	30-60	32548,455	31436,002	38246,173
8	90	60-90	32802,124	32472,917	41513,790
9	120	90-120	34040,448	35475,467	42849,073
10	180	120-180	34399,769	34709,386	41704,379
11	240	180-240	35328,086	35472,543	43282,346
12	360	240-360	35138,241	34744,160	42753,289

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	628,646	549,297	1844,450
3	2-5	3,5	3058,081	3648,527	9137,767
4	5-10	7,5	8854,118	7685,904	13177,367
5	10-15	12,5	8683,632	8467,172	9455,896
6	15-30	22,5	8134,433	8863,033	5846,984
7	30-60	45	3189,544	2222,070	-1216,292
8	60-90	75	253,669	1036,915	3267,617
9	90-120	105	1238,324	3002,550	1335,283
10	120-180	150	359,321	-766,081	-1144,695
11	180-240	210	928,317	763,157	1577,967
12	240-360	300	-189,845	-728,383	-529,057
		sum	35138,241	34744,160	42753,289

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	628,646	549,297	1844,450
3	2-5	3,5	10703,284	12769,844	31982,186
4	5-10	7,5	66405,887	57644,278	98830,253
5	10-15	12,5	108545,402	105839,648	118198,698
6	15-30	22,5	183024,738	199418,238	131557,148
7	30-60	45	143529,496	99993,148	-54733,123
8	60-90	75	19025,164	77768,606	245071,274
9	90-120	105	130024,047	315267,706	140204,690
10	120-180	150	53898,087	-114912,106	-171704,184
11	180-240	210	194946,621	160262,903	331373,107
12	240-360	300	-56953,440	-218514,952	-158717,095
		sum	853777,933	696086,611	713907,405

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
24,298	20,035	16,698	20,344	3,110

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,748	0,652	1,982
7,701	8,454	20,679
48,263	47,730	94,426
100,424	95,672	155,242
451,330	441,322	589,084
1104,736	1080,047	1252,824
1166,180	1138,082	1285,896
1192,805	1210,017	1360,104
2442,629	2499,687	2726,354
2488,585	2499,583	2740,324
5029,882	5001,642	5548,291

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14033,284	14022,887	15775,208

Average AUC0-360 (µg/ml.min)		14610,459
	STDEV	1008,715

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,662	1,449	4,405
5	9,747	11,075	26,231
10	33,154	31,352	57,704
15	56,111	53,690	80,289

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,894	3,705	5,644	4,414	0,873

Table 60: Table containing the AUC, DRi and MDT values and information regarding formula 4F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	10,454	4380,104	7,182	3033,189	2,104	829,356
3	5	36,406	15253,688	30,359	12820,741	15,346	6050,089
4	10	70,198	29412,532	63,117	26654,697	41,876	16509,031
5	15	86,751	36348,082	82,916	35015,744	64,982	25618,328
6	30	98,169	41132,341	97,250	41068,904	82,599	32563,638
7	60	93,771	39289,529	100,485	42435,068	91,297	35992,523
8	90	97,447	40829,500	100,752	42547,774	91,648	36131,071
9	120	94,189	39464,484	103,118	43547,086	96,512	38048,535
10	180	103,280	43273,763	103,684	43786,258	91,556	36094,794
11	240	103,455	43347,041	104,272	44034,556	96,534	38057,080
12	360	103,144	43216,853	95,899	40498,411	97,342	38375,791

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41899,345	42230,315	39423,591

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4380,104	3033,189	829,356
3	5	2-5	15253,688	12820,741	6050,089
4	10	5-10	29412,532	26654,697	16509,031
5	15	10-15	36348,082	35015,744	25618,328
6	30	15-30	41132,341	41068,904	32563,638
7	60	30-60	39289,529	42435,068	35992,523
8	90	60-90	40829,500	42547,774	36131,071
9	120	90-120	39464,484	43547,086	38048,535
10	180	120-180	43273,763	43786,258	36094,794
11	240	180-240	43347,041	44034,556	38057,080
12	360	240-360	43216,853	40498,411	38375,791

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4380,104	3033,189	829,356
3	2-5	3,5	10873,584	9787,553	5220,734
4	5-10	7,5	14158,844	13833,956	10458,942
5	10-15	12,5	6935,550	8361,046	9109,298
6	15-30	22,5	4784,259	6053,160	6945,310
7	30-60	45	-1842,813	1366,164	3428,885
8	60-90	75	1539,971	112,706	138,547
9	90-120	105	-1365,016	999,312	1917,464
10	120-180	150	3809,279	239,172	-1953,741
11	180-240	210	73,278	248,298	1962,286
12	240-360	300	-130,187	-3536,145	318,710
		sum	43216,853	40498,411	38375,791

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4380,104	3033,189	829,356
3	2-5	3,5	38057,544	34256,434	18272,567
4	5-10	7,5	106191,328	103754,671	78442,061
5	10-15	12,5	86694,378	104513,079	113866,223
6	15-30	22,5	107645,837	136196,108	156269,473
7	30-60	45	-82926,564	61477,386	154299,820
8	60-90	75	115497,826	8452,936	10391,059
9	90-120	105	-143326,657	104927,735	201333,757
10	120-180	150	571391,861	35875,861	-293061,081
11	180-240	210	15388,299	52142,543	412080,062
12	240-360	300	-39056,209	-1060843,527	95613,048
		sum	779937,747	-416213,587	948336,344

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
18,047	-10,277	24,712	10,827	15,169

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
4,704	3,232	0,947
31,630	25,341	11,779
119,929	105,161	64,375
176,568	164,288	120,216
624,106	608,060	498,088
1295,599	1334,709	1173,800
1290,721	1358,347	1234,881
1293,539	1376,121	1270,083
2665,832	2791,834	2538,924
2790,929	2807,417	2539,216
5578,190	5404,625	5234,651

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15871,747	15979,134	14686,959

Average AUC0-360 (µg/ml.min)		15512,614
	STDEV	717,051

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	10,454	7,182	2,104
5	36,406	30,359	15,346
10	70,198	63,117	41,876
15	86,751	82,916	64,982

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,044	5,806	4,550	5,467	0,655

Table 61: Table containing the AUC, DRi and MDT values and information regarding formula 5A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	14,265	5604,400	4,321	1654,142	11,698	4400,257
3	5	21,786	8558,904	18,423	7053,213	24,181	9095,479
4	10	42,974	16883,253	42,105	16120,005	44,374	16691,058
5	15	43,209	16975,566	42,335	16208,273	44,617	16782,368
6	30	81,245	31918,587	76,710	29368,796	78,433	29501,999
7	60	85,275	33501,912	82,749	31680,896	85,770	32261,776
8	90	85,507	33593,017	84,660	32412,681	91,277	34333,346
9	120	91,317	35875,742	85,959	32909,866	85,747	32253,288
10	180	96,549	37930,977	87,113	33351,600	88,285	33207,789
11	240	84,441	33174,127	80,848	30953,164	89,319	33596,711
12	360	97,005	38110,113	89,729	34353,106	92,377	34747,197

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39286,888	38285,539	37614,442

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	5604,400	1654,142	4400,257
3	5	2-5	8558,904	7053,213	9095,479
4	10	5-10	16883,253	16120,005	16691,058
5	15	10-15	16975,566	16208,273	16782,368
6	30	15-30	31918,587	29368,796	29501,999
7	60	30-60	33501,912	31680,896	32261,776
8	90	60-90	33593,017	32412,681	34333,346
9	120	90-120	35875,742	32909,866	32253,288
10	180	120-180	37930,977	33351,600	33207,789
11	240	180-240	33174,127	30953,164	33596,711
12	360	240-360	38110,113	34353,106	34747,197

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	5604,400	1654,142	4400,257
3	2-5	3,5	2954,503	5399,072	4695,222
4	5-10	7,5	8324,349	9066,792	7595,579
5	10-15	12,5	92,313	88,267	91,310
6	15-30	22,5	14943,021	13160,523	12719,631
7	30-60	45	1583,325	2312,100	2759,777
8	60-90	75	91,105	731,785	2071,569
9	90-120	105	2282,725	497,185	-2080,058
10	120-180	150	2055,235	441,735	954,501
11	180-240	210	-4756,850	-2398,437	388,922
12	240-360	300	4935,985	3399,942	1150,487
		sum	38110,113	34353,106	34747,197

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	5604,400	1654,142	4400,257
3	2-5	3,5	10340,762	18896,751	16433,278
4	5-10	7,5	62432,619	68000,940	56966,841
5	10-15	12,5	1153,915	1103,341	1141,380
6	15-30	22,5	336217,980	296111,770	286191,702
7	30-60	45	71249,615	104044,498	124189,971
8	60-90	75	6832,876	54883,889	155367,700
9	90-120	105	239686,172	52204,417	-218406,044
10	120-180	150	308285,223	66260,194	143175,090
11	180-240	210	-998938,483	-503671,666	81673,577
12	240-360	300	1480795,558	1019982,629	345146,071
		sum	1523660,637	1179470,907	996279,822

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
39,980	34,334	28,672	34,329	4,617

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
6,419	1,944	5,264
24,334	15,352	24,218
72,855	68,093	77,124
96,956	94,995	100,115
420,033	401,777	415,292
1124,010	1076,347	1108,365
1152,778	1130,013	1195,065
1193,564	1151,681	1194,913
2536,192	2336,469	2349,429
2443,357	2267,473	2397,645
4899,025	4605,575	4905,790

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13969,523	13149,720	13773,220

Average AUC0-360 (µg/ml.min)		13630,821
	STDEV	428,051

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	14,265	4,321	11,698
5	21,786	18,423	24,181
10	42,974	42,105	44,374
15	43,209	42,335	44,617

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,902	3,156	3,071	3,043	0,105

Table 62: Table containing the AUC, DRi and MDT values and information regarding formula 5B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	12,568	4818,299	9,165	3397,341	13,872	5534,052
3	5	26,324	10091,913	25,524	9461,536	34,737	13857,815
4	10	34,451	13207,549	46,799	17347,605	64,310	25655,546
5	15	65,186	24990,101	64,311	23839,384	81,377	32464,143
6	30	74,309	28487,782	73,302	27172,051	89,016	35511,704
7	60	74,715	28643,407	73,702	27320,370	89,502	35705,560
8	90	81,999	31435,879	81,116	30068,741	98,503	39296,142
9	120	83,707	32090,461	83,732	31038,280	93,817	37426,883
10	180	83,122	31866,375	86,413	32032,271	95,473	38087,423
11	240	84,803	32510,599	85,685	31762,281	92,995	37098,897
12	360	89,895	34462,711	91,528	33928,134	94,407	37662,415

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38336,770	37068,712	39893,530

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4818,299	3397,341	5534,052
3	5	2-5	10091,913	9461,536	13857,815
4	10	5-10	13207,549	17347,605	25655,546
5	15	10-15	24990,101	23839,384	32464,143
6	30	15-30	28487,782	27172,051	35511,704
7	60	30-60	28643,407	27320,370	35705,560
8	90	60-90	31435,879	30068,741	39296,142
9	120	90-120	32090,461	31038,280	37426,883
10	180	120-180	31866,375	32032,271	38087,423
11	240	180-240	32510,599	31762,281	37098,897
12	360	240-360	34462,711	33928,134	37662,415

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4818,299	3397,341	5534,052
3	2-5	3,5	5273,613	6064,194	8323,763
4	5-10	7,5	3115,636	7886,070	11797,730
5	10-15	12,5	11782,552	6491,779	6808,597
6	15-30	22,5	3497,682	3332,667	3047,561
7	30-60	45	155,625	148,319	193,856
8	60-90	75	2792,472	2748,371	3590,582
9	90-120	105	654,582	969,539	-1869,259
10	120-180	150	-224,086	993,991	660,540
11	180-240	210	644,224	-269,990	-988,527
12	240-360	300	1952,112	2165,853	563,518
		sum	34462,711	33928,134	37662,415

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4818,299	3397,341	5534,052
3	2-5	3,5	18457,647	21224,681	29133,172
4	5-10	7,5	23367,272	59145,522	88482,977
5	10-15	12,5	147281,895	81147,231	85107,467
6	15-30	22,5	78697,837	74985,012	68570,128
7	30-60	45	7003,108	6674,365	8723,520
8	60-90	75	209435,365	206127,834	269293,642
9	90-120	105	68731,116	101801,584	-196272,184
10	120-180	150	-33612,871	149098,598	99081,023
11	180-240	210	135287,061	-56697,906	-207590,619
12	240-360	300	585633,527	649755,863	169055,439
		sum	1245100,257	1296660,125	419118,616

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
36,129	38,218	11,128	28,492	12,307

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
5,656	4,124	6,242
26,253	23,415	32,811
68,373	81,363	111,428
112,092	124,999	163,898
470,796	464,444	575,077
1005,916	992,276	1204,999
1057,823	1045,023	1269,032
1118,516	1112,724	1298,156
2252,191	2296,957	2555,410
2266,986	2323,324	2544,311
4716,828	4784,739	5059,857

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13101,427	13253,389	14821,220

Average AUC0-360 (µg/ml.min)		13725,345
	STDEV	952,092

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	12,568	9,165	13,872
5	26,324	25,524	34,737
10	34,451	46,799	64,310
15	65,186	64,311	81,377

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,971	4,326	5,507	4,602	0,657

Table 63: Table containing the AUC, DRi and MDT values and information regarding formula 5C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,774	1709,339	8,514	3337,768	7,896	2927,288
3	5	19,796	7087,464	25,072	9828,582	24,930	9241,989
4	10	39,234	14046,602	50,209	19682,567	50,953	18888,942
5	15	65,659	23507,181	69,144	27105,361	70,126	25996,940
6	30	79,635	28510,997	80,718	31642,306	89,997	33363,535
7	60	80,968	28988,158	88,459	34676,769	85,110	31551,528
8	90	83,150	29769,431	91,330	35802,185	85,936	31857,876
9	120	84,819	30367,081	90,343	35415,445	91,128	33782,646
10	180	86,848	31093,488	94,034	36862,254	88,722	32890,718
11	240	87,419	31297,923	96,793	37943,828	91,535	33933,531
12	360	88,400	31649,150	89,152	34948,649	88,238	32711,426

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
35802,103	39201,085	37071,661

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1709,339	3337,768	2927,288
3	5	2-5	7087,464	9828,582	9241,989
4	10	5-10	14046,602	19682,567	18888,942
5	15	10-15	23507,181	27105,361	25996,940
6	30	15-30	28510,997	31642,306	33363,535
7	60	30-60	28988,158	34676,769	31551,528
8	90	60-90	29769,431	35802,185	31857,876
9	120	90-120	30367,081	35415,445	33782,646
10	180	120-180	31093,488	36862,254	32890,718
11	240	180-240	31297,923	37943,828	33933,531
12	360	240-360	31649,150	34948,649	32711,426

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1709,339	3337,768	2927,288
3	2-5	3,5	5378,124	6490,814	6314,700
4	5-10	7,5	6959,139	9853,985	9646,953
5	10-15	12,5	9460,579	7422,794	7107,998
6	15-30	22,5	5003,816	4536,946	7366,595
7	30-60	45	477,160	3034,463	-1812,007
8	60-90	75	781,273	1125,416	306,348
9	90-120	105	597,650	-386,740	1924,769
10	120-180	150	726,406	1446,809	-891,928
11	180-240	210	204,435	1081,575	1042,813
12	240-360	300	351,228	-2995,180	-1222,106
		sum	31649,150	34948,649	32711,426

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1709,339	3337,768	2927,288
3	2-5	3,5	18823,435	22717,848	22101,451
4	5-10	7,5	52193,539	73904,890	72352,148
5	10-15	12,5	118257,239	92784,920	88849,974
6	15-30	22,5	112585,861	102081,275	165748,393
7	30-60	45	21472,221	136550,842	-81540,303
8	60-90	75	58595,506	84406,183	22976,108
9	90-120	105	62753,251	-40607,704	202100,797
10	120-180	150	108960,948	217021,341	-133789,168
11	180-240	210	42931,342	227130,646	218990,829
12	240-360	300	105368,281	-898553,980	-366631,650
		sum	703650,963	20774,029	214085,867

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
22,233	0,594	6,545	9,791	9,127

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,148	3,832	3,553
16,585	22,671	22,158
66,409	84,692	85,368
118,004	134,273	136,214
490,366	505,785	540,417
1084,068	1141,942	1181,972
1107,794	1213,571	1154,557
1133,792	1226,290	1195,181
2317,511	2489,087	2427,974
2352,611	2576,159	2433,469
4747,126	5020,516	4853,880

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13436,416	14418,817	14034,743

Average AUC0-360 (µg/ml.min)		13963,325
	STDEV	495,079

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,774	8,514	7,896
5	19,796	25,072	24,930
10	39,234	50,209	50,953
15	65,659	69,144	70,126

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,405	4,711	4,805	4,640	0,171

Table 64: Table containing the AUC, DRi and MDT values and information regarding formula 5D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	6,555	2715,346	2,923	1112,448	2,168	885,434
3	5	22,376	9269,130	13,413	5105,497	13,468	5499,560
4	10	53,052	21976,725	32,244	12273,492	35,964	14685,809
5	15	75,213	31156,680	48,804	18576,844	55,750	22765,267
6	30	78,545	32537,178	67,266	25604,356	73,322	29940,484
7	60	93,946	38917,127	78,855	30015,337	83,881	34252,187
8	90	92,308	38238,272	84,194	32047,772	90,769	37065,197
9	120	96,549	39995,322	90,606	34488,405	94,157	38448,604
10	180	95,385	39513,164	93,986	35774,840	100,826	41171,677
11	240	102,283	42370,680	90,832	34574,373	94,137	38440,480
12	360	93,525	38742,691	85,733	32633,590	91,378	37313,605

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41424,782	38064,170	40834,458

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2715,346	1112,448	885,434
3	5	2-5	9269,130	5105,497	5499,560
4	10	5-10	21976,725	12273,492	14685,809
5	15	10-15	31156,680	18576,844	22765,267
6	30	15-30	32537,178	25604,356	29940,484
7	60	30-60	38917,127	30015,337	34252,187
8	90	60-90	38238,272	32047,772	37065,197
9	120	90-120	39995,322	34488,405	38448,604
10	180	120-180	39513,164	35774,840	41171,677
11	240	180-240	42370,680	34574,373	38440,480
12	360	240-360	38742,691	32633,590	37313,605

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2715,346	1112,448	885,434
3	2-5	3,5	6553,785	3993,050	4614,126
4	5-10	7,5	12707,595	7167,994	9186,250
5	10-15	12,5	9179,955	6303,352	8079,457
6	15-30	22,5	1380,498	7027,512	7175,218
7	30-60	45	6379,950	4410,981	4311,703
8	60-90	75	-678,855	2032,436	2813,010
9	90-120	105	1757,049	2440,632	1383,407
10	120-180	150	-482,158	1286,435	2723,073
11	180-240	210	2857,516	-1200,467	-2731,197
12	240-360	300	-3627,990	-1940,783	-1126,875
		sum	38742,691	32633,590	37313,605

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2715,346	1112,448	885,434
3	2-5	3,5	22938,247	13975,674	16149,440
4	5-10	7,5	95306,963	53759,958	68896,873
5	10-15	12,5	114749,435	78791,906	100993,215
6	15-30	22,5	31061,194	158119,009	161442,397
7	30-60	45	287097,728	198494,136	194026,644
8	60-90	75	-50914,125	152432,688	210975,739
9	90-120	105	184490,171	256266,403	145257,698
10	120-180	150	-72323,671	192965,262	408460,984
11	180-240	210	600078,460	-252098,013	-573551,442
12	240-360	300	-1088396,856	-582234,837	-338062,562
		sum	126802,891	271584,632	395474,419

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
3,273	8,322	10,599	7,398	3,061

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,950	1,315	0,976
19,528	11,026	10,554
84,856	51,364	55,611
144,298	91,179	103,179
518,933	391,737	435,617
1164,319	986,316	1061,115
1257,216	1100,578	1178,888
1274,785	1179,900	1248,255
2591,117	2491,986	2632,272
2668,528	2495,035	2632,003
5286,838	4767,252	5008,908

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15013,367	13567,690	14367,377

Average AUC0-360 (µg/ml.min)		14316,145
	STDEV	724,199

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	6,555	2,923	2,168
5	22,376	13,413	13,468
10	53,052	32,244	35,964
15	75,213	48,804	55,750

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,212	3,379	3,891	4,161	0,772

Table 65: Table containing the AUC, DRi and MDT values and information regarding formula 5E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,168	810,694	1,851	712,368	2,723	967,824
3	5	10,754	4020,713	11,109	4276,608	12,590	4474,502
4	10	30,361	11351,363	31,327	12059,662	33,065	11751,314
5	15	52,049	19459,798	50,784	19549,865	53,563	19035,872
6	30	68,708	25688,419	68,631	26420,275	71,073	25259,177
7	60	77,381	28930,838	77,185	29713,020	78,545	27914,659
8	90	80,790	30205,547	82,332	31694,434	80,399	28573,331
9	120	85,542	31981,940	86,731	33387,840	84,171	29914,015
10	180	90,930	33996,401	91,471	35212,572	87,752	31186,617
11	240	90,651	33892,138	90,072	34673,952	85,520	30393,329
12	360	92,315	34514,392	95,051	36590,873	86,019	30570,663

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37387,603	38495,848	35539,527

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	810,694	712,368	967,824
3	5	2-5	4020,713	4276,608	4474,502
4	10	5-10	11351,363	12059,662	11751,314
5	15	10-15	19459,798	19549,865	19035,872
6	30	15-30	25688,419	26420,275	25259,177
7	60	30-60	28930,838	29713,020	27914,659
8	90	60-90	30205,547	31694,434	28573,331
9	120	90-120	31981,940	33387,840	29914,015
10	180	120-180	33996,401	35212,572	31186,617
11	240	180-240	33892,138	34673,952	30393,329
12	360	240-360	34514,392	36590,873	30570,663

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	810,694	712,368	967,824
3	2-5	3,5	3210,019	3564,240	3506,678
4	5-10	7,5	7330,650	7783,054	7276,812
5	10-15	12,5	8108,435	7490,203	7284,558
6	15-30	22,5	6228,621	6870,410	6223,305
7	30-60	45	3242,419	3292,744	2655,482
8	60-90	75	1274,709	1981,414	658,671
9	90-120	105	1776,394	1693,405	1340,684
10	120-180	150	2014,460	1824,732	1272,602
11	180-240	210	-104,263	-538,619	-793,288
12	240-360	300	622,254	1916,920	177,333
		sum	34514,392	36590,873	30570,663

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	810,694	712,368	967,824
3	2-5	3,5	11235,066	12474,841	12273,374
4	5-10	7,5	54979,876	58372,905	54576,090
5	10-15	12,5	101355,442	93627,542	91056,976
6	15-30	22,5	140143,968	154584,227	140024,361
7	30-60	45	145908,834	148173,502	119496,694
8	60-90	75	95603,164	148606,073	49400,342
9	90-120	105	186521,338	177807,572	140771,868
10	120-180	150	302169,041	273709,803	190890,340
11	180-240	210	-21895,204	-113110,049	-166590,477
12	240-360	300	186676,176	575076,130	53200,000
		sum	1203508,396	1530034,914	686067,392

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
34,870	41,815	22,442	33,042	8,014

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,976	0,833	1,225
8,723	8,748	10,337
46,255	47,741	51,363
92,711	92,375	97,457
407,556	403,028	420,647
986,102	984,261	1009,927
1067,655	1076,740	1072,873
1122,740	1141,176	1110,846
2382,361	2405,728	2320,961
2451,335	2450,831	2339,168
4940,077	4998,332	4631,541

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13506,489	13609,794	13066,344

Average AUC0-360 (µg/ml.min)		13394,209
	STDEV	288,599

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,168	1,851	2,723
5	10,754	11,109	12,590
10	30,361	31,327	33,065
15	52,049	50,784	53,563

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,568	3,524	3,687	3,593	0,069

Table 66: Table containing the AUC, DRi and MDT values and information regarding formula 5F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,491	561,528	4,201	1889,560	1,162	437,499
3	5	5,498	2070,679	16,702	7513,001	6,183	2327,308
4	10	18,001	6779,832	41,250	18555,210	19,138	7203,917
5	15	33,555	12638,144	62,614	28165,187	36,078	13580,246
6	30	55,321	20835,781	77,812	35001,828	58,841	22148,351
7	60	72,339	27245,370	92,271	41505,435	76,643	28849,399
8	90	79,610	29983,950	94,916	42695,303	84,533	31819,340
9	120	77,495	29187,167	99,752	44870,744	90,104	33916,219
10	180	88,164	33205,465	111,067	49960,688	91,691	34513,576
11	240	84,849	31957,107	98,390	44258,180	92,014	34635,174
12	360	87,215	32848,013	99,584	44795,178	92,941	34984,033

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37663,461	44982,306	37641,112

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	561,528	1889,560	437,499
3	5	2-5	2070,679	7513,001	2327,308
4	10	5-10	6779,832	18555,210	7203,917
5	15	10-15	12638,144	28165,187	13580,246
6	30	15-30	20835,781	35001,828	22148,351
7	60	30-60	27245,370	41505,435	28849,399
8	90	60-90	29983,950	42695,303	31819,340
9	120	90-120	29187,167	44870,744	33916,219
10	180	120-180	33205,465	49960,688	34513,576
11	240	180-240	31957,107	44258,180	34635,174
12	360	240-360	32848,013	44795,178	34984,033

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	561,528	1889,560	437,499
3	2-5	3,5	1509,151	5623,441	1889,809
4	5-10	7,5	4709,153	11042,209	4876,610
5	10-15	12,5	5858,312	9609,977	6376,328
6	15-30	22,5	8197,637	6836,641	8568,106
7	30-60	45	6409,588	6503,607	6701,047
8	60-90	75	2738,580	1189,869	2969,941
9	90-120	105	-796,783	2175,441	2096,879
10	120-180	150	4018,298	5089,944	597,357
11	180-240	210	-1248,358	-5702,508	121,598
12	240-360	300	890,906	536,998	348,858
		sum	32848,013	44795,178	34984,033

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	561,528	1889,560	437,499
3	2-5	3,5	5282,028	19682,044	6614,332
4	5-10	7,5	35318,646	82816,565	36574,572
5	10-15	12,5	73228,906	120124,718	79704,104
6	15-30	22,5	184446,843	153824,417	192782,378
7	30-60	45	288431,473	292662,305	301547,132
8	60-90	75	205393,519	89240,150	222745,611
9	90-120	105	-83662,213	228421,261	220172,286
10	120-180	150	602744,719	763491,597	89603,590
11	180-240	210	-262155,271	-1197526,626	25535,545
12	240-360	300	267271,921	161099,257	104657,500
		sum	1316862,100	715725,248	1280374,548

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
40,090	15,978	36,599	30,889	10,640

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,671	1,890	0,523
4,717	14,109	4,958
26,436	65,196	28,486
58,001	116,847	62,119
299,958	473,939	320,352
861,705	1148,060	914,518
1025,657	1263,508	1087,943
1060,458	1314,007	1178,804
2236,386	2846,062	2454,237
2335,672	2827,678	2480,023
4645,718	5345,303	4993,791

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12555,379	15416,600	13525,755

Average AUC0-360 (µg/ml.min)		13832,578
	STDEV	1455,078

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,491	4,201	1,162
5	5,498	16,702	6,183
10	18,001	41,250	19,138
15	33,555	62,614	36,078

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,273	4,324	2,449	3,015	0,928

Table 67: Table containing the AUC, DRi and MDT values and information regarding formula 6A evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,789	2963,232	15,018	5263,556	2,338	794,627
3	5	21,892	8329,192	14,054	4925,562	12,906	4386,306
4	10	44,074	16768,556	35,203	12338,080	30,604	10401,482
5	15	61,034	23220,824	53,006	18577,582	50,509	17166,300
6	30	78,055	29696,642	69,693	24426,080	67,702	23009,889
7	60	86,849	33042,611	82,146	28790,359	77,933	26486,892
8	90	91,103	34661,019	81,612	28603,272	78,392	26642,883
9	120	93,941	35740,683	82,125	28782,925	77,689	26403,913
10	180	92,514	35197,905	84,751	29703,322	80,422	27332,780
11	240	92,191	35074,797	85,129	29835,912	81,655	27751,981
12	360	91,555	34833,127	83,897	29404,281	83,021	28216,180

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38045,994	35047,891	33986,776

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2963,232	5263,556	794,627
3	5	2-5	8329,192	4925,562	4386,306
4	10	5-10	16768,556	12338,080	10401,482
5	15	10-15	23220,824	18577,582	17166,300
6	30	15-30	29696,642	24426,080	23009,889
7	60	30-60	33042,611	28790,359	26486,892
8	90	60-90	34661,019	28603,272	26642,883
9	120	90-120	35740,683	28782,925	26403,913
10	180	120-180	35197,905	29703,322	27332,780
11	240	180-240	35074,797	29835,912	27751,981
12	360	240-360	34833,127	29404,281	28216,180

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2963,232	5263,556	794,627
3	2-5	3,5	5365,960	-337,994	3591,679
4	5-10	7,5	8439,364	7412,517	6015,176
5	10-15	12,5	6452,268	6239,503	6764,818
6	15-30	22,5	6475,818	5848,498	5843,589
7	30-60	45	3345,969	4364,279	3477,004
8	60-90	75	1618,408	-187,087	155,991
9	90-120	105	1079,664	179,653	-238,970
10	120-180	150	-542,778	920,397	928,868
11	180-240	210	-123,108	132,589	419,201
12	240-360	300	-241,670	-431,631	464,199
		sum	34833,127	29404,281	28216,180

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2963,232	5263,556	794,627
3	2-5	3,5	18780,859	-1182,978	12570,876
4	5-10	7,5	63295,233	55593,881	45113,821
5	10-15	12,5	80653,344	77993,784	84560,223
6	15-30	22,5	145705,909	131591,201	131480,760
7	30-60	45	150568,622	196392,568	156465,160
8	60-90	75	121380,598	-14031,547	11699,309
9	90-120	105	113364,679	18863,554	-25091,891
10	120-180	150	-81416,719	138059,582	139330,141
11	180-240	210	-25852,659	27843,760	88032,157
12	240-360	300	-72500,890	-129489,173	139259,574
		sum	516942,208	506898,186	784214,757

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
14,841	17,239	27,793	19,958	5,626

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,505	6,758	1,052
20,035	19,624	10,290
74,213	55,414	48,949
118,246	99,236	91,252
469,422	414,112	398,963
1113,100	1024,915	983,039
1201,176	1105,365	1055,193
1249,045	1105,222	1053,545
2517,140	2252,816	2134,493
2493,512	2293,375	2188,040
4961,137	4563,713	4446,260

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14220,532	12940,549	12411,076

Average AUC0-360 (µg/ml.min)		13190,719
	STDEV	930,307

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,789	15,018	2,338
5	21,892	14,054	12,906
10	44,074	35,203	30,604
15	61,034	53,006	50,509

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,146	3,330	3,460	3,645	0,358

Table 68: Table containing the AUC, DRi and MDT values and information regarding formula 6B evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,135	802,433	2,272	865,123	3,720	1441,888
3	5	9,259	3480,486	12,110	4610,930	16,857	6534,095
4	10	24,388	9167,461	32,295	12296,988	44,230	17144,379
5	15	46,773	17582,305	54,484	20745,604	67,394	26123,031
6	30	69,303	26051,216	74,914	28524,892	80,678	31272,248
7	60	80,673	30325,138	83,909	31949,873	92,936	36023,809
8	90	83,092	31234,579	86,986	33121,232	91,003	35274,448
9	120	84,207	31653,529	87,800	33431,470	88,619	34350,168
10	180	83,177	31266,367	90,151	34326,529	88,069	34136,979
11	240	85,582	32170,627	87,619	33362,493	91,141	35327,967
12	360	90,571	34045,946	90,900	34611,547	95,708	37098,282

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37590,315	38076,673	38761,842

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	802,433	865,123	1441,888
3	5	2-5	3480,486	4610,930	6534,095
4	10	5-10	9167,461	12296,988	17144,379
5	15	10-15	17582,305	20745,604	26123,031
6	30	15-30	26051,216	28524,892	31272,248
7	60	30-60	30325,138	31949,873	36023,809
8	90	60-90	31234,579	33121,232	35274,448
9	120	90-120	31653,529	33431,470	34350,168
10	180	120-180	31266,367	34326,529	34136,979
11	240	180-240	32170,627	33362,493	35327,967
12	360	240-360	34045,946	34611,547	37098,282

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	802,433	865,123	1441,888
3	2-5	3,5	2678,053	3745,807	5092,207
4	5-10	7,5	5686,975	7686,058	10610,284
5	10-15	12,5	8414,844	8448,617	8978,652
6	15-30	22,5	8468,911	7779,288	5149,217
7	30-60	45	4273,922	3424,980	4751,561
8	60-90	75	909,441	1171,360	-749,361
9	90-120	105	418,950	310,237	-924,281
10	120-180	150	-387,162	895,060	-213,189
11	180-240	210	904,260	-964,036	1190,988
12	240-360	300	1875,319	1249,054	1770,316
		sum	34045,946	34611,547	37098,282

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	802,433	865,123	1441,888
3	2-5	3,5	9373,187	13110,325	17822,724
4	5-10	7,5	42652,309	57645,433	79577,127
5	10-15	12,5	105185,556	105607,710	112233,153
6	15-30	22,5	190550,497	175033,977	115857,385
7	30-60	45	192326,481	154124,115	213820,242
8	60-90	75	68208,070	87851,986	-56202,061
9	90-120	105	43989,739	32574,914	-97049,474
10	120-180	150	-58074,295	134258,946	-31978,302
11	180-240	210	189894,628	-202447,643	250107,417
12	240-360	300	562595,810	374716,340	531094,666
		sum	1347504,415	933341,227	1136724,765

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
39,579	26,966	30,641	32,395	5,297

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,961	1,022	1,674
7,691	9,708	13,889
37,853	49,956	68,723
80,056	97,626	125,577
391,758	436,719	499,742
1012,336	1072,060	1171,896
1105,413	1153,541	1241,590
1129,266	1179,806	1212,445
2259,674	2402,345	2385,275
2278,245	2399,899	2419,330
4756,139	4820,009	5044,932

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13059,391	13622,690	14185,073

Average AUC0-360 (µg/ml.min)		13622,385
	STDEV	562,841

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,135	2,272	3,720
5	9,259	12,110	16,857
10	24,388	32,295	44,230
15	46,773	54,484	67,394

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,135	3,739	4,684	3,853	0,638

Table 69: Table containing the AUC, DRi and MDT values and information regarding formula 6C evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,277	513,872	1,394	567,013	1,441	575,260
3	5	9,089	3657,959	8,480	3449,604	5,899	2354,771
4	10	27,235	10961,375	27,349	11124,806	22,932	9154,291
5	15	46,326	18645,130	47,683	19395,864	47,725	19051,148
6	30	66,994	26963,712	68,042	27677,474	66,630	26597,911
7	60	80,320	32327,102	83,121	33810,957	84,690	33806,995
8	90	82,139	33059,388	86,100	35023,017	86,338	34465,102
9	120	91,793	36944,665	99,040	40286,573	93,223	37213,439
10	180	99,377	39997,327	100,437	40854,847	97,436	38895,374
11	240	94,428	38005,173	96,611	39298,351	98,565	39345,767
12	360	87,888	35373,046	99,713	40560,475	93,731	37416,351

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40247,879	40677,036	39918,712

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	513,872	567,013	575,260
3	5	2-5	3657,959	3449,604	2354,771
4	10	5-10	10961,375	11124,806	9154,291
5	15	10-15	18645,130	19395,864	19051,148
6	30	15-30	26963,712	27677,474	26597,911
7	60	30-60	32327,102	33810,957	33806,995
8	90	60-90	33059,388	35023,017	34465,102
9	120	90-120	36944,665	40286,573	37213,439
10	180	120-180	39997,327	40854,847	38895,374
11	240	180-240	38005,173	39298,351	39345,767
12	360	240-360	35373,046	40560,475	37416,351

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	513,872	567,013	575,260
3	2-5	3,5	3144,087	2882,591	1779,511
4	5-10	7,5	7303,417	7675,201	6799,520
5	10-15	12,5	7683,755	8271,058	9896,857
6	15-30	22,5	8318,582	8281,610	7546,763
7	30-60	45	5363,390	6133,482	7209,083
8	60-90	75	732,286	1212,060	658,108
9	90-120	105	3885,277	5263,557	2748,337
10	120-180	150	3052,662	568,273	1681,935
11	180-240	210	-1992,154	-1556,495	450,393
12	240-360	300	-2632,127	1262,123	-1929,416
		sum	35373,046	40560,475	37416,351

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	513,872	567,013	575,260
3	2-5	3,5	11004,303	10089,069	6228,290
4	5-10	7,5	54775,624	57564,010	50996,401
5	10-15	12,5	96046,940	103388,228	123710,710
6	15-30	22,5	187168,085	186336,231	169802,172
7	30-60	45	241352,571	276006,703	324408,755
8	60-90	75	54921,415	90904,502	49358,076
9	90-120	105	407954,080	552673,460	288575,372
10	120-180	150	457899,349	85240,990	252290,293
11	180-240	210	-418352,353	-326864,046	94582,527
12	240-360	300	-789638,086	378637,011	-578824,910
		sum	303645,802	1414543,171	781702,946

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
8,584	34,875	20,892	21,450	10,740

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,575	0,627	0,648
6,997	6,665	4,954
40,864	40,308	32,435
82,755	84,411	79,489
382,455	390,571	385,948
994,370	1020,347	1021,408
1096,601	1142,240	1154,438
1174,043	1249,697	1212,038
2580,799	2692,942	2573,903
2616,371	2660,145	2646,016
4922,525	5300,751	5191,994

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13898,354	14588,704	14303,273

Average AUC0-360 (µg/ml.min)		14263,444
	STDEV	346,894

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,277	1,394	1,441
5	9,089	8,480	5,899
10	27,235	27,349	22,932
15	46,326	47,683	47,725

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,204	3,288	3,206	3,233	0,039

Table 70: Table containing the AUC, DRi and MDT values and information regarding formula 6D evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,568	591,211	1,584	589,112	1,372	474,218
3	5	8,011	3021,303	7,710	2867,679	4,426	1529,533
4	10	24,034	9063,953	24,465	9099,831	15,453	5339,677
5	15	44,063	16617,097	45,005	16739,614	31,354	10834,199
6	30	65,148	24568,993	66,454	24717,625	55,979	19343,078
7	60	82,639	31165,260	79,599	29607,037	72,287	24978,201
8	90	84,500	31867,034	83,448	31038,783	77,421	26752,103
9	120	93,117	35116,912	91,377	33987,936	83,326	28792,453
10	180	89,984	33935,072	88,465	32904,894	83,102	28715,164
11	240	90,056	33962,567	86,937	32336,296	85,319	29481,235
12	360	87,738	33088,161	91,840	34160,077	84,603	29233,854

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37712,530	37195,203	34554,161

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	591,211	589,112	474,218
3	5	2-5	3021,303	2867,679	1529,533
4	10	5-10	9063,953	9099,831	5339,677
5	15	10-15	16617,097	16739,614	10834,199
6	30	15-30	24568,993	24717,625	19343,078
7	60	30-60	31165,260	29607,037	24978,201
8	90	60-90	31867,034	31038,783	26752,103
9	120	90-120	35116,912	33987,936	28792,453
10	180	120-180	33935,072	32904,894	28715,164
11	240	180-240	33962,567	32336,296	29481,235
12	360	240-360	33088,161	34160,077	29233,854

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	591,211	589,112	474,218
3	2-5	3,5	2430,092	2278,567	1055,315
4	5-10	7,5	6042,651	6232,152	3810,144
5	10-15	12,5	7553,144	7639,783	5494,523
6	15-30	22,5	7951,895	7978,011	8508,879
7	30-60	45	6596,267	4889,412	5635,123
8	60-90	75	701,775	1431,747	1773,902
9	90-120	105	3249,878	2949,152	2040,350
10	120-180	150	-1181,840	-1083,041	-77,289
11	180-240	210	27,495	-568,598	766,071
12	240-360	300	-874,406	1823,781	-247,381
		sum	33088,161	34160,077	29233,854

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	591,211	589,112	474,218
3	2-5	3,5	8505,323	7974,985	3693,602
4	5-10	7,5	45319,880	46741,137	28576,078
5	10-15	12,5	94414,300	95497,292	68681,533
6	15-30	22,5	178917,640	179505,240	191449,770
7	30-60	45	296832,025	220023,527	253580,536
8	60-90	75	52633,106	107381,007	133042,632
9	90-120	105	341237,153	309661,003	214236,765
10	120-180	150	-177275,981	-162456,207	-11593,289
11	180-240	210	5773,953	-119405,619	160874,864
12	240-360	300	-262321,758	547134,340	-74214,270
		sum	584626,851	1232645,817	968802,438

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
17,669	36,084	33,140	28,964	8,077

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,705	0,713	0,618
6,466	6,273	3,914
36,051	36,197	22,364
76,609	78,154	52,658
368,586	376,173	294,750
997,563	985,857	865,796
1128,187	1100,570	1010,528
1198,916	1180,072	1085,038
2471,862	2427,875	2246,771
2430,540	2367,929	2273,681
4800,446	4826,972	4587,892

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13515,932	13386,785	12444,010

Average AUC0-360 (µg/ml.min)		13115,576
	STDEV	585,167

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,568	1,584	1,372
5	8,011	7,710	4,426
10	24,034	24,465	15,453
15	44,063	45,005	31,354

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,998	3,065	2,098	2,721	0,441

Table 71: Table containing the AUC, DRi and MDT values and information regarding formula 6E evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,611	3016,510	4,183	1571,198	5,228	1954,676
3	5	26,079	10336,201	15,944	5988,487	16,429	6142,257
4	10	51,920	20578,462	35,320	13266,118	34,939	13062,504
5	15	70,586	27976,636	53,207	19984,559	53,794	20111,647
6	30	82,335	32633,114	70,072	26319,047	69,595	26019,299
7	60	88,623	35125,490	82,088	30832,124	82,100	30694,309
8	90	91,710	36349,066	87,225	32761,770	86,503	32340,636
9	120	95,390	37807,378	89,164	33490,176	88,623	33133,147
10	180	96,103	38090,328	88,853	33373,314	91,953	34378,228
11	240	97,864	38787,947	89,828	33739,410	88,481	33079,894
12	360	95,849	37989,392	92,741	34833,462	92,313	34512,484

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39634,730	37560,021	37386,570

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3016,510	1571,198	1954,676
3	5	2-5	10336,201	5988,487	6142,257
4	10	5-10	20578,462	13266,118	13062,504
5	15	10-15	27976,636	19984,559	20111,647
6	30	15-30	32633,114	26319,047	26019,299
7	60	30-60	35125,490	30832,124	30694,309
8	90	60-90	36349,066	32761,770	32340,636
9	120	90-120	37807,378	33490,176	33133,147
10	180	120-180	38090,328	33373,314	34378,228
11	240	180-240	38787,947	33739,410	33079,894
12	360	240-360	37989,392	34833,462	34512,484

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3016,510	1571,198	1954,676
3	2-5	3,5	7319,691	4417,289	4187,581
4	5-10	7,5	10242,261	7277,631	6920,247
5	10-15	12,5	7398,175	6718,441	7049,143
6	15-30	22,5	4656,477	6334,488	5907,651
7	30-60	45	2492,377	4513,076	4675,011
8	60-90	75	1223,576	1929,646	1646,327
9	90-120	105	1458,312	728,406	792,511
10	120-180	150	282,950	-116,862	1245,080
11	180-240	210	697,619	366,096	-1298,334
12	240-360	300	-798,555	1094,052	1432,590
		sum	37989,392	34833,462	34512,484

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3016,510	1571,198	1954,676
3	2-5	3,5	25618,918	15460,511	14656,534
4	5-10	7,5	76816,956	54582,235	51901,853
5	10-15	12,5	92477,182	83980,512	88114,291
6	15-30	22,5	104770,740	142525,990	132922,158
7	30-60	45	112156,945	203088,426	210375,486
8	60-90	75	91768,191	144723,483	123474,496
9	90-120	105	153122,753	76482,615	83213,692
10	120-180	150	42442,524	-17529,275	186762,070
11	180-240	210	146499,927	76880,094	-272650,056
12	240-360	300	-239566,367	328215,569	429776,871
		sum	609124,280	1109981,359	1050502,072

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
16,034	31,865	30,438	26,113	7,150

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,425	1,882	2,353
22,740	13,586	14,619
87,749	57,672	57,789
137,820	99,593	99,824
516,108	416,067	416,438
1153,964	1027,077	1023,942
1217,249	1142,861	1138,071
1262,923	1190,629	1182,104
2585,155	2403,239	2437,783
2618,554	2412,197	2435,860
5230,232	4929,357	4881,417

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14835,917	13694,159	13690,201

Average AUC0-360 (µg/ml.min)		14073,426
	STDEV	660,340

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,611	4,183	5,228
5	26,079	15,944	16,429
10	51,920	35,320	34,939
15	70,586	53,207	53,794

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,852	3,646	3,635	4,045	0,571

Table 72: Table containing the AUC, DRi and MDT values and information regarding formula 6F evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,583	1029,195	5,709	2191,318	8,869	3578,887
3	5	14,546	5795,610	22,506	8638,389	27,861	11242,968
4	10	41,750	16634,327	48,765	18717,582	53,921	21759,371
5	15	65,784	26209,837	69,589	26710,302	73,181	29531,619
6	30	81,082	32305,077	83,744	32143,534	88,986	35909,393
7	60	91,937	36629,875	93,627	35936,931	96,306	38863,468
8	90	91,783	36568,491	93,602	35927,120	99,640	40208,913
9	120	92,456	36836,736	93,708	35967,861	90,618	36568,149
10	180	91,859	36598,820	94,297	36193,845	95,594	38576,188
11	240	98,376	39195,472	94,773	36376,584	94,507	38137,712
12	360	92,173	36723,875	92,197	35387,869	96,192	38817,416

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39842,397	38382,961	40354,194

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1029,195	2191,318	3578,887
3	5	2-5	5795,610	8638,389	11242,968
4	10	5-10	16634,327	18717,582	21759,371
5	15	10-15	26209,837	26710,302	29531,619
6	30	15-30	32305,077	32143,534	35909,393
7	60	30-60	36629,875	35936,931	38863,468
8	90	60-90	36568,491	35927,120	40208,913
9	120	90-120	36836,736	35967,861	36568,149
10	180	120-180	36598,820	36193,845	38576,188
11	240	180-240	39195,472	36376,584	38137,712
12	360	240-360	36723,875	35387,869	38817,416

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1029,195	2191,318	3578,887
3	2-5	3,5	4766,415	6447,071	7664,081
4	5-10	7,5	10838,718	10079,193	10516,403
5	10-15	12,5	9575,510	7992,720	7772,248
6	15-30	22,5	6095,240	5433,232	6377,774
7	30-60	45	4324,798	3793,397	2954,075
8	60-90	75	-61,384	-9,810	1345,445
9	90-120	105	268,245	40,741	-3640,764
10	120-180	150	-237,916	225,984	2008,039
11	180-240	210	2596,651	182,739	-438,476
12	240-360	300	-2471,597	-988,715	679,705
		sum	36723,875	35387,869	38817,416

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1029,195	2191,318	3578,887
3	2-5	3,5	16682,451	22564,748	26824,284
4	5-10	7,5	81290,384	75593,949	78873,019
5	10-15	12,5	119693,872	99908,994	97153,099
6	15-30	22,5	137142,896	122247,726	143499,921
7	30-60	45	194615,889	170702,854	132933,373
8	60-90	75	-4603,787	-735,781	100908,357
9	90-120	105	28165,758	4277,783	-382280,171
10	120-180	150	-35687,340	33897,625	301205,787
11	180-240	210	545296,728	38375,206	-92080,028
12	240-360	300	-741479,081	-296614,559	203911,418
		sum	342146,966	272409,864	614527,947

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
9,317	7,698	15,831	10,949	3,515

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,162	2,569	3,991
11,562	19,045	24,792
63,334	80,180	92,004
120,976	133,149	142,990
495,673	517,500	547,312
1167,879	1197,258	1250,717
1240,109	1263,796	1322,635
1243,613	1264,340	1284,241
2488,254	2538,061	2513,862
2568,176	2552,437	2566,369
5144,827	5048,178	5148,879

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14545,564	14616,513	14897,792

Average AUC0-360 (µg/ml.min)		14686,623
	STDEV	186,286

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,583	5,709	8,869
5	14,546	22,506	27,861
10	41,750	48,765	53,921
15	65,784	69,589	73,181

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,587	4,808	4,996	4,797	0,167

Table 73: Table containing the AUC, DRi and MDT values and information regarding formula 1A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	28,739	12135,238	30,353	11226,058	47,535	20831,515
3	5	50,754	21431,126	50,177	18558,039	64,577	28300,105
4	10	60,827	25684,357	58,982	21814,888	72,005	31555,084
5	15	70,452	29748,502	66,207	24487,089	79,350	34774,048
6	30	70,835	29910,310	66,567	24620,106	79,781	34963,056
7	60	78,328	33074,181	71,884	26586,508	85,057	37275,079
8	90	85,265	36003,254	79,290	29325,818	91,925	40285,144
9	120	94,793	40026,700	79,935	29564,538	93,788	41101,451
10	180	100,412	42399,300	85,998	31806,952	108,207	47420,154
11	240	104,259	44023,830	91,322	33776,020	100,784	44167,235
12	360	104,134	43970,866	90,549	33489,929	101,767	44598,099

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42225,300	36985,500	43823,700

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	12135,238	11226,058	20831,515
3	5	2-5	21431,126	18558,039	28300,105
4	10	5-10	25684,357	21814,888	31555,084
5	15	10-15	29748,502	24487,089	34774,048
6	30	15-30	29910,310	24620,106	34963,056
7	60	30-60	33074,181	26586,508	37275,079
8	90	60-90	36003,254	29325,818	40285,144
9	120	90-120	40026,700	29564,538	41101,451
10	180	120-180	42399,300	31806,952	47420,154
11	240	180-240	44023,830	33776,020	44167,235
12	360	240-360	43970,866	33489,929	44598,099

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	12135,238	11226,058	20831,515
3	2-5	3,5	9295,888	7331,981	7468,590
4	5-10	7,5	4253,231	3256,849	3254,979
5	10-15	12,5	4064,145	2672,201	3218,964
6	15-30	22,5	161,808	133,017	189,008
7	30-60	45	3163,870	1966,402	2312,023
8	60-90	75	2929,073	2739,311	3010,064
9	90-120	105	4023,446	238,719	816,307
10	120-180	150	2372,600	2242,414	6318,703
11	180-240	210	1624,531	1969,068	-3252,920
12	240-360	300	-52,964	-286,091	430,865
		sum	43970,866	33489,929	44598,099

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	12135,238	11226,058	20831,515
3	2-5	3,5	32535,607	25661,934	26140,065
4	5-10	7,5	31899,233	24426,366	24412,344
5	10-15	12,5	50801,814	33402,511	40237,055
6	15-30	22,5	3640,681	2992,880	4252,684
7	30-60	45	142374,172	88488,083	104041,035
8	60-90	75	219680,512	205448,288	225754,815
9	90-120	105	422461,781	25065,530	85712,286
10	120-180	150	355889,946	336362,118	947805,458
11	180-240	210	341151,440	413504,374	-683113,123
12	240-360	300	-15889,224	-85827,364	129259,356
		sum	1596681,200	1080750,778	925333,489

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
36,312	32,271	20,748	29,777	6,594

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
12,933	13,659	21,391
53,658	54,357	75,676
125,529	122,804	153,655
147,689	140,838	170,274
476,843	448,113	537,067
1006,850	934,541	1112,657
1104,250	1020,422	1194,631
1215,390	1074,772	1253,567
2635,271	2240,108	2726,930
2763,064	2393,830	2821,372
5626,619	4910,521	5468,876

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15168,095	13353,965	15536,096

Average AUC0-360 (µg/ml.min)	14686,052
STDEV	1168,203

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	28,739	30,353	47,535
5	50,754	50,177	64,577
10	60,827	58,982	72,005
15	70,452	66,207	79,350

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,205	3,873	4,303	4,127	0,184

Table 74: Table containing the AUC, DRi and MDT values and information regarding formula 1B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	38,030	15728,180	63,581	27386,196	52,314	22170,757
3	5	19,613	8111,590	78,622	33864,876	79,503	33693,442
4	10	73,080	30224,238	83,583	36001,848	93,206	39500,705
5	15	77,983	32251,817	89,611	38598,259	97,252	41215,463
6	30	78,408	32427,725	90,098	38808,034	97,781	41439,862
7	60	83,202	34410,505	96,729	41664,092	96,435	40869,398
8	90	91,440	37817,450	106,330	45799,606	104,123	44127,562
9	120	98,370	40683,501	100,986	43497,797	98,140	41591,823
10	180	101,150	41833,446	106,354	45810,117	102,154	43293,131
11	240	100,983	41764,377	104,634	45069,104	102,924	43619,500
12	360	102,722	42483,460	101,391	43672,376	104,643	44347,604

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41357,700	43073,100	42380,100

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	15728,180	27386,196	22170,757
3	5	2-5	8111,590	33864,876	33693,442
4	10	5-10	30224,238	36001,848	39500,705
5	15	10-15	32251,817	38598,259	41215,463
6	30	15-30	32427,725	38808,034	41439,862
7	60	30-60	34410,505	41664,092	40869,398
8	90	60-90	37817,450	45799,606	44127,562
9	120	90-120	40683,501	43497,797	41591,823
10	180	120-180	41833,446	45810,117	43293,131
11	240	180-240	41764,377	45069,104	43619,500
12	360	240-360	42483,460	43672,376	44347,604

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	15728,180	27386,196	22170,757
3	2-5	3,5	-7616,591	6478,680	11522,685
4	5-10	7,5	22112,648	2136,972	5807,263
5	10-15	12,5	2027,579	2596,411	1714,758
6	15-30	22,5	175,908	209,775	224,398
7	30-60	45	1982,780	2856,058	-570,464
8	60-90	75	3406,945	4135,514	3258,165
9	90-120	105	2866,051	-2301,809	-2535,739
10	120-180	150	1149,945	2312,320	1701,308
11	180-240	210	-69,069	-741,013	326,369
12	240-360	300	719,083	-1396,728	728,104
		sum	42483,460	43672,376	44347,604

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	15728,180	27386,196	22170,757
3	2-5	3,5	-26658,067	22675,380	40329,398
4	5-10	7,5	165844,862	16027,288	43554,473
5	10-15	12,5	25344,739	32455,138	21434,477
6	15-30	22,5	3957,932	4719,934	5048,961
7	30-60	45	89225,102	128522,632	-25670,882
8	60-90	75	255520,891	310163,544	244362,349
9	90-120	105	300935,373	-241689,918	-266252,612
10	120-180	150	172491,734	346847,999	255196,219
11	180-240	210	-14504,503	-155612,794	68537,412
12	240-360	300	215724,827	-419018,307	218431,221
		sum	1203611,069	72477,092	627141,773

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
28,331	1,660	14,142	14,711	10,896

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
17,113	28,611	23,541
38,909	95,987	88,977
104,280	182,481	194,297
169,946	194,843	214,265
527,818	606,518	658,238
1090,868	1261,081	1310,963
1178,834	1370,647	1353,771
1281,216	1399,383	1365,277
2693,522	2799,095	2703,974
2728,804	2848,343	2768,565
5500,044	5562,683	5604,309

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15331,354	16349,671	16286,177

Average AUC0-360 (µg/ml.min)		15989,068
	STDEV	570,480

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	38,030	63,581	52,314
5	19,613	78,622	79,503
10	73,080	83,583	93,206
15	77,983	89,611	97,252

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,953	4,569	5,566	5,029	0,410

Table 75: Table containing the AUC, DRi and MDT values and information regarding formula 1C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	12,535	6399,336	7,963	3016,880	6,960	2751,838
3	5	38,507	19658,872	24,842	9411,652	22,924	9063,512
4	10	63,640	32489,681	50,534	19145,560	44,564	17619,611
5	15	82,207	41968,769	74,631	28274,882	67,493	26685,128
6	30	89,779	45834,594	79,193	30003,350	69,547	27497,516
7	60	103,221	52696,794	93,547	35441,642	86,302	34121,872
8	90	101,355	51744,234	89,752	34003,811	94,395	37321,607
9	120	115,138	58780,748	90,689	34358,630	96,322	38083,810
10	180	126,056	64354,992	87,777	33255,634	97,624	38598,424
11	240	97,903	49982,166	80,337	30436,948	87,436	34570,534
12	360	89,321	45600,417	90,855	34421,731	85,173	33675,705

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
51052,500	37886,400	39537,900

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	6399,336	3016,880	2751,838
3	5	2-5	19658,872	9411,652	9063,512
4	10	5-10	32489,681	19145,560	17619,611
5	15	10-15	41968,769	28274,882	26685,128
6	30	15-30	45834,594	30003,350	27497,516
7	60	30-60	52696,794	35441,642	34121,872
8	90	60-90	51744,234	34003,811	37321,607
9	120	90-120	58780,748	34358,630	38083,810
10	180	120-180	64354,992	33255,634	38598,424
11	240	180-240	49982,166	30436,948	34570,534
12	360	240-360	45600,417	34421,731	33675,705

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	6399,336	3016,880	2751,838
3	2-5	3,5	13259,536	6394,772	6311,674
4	5-10	7,5	12830,808	9733,908	8556,099
5	10-15	12,5	9479,088	9129,322	9065,517
6	15-30	22,5	3865,826	1728,468	812,388
7	30-60	45	6862,200	5438,292	6624,355
8	60-90	75	-952,560	-1437,831	3199,736
9	90-120	105	7036,514	354,819	762,203
10	120-180	150	5574,244	-1102,996	514,614
11	180-240	210	-14372,825	-2818,686	-4027,890
12	240-360	300	-4381,750	3984,782	-894,829
		sum	45600,417	34421,731	33675,705

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	6399,336	3016,880	2751,838
3	2-5	3,5	46408,376	22381,703	22090,860
4	5-10	7,5	96231,063	73004,310	64170,744
5	10-15	12,5	118488,598	114116,526	113318,957
6	15-30	22,5	86981,075	38890,530	18278,737
7	30-60	45	308798,988	244723,132	298095,997
8	60-90	75	-71441,986	-107837,323	239980,165
9	90-120	105	738833,923	37256,036	80031,299
10	120-180	150	836136,584	-165449,441	77192,136
11	180-240	210	-3018293,257	-591924,017	-845856,944
12	240-360	300	-1314524,981	1195434,724	-268448,674
		sum	-2165982,280	863613,059	-198394,884

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-47,499	25,089	-5,891	-9,434	29,740

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
5,641	3,583	3,132
34,453	22,143	20,171
114,915	84,798	75,923
164,078	140,810	126,063
580,454	519,155	462,509
1302,751	1165,995	1051,980
1380,886	1237,269	1219,699
1461,326	1217,974	1287,338
3256,124	2409,288	2618,273
3023,459	2269,548	2498,314
5055,051	4622,198	4660,461

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16379,138	13692,762	14023,865

Average AUC0-360 (µg/ml.min)		14698,588
	STDEV	1464,784

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	12,535	7,963	6,960
5	38,507	24,842	22,924
10	63,640	50,534	44,564
15	82,207	74,631	67,493

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,543	5,053	4,545	5,047	0,407

Table 76: Table containing the AUC, DRi and MDT values and information regarding formula 1D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,572	1889,496	5,628	2030,895	10,492	4963,066
3	5	28,993	11982,612	30,891	11146,901	40,774	19287,893
4	10	49,684	20533,701	50,230	18125,434	72,632	34357,919
5	15	75,669	31273,079	70,778	25540,133	90,758	42931,974
6	30	82,789	34215,945	75,547	27260,965	90,273	42702,913
7	60	95,278	39377,193	84,984	30665,976	115,416	54596,517
8	90	102,046	42174,513	89,098	32150,669	116,798	55250,301
9	120	98,350	40646,956	84,802	30600,353	109,237	51673,235
10	180	96,315	39805,806	82,950	29932,149	94,106	44515,972
11	240	95,369	39414,916	84,607	30530,034	95,220	45043,025
12	360	95,499	39468,861	85,358	30801,048	98,045	46379,014

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41328,900	36084,600	47304,000

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1889,496	2030,895	4963,066
3	5	2-5	11982,612	11146,901	19287,893
4	10	5-10	20533,701	18125,434	34357,919
5	15	10-15	31273,079	25540,133	42931,974
6	30	15-30	34215,945	27260,965	42702,913
7	60	30-60	39377,193	30665,976	54596,517
8	90	60-90	42174,513	32150,669	55250,301
9	120	90-120	40646,956	30600,353	51673,235
10	180	120-180	39805,806	29932,149	44515,972
11	240	180-240	39414,916	30530,034	45043,025
12	360	240-360	39468,861	30801,048	46379,014

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1889,496	2030,895	4963,066
3	2-5	3,5	10093,116	9116,006	14324,827
4	5-10	7,5	8551,089	6978,533	15070,027
5	10-15	12,5	10739,378	7414,699	8574,054
6	15-30	22,5	2942,866	1720,832	-229,060
7	30-60	45	5161,248	3405,011	11893,604
8	60-90	75	2797,320	1484,693	653,784
9	90-120	105	-1527,557	-1550,316	-3577,066
10	120-180	150	-841,150	-668,204	-7157,263
11	180-240	210	-390,890	597,885	527,052
12	240-360	300	53,945	271,015	1335,990
		sum	39468,861	30801,048	46379,014

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1889,496	2030,895	4963,066
3	2-5	3,5	35325,906	31906,023	50136,894
4	5-10	7,5	64133,167	52338,997	113025,199
5	10-15	12,5	134242,220	92683,741	107175,680
6	15-30	22,5	66214,485	38718,709	-5153,858
7	30-60	45	232256,172	153225,502	535212,173
8	60-90	75	209799,018	111351,952	49033,808
9	90-120	105	-160393,481	-162783,199	-375591,950
10	120-180	150	-126172,540	-100230,545	-1073589,392
11	180-240	210	-82086,849	125555,787	110680,965
12	240-360	300	16183,581	81304,395	400796,864
		sum	391391,175	426102,256	-83310,551

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
9,916	13,834	-1,796	7,318	6,640

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,057	2,533	4,721
22,656	24,650	34,605
88,512	91,262	127,582
141,021	136,135	183,813
534,796	493,850	610,980
1201,952	1083,584	1388,405
1331,935	1175,051	1567,449
1352,673	1173,823	1525,735
2627,973	2264,647	2745,126
2587,729	2262,016	2555,907
5153,445	4589,047	5218,153

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15044,750	13296,597	15962,477

Average AUC0-360 (µg/ml.min)	14767,941
STDEV	1354,325

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,572	5,628	10,492
5	28,993	30,891	40,774
10	49,684	50,230	72,632
15	75,669	70,778	90,758

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,154	4,836	6,292	5,427	0,625

Table 77: Table containing the AUC, DRi and MDT values and information regarding formula 1E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,152	66,773	0,111	49,027	0,715	286,908
3	5	69,609	30504,569	63,462	27927,316	32,206	12930,558
4	10	100,290	43949,927	93,291	41054,173	67,121	26949,046
5	15	102,538	44935,031	101,013	44452,361	85,901	34488,989
6	30	107,278	47012,377	108,658	47816,673	94,719	38029,433
7	60	107,837	47257,389	108,485	47740,392	99,136	39802,866
8	90	108,205	47418,592	107,383	47255,425	95,588	38378,360
9	120	104,189	45658,853	108,031	47540,845	89,632	35987,090
10	180	98,679	43243,886	105,385	46376,504	89,373	35883,315
11	240	99,396	43558,441	91,741	40372,039	92,817	37266,118
12	360	83,764	36707,929	83,609	36793,300	83,573	33554,422

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
43822,973	44006,537	40149,920

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	66,773	49,027	286,908
3	5	2-5	30504,569	27927,316	12930,558
4	10	5-10	43949,927	41054,173	26949,046
5	15	10-15	44935,031	44452,361	34488,989
6	30	15-30	47012,377	47816,673	38029,433
7	60	30-60	47257,389	47740,392	39802,866
8	90	60-90	47418,592	47255,425	38378,360
9	120	90-120	45658,853	47540,845	35987,090
10	180	120-180	43243,886	46376,504	35883,315
11	240	180-240	43558,441	40372,039	37266,118
12	360	240-360	36707,929	36793,300	33554,422

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	66,773	49,027	286,908
3	2-5	3,5	30437,796	27878,289	12643,649
4	5-10	7,5	13445,357	13126,857	14018,488
5	10-15	12,5	985,104	3398,188	7539,943
6	15-30	22,5	2077,346	3364,312	3540,443
7	30-60	45	245,012	-76,282	1773,434
8	60-90	75	161,204	-484,967	-1424,506
9	90-120	105	-1759,739	285,420	-2391,270
10	120-180	150	-2414,967	-1164,341	-103,775
11	180-240	210	314,555	-6004,466	1382,803
12	240-360	300	-6850,512	-3578,738	-3711,697
		sum	36707,929	36793,300	33554,422

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	66,773	49,027	286,908
3	2-5	3,5	106532,287	97574,013	44252,773
4	5-10	7,5	100840,178	98451,424	105138,662
5	10-15	12,5	12313,805	42477,355	94249,294
6	15-30	22,5	46740,285	75697,029	79659,969
7	30-60	45	11025,535	-3432,673	79804,509
8	60-90	75	12090,271	-36372,489	-106837,946
9	90-120	105	-184772,642	29969,049	-251083,324
10	120-180	150	-362245,026	-174651,078	-15566,273
11	180-240	210	66056,586	-1260937,767	290388,609
12	240-360	300	-2055153,537	-1073621,499	-1113508,959
		sum	-2246505,484	-2204797,610	-793215,778

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-61,199	-59,924	-23,640	-48,254	17,413

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,069	0,050	0,322
47,089	42,912	22,221
191,136	176,347	111,743
228,181	218,592	172,149
708,127	707,640	609,589
1452,026	1465,715	1308,516
1458,283	1457,106	1314,382
1433,661	1454,045	1250,231
2738,716	2881,127	2416,569
2674,012	2661,208	2459,575
4945,333	4734,442	4762,536

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15876,632	15799,184	14427,833

Average AUC0-360 (µg/ml.min)		15367,883
	STDEV	815,027

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,152	0,111	0,715
5	69,609	63,462	32,206
10	100,290	93,291	67,121
15	102,538	101,013	85,901

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
7,673	7,475	6,248	7,132	0,630

Table 78: Table containing the AUC, DRi and MDT values and information regarding formula 1F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,902	1020,924	3,203	1205,460	3,726	1352,530
3	5	9,506	3343,781	16,332	6146,811	13,266	4815,494
4	10	29,385	10336,996	44,558	16769,873	36,654	13305,519
5	15	46,810	16466,342	67,232	25303,465	58,052	21073,000
6	30	76,032	26745,957	91,531	34448,215	80,275	29140,293
7	60	86,051	30270,292	91,603	34475,483	89,631	32536,464
8	90	86,858	30554,152	92,928	34974,116	89,368	32441,031
9	120	71,986	25322,869	80,945	30464,179	74,188	26930,736
10	180	74,006	26033,407	85,230	32076,985	82,203	29840,149
11	240	74,189	26097,792	75,833	28540,349	73,069	26524,464
12	360	70,232	24705,682	75,260	28324,614	69,772	25327,706

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
35177,310	37635,777	36300,507

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1020,924	1205,460	1352,530
3	5	2-5	3343,781	6146,811	4815,494
4	10	5-10	10336,996	16769,873	13305,519
5	15	10-15	16466,342	25303,465	21073,000
6	30	15-30	26745,957	34448,215	29140,293
7	60	30-60	30270,292	34475,483	32536,464
8	90	60-90	30554,152	34974,116	32441,031
9	120	90-120	25322,869	30464,179	26930,736
10	180	120-180	26033,407	32076,985	29840,149
11	240	180-240	26097,792	28540,349	26524,464
12	360	240-360	24705,682	28324,614	25327,706

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1020,924	1205,460	1352,530
3	2-5	3,5	2322,858	4941,351	3462,964
4	5-10	7,5	6993,214	10623,062	8490,025
5	10-15	12,5	6129,347	8533,592	7767,481
6	15-30	22,5	10279,615	9144,750	8067,293
7	30-60	45	3524,335	27,268	3396,171
8	60-90	75	283,859	498,632	-95,433
9	90-120	105	-5231,283	-4509,937	-5510,294
10	120-180	150	710,538	1612,806	2909,412
11	180-240	210	64,385	-3536,635	-3315,685
12	240-360	300	-1392,109	-215,735	-1196,757
		sum	24705,682	28324,614	25327,706

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1020,924	1205,460	1352,530
3	2-5	3,5	8130,002	17294,730	12120,373
4	5-10	7,5	52449,109	79672,964	63675,189
5	10-15	12,5	76616,833	106669,897	97093,510
6	15-30	22,5	231291,334	205756,882	181514,096
7	30-60	45	158595,078	1227,066	152827,688
8	60-90	75	21289,438	37397,417	-7157,474
9	90-120	105	-549284,706	-473543,378	-578580,914
10	120-180	150	106580,735	241920,914	436411,862
11	180-240	210	13520,768	-742693,451	-696293,911
12	240-360	300	-417632,841	-64720,526	-359027,248
		sum	-297423,327	-589812,026	-696064,299

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-12,039	-20,823	-27,482	-20,115	6,325

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,306	1,441	1,677
8,375	13,186	11,469
43,752	68,502	56,159
85,719	125,765	106,544
414,590	535,825	466,853
1094,057	1236,151	1146,866
1167,130	1245,583	1208,242
1072,197	1173,640	1104,005
1970,900	2243,359	2111,284
2000,640	2174,351	2096,175
3899,371	4079,507	3856,719

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
11758,037	12897,310	12165,994

Average AUC0-360 (µg/ml.min)		12273,780
	STDEV	577,234

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,902	3,203	3,726
5	9,506	16,332	13,266
10	29,385	44,558	36,654
15	46,810	67,232	58,052

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,232	4,703	3,996	3,977	0,600

Table 79: Table containing the AUC, DRi and MDT values and information regarding formula 2A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	6,493	2421,501	5,684	2159,467	6,601	2665,986
3	5	23,820	8883,080	20,598	7824,988	23,880	9643,910
4	10	41,748	15568,885	39,428	14978,454	43,376	17517,280
5	15	56,987	21251,809	61,206	23251,444	61,664	24902,820
6	30	73,209	27301,187	68,249	25927,300	68,166	27528,770
7	60	73,344	27351,600	70,139	26645,262	75,786	30605,905
8	90	75,759	28252,280	79,706	30279,487	79,772	32215,541
9	120	90,946	33915,612	93,380	35474,050	87,740	35433,627
10	180	83,293	31061,658	81,320	30892,568	80,995	32709,643
11	240	86,961	32429,425	92,796	35252,241	99,715	40269,648
12	360	87,925	32788,970	89,132	33860,315	95,574	38597,168

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37292,103	37989,067	40384,660

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2421,501	2159,467	2665,986
3	5	2-5	8883,080	7824,988	9643,910
4	10	5-10	15568,885	14978,454	17517,280
5	15	10-15	21251,809	23251,444	24902,820
6	30	15-30	27301,187	25927,300	27528,770
7	60	30-60	27351,600	26645,262	30605,905
8	90	60-90	28252,280	30279,487	32215,541
9	120	90-120	33915,612	35474,050	35433,627
10	180	120-180	31061,658	30892,568	32709,643
11	240	180-240	32429,425	35252,241	40269,648
12	360	240-360	32788,970	33860,315	38597,168

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2421,501	2159,467	2665,986
3	2-5	3,5	6461,580	5665,521	6977,924
4	5-10	7,5	6685,805	7153,466	7873,370
5	10-15	12,5	5682,924	8272,990	7385,540
6	15-30	22,5	6049,378	2675,856	2625,950
7	30-60	45	50,413	717,962	3077,135
8	60-90	75	900,679	3634,225	1609,636
9	90-120	105	5663,332	5194,562	3218,086
10	120-180	150	-2853,954	-4581,481	-2723,984
11	180-240	210	1367,767	4359,672	7560,005
12	240-360	300	359,545	-1391,926	-1672,480
		sum	32788,970	33860,315	38597,168

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2421,501	2159,467	2665,986
3	2-5	3,5	22615,529	19829,322	24422,734
4	5-10	7,5	50143,538	53650,997	59050,275
5	10-15	12,5	71036,546	103412,376	92319,250
6	15-30	22,5	136110,998	60206,761	59083,879
7	30-60	45	2268,603	32308,294	138471,072
8	60-90	75	67550,962	272566,863	120722,712
9	90-120	105	594649,889	545429,056	337898,999
10	120-180	150	-428093,089	-687222,216	-408597,531
11	180-240	210	287231,054	915531,160	1587601,056
12	240-360	300	107863,496	-417577,697	-501744,002
		sum	913799,026	900294,385	1511894,430

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
27,869	26,588	39,171	31,210	5,654

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,922	2,558	2,971
20,462	17,741	20,575
73,765	67,530	75,663
111,078	113,213	118,170
439,413	436,911	438,178
989,234	934,124	971,679
1006,450	1011,454	1050,014

1125,260	1168,327	1130,706
2352,222	2358,440	2277,930
2298,421	2350,558	2439,591
4721,902	4912,042	5272,804

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13141,129	13372,896	13798,281

Average AUC0-360 (µg/ml.min)		13437,436
	STDEV	333,296

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	6,493	5,684	6,601
5	23,820	20,598	23,880
10	41,748	39,428	43,376
15	56,987	61,206	61,664

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,877	4,118	4,182	4,059	0,131

Table 80: Table containing the AUC, DRi and MDT values and information regarding formula 2B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	15,196	5823,581	15,475	5356,646	15,857	6251,221
3	5	39,221	15030,796	38,530	13337,457	44,054	17367,081
4	10	62,806	24069,114	60,559	20962,913	69,022	27209,740
5	15	80,178	30726,696	76,826	26593,495	85,049	33528,053
6	30	83,708	32079,539	79,901	27657,982	87,682	34565,986
7	60	85,185	32645,658	82,851	28679,088	93,753	36959,361
8	90	87,991	33720,799	83,295	28832,769	92,110	36311,583
9	120	86,972	33330,453	84,851	29371,520	92,241	36363,110
10	180	94,625	36263,433	84,524	29258,322	97,338	38372,452
11	240	87,311	33460,393	84,387	29210,751	93,599	36898,324
12	360	87,878	33677,656	85,470	29585,825	95,157	37512,589

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38323,218	34615,400	39421,876

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	5823,581	5356,646	6251,221
3	5	2-5	15030,796	13337,457	17367,081
4	10	5-10	24069,114	20962,913	27209,740
5	15	10-15	30726,696	26593,495	33528,053
6	30	15-30	32079,539	27657,982	34565,986
7	60	30-60	32645,658	28679,088	36959,361
8	90	60-90	33720,799	28832,769	36311,583
9	120	90-120	33330,453	29371,520	36363,110
10	180	120-180	36263,433	29258,322	38372,452
11	240	180-240	33460,393	29210,751	36898,324
12	360	240-360	33677,656	29585,825	37512,589

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	5823,581	5356,646	6251,221
3	2-5	3,5	9207,216	7980,812	11115,860
4	5-10	7,5	9038,318	7625,455	9842,659
5	10-15	12,5	6657,582	5630,583	6318,313
6	15-30	22,5	1352,843	1064,486	1037,932
7	30-60	45	566,120	1021,106	2393,375
8	60-90	75	1075,140	153,680	-647,778
9	90-120	105	-390,346	538,752	51,527
10	120-180	150	2932,981	-113,199	2009,342
11	180-240	210	-2803,040	-47,571	-1474,127
12	240-360	300	217,262	375,074	614,265
		sum	33677,656	29585,825	37512,589

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	5823,581	5356,646	6251,221
3	2-5	3,5	32225,254	27932,841	38905,510
4	5-10	7,5	67787,386	57190,915	73819,940
5	10-15	12,5	83219,772	70382,283	78978,919
6	15-30	22,5	30438,958	23950,943	23353,479
7	30-60	45	25475,392	45949,787	107701,892
8	60-90	75	80635,535	11526,035	-48583,369
9	90-120	105	-40986,359	56568,945	5410,354
10	120-180	150	439947,104	-16979,806	301401,256
11	180-240	210	-588638,438	-9989,826	-309566,761
12	240-360	300	65178,719	112522,195	184279,350
		sum	201106,903	384410,958	461951,790

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
5,972	12,993	12,315	10,426	3,162

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
6,838	6,964	7,136
36,732	36,453	40,440
114,780	111,476	127,211
160,856	154,558	173,330
553,114	528,952	582,969
1140,027	1098,572	1224,691
1168,935	1121,481	1254,580
1180,997	1134,983	1244,370
2451,562	2286,563	2559,315
2456,139	2280,293	2577,644
4730,102	4586,131	5096,395

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14000,082	13346,426	14888,082

Average AUC0-360 (µg/ml.min)		14078,197
	STDEV	773,791

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	15,196	15,475	15,857
5	39,221	38,530	44,054
10	62,806	60,559	69,022
15	80,178	76,826	85,049

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,321	5,072	5,687	5,360	0,253

Table 81: Table containing the AUC, DRi and MDT values and information regarding formula 2C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	16,216	6967,226	24,544	10107,815	19,197	7184,038
3	5	48,279	20742,642	56,378	23218,244	42,910	16058,095
4	10	72,326	31074,489	81,499	33563,550	74,636	27930,697
5	15	74,657	32075,873	83,409	34350,175	79,148	29619,404
6	30	87,010	37383,402	93,940	38687,370	88,817	33237,671
7	60	106,085	45578,644	93,381	38457,099	84,534	31634,864
8	90	104,553	44920,529	86,566	35650,294	89,891	33639,670
9	120	96,104	41290,615	94,526	38928,526	92,402	34579,111
10	180	102,977	44243,602	101,686	41877,362	87,132	32607,125
11	240	85,244	36624,715	95,082	39157,571	92,188	34499,032
12	360	91,502	39313,095	94,582	38951,585	85,700	32071,104

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42964,347	41182,923	37422,640

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	6967,226	10107,815	7184,038
3	5	2-5	20742,642	23218,244	16058,095
4	10	5-10	31074,489	33563,550	27930,697
5	15	10-15	32075,873	34350,175	29619,404
6	30	15-30	37383,402	38687,370	33237,671
7	60	30-60	45578,644	38457,099	31634,864
8	90	60-90	44920,529	35650,294	33639,670
9	120	90-120	41290,615	38928,526	34579,111
10	180	120-180	44243,602	41877,362	32607,125
11	240	180-240	36624,715	39157,571	34499,032
12	360	240-360	39313,095	38951,585	32071,104

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	6967,226	10107,815	7184,038
3	2-5	3,5	13775,416	13110,429	8874,057
4	5-10	7,5	10331,847	10345,306	11872,602
5	10-15	12,5	1001,384	786,624	1688,707
6	15-30	22,5	5307,529	4337,196	3618,267
7	30-60	45	8195,242	-230,272	-1602,807
8	60-90	75	-658,115	-2806,804	2004,806
9	90-120	105	-3629,914	3278,232	939,441
10	120-180	150	2952,987	2948,836	-1971,985
11	180-240	210	-7618,887	-2719,791	1891,907
12	240-360	300	2688,380	-205,986	-2427,929
		sum	39313,095	38951,585	32071,104

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	6967,226	10107,815	7184,038
3	2-5	3,5	48213,957	45886,503	31059,199
4	5-10	7,5	77488,851	77589,797	89044,515
5	10-15	12,5	12517,300	9832,804	21108,833
6	15-30	22,5	119419,402	97586,903	81411,013
7	30-60	45	368785,902	-10362,234	-72126,317
8	60-90	75	-49358,608	-210510,326	150360,471
9	90-120	105	-381141,016	344214,347	98641,274
10	120-180	150	442948,093	442325,442	-295797,787
11	180-240	210	-1599966,279	-571156,202	397300,461
12	240-360	300	806513,985	-61795,739	-728378,557
		sum	-147611,188	173719,110	-220192,856

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-3,755	4,460	-6,866	-2,054	4,778

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
7,297	11,045	8,639
43,534	54,622	41,922
135,681	155,112	132,239
165,356	185,521	173,007
545,627	598,553	566,883
1303,392	1264,420	1170,120
1421,805	1214,642	1177,370
1354,438	1222,368	1230,476
2687,605	2648,864	2423,704
2540,996	2656,372	2420,816
4772,145	5120,926	4802,958

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14977,876	15132,445	14148,135

Average AUC0-360 (µg/ml.min)		14752,819
	STDEV	529,344

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	16,216	24,544	19,197
5	48,279	56,378	42,910
10	72,326	81,499	74,636
15	74,657	83,409	79,148

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,117	5,521	5,394	5,344	0,169

Table 82: Table containing the AUC, DRi and MDT values and information regarding formula 2D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	19,199	7439,314	12,720	5246,752	22,591	9751,155
3	5	47,304	18330,097	38,997	16085,539	59,157	25534,386
4	10	84,364	32690,539	66,018	27231,265	63,508	27412,305
5	15	88,825	34419,247	79,433	32764,527	90,404	39021,619
6	30	91,289	35374,113	87,024	35895,594	91,061	39305,142
7	60	94,040	36440,015	80,071	33027,568	91,207	39368,441
8	90	92,734	35933,814	92,371	38101,258	89,074	38447,414
9	120	94,889	36768,741	101,847	42009,924	106,577	46002,550
10	180	95,678	37074,501	93,370	38513,290	99,920	43129,241
11	240	92,726	35930,778	89,149	36772,392	92,863	40083,207
12	360	86,317	33447,198	90,073	37153,357	104,860	45261,637

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38749,417	41248,053	43163,680

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	7439,314	5246,752	9751,155
3	5	2-5	18330,097	16085,539	25534,386
4	10	5-10	32690,539	27231,265	27412,305
5	15	10-15	34419,247	32764,527	39021,619
6	30	15-30	35374,113	35895,594	39305,142
7	60	30-60	36440,015	33027,568	39368,441
8	90	60-90	35933,814	38101,258	38447,414
9	120	90-120	36768,741	42009,924	46002,550
10	180	120-180	37074,501	38513,290	43129,241
11	240	180-240	35930,778	36772,392	40083,207
12	360	240-360	33447,198	37153,357	45261,637

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	7439,314	5246,752	9751,155
3	2-5	3,5	10890,783	10838,787	15783,231
4	5-10	7,5	14360,441	11145,726	1877,918
5	10-15	12,5	1728,709	5533,262	11609,314
6	15-30	22,5	954,865	3131,067	283,523
7	30-60	45	1065,902	-2868,026	63,300
8	60-90	75	-506,201	5073,690	-921,028
9	90-120	105	834,927	3908,666	7555,136
10	120-180	150	305,760	-3496,633	-2873,308
11	180-240	210	-1143,723	-1740,899	-3046,034
12	240-360	300	-2483,579	380,966	5178,430
		sum	33447,198	37153,357	45261,637

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	7439,314	5246,752	9751,155
3	2-5	3,5	38117,742	37935,753	55241,309
4	5-10	7,5	107703,310	83592,948	14084,389
5	10-15	12,5	21608,859	69165,771	145116,425
6	15-30	22,5	21484,471	70449,002	6379,272
7	30-60	45	47965,607	-129061,187	2848,483
8	60-90	75	-37965,100	380526,787	-69077,075
9	90-120	105	87667,350	410409,881	793289,288
10	120-180	150	45864,001	-524494,969	-430996,272
11	180-240	210	-240181,897	-365588,728	-639667,193
12	240-360	300	-745073,784	114289,699	1553529,052
		sum	-645370,127	152471,710	1440498,834

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-19,295	4,104	31,826	5,545	20,895

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
8,639	5,724	10,166
44,889	34,909	55,180
148,127	118,142	137,998
194,838	163,633	173,151
607,887	561,791	612,443
1250,975	1127,887	1230,309
1260,724	1163,981	1216,896
1266,451	1310,972	1320,641
2572,642	2635,430	2787,712
2543,448	2464,011	2602,577
4834,151	4839,005	5338,541

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14732,771	14425,485	15485,614

Average AUC0-360 (µg/ml.min)		14881,290
	STDEV	545,446

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	19,199	12,720	22,591
5	47,304	38,997	59,157
10	84,364	66,018	63,508
15	88,825	79,433	90,404

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,145	5,430	5,522	5,699	0,318

Table 83: Table containing the AUC, DRi and MDT values and information regarding formula 2E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,711	260,844	1,421	556,882	0,711	256,398
3	5	8,273	3034,490	12,100	4742,881	9,879	3561,798
4	10	26,470	9709,582	30,814	12077,983	29,491	10633,249
5	15	45,671	16752,620	47,956	18796,938	50,051	18046,219
6	30	68,691	25196,862	70,264	27541,140	70,166	25299,208
7	60	80,747	29618,881	77,237	30274,429	81,582	29415,277
8	90	84,440	30973,696	81,505	31947,211	86,375	31143,303
9	120	81,353	29841,360	87,953	34474,436	89,027	32099,627
10	180	90,571	33222,558	96,782	37935,134	82,643	29797,658
11	240	83,026	30454,851	82,999	32532,947	84,491	30464,169
12	360	84,556	31016,105	80,336	31489,049	81,908	29532,609

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
36681,243	39196,593	36055,997

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	260,844	556,882	256,398
3	5	2-5	3034,490	4742,881	3561,798
4	10	5-10	9709,582	12077,983	10633,249
5	15	10-15	16752,620	18796,938	18046,219
6	30	15-30	25196,862	27541,140	25299,208
7	60	30-60	29618,881	30274,429	29415,277
8	90	60-90	30973,696	31947,211	31143,303
9	120	90-120	29841,360	34474,436	32099,627
10	180	120-180	33222,558	37935,134	29797,658
11	240	180-240	30454,851	32532,947	30464,169
12	360	240-360	31016,105	31489,049	29532,609

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	260,844	556,882	256,398
3	2-5	3,5	2773,645	4185,999	3305,400
4	5-10	7,5	6675,093	7335,102	7071,450
5	10-15	12,5	7043,037	6718,954	7412,970
6	15-30	22,5	8444,243	8744,202	7252,989
7	30-60	45	4422,019	2733,290	4116,069
8	60-90	75	1354,815	1672,782	1728,026
9	90-120	105	-1132,336	2527,225	956,324
10	120-180	150	3381,199	3460,698	-2301,969
11	180-240	210	-2767,707	-5402,187	666,511
12	240-360	300	561,253	-1043,897	-931,559
		sum	31016,105	31489,049	29532,609

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	260,844	556,882	256,398
3	2-5	3,5	9707,759	14650,998	11568,900
4	5-10	7,5	50063,195	55013,266	53035,878
5	10-15	12,5	88037,965	83986,928	92662,131
6	15-30	22,5	189995,459	196744,542	163192,245
7	30-60	45	198990,854	122998,039	185223,127
8	60-90	75	101611,120	125458,617	129601,945
9	90-120	105	-118895,322	265358,662	100413,992
10	120-180	150	507179,777	519104,681	-345295,371
11	180-240	210	-581218,467	-1134459,355	139967,242
12	240-360	300	168375,964	-313169,167	-279467,804
		sum	614109,149	-63755,908	251158,684

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
19,800	-2,025	8,504	8,760	8,912

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,320	0,639	0,320
6,064	9,127	7,148
39,086	48,278	44,291
81,159	88,616	89,484
385,972	398,991	405,732
1008,707	995,635	1024,303
1115,011	1071,512	1133,710
1119,105	1143,840	1183,963
2320,976	2493,914	2317,543
2343,555	2427,045	2256,309
4524,699	4410,062	4492,770

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12944,653	13087,658	12955,574

Average AUC0-360 (µg/ml.min)		12995,962
	STDEV	79,599

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,711	1,421	0,711
5	8,273	12,100	9,879
10	26,470	30,814	29,491
15	45,671	47,956	50,051

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,173	3,352	3,483	3,336	0,127

Table 84: Table containing the AUC, DRi and MDT values and information regarding formula 2F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,135	751,990	1,567	540,254	1,763	624,476
3	5	11,411	4019,487	9,780	3370,823	12,336	4369,728
4	10	30,805	10851,112	29,871	10296,077	33,984	12037,962
5	15	49,610	17475,303	49,272	16982,942	55,889	19796,949
6	30	69,493	24478,827	69,262	23873,116	68,708	24337,760
7	60	79,516	28009,703	84,207	29024,547	76,720	27175,656
8	90	84,142	29639,035	82,486	28431,121	84,287	29855,931
9	120	78,416	27622,036	80,407	27714,541	80,825	28629,723
10	180	86,975	30637,168	85,106	29334,396	76,741	27183,271
11	240	84,797	29869,659	83,278	28704,383	79,496	28159,185
12	360	77,850	27422,868	79,294	27331,104	87,462	30980,606

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
35225,067	34468,000	35421,950

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	751,990	540,254	624,476
3	5	2-5	4019,487	3370,823	4369,728
4	10	5-10	10851,112	10296,077	12037,962
5	15	10-15	17475,303	16982,942	19796,949
6	30	15-30	24478,827	23873,116	24337,760
7	60	30-60	28009,703	29024,547	27175,656
8	90	60-90	29639,035	28431,121	29855,931
9	120	90-120	27622,036	27714,541	28629,723
10	180	120-180	30637,168	29334,396	27183,271
11	240	180-240	29869,659	28704,383	28159,185
12	360	240-360	27422,868	27331,104	30980,606

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	751,990	540,254	624,476
3	2-5	3,5	3267,497	2830,569	3745,252
4	5-10	7,5	6831,625	6925,254	7668,234
5	10-15	12,5	6624,191	6686,866	7758,987
6	15-30	22,5	7003,523	6890,173	4540,811
7	30-60	45	3530,877	5151,431	2837,896
8	60-90	75	1629,332	-593,425	2680,275
9	90-120	105	-2016,999	-716,580	-1226,209
10	120-180	150	3015,132	1619,854	-1446,452
11	180-240	210	-767,509	-630,013	975,914
12	240-360	300	-2446,791	-1373,279	2821,421
		sum	27422,868	27331,104	30980,606

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	751,990	540,254	624,476
3	2-5	3,5	11436,241	9906,991	13108,381
4	5-10	7,5	51237,186	51939,404	57511,756
5	10-15	12,5	82802,390	83585,822	96987,340
6	15-30	22,5	157579,271	155028,894	102168,252
7	30-60	45	158889,447	231814,406	127705,313
8	60-90	75	122199,888	-44506,911	201020,660
9	90-120	105	-211784,886	-75240,878	-128751,923
10	120-180	150	452269,852	242978,123	-216967,753
11	180-240	210	-161176,946	-132302,652	204941,957
12	240-360	300	-734037,334	-411983,664	846426,299
		sum	-69832,902	111759,789	1304774,758

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-2,547	4,089	42,116	14,553	19,677

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,961	0,705	0,793
9,143	7,659	9,517
47,493	44,607	52,111
90,467	89,036	101,108
401,973	400,050	420,515
1005,811	1035,915	981,639
1104,693	1125,176	1086,793
1097,265	1099,522	1114,502
2232,783	2234,422	2127,143
2318,923	2273,191	2109,210
4391,470	4389,457	4507,867

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12700,982	12699,742	12511,196

Average AUC0-360 (µg/ml.min)		12637,307
	STDEV	109,217

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,135	1,567	1,763
5	11,411	9,780	12,336
10	30,805	29,871	33,984
15	49,610	49,272	55,889

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,433	3,423	3,874	3,576	0,210

Table 85: Table containing the AUC, DRi and MDT values and information regarding formula 3A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	13,351	6107,667	12,796	5870,315	21,613	9853,248
3	5	36,561	16725,194	34,475	15816,149	56,398	25710,961
4	10	72,549	33188,631	57,134	26211,956	78,810	35928,506
5	15	87,293	39933,620	68,088	31237,191	91,810	41855,231
6	30	89,338	40869,007	73,555	33745,542	88,570	40377,758
7	60	88,260	40375,663	81,155	37232,014	100,911	46004,002
8	90	102,528	46902,975	88,197	40462,930	96,431	43961,529
9	120	93,482	42764,719	87,313	40057,446	91,333	41637,519
10	180	106,031	48505,676	86,586	39723,939	94,257	42970,699
11	240	106,528	48732,778	91,567	42008,875	98,594	44947,619
12	360	96,929	44341,675	111,973	51370,502	112,071	51091,946

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
45746,507	45877,763	45588,747

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	6107,667	5870,315	9853,248
3	5	2-5	16725,194	15816,149	25710,961
4	10	5-10	33188,631	26211,956	35928,506
5	15	10-15	39933,620	31237,191	41855,231
6	30	15-30	40869,007	33745,542	40377,758
7	60	30-60	40375,663	37232,014	46004,002
8	90	60-90	46902,975	40462,930	43961,529
9	120	90-120	42764,719	40057,446	41637,519
10	180	120-180	48505,676	39723,939	42970,699
11	240	180-240	48732,778	42008,875	44947,619
12	360	240-360	44341,675	51370,502	51091,946

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	6107,667	5870,315	9853,248
3	2-5	3,5	10617,527	9945,835	15857,713
4	5-10	7,5	16463,437	10395,807	10217,545
5	10-15	12,5	6744,989	5025,235	5926,725
6	15-30	22,5	935,386	2508,351	-1477,473
7	30-60	45	-493,343	3486,472	5626,244
8	60-90	75	6527,311	3230,916	-2042,473
9	90-120	105	-4138,255	-405,484	-2324,009
10	120-180	150	5740,957	-333,507	1333,180
11	180-240	210	227,102	2284,935	1976,919
12	240-360	300	-4391,104	9361,628	6144,327
		sum	44341,675	51370,502	51091,946

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	6107,667	5870,315	9853,248
3	2-5	3,5	37161,344	34810,421	55501,997
4	5-10	7,5	123475,780	77968,551	76631,588
5	10-15	12,5	84312,365	62815,437	74084,058
6	15-30	22,5	21046,189	56437,890	-33243,145
7	30-60	45	-22200,441	156891,246	253180,988
8	60-90	75	489548,334	242318,700	-153185,506
9	90-120	105	-434516,812	-42575,810	-244020,971
10	120-180	150	861143,537	-50026,019	199977,007
11	180-240	210	47691,467	479836,433	415153,077
12	240-360	300	-1317331,090	2808488,277	1843298,236
		sum	-103561,659	3832835,439	2497230,578

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-2,336	74,612	48,877	40,384	31,982

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
6,008	5,758	9,726
33,690	31,907	52,657
122,748	103,060	152,109
179,823	140,875	191,948
596,130	478,046	608,783
1198,783	1044,294	1278,993
1287,816	1143,127	1332,055
1323,067	1184,697	1267,404
2693,430	2347,649	2505,467
2869,551	2405,071	2603,487
5493,338	5495,567	5687,957

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15804,385	14380,050	15690,586

Average AUC0-360 (µg/ml.min)		15291,674
	STDEV	791,537

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	13,351	12,796	21,613
5	36,561	34,475	56,398
10	72,549	57,134	78,810
15	87,293	68,088	91,810

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,045	4,602	6,027	5,558	0,676

Table 86: Table containing the AUC, DRi and MDT values and information regarding formula 3B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	22,410	10257,735	22,804	8866,452	38,856	17802,456
3	5	51,762	23692,657	51,684	20095,015	75,144	34427,977
4	10	73,903	33826,970	76,974	29927,825	101,199	46365,511
5	15	92,498	42338,547	92,618	36010,135	102,896	47143,020
6	30	88,525	40519,979	86,565	33656,893	108,982	49931,202
7	60	96,715	44268,815	89,694	34873,391	106,776	48920,864
8	90	97,997	44855,574	88,575	34438,466	109,880	50342,861
9	120	98,900	45268,632	90,544	35203,929	93,531	42852,416
10	180	88,957	40717,538	95,172	37003,091	112,149	51382,333
11	240	98,696	45175,599	92,938	36134,507	110,593	50669,577
12	360	113,018	51730,882	94,263	36649,904	112,803	51682,175

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
45772,270	38880,367	45816,143

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	10257,735	8866,452	17802,456
3	5	2-5	23692,657	20095,015	34427,977
4	10	5-10	33826,970	29927,825	46365,511
5	15	10-15	42338,547	36010,135	47143,020
6	30	15-30	40519,979	33656,893	49931,202
7	60	30-60	44268,815	34873,391	48920,864
8	90	60-90	44855,574	34438,466	50342,861
9	120	90-120	45268,632	35203,929	42852,416
10	180	120-180	40717,538	37003,091	51382,333
11	240	180-240	45175,599	36134,507	50669,577
12	360	240-360	51730,882	36649,904	51682,175

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	10257,735	8866,452	17802,456
3	2-5	3,5	13434,922	11228,563	16625,521
4	5-10	7,5	10134,312	9832,810	11937,534
5	10-15	12,5	8511,578	6082,310	777,509
6	15-30	22,5	-1818,568	-2353,241	2788,182
7	30-60	45	3748,836	1216,498	-1010,338
8	60-90	75	586,759	-434,926	1421,997
9	90-120	105	413,058	765,463	-7490,445
10	120-180	150	-4551,093	1799,163	8529,918
11	180-240	210	4458,061	-868,584	-712,756
12	240-360	300	6555,282	515,397	1012,597
		sum	51730,882	36649,904	51682,175

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	10257,735	8866,452	17802,456
3	2-5	3,5	47022,228	39299,972	58189,323
4	5-10	7,5	76007,341	73746,071	89531,503
5	10-15	12,5	106394,722	76028,877	9718,867
6	15-30	22,5	-40917,782	-52947,931	62734,094
7	30-60	45	168697,600	54742,404	-45465,226
8	60-90	75	44006,930	-32619,428	106649,800
9	90-120	105	43371,091	80373,638	-786496,772
10	120-180	150	-682664,022	269874,385	1279487,638
11	180-240	210	936192,783	-182402,680	-149678,738
12	240-360	300	1966584,672	154619,058	303779,131
		sum	2674953,298	489580,819	946252,076

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
51,709	13,358	18,309	27,792	17,032

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
10,085	10,262	17,485
50,066	50,280	76,950
141,373	144,741	198,386
187,201	190,791	229,607
610,954	604,743	715,087
1250,374	1189,751	1456,368
1314,310	1203,320	1462,432
1329,054	1209,058	1373,027
2536,062	2507,165	2776,683
2533,318	2539,476	3007,020
5716,288	5054,425	6031,711

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15679,087	14704,010	17344,757

Average AUC0-360 (µg/ml.min)		15909,285
	STDEV	1335,339

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	22,410	22,804	38,856
5	51,762	51,684	75,144
10	73,903	76,974	101,199
15	92,498	92,618	102,896

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,968	6,038	6,522	6,176	0,246

Table 87: Table containing the AUC, DRi and MDT values and information regarding formula 3C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,750	3303,600	12,330	5128,200	6,468	2504,844
3	5	29,830	12716,364	42,807	17803,333	24,294	9408,131
4	10	67,420	28740,531	89,781	37339,917	55,505	21494,786
5	15	79,687	33969,962	85,919	35733,555	71,708	27769,440
6	30	102,015	43487,958	100,299	41714,233	81,654	31621,075
7	60	98,007	41779,708	83,392	34682,584	82,025	31764,686
8	90	100,944	43031,426	102,691	42709,315	86,678	33566,750
9	120	100,834	42984,702	87,025	36193,530	89,657	34720,391
10	180	105,257	44870,212	91,540	38071,634	90,297	34968,373
11	240	95,684	40789,256	83,726	34821,659	85,287	33027,970
12	360	90,946	38769,649	88,473	36795,924	86,022	33312,667

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42629,140	41589,990	38725,823

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3303,600	5128,200	2504,844
3	5	2-5	12716,364	17803,333	9408,131
4	10	5-10	28740,531	37339,917	21494,786
5	15	10-15	33969,962	35733,555	27769,440
6	30	15-30	43487,958	41714,233	31621,075
7	60	30-60	41779,708	34682,584	31764,686
8	90	60-90	43031,426	42709,315	33566,750
9	120	90-120	42984,702	36193,530	34720,391
10	180	120-180	44870,212	38071,634	34968,373
11	240	180-240	40789,256	34821,659	33027,970
12	360	240-360	38769,649	36795,924	33312,667

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3303,600	5128,200	2504,844
3	2-5	3,5	9412,763	12675,133	6903,288
4	5-10	7,5	16024,167	19536,585	12086,655
5	10-15	12,5	5229,431	-1606,363	6274,654
6	15-30	22,5	9517,996	5980,678	3851,635
7	30-60	45	-1708,250	-7031,649	143,611
8	60-90	75	1251,718	8026,731	1802,064
9	90-120	105	-46,724	-6515,786	1153,641
10	120-180	150	1885,510	1878,105	247,982
11	180-240	210	-4080,956	-3249,975	-1940,403
12	240-360	300	-2019,607	1974,265	284,697
		sum	38769,649	36795,924	33312,667

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3303,600	5128,200	2504,844
3	2-5	3,5	32944,671	44362,966	24161,507
4	5-10	7,5	120181,256	146524,384	90649,909
5	10-15	12,5	65367,883	-20079,536	78433,179
6	15-30	22,5	214154,905	134565,260	86661,795
7	30-60	45	-76871,234	-316424,192	6462,479
8	60-90	75	93878,839	602004,836	135154,797
9	90-120	105	-4905,982	-684157,492	121132,272
10	120-180	150	282826,450	281715,702	37197,349
11	180-240	210	-857000,758	-682494,817	-407484,587
12	240-360	300	-605882,178	592279,453	85409,086
		sum	-732002,546	103424,765	260282,628

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-18,881	2,811	7,813	-2,752	11,586

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,487	5,549	2,911
25,366	37,218	20,765
109,406	149,161	89,774
165,495	197,662	143,114
613,244	628,484	517,595
1350,149	1239,910	1104,828
1342,920	1256,060	1138,742
1362,000	1280,583	1190,261
2782,231	2410,627	2429,382
2712,705	2366,097	2370,384
5039,019	4649,375	4625,330

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15506,023	14220,726	13633,086

Average AUC0-360 (µg/ml.min)			14453,278
		STDEV	957,880

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,750	12,330	6,468
5	29,830	42,807	24,294
10	67,420	89,781	55,505
15	79,687	85,919	71,708

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,712	6,353	5,054	5,706	0,531

Table 88: Table containing the AUC, DRi and MDT values and information regarding formula 3D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,742	1441,662	3,970	1751,430	1,409	539,102
3	5	23,541	9069,098	25,700	11336,735	16,167	6186,129
4	10	53,130	20468,019	58,090	25625,034	45,906	17565,617
5	15	78,341	30180,139	76,158	33595,076	72,963	27918,603
6	30	86,055	33152,202	88,263	38935,072	84,546	32350,837
7	60	88,126	33949,971	94,213	41559,589	87,564	33505,912
8	90	95,122	36644,847	104,449	46075,066	90,300	34552,480
9	120	91,562	35273,527	90,664	39994,041	94,480	36152,022
10	180	90,381	34818,640	103,864	45816,981	81,405	31149,042
11	240	90,484	34858,420	102,582	45251,564	87,907	33636,829
12	360	82,907	31939,298	108,920	48047,262	87,885	33628,512

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38524,230	44112,517	38264,303

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1441,662	1751,430	539,102
3	5	2-5	9069,098	11336,735	6186,129
4	10	5-10	20468,019	25625,034	17565,617
5	15	10-15	30180,139	33595,076	27918,603
6	30	15-30	33152,202	38935,072	32350,837
7	60	30-60	33949,971	41559,589	33505,912
8	90	60-90	36644,847	46075,066	34552,480
9	120	90-120	35273,527	39994,041	36152,022
10	180	120-180	34818,640	45816,981	31149,042
11	240	180-240	34858,420	45251,564	33636,829
12	360	240-360	31939,298	48047,262	33628,512

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1441,662	1751,430	539,102
3	2-5	3,5	7627,436	9585,305	5647,027
4	5-10	7,5	11398,920	14288,298	11379,489
5	10-15	12,5	9712,120	7970,043	10352,985
6	15-30	22,5	2972,063	5339,996	4432,235
7	30-60	45	797,769	2624,517	1155,075
8	60-90	75	2694,876	4515,477	1046,568
9	90-120	105	-1371,320	-6081,025	1599,542
10	120-180	150	-454,887	5822,939	-5002,981
11	180-240	210	39,780	-565,417	2487,788
12	240-360	300	-2919,122	2795,699	-8,317
		sum	31939,298	48047,262	33628,512

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1441,662	1751,430	539,102
3	2-5	3,5	26696,026	33548,567	19764,594
4	5-10	7,5	85491,901	107162,237	85346,167
5	10-15	12,5	121401,501	99625,532	129412,315
6	15-30	22,5	66871,429	120149,915	99725,278
7	30-60	45	35899,588	118103,258	51978,371
8	60-90	75	202115,708	338660,776	78492,605
9	90-120	105	-143988,590	-638507,603	167951,948
10	120-180	150	-68233,070	873440,900	-750447,075
11	180-240	210	8353,765	-118737,607	522435,383
12	240-360	300	-875736,601	838709,646	-2495,210
		sum	-539686,680	1773907,053	402703,475

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-16,897	36,920	11,975	10,666	21,990

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,684	1,787	0,634
18,416	20,027	11,864
86,255	94,263	69,832
147,905	151,029	133,727
554,837	554,920	531,590
1175,727	1231,712	1161,744
1236,923	1340,966	1200,582
1260,114	1317,011	1247,260
2456,231	2626,123	2374,444
2441,685	2787,022	2285,705
4681,569	5710,552	4746,367

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14061,346	15835,411	13763,748

Average AUC0-360 (µg/ml.min)		14553,502
	STDEV	1120,094

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,742	3,970	1,409
5	23,541	25,700	16,167
10	53,130	58,090	45,906
15	78,341	76,158	72,963

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,466	5,433	5,120	5,340	0,156

Table 89: Table containing the AUC, DRi and MDT values and information regarding formula 3E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,711	272,574	0,711	221,579	1,908	862,821
3	5	9,373	3592,865	7,117	2217,634	12,307	5565,118
4	10	31,850	12208,180	24,150	7524,917	37,561	16984,402
5	15	52,779	20230,706	43,881	13673,155	59,669	26981,145
6	30	69,103	26487,656	57,565	17936,822	67,219	30394,954
7	60	70,353	26966,683	58,628	18268,121	77,698	35133,199
8	90	73,478	28164,778	70,391	21933,630	82,851	37463,131
9	120	78,403	30052,422	72,228	22505,773	77,761	35161,926
10	180	77,705	29785,015	76,937	23973,211	107,196	48471,365
11	240	82,670	31687,865	69,668	21708,064	81,401	36807,783
12	360	90,468	34677,068	70,764	22049,785	111,649	50484,933

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38330,710	31159,510	45217,693

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	272,574	221,579	862,821
3	5	2-5	3592,865	2217,634	5565,118
4	10	5-10	12208,180	7524,917	16984,402
5	15	10-15	20230,706	13673,155	26981,145
6	30	15-30	26487,656	17936,822	30394,954
7	60	30-60	26966,683	18268,121	35133,199
8	90	60-90	28164,778	21933,630	37463,131
9	120	90-120	30052,422	22505,773	35161,926
10	180	120-180	29785,015	23973,211	48471,365
11	240	180-240	31687,865	21708,064	36807,783
12	360	240-360	34677,068	22049,785	50484,933

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	272,574	221,579	862,821
3	2-5	3,5	3320,291	1996,055	4702,298
4	5-10	7,5	8615,314	5307,283	11419,284
5	10-15	12,5	8022,526	6148,238	9996,743
6	15-30	22,5	6256,951	4263,667	3413,809
7	30-60	45	479,027	331,299	4738,245
8	60-90	75	1198,095	3665,510	2329,932
9	90-120	105	1887,644	572,142	-2301,205
10	120-180	150	-267,406	1467,439	13309,439
11	180-240	210	1902,850	-2265,148	-11663,582
12	240-360	300	2989,202	341,721	13677,150
		sum	34677,068	22049,785	50484,933

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	272,574	221,579	862,821
3	2-5	3,5	11621,019	6986,193	16458,042
4	5-10	7,5	64614,859	39804,620	85644,628
5	10-15	12,5	100281,576	76852,976	124959,282
6	15-30	22,5	140781,387	95932,515	76810,710
7	30-60	45	21556,198	14908,441	213221,018
8	60-90	75	89857,122	274913,240	174744,892
9	90-120	105	198202,612	60074,958	-241626,494
10	120-180	150	-40110,959	220115,780	1996415,868
11	180-240	210	399598,504	-475681,003	-2449352,236
12	240-360	300	896760,684	102516,327	4103145,045
		sum	1883435,575	416645,624	4101283,576

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
54,314	18,896	81,238	51,482	25,530

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,320	0,320	0,859
6,807	5,284	9,595
46,376	35,175	56,102
95,208	76,535	109,385
411,353	342,379	428,249
941,326	784,298	978,190
970,860	870,880	1083,702
1025,199	962,679	1084,131
2107,463	2013,723	2496,920
2165,063	1979,162	2546,058
4674,720	3791,658	5212,348

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12444,692	10862,092	14005,539

Average AUC0-360 (µg/ml.min)		12437,441
	STDEV	1571,736

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,711	0,711	1,908
5	9,373	7,117	12,307
10	31,850	24,150	37,561
15	52,779	43,881	59,669

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,702	3,024	4,174	3,633	0,472

Table 90: Table containing the AUC, DRi and MDT values and information regarding formula 3F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,821	1705,814	4,154	1811,955	0,711	231,919
3	5	28,768	12843,983	27,757	12107,217	7,599	2478,146
4	10	69,169	30881,135	65,365	28511,327	30,031	9794,125
5	15	81,761	36503,289	85,313	37212,342	51,896	16925,042
6	30	87,256	38956,425	84,641	36919,145	73,243	23887,037
7	60	88,562	39539,666	85,648	37358,568	76,311	24887,755
8	90	91,644	40915,371	89,167	38893,338	77,738	25353,130
9	120	99,738	44529,175	94,314	41138,580	69,323	22608,750
10	180	110,237	49216,802	97,659	42597,715	76,108	24821,564
11	240	98,892	44151,299	89,296	38949,672	80,527	26262,790
12	360	104,390	46606,350	107,701	46977,677	67,225	21924,435

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
44646,170	43618,757	32613,540

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1705,814	1811,955	231,919
3	5	2-5	12843,983	12107,217	2478,146
4	10	5-10	30881,135	28511,327	9794,125
5	15	10-15	36503,289	37212,342	16925,042
6	30	15-30	38956,425	36919,145	23887,037
7	60	30-60	39539,666	37358,568	24887,755
8	90	60-90	40915,371	38893,338	25353,130
9	120	90-120	44529,175	41138,580	22608,750
10	180	120-180	49216,802	42597,715	24821,564
11	240	180-240	44151,299	38949,672	26262,790
12	360	240-360	46606,350	46977,677	21924,435

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1705,814	1811,955	231,919
3	2-5	3,5	11138,168	10295,262	2246,227
4	5-10	7,5	18037,152	16404,110	7315,979
5	10-15	12,5	5622,154	8701,016	7130,917

6	15-30	22,5	2453,136	-293,197	6961,995
7	30-60	45	583,241	439,422	1000,718
8	60-90	75	1375,705	1534,770	465,375
9	90-120	105	3613,804	2245,242	-2744,380
10	120-180	150	4687,627	1459,135	2212,814
11	180-240	210	-5065,503	-3648,043	1441,226
12	240-360	300	2455,051	8028,005	-4338,355
		sum	46606,350	46977,677	21924,435

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1705,814	1811,955	231,919
3	2-5	3,5	38983,590	36033,415	7861,796
4	5-10	7,5	135278,639	123030,823	54869,845
5	10-15	12,5	70276,930	108762,697	89136,462
6	15-30	22,5	55195,564	-6596,933	156644,886
7	30-60	45	26245,830	19773,998	45032,293
8	60-90	75	103177,850	115107,745	34903,131
9	90-120	105	379449,452	235750,441	-288159,872
10	120-180	150	703144,106	218870,305	331922,089
11	180-240	210	-1063755,631	-766089,040	302657,436
12	240-360	300	736515,189	2408401,572	-1301506,528
		sum	1186217,334	2494856,977	-566406,543

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
25,452	53,107	-25,834	17,575	32,706

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,719	1,869	0,320
21,998	21,540	5,609
110,179	104,762	42,333
169,796	169,512	92,167
570,433	573,592	422,342
1186,773	1149,447	1009,488
1216,390	1179,998	1039,832
1291,826	1238,493	992,663
2834,668	2591,637	1963,323
2823,242	2523,891	2114,578
5488,615	5318,901	3989,310

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15715,639	14873,643	11671,966

Average AUC0-360 (µg/ml.min)		14087,083
	STDEV	2133,502

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,821	4,154	0,711
5	28,768	27,757	7,599
10	69,169	65,365	30,031
15	81,761	85,313	51,896

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,999	6,112	3,624	5,245	1,147

Table 91: Table containing the AUC, DRi and MDT values and information regarding formula 4A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	6,042	2218,581	5,619	2214,713	6,674	2592,858
3	5	24,911	9146,849	21,252	8376,209	24,427	9489,894
4	10	56,051	20580,898	45,147	17793,808	53,113	20634,180
5	15	65,999	24233,608	61,993	24433,339	69,015	26812,081
6	30	90,662	33289,110	92,111	36303,546	95,925	37266,640
7	60	71,400	26216,523	90,108	35514,137	76,423	29690,048
8	90	76,998	28272,245	87,424	34456,485	78,100	30341,476
9	120	83,214	30554,558	97,316	38354,993	86,475	33595,395
10	180	75,459	27707,103	75,849	29894,385	79,114	30735,715
11	240	90,397	33191,767	80,860	31869,458	78,646	30553,876
12	360	79,835	29313,899	82,828	32644,793	80,204	31159,199

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
36717,965	39412,907	38849,697

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2218,581	2214,713	2592,858
3	5	2-5	9146,849	8376,209	9489,894
4	10	5-10	20580,898	17793,808	20634,180
5	15	10-15	24233,608	24433,339	26812,081
6	30	15-30	33289,110	36303,546	37266,640
7	60	30-60	26216,523	35514,137	29690,048
8	90	60-90	28272,245	34456,485	30341,476
9	120	90-120	30554,558	38354,993	33595,395
10	180	120-180	27707,103	29894,385	30735,715
11	240	180-240	33191,767	31869,458	30553,876
12	360	240-360	29313,899	32644,793	31159,199

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2218,581	2214,713	2592,858
3	2-5	3,5	6928,267	6161,496	6897,036
4	5-10	7,5	11434,050	9417,599	11144,286
5	10-15	12,5	3652,709	6639,531	6177,901
6	15-30	22,5	9055,502	11870,207	10454,559
7	30-60	45	-7072,587	-789,410	-7576,593
8	60-90	75	2055,723	-1057,651	651,428
9	90-120	105	2282,313	3898,507	3253,919
10	120-180	150	-2847,456	-8460,608	-2859,680
11	180-240	210	5484,664	1975,073	-181,839
12	240-360	300	-3877,867	775,335	605,323
		sum	29313,899	32644,793	31159,199

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2218,581	2214,713	2592,858
3	2-5	3,5	24248,936	21565,236	24139,627
4	5-10	7,5	85755,374	70631,992	83582,149
5	10-15	12,5	45658,865	82994,134	77223,764
6	15-30	22,5	203748,804	267079,664	235227,575
7	30-60	45	-318266,425	-35523,437	-340946,665
8	60-90	75	154179,188	-79323,827	48857,091
9	90-120	105	239642,881	409343,276	341661,547
10	120-180	150	-427118,328	-1269091,215	-428951,971
11	180-240	210	1151779,371	414765,373	-38186,182
12	240-360	300	-1163360,217	232600,378	181596,912
		sum	-1512,970	117256,286	186796,704

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-0,052	3,592	5,995	3,178	2,486

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,719	2,529	3,003
20,893	18,138	20,993
91,083	74,700	87,233
137,307	120,533	137,394
528,731	520,101	556,673
1093,914	1229,976	1163,349
1001,687	1198,343	1043,027
1081,435	1246,996	1110,881
2142,092	2337,728	2235,461
2239,053	2115,581	2129,771
4596,260	4419,580	4288,973

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12935,174	13284,204	12776,758

Average AUC0-360 (µg/ml.min)		12998,712
	STDEV	259,621

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	6,042	5,619	6,674
5	24,911	21,252	24,427
10	56,051	45,147	53,113
15	65,999	61,993	69,015

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,745	4,298	4,834	4,625	0,235

Table 92: Table containing the AUC, DRi and MDT values and information regarding formula 4B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	10,745	4105,246	10,477	4213,978	12,397	5605,405
3	5	32,719	12500,611	34,074	13704,739	39,062	17662,133
4	10	57,177	21844,714	59,399	23891,046	67,024	30305,492
5	15	77,635	29660,627	79,259	31878,766	85,594	38701,967
6	30	91,016	34773,035	99,311	39944,101	103,761	46916,414
7	60	94,334	36040,893	87,698	35273,098	80,303	36309,328
8	90	90,423	34546,403	73,193	29439,209	79,121	35774,893
9	120	79,297	30295,693	96,816	38940,477	111,644	50480,452
10	180	74,909	28619,436	86,960	34976,389	87,747	39675,236
11	240	76,356	29172,091	81,478	32771,356	75,444	34112,444
12	360	82,598	31556,875	74,517	29971,472	89,713	40564,377

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
38205,447	40221,090	45215,687

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	4105,246	4213,978	5605,405
3	5	2-5	12500,611	13704,739	17662,133
4	10	5-10	21844,714	23891,046	30305,492
5	15	10-15	29660,627	31878,766	38701,967
6	30	15-30	34773,035	39944,101	46916,414
7	60	30-60	36040,893	35273,098	36309,328
8	90	60-90	34546,403	29439,209	35774,893
9	120	90-120	30295,693	38940,477	50480,452
10	180	120-180	28619,436	34976,389	39675,236
11	240	180-240	29172,091	32771,356	34112,444
12	360	240-360	31556,875	29971,472	40564,377

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	4105,246	4213,978	5605,405
3	2-5	3,5	8395,365	9490,760	12056,727
4	5-10	7,5	9344,103	10186,307	12643,359
5	10-15	12,5	7815,913	7987,720	8396,475
6	15-30	22,5	5112,408	8065,335	8214,447
7	30-60	45	1267,858	-4671,003	-10607,087
8	60-90	75	-1494,490	-5833,889	-534,435
9	90-120	105	-4250,710	9501,268	14705,559
10	120-180	150	-1676,257	-3964,088	-10805,217
11	180-240	210	552,655	-2205,033	-5562,791
12	240-360	300	2384,784	-2799,884	6451,932
		sum	31556,875	29971,472	40564,377

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	4105,246	4213,978	5605,405
3	2-5	3,5	29383,779	33217,661	42198,546
4	5-10	7,5	70080,770	76397,304	94825,194
5	10-15	12,5	97698,913	99846,497	104955,936
6	15-30	22,5	115029,171	181470,035	184825,064
7	30-60	45	57053,609	-210195,118	-477318,894
8	60-90	75	-112086,762	-437541,652	-40082,590
9	90-120	105	-446324,518	997633,091	1544083,714
10	120-180	150	-251438,535	-594613,201	-1620782,525
11	180-240	210	116057,582	-463056,868	-1168186,117
12	240-360	300	715435,194	-839965,326	1935579,718
		sum	394994,449	-1152593,598	605703,451

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
12,517	-38,456	14,932	-3,669	24,618

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
4,835	4,715	5,579
29,339	30,072	34,735
101,133	105,157	119,347
151,663	155,990	171,696
569,195	602,674	639,075
1251,115	1262,313	1242,431
1247,111	1086,018	1076,106
1145,607	1147,564	1287,658
2081,782	2480,981	2691,769
2042,080	2273,918	2203,071
4291,750	4211,861	4459,236

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12915,609	13361,263	13930,702

Average AUC0-360 (µg/ml.min)		13402,525
	STDEV	508,803

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	10,745	10,477	12,397
5	32,719	34,074	39,062
10	57,177	59,399	67,024
15	77,635	79,259	85,594

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,231	5,373	5,819	5,474	0,251

Table 93: Table containing the AUC, DRi and MDT values and information regarding formula 4C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,880	830,344	2,975	1269,340	2,139	825,542
3	5	14,624	6459,140	18,457	7875,528	14,361	5541,740
4	10	40,555	17911,972	46,766	19954,803	38,667	14921,792
5	15	58,967	26044,048	79,632	33978,412	67,679	26117,504
6	30	78,342	34601,580	81,732	34874,522	76,185	29399,678
7	60	85,601	37807,643	87,238	37224,076	84,815	32730,165
8	90	109,055	48166,589	90,989	38824,528	86,211	33268,904
9	120	84,816	37460,831	79,173	33782,621	89,723	34624,328
10	180	86,698	38292,135	97,737	41703,940	84,340	32546,905
11	240	94,665	41811,000	96,535	41191,245	95,284	36770,242
12	360	100,132	44225,448	105,357	44955,321	94,826	36593,366

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
44167,260	42669,550	38590,087

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	830,344	1269,340	825,542
3	5	2-5	6459,140	7875,528	5541,740
4	10	5-10	17911,972	19954,803	14921,792
5	15	10-15	26044,048	33978,412	26117,504
6	30	15-30	34601,580	34874,522	29399,678
7	60	30-60	37807,643	37224,076	32730,165
8	90	60-90	48166,589	38824,528	33268,904
9	120	90-120	37460,831	33782,621	34624,328
10	180	120-180	38292,135	41703,940	32546,905
11	240	180-240	41811,000	41191,245	36770,242
12	360	240-360	44225,448	44955,321	36593,366

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	830,344	1269,340	825,542
3	2-5	3,5	5628,796	6606,188	4716,198
4	5-10	7,5	11452,832	12079,275	9380,053
5	10-15	12,5	8132,076	14023,609	11195,711
6	15-30	22,5	8557,532	896,110	3282,174
7	30-60	45	3206,063	2349,554	3330,486
8	60-90	75	10358,946	1600,452	538,740
9	90-120	105	-10705,758	-5041,908	1355,424
10	120-180	150	831,304	7921,319	-2077,423
11	180-240	210	3518,866	-512,695	4223,337
12	240-360	300	2414,448	3764,076	-176,876
		sum	44225,448	44955,321	36593,366

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	830,344	1269,340	825,542
3	2-5	3,5	19700,785	23121,656	16506,692
4	5-10	7,5	85896,242	90594,566	70350,395
5	10-15	12,5	101650,949	175295,116	139946,393
6	15-30	22,5	192544,471	20162,469	73848,920
7	30-60	45	144272,846	105729,930	149871,891
8	60-90	75	776920,915	120033,922	40405,488
9	90-120	105	-1124104,642	-529400,317	142319,477
10	120-180	150	124695,626	1188197,887	-311613,521
11	180-240	210	738961,773	-107665,916	886900,812
12	240-360	300	724334,340	1129222,775	-53062,798
		sum	1785703,647	2216561,428	1156299,291

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
40,377	49,306	31,599	40,427	7,229

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,846	1,339	0,963
11,140	14,466	11,137
62,077	73,376	59,656
111,962	142,197	119,640
463,418	544,601	485,540
1106,617	1140,545	1086,747
1313,928	1203,031	1154,425
1308,628	1148,590	1187,557
2315,437	2388,281	2349,856
2448,403	2622,678	2424,927
5259,516	5451,094	5132,970

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14401,971	14730,198	14013,419

Average AUC0-360 (µg/ml.min)		14381,863
	STDEV	358,812

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,880	2,975	2,139
5	14,624	18,457	14,361
10	40,555	46,766	38,667
15	58,967	79,632	67,679

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,185	5,458	4,636	4,760	0,527

Table 94: Table containing the AUC, DRi and MDT values and information regarding formula 4D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	8,148	3516,842	3,716	1680,146	3,825	1637,873
3	5	32,029	13824,315	22,754	10289,397	22,297	9547,290
4	10	59,431	25651,320	52,105	23561,478	50,589	21661,262
5	15	82,943	35799,260	68,893	31153,088	63,348	27124,557
6	30	89,035	38428,800	104,551	47277,326	95,663	40961,059
7	60	106,571	45997,356	102,869	46516,571	98,142	42022,455
8	90	95,209	41093,234	91,005	41151,858	89,143	38169,175
9	120	91,253	39385,739	87,318	39484,678	87,287	37374,854
10	180	93,931	40541,747	93,693	42367,112	90,274	38653,718
11	240	98,361	42453,690	84,655	38280,525	87,433	37437,358
12	360	96,600	41693,942	102,131	46182,887	105,724	45268,973

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
43161,243	45219,237	42818,143

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3516,842	1680,146	1637,873
3	5	2-5	13824,315	10289,397	9547,290
4	10	5-10	25651,320	23561,478	21661,262
5	15	10-15	35799,260	31153,088	27124,557
6	30	15-30	38428,800	47277,326	40961,059
7	60	30-60	45997,356	46516,571	42022,455
8	90	60-90	41093,234	41151,858	38169,175
9	120	90-120	39385,739	39484,678	37374,854
10	180	120-180	40541,747	42367,112	38653,718
11	240	180-240	42453,690	38280,525	37437,358
12	360	240-360	41693,942	46182,887	45268,973

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3516,842	1680,146	1637,873
3	2-5	3,5	10307,473	8609,251	7909,417
4	5-10	7,5	11827,005	13272,080	12113,972
5	10-15	12,5	10147,940	7591,610	5463,296
6	15-30	22,5	2629,539	16124,238	13836,502
7	30-60	45	7568,557	-760,755	1061,397
8	60-90	75	-4904,123	-5364,713	-3853,280
9	90-120	105	-1707,494	-1667,179	-794,321
10	120-180	150	1156,007	2882,434	1278,863
11	180-240	210	1911,944	-4086,587	-1216,359
12	240-360	300	-759,748	7902,361	7831,615
		sum	41693,942	46182,887	45268,973

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3516,842	1680,146	1637,873
3	2-5	3,5	36076,157	30132,380	27682,959
4	5-10	7,5	88702,536	99540,603	90854,788
5	10-15	12,5	126849,251	94895,127	68291,194
6	15-30	22,5	59164,633	362795,359	311321,284
7	30-60	45	340585,051	-34233,977	47762,846
8	60-90	75	-367809,192	-402353,510	-288996,037
9	90-120	105	-179286,903	-175053,826	-83403,664
10	120-180	150	173401,094	432365,127	191829,511
11	180-240	210	401508,159	-858183,290	-255435,493
12	240-360	300	-227924,402	2370708,362	2349484,387
		sum	454783,227	1922292,502	2461029,648

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
10,908	41,623	54,365	35,632	18,240

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,667	1,672	1,721
27,120	17,867	17,633
102,893	84,217	81,997
160,171	136,123	128,179
580,427	585,376	536,663
1320,343	1400,087	1308,181
1362,012	1308,651	1264,169
1258,613	1203,684	1190,902
2499,977	2443,648	2397,081
2595,936	2407,699	2399,052
5263,950	5043,234	5215,245

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15175,110	14632,259	14540,823

Average AUC0-360 (µg/ml.min)		14782,731
	STDEV	342,872

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	8,148	3,716	3,825
5	32,029	22,754	22,297
10	59,431	52,105	50,589
15	82,943	68,893	63,348

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,674	4,905	4,550	5,043	0,469

Table 95: Table containing the AUC, DRi and MDT values and information regarding formula 4E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,206	892,613	6,253	2610,898	3,541	1365,656
3	5	14,965	6055,624	29,146	12169,210	19,562	7545,172
4	10	41,430	16764,235	63,658	26578,642	50,018	19291,892
5	15	65,199	26382,374	80,105	33445,374	77,204	29777,417
6	30	75,945	30730,733	80,587	33646,843	80,510	31052,433
7	60	74,044	29961,381	77,014	32154,826	79,292	30582,844
8	90	76,602	30996,628	90,107	37621,464	80,208	30935,956
9	120	82,274	33291,418	92,962	38813,639	94,499	36448,175
10	180	96,432	39020,410	96,567	40318,728	91,124	35146,383
11	240	99,912	40428,671	86,494	36113,148	95,234	36731,573
12	360	80,748	32674,076	97,047	40519,193	87,268	33659,008

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40464,320	41752,097	38569,790

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	892,613	2610,898	1365,656
3	5	2-5	6055,624	12169,210	7545,172
4	10	5-10	16764,235	26578,642	19291,892
5	15	10-15	26382,374	33445,374	29777,417
6	30	15-30	30730,733	33646,843	31052,433
7	60	30-60	29961,381	32154,826	30582,844
8	90	60-90	30996,628	37621,464	30935,956
9	120	90-120	33291,418	38813,639	36448,175
10	180	120-180	39020,410	40318,728	35146,383
11	240	180-240	40428,671	36113,148	36731,573
12	360	240-360	32674,076	40519,193	33659,008

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	892,613	2610,898	1365,656
3	2-5	3,5	5163,011	9558,313	6179,515
4	5-10	7,5	10708,611	14409,432	11746,720
5	10-15	12,5	9618,139	6866,732	10485,526
6	15-30	22,5	4348,359	201,468	1275,016
7	30-60	45	-769,352	-1492,017	-469,590
8	60-90	75	1035,247	5466,638	353,112
9	90-120	105	2294,790	1192,175	5512,220
10	120-180	150	5728,992	1505,089	-1301,792
11	180-240	210	1408,262	-4205,580	1585,190
12	240-360	300	-7754,596	4406,045	-3072,565
		sum	32674,076	40519,193	33659,008

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	892,613	2610,898	1365,656
3	2-5	3,5	18070,538	33454,094	21628,303
4	5-10	7,5	80314,581	108070,740	88100,400
5	10-15	12,5	120226,738	85834,149	131069,075
6	15-30	22,5	97838,080	4533,041	28687,853
7	30-60	45	-34620,823	-67140,773	-21131,531
8	60-90	75	77643,537	409997,857	26483,399
9	90-120	105	240952,936	125178,404	578783,078
10	120-180	150	859348,757	225763,380	-195268,847
11	180-240	210	295734,931	-883171,895	332889,858
12	240-360	300	-2326378,682	1321813,649	-921769,412
		sum	-569976,793	1366943,545	70837,832

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-17,444	33,736	2,105	6,132	21,087

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,993	2,814	1,593
11,591	23,895	15,595
63,444	104,405	78,278
119,957	161,733	143,125
476,362	542,335	532,284
1012,427	1063,806	1078,663
1016,863	1128,063	1076,625
1072,412	1235,715	1179,272
2412,520	2558,643	2505,916
2650,638	2471,326	2515,835
4877,814	4955,615	4927,550

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13715,021	14248,350	14054,736

Average AUC0-360 (µg/ml.min)		14006,036
	STDEV	269,979

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,206	6,253	3,541
5	14,965	29,146	19,562
10	41,430	63,658	50,018
15	65,199	80,105	77,204

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,552	5,695	5,369	5,206	0,481

Table 96: Table containing the AUC, DRi and MDT values and information regarding formula 4F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,664	2386,267	4,049	1819,802	1,601	631,021
3	5	28,899	12175,750	22,364	10051,537	12,442	4902,432
4	10	65,002	27386,939	50,936	22893,443	35,909	14148,831
5	15	90,590	38168,148	81,959	36837,149	56,596	22299,994
6	30	91,848	38698,096	88,042	39571,257	77,607	30578,905
7	60	84,168	35462,234	84,012	37759,609	78,567	30957,287
8	90	92,962	39167,534	93,045	41819,590	83,535	32914,688
9	120	86,645	36505,670	77,272	34730,482	84,565	33320,529
10	180	104,031	43831,067	105,292	47324,244	93,761	36944,033
11	240	102,319	43109,733	92,105	41397,396	83,730	32991,651
12	360	102,538	43202,019	110,977	49879,428	97,290	38334,423

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
42132,627	44945,710	39402,337

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2386,267	1819,802	631,021
3	5	2-5	12175,750	10051,537	4902,432
4	10	5-10	27386,939	22893,443	14148,831
5	15	10-15	38168,148	36837,149	22299,994
6	30	15-30	38698,096	39571,257	30578,905
7	60	30-60	35462,234	37759,609	30957,287
8	90	60-90	39167,534	41819,590	32914,688
9	120	90-120	36505,670	34730,482	33320,529
10	180	120-180	43831,067	47324,244	36944,033
11	240	180-240	43109,733	41397,396	32991,651
12	360	240-360	43202,019	49879,428	38334,423

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2386,267	1819,802	631,021
3	2-5	3,5	9789,483	8231,735	4271,411
4	5-10	7,5	15211,189	12841,907	9246,399
5	10-15	12,5	10781,209	13943,706	8151,163
6	15-30	22,5	529,949	2734,109	8278,911
7	30-60	45	-3235,862	-1811,649	378,382
8	60-90	75	3705,299	4059,981	1957,401
9	90-120	105	-2661,863	-7089,107	405,841
10	120-180	150	7325,397	12593,762	3623,504
11	180-240	210	-721,335	-5926,848	-3952,382
12	240-360	300	92,286	8482,032	5342,772
		sum	43202,019	49879,428	38334,423

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2386,267	1819,802	631,021
3	2-5	3,5	34263,190	28811,071	14949,939
4	5-10	7,5	114083,918	96314,301	69347,991
5	10-15	12,5	134765,108	174296,319	101889,538
6	15-30	22,5	11923,845	61517,443	186275,495
7	30-60	45	-145613,791	-81524,193	17027,209
8	60-90	75	277897,443	304498,585	146805,080
9	90-120	105	-279495,622	-744356,280	42613,287
10	120-180	150	1098809,541	1889064,307	543525,561
11	180-240	210	-151480,317	-1244638,155	-830000,201
12	240-360	300	27685,817	2544609,695	1602831,600
		sum	1125225,399	3030412,894	1895896,520

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
26,046	60,755	49,457	45,419	14,455

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,549	1,822	0,721
23,330	17,829	9,479
105,638	82,462	54,394
175,041	149,507	104,067
615,731	573,755	452,933
1188,111	1161,364	1054,174
1195,631	1195,130	1094,189
1212,348	1149,638	1134,673
2574,124	2464,615	2407,399
2785,729	2664,864	2396,131
5531,146	5483,225	4887,538

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
15409,378	14944,211	13595,699

Average AUC0-360 (µg/ml.min)		14649,762
	STDEV	942,010

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,664	4,049	1,601
5	28,899	22,364	12,442
10	65,002	50,936	35,909
15	90,590	81,959	56,596

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
6,352	5,624	3,965	5,314	0,999

Table 97: Table containing the AUC, DRi and MDT values and information regarding formula 5A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,430	3073,850	5,480	2166,474	7,523	2849,737
3	5	27,738	11476,030	18,892	7468,672	15,487	5866,455
4	10	55,986	23162,919	35,788	14148,532	33,921	12849,528
5	15	69,062	28573,004	47,170	18648,437	48,092	18217,387
6	30	91,718	37946,234	61,105	24157,463	62,980	23857,117
7	60	84,562	34985,783	72,691	28737,754	66,914	25347,303
8	90	102,155	42264,525	81,098	32061,268	80,865	30631,975
9	120	92,402	38229,327	91,021	35984,557	86,011	32581,453
10	180	88,574	36645,454	88,067	34816,759	84,855	32143,423
11	240	93,388	38637,290	95,041	37573,727	86,233	32665,551
12	360	83,352	34485,277	97,615	38591,412	93,532	35430,464

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41372,857	39534,190	37880,520

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	3073,850	2166,474	2849,737
3	5	2-5	11476,030	7468,672	5866,455
4	10	5-10	23162,919	14148,532	12849,528
5	15	10-15	28573,004	18648,437	18217,387
6	30	15-30	37946,234	24157,463	23857,117
7	60	30-60	34985,783	28737,754	25347,303
8	90	60-90	42264,525	32061,268	30631,975
9	120	90-120	38229,327	35984,557	32581,453
10	180	120-180	36645,454	34816,759	32143,423
11	240	180-240	38637,290	37573,727	32665,551
12	360	240-360	34485,277	38591,412	35430,464

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	3073,850	2166,474	2849,737
3	2-5	3,5	8402,180	5302,199	3016,717
4	5-10	7,5	11686,889	6679,859	6983,073
5	10-15	12,5	5410,085	4499,905	5367,860
6	15-30	22,5	9373,230	5509,026	5639,730
7	30-60	45	-2960,451	4580,291	1490,185
8	60-90	75	7278,742	3323,514	5284,672
9	90-120	105	-4035,199	3923,288	1949,478
10	120-180	150	-1583,872	-1167,798	-438,030
11	180-240	210	1991,836	2756,968	522,128
12	240-360	300	-4152,013	1017,685	2764,913
		sum	34485,277	38591,412	35430,464

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	3073,850	2166,474	2849,737
3	2-5	3,5	29407,631	18557,695	10558,511
4	5-10	7,5	87651,666	50098,946	52373,046
5	10-15	12,5	67626,062	56248,814	67098,248
6	15-30	22,5	210897,677	123953,083	126893,920
7	30-60	45	-133220,292	206113,110	67058,341
8	60-90	75	545905,650	249263,556	396350,428
9	90-120	105	-423695,850	411945,284	204695,200
10	120-180	150	-237580,820	-175169,651	-65704,463
11	180-240	210	418285,506	578963,277	109646,802
12	240-360	300	-1245603,912	305305,467	829473,955
		sum	-677252,832	1827446,056	1801293,725

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-19,639	47,354	50,840	26,185	32,434

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,343	2,466	3,385
23,738	16,451	15,532
94,189	61,515	55,584
140,679	93,328	92,265
542,632	365,430	374,867
1189,889	903,124	876,783
1260,342	1038,072	997,505
1313,261	1161,803	1126,412
2443,171	2417,699	2306,689
2456,483	2471,966	2309,686
4771,992	5201,722	4853,662

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14239,719	13733,576	13012,369

Average AUC0-360 (µg/ml.min)		13661,888
	STDEV	616,808

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,430	5,480	7,523
5	27,738	18,892	15,487
10	55,986	35,788	33,921
15	69,062	47,170	48,092

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,852	3,244	3,223	3,773	0,763

Table 98: Table containing the AUC, DRi and MDT values and information regarding formula 5B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	16,601	7345,443	17,241	7834,884	18,046	8135,337
3	5	37,982	16805,233	39,711	18045,538	45,196	20374,746
4	10	63,034	27889,886	64,789	29441,669	82,122	37021,737
5	15	72,103	31902,549	71,526	32502,874	110,368	49755,370
6	30	87,302	38627,452	80,005	36355,736	110,320	49733,490
7	60	90,146	39885,895	86,014	39086,572	111,312	50180,822
8	90	96,927	42885,903	88,172	40066,983	108,371	48855,269
9	120	109,249	48337,841	101,816	46267,067	104,235	46990,551
10	180	93,212	41242,512	91,752	41693,940	99,087	44669,877
11	240	85,598	37873,429	112,203	50987,173	104,755	47225,066
12	360	101,033	44702,872	96,760	43969,641	106,707	48104,756

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
44245,707	45442,057	45081,297

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	7345,443	7834,884	8135,337
3	5	2-5	16805,233	18045,538	20374,746
4	10	5-10	27889,886	29441,669	37021,737
5	15	10-15	31902,549	32502,874	49755,370
6	30	15-30	38627,452	36355,736	49733,490
7	60	30-60	39885,895	39086,572	50180,822
8	90	60-90	42885,903	40066,983	48855,269
9	120	90-120	48337,841	46267,067	46990,551
10	180	120-180	41242,512	41693,940	44669,877
11	240	180-240	37873,429	50987,173	47225,066
12	360	240-360	44702,872	43969,641	48104,756

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	7345,443	7834,884	8135,337
3	2-5	3,5	9459,790	10210,654	12239,409
4	5-10	7,5	11084,653	11396,131	16646,990
5	10-15	12,5	4012,663	3061,205	12733,633
6	15-30	22,5	6724,903	3852,862	-21,880
7	30-60	45	1258,443	2730,836	447,333
8	60-90	75	3000,008	980,411	-1325,553
9	90-120	105	5451,938	6200,084	-1864,718
10	120-180	150	-7095,329	-4573,128	-2320,674
11	180-240	210	-3369,083	9293,233	2555,189
12	240-360	300	6829,443	-7017,533	879,690
		sum	44702,872	43969,641	48104,756

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	7345,443	7834,884	8135,337
3	2-5	3,5	33109,266	35737,290	42837,931
4	5-10	7,5	83134,897	85470,983	124852,428
5	10-15	12,5	50158,290	38265,064	159170,417
6	15-30	22,5	151310,321	86689,391	-492,304
7	30-60	45	56629,916	122887,607	20129,968
8	60-90	75	225000,616	73530,858	-99416,503
9	90-120	105	572453,466	651008,851	-195795,418
10	120-180	150	-1064299,338	-685969,164	-348101,076
11	180-240	210	-707507,422	1951579,026	536589,762
12	240-360	300	2048832,953	-2105259,798	263907,024
		sum	1456168,407	261774,991	511817,565

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
32,574	5,954	10,640	16,389	11,603

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
7,471	7,759	8,121
36,844	38,443	42,688
113,643	117,563	143,232
152,029	153,355	216,552
537,993	511,416	744,821
1197,777	1120,626	1496,012
1262,743	1175,753	1482,862
1391,684	1282,413	1435,095
2733,225	2613,160	2744,854
2413,941	2753,386	2751,877
5039,043	5641,985	5709,475

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14886,392	15415,858	16775,588

Average AUC0-360 (µg/ml.min)		15692,613
	STDEV	974,531

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	16,601	17,241	18,046
5	37,982	39,711	45,196
10	63,034	64,789	82,122
15	72,103	71,526	110,368

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,831	4,805	7,387	5,674	1,211

Table 99: Table containing the AUC, DRi and MDT values and information regarding formula 5C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	6,729	2357,764	8,228	3616,354	10,350	4252,289
3	5	24,490	8581,060	31,645	13908,176	35,859	14733,362
4	10	49,977	17511,723	61,994	27247,043	64,890	26660,956
5	15	65,891	23087,989	82,053	36063,298	79,879	32819,495
6	30	81,435	28534,301	86,778	38139,713	85,882	35285,662
7	60	74,199	25998,860	83,160	36549,660	85,008	34926,834
8	90	78,756	27595,579	89,059	39142,220	81,680	33559,394
9	120	74,610	26142,873	103,632	45547,405	101,448	41681,263
10	180	86,517	30315,091	108,521	47696,081	88,622	36411,699
11	240	76,985	26974,937	79,603	34986,216	82,949	34080,789
12	360	81,868	28685,919	85,993	37794,881	92,332	37935,940

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
35039,423	43951,010	41086,387

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2357,764	3616,354	4252,289
3	5	2-5	8581,060	13908,176	14733,362
4	10	5-10	17511,723	27247,043	26660,956
5	15	10-15	23087,989	36063,298	32819,495
6	30	15-30	28534,301	38139,713	35285,662
7	60	30-60	25998,860	36549,660	34926,834
8	90	60-90	27595,579	39142,220	33559,394
9	120	90-120	26142,873	45547,405	41681,263
10	180	120-180	30315,091	47696,081	36411,699
11	240	180-240	26974,937	34986,216	34080,789
12	360	240-360	28685,919	37794,881	37935,940

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2357,764	3616,354	4252,289
3	2-5	3,5	6223,296	10291,822	10481,073
4	5-10	7,5	8930,664	13338,867	11927,594
5	10-15	12,5	5576,266	8816,254	6158,538
6	15-30	22,5	5446,312	2076,416	2466,167
7	30-60	45	-2535,441	-1590,053	-358,828
8	60-90	75	1596,719	2592,560	-1367,439
9	90-120	105	-1452,706	6405,185	8121,869
10	120-180	150	4172,218	2148,676	-5269,564
11	180-240	210	-3340,154	-12709,865	-2330,910
12	240-360	300	1710,982	2808,665	3855,151
		sum	28685,919	37794,881	37935,940

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2357,764	3616,354	4252,289
3	2-5	3,5	21781,535	36021,376	36683,755
4	5-10	7,5	66979,977	100041,506	89456,959
5	10-15	12,5	69703,326	110203,178	76981,728
6	15-30	22,5	122542,013	46719,354	55488,763
7	30-60	45	-114094,851	-71552,407	-16147,254
8	60-90	75	119753,934	194441,981	-102557,962
9	90-120	105	-152534,093	672544,432	852796,244
10	120-180	150	625832,651	322301,438	-790434,617
11	180-240	210	-701432,327	-2669071,694	-489491,138
12	240-360	300	513294,675	842599,463	1156545,263
		sum	574184,605	-412135,018	873574,031

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
20,016	-10,905	23,028	10,713	15,335

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,028	3,703	4,657
21,073	26,914	31,191
83,775	105,344	113,343
130,352	162,053	162,865
497,226	569,805	559,443
1050,528	1147,080	1153,507
1032,444	1162,477	1125,147
1035,218	1300,664	1236,114
2175,214	2864,069	2565,947
2207,272	2539,671	2316,214
4289,006	4471,091	4732,594

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12525,137	14352,870	14001,022

Average AUC0-360 (µg/ml.min)		13626,343
	STDEV	969,763

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	6,729	8,228	10,350
5	24,490	31,645	35,859
10	49,977	61,994	64,890
15	65,891	82,053	79,879

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,576	5,686	5,528	5,263	0,490

Table 100: Table containing the AUC, DRi and MDT values and information regarding formula 5D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,030	1236,339	2,711	1108,463	2,356	908,738
3	5	14,714	6004,370	15,093	6170,748	14,864	5734,288
4	10	39,068	15943,119	40,910	16726,522	35,707	13775,212
5	15	65,795	26849,802	65,751	26882,835	54,341	20963,903
6	30	93,481	38147,899	94,820	38768,058	83,980	32398,028
7	60	97,587	39823,394	96,115	39297,688	88,092	33984,655
8	90	96,518	39387,428	80,425	32882,711	84,176	32473,972
9	120	100,761	41118,833	97,405	39825,140	92,587	35718,741
10	180	95,922	39144,214	100,953	41275,558	95,256	36748,152
11	240	91,697	37419,775	81,328	33251,542	75,108	28975,455
12	360	82,845	33807,413	83,172	34005,812	72,130	27826,559

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40808,243	40885,940	38578,493

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1236,339	1108,463	908,738
3	5	2-5	6004,370	6170,748	5734,288
4	10	5-10	15943,119	16726,522	13775,212
5	15	10-15	26849,802	26882,835	20963,903
6	30	15-30	38147,899	38768,058	32398,028
7	60	30-60	39823,394	39297,688	33984,655
8	90	60-90	39387,428	32882,711	32473,972
9	120	90-120	41118,833	39825,140	35718,741
10	180	120-180	39144,214	41275,558	36748,152
11	240	180-240	37419,775	33251,542	28975,455
12	360	240-360	33807,413	34005,812	27826,559

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1236,339	1108,463	908,738
3	2-5	3,5	4768,032	5062,285	4825,550
4	5-10	7,5	9938,749	10555,774	8040,923
5	10-15	12,5	10906,683	10156,313	7188,691
6	15-30	22,5	11298,096	11885,223	11434,126
7	30-60	45	1675,496	529,629	1586,627
8	60-90	75	-435,966	-6414,977	-1510,683
9	90-120	105	1731,405	6942,429	3244,769
10	120-180	150	-1974,619	1450,418	1029,411
11	180-240	210	-1724,439	-8024,015	-7772,696
12	240-360	300	-3612,362	754,270	-1148,896
		sum	33807,413	34005,812	27826,559

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1236,339	1108,463	908,738
3	2-5	3,5	16688,111	17717,998	16889,426
4	5-10	7,5	74540,614	79168,304	60306,925
5	10-15	12,5	136333,540	126953,914	89858,638
6	15-30	22,5	254207,168	267417,519	257267,827
7	30-60	45	75397,310	23833,323	71398,218
8	60-90	75	-32697,479	-481123,280	-113301,225
9	90-120	105	181797,500	728955,071	340700,725
10	120-180	150	-296192,780	217562,668	154411,610
11	180-240	210	-362132,150	-1685043,249	-1632266,245
12	240-360	300	-1083708,748	226280,963	-344668,832
		sum	-1034530,574	-477168,306	-1098494,196

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-30,601	-14,032	-39,476	-28,036	10,545

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,363	1,220	1,060
11,977	12,018	11,623
60,505	63,003	56,892
117,971	119,994	101,304
537,556	541,927	466,831
1289,706	1288,814	1161,484
1310,208	1191,651	1162,813
1331,636	1200,359	1193,154
2655,226	2677,838	2535,877
2532,856	2460,787	2299,905
4712,612	4441,499	3975,413

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14561,616	13999,109	12966,357

Average AUC0-360 (µg/ml.min)		13842,360
	STDEV	809,099

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,030	2,711	2,356
5	14,714	15,093	14,864
10	39,068	40,910	35,707
15	65,795	65,751	54,341

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,508	4,555	3,785	4,283	0,353

Table 101: Table containing the AUC, DRi and MDT values and information regarding formula 5E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,944	1175,704	3,310	1354,736	2,253	878,005
3	5	17,161	6853,861	12,574	5147,115	14,863	5791,477
4	10	41,449	16554,541	30,331	12415,289	36,585	14255,216
5	15	55,941	22342,757	45,102	18461,737	62,807	24472,750
6	30	86,482	34540,544	62,620	25632,349	82,850	32282,314
7	60	83,992	33546,054	72,407	29638,537	92,925	36208,031
8	90	80,810	32275,175	82,303	33689,249	96,209	37487,659
9	120	91,080	36377,127	101,070	41370,966	87,075	33928,396
10	180	77,069	30781,071	75,796	31025,535	84,949	33100,006
11	240	97,610	38984,968	93,288	38185,652	90,182	35139,000
12	360	98,616	39387,020	91,044	37267,125	93,894	36585,685

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39939,633	40933,167	38964,730

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1175,704	1354,736	878,005
3	5	2-5	6853,861	5147,115	5791,477
4	10	5-10	16554,541	12415,289	14255,216
5	15	10-15	22342,757	18461,737	24472,750
6	30	15-30	34540,544	25632,349	32282,314
7	60	30-60	33546,054	29638,537	36208,031
8	90	60-90	32275,175	33689,249	37487,659
9	120	90-120	36377,127	41370,966	33928,396
10	180	120-180	30781,071	31025,535	33100,006
11	240	180-240	38984,968	38185,652	35139,000
12	360	240-360	39387,020	37267,125	36585,685

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1175,704	1354,736	878,005
3	2-5	3,5	5678,157	3792,379	4913,472
4	5-10	7,5	9700,679	7268,174	8463,739
5	10-15	12,5	5788,216	6046,449	10217,534
6	15-30	22,5	12197,788	7170,611	7809,565
7	30-60	45	-994,490	4006,188	3925,717
8	60-90	75	-1270,879	4050,712	1279,627
9	90-120	105	4101,952	7681,717	-3559,263
10	120-180	150	-5596,055	-10345,432	-828,390
11	180-240	210	8203,897	7160,117	2038,994
12	240-360	300	402,052	-918,527	1446,685
		sum	39387,020	37267,125	36585,685

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1175,704	1354,736	878,005
3	2-5	3,5	19873,549	13273,326	17197,151
4	5-10	7,5	72755,096	54511,304	63478,043
5	10-15	12,5	72352,700	75580,608	127719,169
6	15-30	22,5	274450,220	161338,759	175715,202
7	30-60	45	-44752,063	180278,459	176657,283
8	60-90	75	-95315,935	303803,436	95972,054
9	90-120	105	430704,913	806580,267	-373722,607
10	120-180	150	-839408,315	-1551814,755	-124258,524
11	180-240	210	1722818,273	1503624,592	428188,709
12	240-360	300	120615,720	-275558,035	434005,518
		sum	1735269,862	1272972,697	1021830,004

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
44,057	34,158	27,930	35,382	6,640

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,325	1,489	1,014
13,570	10,722	11,554
65,936	48,268	57,879
109,564	84,862	111,816
480,678	363,562	491,594
1150,698	911,433	1186,483
1112,412	1044,294	1276,657
1160,259	1237,765	1237,166
2270,015	2387,679	2322,314
2358,163	2282,626	2364,258
5298,105	4976,954	4970,050

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14020,724	13349,655	14030,785

Average AUC0-360 (µg/ml.min)		13800,388
	STDEV	390,379

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,944	3,310	2,253
5	17,161	12,574	14,863
10	41,449	30,331	36,585
15	55,941	45,102	62,807

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,977	3,116	4,297	3,797	0,499

Table 102: Table containing the AUC, DRi and MDT values and information regarding formula 5F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,711	281,873	1,329	601,790	0,711	290,774
3	5	5,492	2176,882	14,781	6693,704	4,853	1984,531
4	10	19,656	7791,398	34,859	15786,139	17,839	7294,505
5	15	36,683	14540,463	51,727	23424,751	33,093	13531,691
6	30	62,900	24932,418	67,719	30666,559	62,840	25695,116
7	60	74,063	29357,218	84,740	38374,578	76,146	31136,140
8	90	76,540	30339,392	83,030	37600,134	91,458	37397,153
9	120	82,808	32823,584	85,598	38763,129	83,571	34172,192
10	180	70,832	28076,526	85,730	38823,140	76,471	31269,236
11	240	92,173	36536,048	104,062	47124,906	89,655	36659,806
12	360	96,597	38289,699	111,815	50635,846	94,757	38746,397

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39638,397	45285,227	40890,067

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	281,873	601,790	290,774
3	5	2-5	2176,882	6693,704	1984,531
4	10	5-10	7791,398	15786,139	7294,505
5	15	10-15	14540,463	23424,751	13531,691
6	30	15-30	24932,418	30666,559	25695,116
7	60	30-60	29357,218	38374,578	31136,140
8	90	60-90	30339,392	37600,134	37397,153
9	120	90-120	32823,584	38763,129	34172,192
10	180	120-180	28076,526	38823,140	31269,236
11	240	180-240	36536,048	47124,906	36659,806
12	360	240-360	38289,699	50635,846	38746,397

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	281,873	601,790	290,774
3	2-5	3,5	1895,009	6091,914	1693,757
4	5-10	7,5	5614,516	9092,435	5309,974
5	10-15	12,5	6749,065	7638,611	6237,186
6	15-30	22,5	10391,954	7241,808	12163,425
7	30-60	45	4424,800	7708,019	5441,024
8	60-90	75	982,174	-774,444	6261,013
9	90-120	105	2484,192	1162,995	-3224,961
10	120-180	150	-4747,058	60,011	-2902,956
11	180-240	210	8459,522	8301,766	5390,569
12	240-360	300	1753,652	3510,939	2086,591
		sum	38289,699	50635,846	38746,397

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	281,873	601,790	290,774
3	2-5	3,5	6632,531	21321,699	5928,151
4	5-10	7,5	42108,872	68193,262	39824,805
5	10-15	12,5	84363,313	95482,643	77964,821
6	15-30	22,5	233818,974	162940,690	273677,065
7	30-60	45	199115,998	346860,852	244846,085
8	60-90	75	73663,067	-58083,335	469575,973
9	90-120	105	260840,176	122114,521	-338620,890
10	120-180	150	-712058,775	9001,697	-435443,368
11	180-240	210	1776499,666	1743370,865	1132019,587
12	240-360	300	526095,481	1053281,819	625977,449
		sum	2491361,177	3565086,503	2096040,450

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
65,066	70,406	54,096	63,190	6,789

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,320	0,598	0,320
4,187	10,874	3,756
28,292	55,846	25,529
63,381	97,410	57,299
336,091	403,130	323,772
924,495	1029,094	938,152
1016,570	1132,443	1131,325
1075,599	1138,234	1181,444
2074,129	2312,928	2160,572
2200,568	2562,201	2242,701
5096,814	5828,701	4979,125

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
12820,445	14571,459	13043,995

Average AUC0-360 (µg/ml.min)		13478,633
	STDEV	952,993

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,711	1,329	0,711
5	5,492	14,781	4,853
10	19,656	34,859	17,839
15	36,683	51,727	33,093

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,516	3,645	2,271	2,811	0,598

Table 103: Table containing the AUC, DRi and MDT values and information regarding formula 6A evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,708	1954,048	9,639	4240,282	7,399	2740,417
3	5	20,345	8443,966	33,251	14628,177	22,917	8488,532
4	10	48,374	20076,975	62,666	27568,558	42,005	15558,597
5	15	58,780	24395,954	95,760	42127,642	55,078	20400,833
6	30	75,399	31293,091	101,628	44709,406	63,452	23502,552
7	60	88,202	36607,017	101,258	44546,679	85,273	31585,353
8	90	87,706	36400,954	102,149	44938,286	82,855	30689,386
9	120	98,614	40928,349	101,946	44849,083	69,947	25908,429
10	180	98,259	40780,985	102,194	44958,125	65,056	24096,669
11	240	99,521	41304,856	107,090	47112,276	82,385	30515,630
12	360	97,436	40439,591	104,180	45831,914	89,420	33121,215

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41503,543	43993,090	37040,083

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1954,048	4240,282	2740,417
3	5	2-5	8443,966	14628,177	8488,532
4	10	5-10	20076,975	27568,558	15558,597
5	15	10-15	24395,954	42127,642	20400,833
6	30	15-30	31293,091	44709,406	23502,552
7	60	30-60	36607,017	44546,679	31585,353
8	90	60-90	36400,954	44938,286	30689,386
9	120	90-120	40928,349	44849,083	25908,429
10	180	120-180	40780,985	44958,125	24096,669
11	240	180-240	41304,856	47112,276	30515,630
12	360	240-360	40439,591	45831,914	33121,215

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1954,048	4240,282	2740,417
3	2-5	3,5	6489,918	10387,895	5748,115
4	5-10	7,5	11633,009	12940,381	7070,065
5	10-15	12,5	4318,978	14559,084	4842,236
6	15-30	22,5	6897,137	2581,764	3101,718
7	30-60	45	5313,926	-162,727	8082,802
8	60-90	75	-206,063	391,607	-895,968
9	90-120	105	4527,394	-89,203	-4780,957
10	120-180	150	-147,363	109,041	-1811,760
11	180-240	210	523,870	2154,152	6418,961
12	240-360	300	-865,265	-1280,362	2605,585
		sum	40439,591	45831,914	33121,215

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1954,048	4240,282	2740,417
3	2-5	3,5	22714,712	36357,631	20118,402
4	5-10	7,5	87247,570	97052,857	53025,486
5	10-15	12,5	53987,228	181988,551	60527,955
6	15-30	22,5	155185,591	58089,698	69788,661
7	30-60	45	239126,662	-7322,731	363726,073
8	60-90	75	-15454,690	29370,547	-67197,570
9	90-120	105	475376,410	-9366,292	-502000,500
10	120-180	150	-22104,480	16356,196	-271764,006
11	180-240	210	110012,776	452371,820	1347981,827
12	240-360	300	-259579,556	-384108,557	781675,627
		sum	848466,272	475030,003	1858622,373

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
20,981	10,365	56,116	29,154	19,551

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,119	4,337	3,329
16,911	28,950	20,463
77,309	107,906	73,037
120,549	178,229	109,218
452,854	666,184	400,037
1104,305	1369,485	1003,895
1187,378	1372,996	1134,864
1257,658	1377,636	1031,410
2657,788	2755,881	1822,536
2670,034	2825,331	1990,455
5317,859	5704,289	4638,744

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14864,764	16391,226	12227,988

Average AUC0-360 (µg/ml.min)		14494,659
	STDEV	2106,151

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,708	9,639	7,399
5	20,345	33,251	22,917
10	48,374	62,666	42,005
15	58,780	95,760	55,078

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,226	6,435	3,755	4,805	1,169

Table 104: Table containing the AUC, DRi and MDT values and information regarding formula 6B evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,566	2113,746	3,702	1322,049	5,018	1979,678
3	5	18,572	7053,061	17,903	6392,927	22,739	8971,473
4	10	37,808	14357,990	41,592	14852,349	52,120	20562,858
5	15	54,608	20738,407	61,839	22082,555	69,904	27579,250
6	30	75,265	28582,880	71,005	25355,650	80,733	31851,811
7	60	80,663	30633,172	81,331	29043,032	87,662	34585,504
8	90	84,382	32045,293	79,763	28482,967	89,181	35184,824
9	120	75,911	28828,383	72,850	26014,402	86,109	33972,748
10	180	83,733	31798,848	77,795	27780,446	83,558	32966,221
11	240	89,360	33935,971	77,344	27619,274	93,319	36817,242
12	360	93,769	35610,298	82,430	29435,488	94,956	37463,448

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37976,533	35709,600	39453,287

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2113,746	1322,049	1979,678
3	5	2-5	7053,061	6392,927	8971,473
4	10	5-10	14357,990	14852,349	20562,858
5	15	10-15	20738,407	22082,555	27579,250
6	30	15-30	28582,880	25355,650	31851,811
7	60	30-60	30633,172	29043,032	34585,504
8	90	60-90	32045,293	28482,967	35184,824
9	120	90-120	28828,383	26014,402	33972,748
10	180	120-180	31798,848	27780,446	32966,221
11	240	180-240	33935,971	27619,274	36817,242
12	360	240-360	35610,298	29435,488	37463,448

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2113,746	1322,049	1979,678
3	2-5	3,5	4939,315	5070,878	6991,795
4	5-10	7,5	7304,928	8459,422	11591,385
5	10-15	12,5	6380,417	7230,206	7016,392
6	15-30	22,5	7844,473	3273,095	4272,560
7	30-60	45	2050,292	3687,382	2733,694
8	60-90	75	1412,121	-560,065	599,320
9	90-120	105	-3216,909	-2468,565	-1212,076
10	120-180	150	2970,465	1766,044	-1006,526
11	180-240	210	2137,122	-161,172	3851,021
12	240-360	300	1674,328	1816,214	646,206
		sum	35610,298	29435,488	37463,448

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2113,746	1322,049	1979,678
3	2-5	3,5	17287,604	17748,072	24471,281
4	5-10	7,5	54786,963	63445,665	86935,390
5	10-15	12,5	79755,213	90377,581	87704,900
6	15-30	22,5	176500,651	73644,635	96132,609
7	30-60	45	92263,144	165932,195	123016,225
8	60-90	75	105909,050	-42004,850	44948,983
9	90-120	105	-337775,477	-259199,322	-127268,022
10	120-180	150	445569,758	264906,598	-150978,961
11	180-240	210	448795,700	-33846,176	808714,347
12	240-360	300	502298,259	544864,131	193861,761
		sum	1587504,609	887190,578	1189518,191

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
44,580	30,140	31,751	35,491	6,461

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,505	1,666	2,258
16,293	14,583	18,736
63,427	66,931	84,216
103,968	116,360	137,276
438,322	448,350	508,398
1052,514	1028,270	1136,665
1114,055	1087,384	1193,689
1081,977	1030,135	1183,206
2155,193	2033,712	2290,496
2336,759	2094,384	2387,828
4944,499	4313,906	5083,426

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13309,512	12235,683	14026,196

Average AUC0-360 (µg/ml.min)		13190,464
	STDEV	901,174

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,566	3,702	5,018
5	18,572	17,903	22,739
10	37,808	41,592	52,120
15	54,608	61,839	69,904

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,722	4,291	4,926	4,313	0,492

Table 105: Table containing the AUC, DRi and MDT values and information regarding formula 6C evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,567	637,530	1,927	810,215	1,484	668,591
3	5	10,824	4402,580	10,002	4204,626	9,864	4442,528
4	10	28,496	11590,706	32,870	13817,489	29,286	13190,466
5	15	44,409	18063,003	45,683	19203,383	52,836	23797,145
6	30	59,951	24384,712	67,459	28357,232	76,939	34653,188
7	60	78,779	32042,569	72,068	30294,950	81,933	36902,491
8	90	75,503	30710,153	95,900	40312,966	91,379	41157,001
9	120	86,861	35330,091	79,037	33224,229	109,398	49272,759
10	180	100,430	40849,116	83,926	35279,407	111,209	50088,535
11	240	94,017	38240,608	98,099	41237,282	109,906	49501,450
12	360	94,386	38390,664	103,794	43631,368	107,854	48577,307

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40674,183	42036,537	45039,823

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	637,530	810,215	668,591
3	5	2-5	4402,580	4204,626	4442,528
4	10	5-10	11590,706	13817,489	13190,466
5	15	10-15	18063,003	19203,383	23797,145
6	30	15-30	24384,712	28357,232	34653,188
7	60	30-60	32042,569	30294,950	36902,491
8	90	60-90	30710,153	40312,966	41157,001
9	120	90-120	35330,091	33224,229	49272,759
10	180	120-180	40849,116	35279,407	50088,535
11	240	180-240	38240,608	41237,282	49501,450
12	360	240-360	38390,664	43631,368	48577,307

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	637,530	810,215	668,591
3	2-5	3,5	3765,050	3394,411	3773,937
4	5-10	7,5	7188,126	9612,863	8747,938
5	10-15	12,5	6472,297	5385,894	10606,678
6	15-30	22,5	6321,709	9153,849	10856,043
7	30-60	45	7657,857	1937,718	2249,304
8	60-90	75	-1332,416	10018,016	4254,510
9	90-120	105	4619,938	-7088,737	8115,757
10	120-180	150	5519,025	2055,178	815,777
11	180-240	210	-2608,507	5957,875	-587,086
12	240-360	300	150,056	2394,086	-924,143
		sum	38390,664	43631,368	48577,307

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	637,530	810,215	668,591
3	2-5	3,5	13177,675	11880,437	13208,779
4	5-10	7,5	53910,944	72096,475	65609,538
5	10-15	12,5	80903,712	67323,676	132583,478
6	15-30	22,5	142238,448	205961,592	244260,971
7	30-60	45	344603,582	87197,322	101218,662
8	60-90	75	-99931,196	751351,196	319088,243
9	90-120	105	485093,467	-744317,394	852154,514
10	120-180	150	827853,705	308276,758	122366,527
11	180-240	210	-547786,544	1251153,681	-123288,009
12	240-360	300	45016,780	718225,886	-277242,911
		sum	1345718,104	2729959,845	1450628,384

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
35,053	62,569	29,862	42,495	14,352

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,705	0,867	0,668
8,364	8,053	7,660
44,236	48,232	44,044
82,019	88,372	92,387
352,216	381,851	437,990
936,427	941,805	1072,386
1041,400	1133,784	1169,857
1095,957	1180,821	1355,247
2528,433	2199,989	2978,203
2625,034	2457,327	2985,058
5086,874	5451,100	5879,522

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13801,665	13892,200	16023,022

Average AUC0-360 (µg/ml.min)		14572,296
	STDEV	1257,181

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,567	1,927	1,484
5	10,824	10,002	9,864
10	28,496	32,870	29,286
15	44,409	45,683	52,836

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,100	3,276	3,616	3,330	0,214

Table 106: Table containing the AUC, DRi and MDT values and information regarding formula 6D evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,567	656,102	1,927	832,988	1,484	675,210
3	5	10,824	4530,828	10,002	4322,805	9,864	4486,507
4	10	28,496	11928,346	32,870	14205,856	29,280	13318,351
5	15	44,409	18589,182	45,683	19743,131	52,836	24032,712
6	30	59,951	25095,043	67,459	29154,266	76,939	34996,226
7	60	78,779	32975,975	72,068	31146,447	81,933	37267,797
8	90	75,503	31604,746	95,900	41446,038	91,379	41564,425
9	120	86,861	36359,263	79,037	34158,059	109,398	49760,525
10	180	100,430	42039,058	83,926	36271,002	111,209	50584,377
11	240	94,017	39354,565	98,099	42396,334	112,310	51085,158
12	360	96,190	40264,315	104,732	45263,000	111,617	50769,809

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41859,030	43218,053	45485,700

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	656,102	832,988	675,210
3	5	2-5	4530,828	4322,805	4486,507
4	10	5-10	11928,346	14205,856	13318,351
5	15	10-15	18589,182	19743,131	24032,712
6	30	15-30	25095,043	29154,266	34996,226
7	60	30-60	32975,975	31146,447	37267,797
8	90	60-90	31604,746	41446,038	41564,425
9	120	90-120	36359,263	34158,059	49760,525
10	180	120-180	42039,058	36271,002	50584,377
11	240	180-240	39354,565	42396,334	51085,158
12	360	240-360	40264,315	45263,000	50769,809

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	656,102	832,988	675,210
3	2-5	3,5	3874,727	3489,817	3811,297
4	5-10	7,5	7397,517	9883,051	8831,844
5	10-15	12,5	6660,836	5537,275	10714,361
6	15-30	22,5	6505,861	9411,135	10963,514
7	30-60	45	7880,932	1992,182	2271,571
8	60-90	75	-1371,229	10299,591	4296,628
9	90-120	105	4754,517	-7287,979	8196,100
10	120-180	150	5679,795	2112,943	823,853
11	180-240	210	-2684,494	6125,332	500,781
12	240-360	300	909,750	2866,666	-315,349
		sum	40264,315	45263,000	50769,809

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	656,102	832,988	675,210
3	2-5	3,5	13561,544	12214,359	13339,541
4	5-10	7,5	55481,380	74122,883	66238,831
5	10-15	12,5	83260,453	69215,936	133929,508
6	15-30	22,5	146381,881	211750,534	246679,059
7	30-60	45	354641,950	89648,168	102220,687
8	60-90	75	-102842,211	772469,348	322247,092
9	90-120	105	499224,331	-765237,847	860590,511
10	120-180	150	851969,240	316941,462	123577,908
11	180-240	210	-563743,670	1286319,730	105163,949
12	240-360	300	272925,010	859999,778	-94604,640
		sum	1611516,009	2928277,339	1880057,657

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
40,023	64,695	37,031	47,250	12,396

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,705	0,867	0,668
8,364	8,053	7,660
44,236	48,232	44,037
82,019	88,372	92,381
352,216	381,851	437,990
936,427	941,805	1072,386
1041,400	1133,784	1169,857
1095,957	1180,821	1355,247
2528,433	2199,989	2978,202
2625,034	2457,327	3017,517
5135,594	5476,420	6046,041

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13850,385	13917,520	16221,984

Average AUC0-360 (µg/ml.min)		14663,296
	STDEV	1350,281

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,567	1,927	1,484
5	10,824	10,002	9,864
10	28,496	32,870	29,280
15	44,409	45,683	52,836

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,100	3,276	3,616	3,330	0,214

Table 107: Table containing the AUC, DRi and MDT values and information regarding formula 6E evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,732	2045,571	11,474	4920,122	11,108	4924,243
3	5	19,539	8446,837	34,878	14955,620	26,919	11932,974
4	10	43,488	18799,914	58,811	25218,251	56,416	25009,381
5	15	60,869	26313,538	92,234	39550,409	83,926	37204,489
6	30	80,883	34965,413	87,912	37696,753	102,894	45612,833
7	60	89,308	38607,627	88,012	37739,930	80,090	35503,979
8	90	100,514	43451,911	96,459	41361,921	107,892	47828,326
9	120	85,718	37055,929	105,877	45400,575	109,457	48522,210
10	180	88,885	38424,965	80,427	34487,247	103,404	45838,920
11	240	97,235	42034,364	76,957	32999,602	97,225	43099,865
12	360	106,740	46143,645	76,480	32794,807	102,791	45567,292

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
43229,823	42880,337	44330,007

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2045,571	4920,122	4924,243
3	5	2-5	8446,837	14955,620	11932,974
4	10	5-10	18799,914	25218,251	25009,381
5	15	10-15	26313,538	39550,409	37204,489
6	30	15-30	34965,413	37696,753	45612,833
7	60	30-60	38607,627	37739,930	35503,979
8	90	60-90	43451,911	41361,921	47828,326
9	120	90-120	37055,929	45400,575	48522,210
10	180	120-180	38424,965	34487,247	45838,920
11	240	180-240	42034,364	32999,602	43099,865
12	360	240-360	46143,645	32794,807	45567,292

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2045,571	4920,122	4924,243
3	2-5	3,5	6401,266	10035,499	7008,731
4	5-10	7,5	10353,077	10262,630	13076,407
5	10-15	12,5	7513,624	14332,158	12195,108
6	15-30	22,5	8651,875	-1853,655	8408,344
7	30-60	45	3642,214	43,177	-10108,854
8	60-90	75	4844,284	3621,991	12324,348
9	90-120	105	-6395,982	4038,654	693,883
10	120-180	150	1369,037	-10913,328	-2683,290
11	180-240	210	3609,398	-1487,644	-2739,054
12	240-360	300	4109,281	-204,795	2467,426
		sum	46143,645	32794,807	45567,292

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2045,571	4920,122	4924,243
3	2-5	3,5	22404,431	35124,245	24530,558
4	5-10	7,5	77648,074	76969,728	98073,052
5	10-15	12,5	93920,305	179151,973	152438,853
6	15-30	22,5	194667,177	-41707,242	189187,744
7	30-60	45	163899,631	1942,956	-454898,438
8	60-90	75	363321,314	271649,315	924326,064
9	90-120	105	-671578,134	424058,631	72857,734
10	120-180	150	205355,537	-1636999,203	-402493,475
11	180-240	210	757973,683	-312405,275	-575201,429
12	240-360	300	1232784,338	-61438,523	740227,924
		sum	2442441,927	-1058733,273	773972,830

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
52,931	-32,284	16,985	12,544	34,930

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,129	5,163	4,999
16,383	31,287	25,668
70,906	105,399	93,752
117,402	169,926	157,885
478,412	607,992	630,518
1148,786	1187,485	1235,142
1281,296	1245,180	1268,877
1257,067	1365,770	1467,101
2357,151	2515,105	2873,618
2512,619	2124,686	2708,490
5507,324	4142,806	5400,435

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14749,474	13500,801	15866,484

Average AUC0-360 (µg/ml.min)		14705,586
	STDEV	1183,452

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,732	11,474	11,108
5	19,539	34,878	26,919
10	43,488	58,811	56,416
15	60,869	92,234	83,926

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,235	6,070	5,619	5,308	0,781

Table 108: Table containing the AUC, DRi and MDT values and information regarding formula 6F evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,827	1599,155	4,043	1831,977	20,170	7685,715
3	5	17,708	7399,996	21,691	9828,833	46,513	17723,136
4	10	42,366	17704,837	58,683	26590,926	65,360	24904,948
5	15	60,676	25356,256	91,178	41315,142	73,432	27980,407
6	30	84,398	35269,767	107,150	48552,787	89,812	34222,125
7	60	98,172	41025,795	97,008	43956,774	75,252	28674,147
8	90	80,756	33747,705	101,707	46086,357	72,145	27490,101
9	120	80,310	33561,295	108,402	49119,946	77,686	29601,529
10	180	92,548	38675,495	104,389	47301,410	81,105	30904,212
11	240	84,871	35467,204	105,137	47640,271	76,017	28965,666
12	360	99,589	41618,178	108,374	49107,393	91,730	34952,922

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41789,757	45312,740	38103,987

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1599,155	1831,977	7685,715
3	5	2-5	7399,996	9828,833	17723,136
4	10	5-10	17704,837	26590,926	24904,948
5	15	10-15	25356,256	41315,142	27980,407
6	30	15-30	35269,767	48552,787	34222,125
7	60	30-60	41025,795	43956,774	28674,147
8	90	60-90	33747,705	46086,357	27490,101
9	120	90-120	33561,295	49119,946	29601,529
10	180	120-180	38675,495	47301,410	30904,212
11	240	180-240	35467,204	47640,271	28965,666
12	360	240-360	41618,178	49107,393	34952,922

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1599,155	1831,977	7685,715
3	2-5	3,5	5800,841	7996,856	10037,421
4	5-10	7,5	10304,842	16762,093	7181,811
5	10-15	12,5	7651,419	14724,216	3075,459
6	15-30	22,5	9913,511	7237,645	6241,718
7	30-60	45	5756,028	-4596,013	-5547,978
8	60-90	75	-7278,090	2129,583	-1184,046
9	90-120	105	-186,410	3033,589	2111,428
10	120-180	150	5114,199	-1818,536	1302,683
11	180-240	210	-3208,291	338,861	-1938,546
12	240-360	300	6150,974	1467,122	5987,256
		sum	41618,178	49107,393	34952,922

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1599,155	1831,977	7685,715
3	2-5	3,5	20302,944	27988,995	35130,974
4	5-10	7,5	77286,311	125715,694	53863,584
5	10-15	12,5	95642,737	184052,705	38443,238
6	15-30	22,5	223053,987	162847,023	140438,664
7	30-60	45	259021,270	-206820,604	-249659,014
8	60-90	75	-545856,770	159718,738	-88803,458
9	90-120	105	-19573,032	318526,857	221699,955
10	120-180	150	767129,920	-272780,457	195402,418
11	180-240	210	-673741,061	71160,805	-407094,620
12	240-360	300	1845292,228	440136,629	1796176,771
		sum	2050157,689	1012378,362	1743284,227

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
49,261	20,616	49,875	39,917	13,651

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,722	1,819	9,077
14,536	17,370	45,011
67,583	90,421	125,857
115,923	168,593	156,141
489,624	669,358	550,949
1232,348	1378,066	1114,187
1207,763	1341,325	994,932
1087,194	1418,238	1011,360
2333,578	2872,676	2143,680
2395,148	2828,592	2121,152
4980,420	5764,796	4529,190

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13925,838	16551,256	12801,536

Average AUC0-360 (µg/ml.min)		14426,210
	STDEV	1924,287

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,827	4,043	20,170
5	17,708	21,691	46,513
10	42,366	58,683	65,360
15	60,676	91,178	73,432

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,241	6,349	4,778	5,123	0,894

Table 109: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.5mm beads) evaluated in the pH 1.2 environment using 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,565	77,353	1,756	85,872	1,298	60,107
3	5	1,403	69,348	1,889	92,354	1,455	67,349
4	10	1,643	81,173	2,264	110,715	1,519	70,317
5	15	2,138	105,649	2,549	124,621	1,897	87,825
6	30	2,448	120,974	2,998	146,575	2,259	104,567
7	60	3,171	156,719	3,643	178,140	2,942	136,211
8	90	4,200	207,548	4,903	239,716	4,086	189,168
9	120	5,306	262,186	5,677	277,562	5,154	238,605
10	180	6,900	340,989	6,893	337,023	6,390	295,863
11	240	8,184	404,415	8,338	407,666	8,750	405,127
12	360	10,530	520,367	10,544	515,516	8,988	416,131

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
4941,639	4889,263	4629,892

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	77,353	85,872	60,107
3	5	2-5	69,348	92,354	67,349
4	10	5-10	81,173	110,715	70,317
5	15	10-15	105,649	124,621	87,825
6	30	15-30	120,974	146,575	104,567
7	60	30-60	156,719	178,140	136,211
8	90	60-90	207,548	239,716	189,168
9	120	90-120	262,186	277,562	238,605
10	180	120-180	340,989	337,023	295,863
11	240	180-240	404,415	407,666	405,127
12	360	240-360	520,367	515,516	416,131

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	77,353	85,872	60,107
3	2-5	3,5	-8,005	6,482	7,242
4	5-10	7,5	11,825	18,361	2,968
5	10-15	12,5	24,476	13,906	17,508
6	15-30	22,5	15,325	21,954	16,742
7	30-60	45	35,745	31,565	31,644
8	60-90	75	50,829	61,576	52,957
9	90-120	105	54,638	37,846	49,438
10	120-180	150	78,803	59,462	57,257
11	180-240	210	63,426	70,643	109,265
12	240-360	300	115,952	107,851	11,004
		sum	520,367	515,516	416,131

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	77,353	85,872	60,107
3	2-5	3,5	-28,018	22,685	25,348
4	5-10	7,5	88,688	137,708	22,262
5	10-15	12,5	305,945	173,829	218,845
6	15-30	22,5	344,819	493,966	376,684
7	30-60	45	1608,517	1420,407	1424,000
8	60-90	75	3812,161	4618,206	3971,753
9	90-120	105	5736,999	3973,809	5190,956
10	120-180	150	11820,438	8919,232	8588,613
11	180-240	210	13319,467	14834,927	22945,579
12	240-360	300	34785,750	32355,158	3301,211
		sum	71872,119	67035,800	46125,357

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
138,118	130,036	110,843	126,332	11,439

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,704	0,790	0,584
2,004	2,461	1,858
3,427	4,673	3,345
4,253	5,415	3,843
15,478	18,720	14,025
37,931	44,829	35,103
49,757	57,688	47,438
64,163	71,414	62,366
164,781	169,696	155,842
203,636	205,620	204,397
505,280	509,809	478,931

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
1051,414	1091,117	1007,732

Average AUC0-360 (µg/ml.min)		1050,087
	STDEV	41,708

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,565	1,756	1,298
5	1,403	1,889	1,455
10	1,643	2,264	1,519
15	2,138	2,549	1,897

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,104	0,132	0,094	0,110	0,016

Table 110: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.75 mm beads) evaluated in the pH 1.2 environment using 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,402	75,130	1,623	84,993	1,391	72,294
3	5	1,508	80,795	1,775	92,955	1,516	78,754
4	10	1,833	98,224	2,156	112,916	1,953	101,466
5	15	2,229	119,409	2,412	126,317	2,402	124,789
6	30	3,070	164,505	2,900	151,910	2,547	132,345
7	60	3,602	192,961	3,646	190,981	3,366	174,877
8	90	4,921	263,671	4,779	250,275	4,548	236,281
9	120	6,124	328,113	6,060	317,377	5,832	303,026
10	180	7,798	417,785	7,331	383,950	7,452	387,160
11	240	9,707	520,093	8,845	463,249	8,681	451,018
12	360	11,851	634,939	11,201	586,654	10,924	567,586

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
5357,662	5237,442	5195,713

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	75,130	84,993	72,294
3	5	2-5	80,795	92,955	78,754
4	10	5-10	98,224	112,916	101,466
5	15	10-15	119,409	126,317	124,789
6	30	15-30	164,505	151,910	132,345
7	60	30-60	192,961	190,981	174,877
8	90	60-90	263,671	250,275	236,281
9	120	90-120	328,113	317,377	303,026
10	180	120-180	417,785	383,950	387,160
11	240	180-240	520,093	463,249	451,018
12	360	240-360	634,939	586,654	567,586

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	75,130	84,993	72,294
3	2-5	3,5	5,666	7,962	6,460
4	5-10	7,5	17,428	19,961	22,713
5	10-15	12,5	21,185	13,401	23,322
6	15-30	22,5	45,097	25,593	7,556
7	30-60	45	28,456	39,071	42,532
8	60-90	75	70,710	59,294	61,404
9	90-120	105	64,443	67,102	66,744
10	120-180	150	89,671	66,574	84,134
11	180-240	210	102,308	79,298	63,858
12	240-360	300	114,846	123,405	116,567
		sum	634,939	586,654	567,586

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	75,130	84,993	72,294
3	2-5	3,5	19,831	27,866	22,609
4	5-10	7,5	130,711	149,707	170,346
5	10-15	12,5	264,813	167,518	291,531
6	15-30	22,5	1014,676	575,838	170,003
7	30-60	45	1280,510	1758,217	1913,950
8	60-90	75	5303,236	4447,021	4605,334
9	90-120	105	6766,467	7045,666	7008,168
10	120-180	150	13450,663	9986,073	12620,148
11	180-240	210	21484,730	16652,659	13410,216
12	240-360	300	34453,942	37021,453	34970,239
		sum	84244,707	77917,011	75254,837

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
132,682	132,816	132,588	132,695	0,094

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,631	0,730	0,626
1,964	2,293	1,962
3,759	4,422	3,902
4,570	5,139	4,899
17,885	17,929	16,703
45,036	44,192	39,913
57,530	56,869	53,416
74,558	73,159	70,064
187,948	180,774	179,331
236,322	218,374	217,783
582,080	541,244	529,327

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
1212,283	1145,124	1117,925

Average AUC0-360 (µg/ml.min)		1158,444
	STDEV	48,569

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,402	1,623	1,391
5	1,508	1,775	1,516
10	1,833	2,156	1,953
15	2,229	2,412	2,402

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,117	0,127	0,130	0,125	0,006

Table 111: Table containing the AUC, DRi and MDT values and information regarding the control formulation (1 mm beads) evaluated in the pH 1.2 environment using 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,363	79,402	1,399	80,045	1,413	95,132
3	5	1,499	87,266	1,475	84,406	1,862	125,359
4	10	1,925	112,085	1,934	110,645	2,087	140,490
5	15	2,257	131,434	2,321	132,765	2,633	177,239
6	30	2,759	160,657	2,918	166,911	3,374	227,153
7	60	3,783	220,335	4,305	246,287	4,699	316,335
8	90	5,092	296,529	5,557	317,927	6,294	423,675
9	120	5,867	341,671	6,905	395,023	8,350	562,130
10	180	7,404	431,189	8,445	483,111	9,985	672,177
11	240	8,642	503,289	10,085	576,921	11,660	784,910
12	360	10,963	638,451	12,892	737,513	14,839	998,925

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
5823,574	5720,839	6731,901

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	79,402	80,045	95,132
3	5	2-5	87,266	84,406	125,359
4	10	5-10	112,085	110,645	140,490
5	15	10-15	131,434	132,765	177,239
6	30	15-30	160,657	166,911	227,153
7	60	30-60	220,335	246,287	316,335
8	90	60-90	296,529	317,927	423,675
9	120	90-120	341,671	395,023	562,130
10	180	120-180	431,189	483,111	672,177
11	240	180-240	503,289	576,921	784,910
12	360	240-360	638,451	737,513	998,925

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	79,402	80,045	95,132
3	2-5	3,5	7,864	4,361	30,227
4	5-10	7,5	24,819	26,239	15,131
5	10-15	12,5	19,349	22,120	36,749
6	15-30	22,5	29,222	34,146	49,914
7	30-60	45	59,678	79,375	89,182
8	60-90	75	76,195	71,640	107,340
9	90-120	105	45,142	77,096	138,455
10	120-180	150	89,518	88,089	110,047
11	180-240	210	72,100	93,809	112,734
12	240-360	300	135,161	160,592	214,015
		sum	638,451	737,513	998,925

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	79,402	80,045	95,132
3	2-5	3,5	27,525	15,264	105,794
4	5-10	7,5	186,142	196,795	113,483
5	10-15	12,5	241,864	276,502	459,362
6	15-30	22,5	657,498	768,287	1123,068
7	30-60	45	2685,518	3571,893	4013,188
8	60-90	75	5714,600	5372,994	8050,508
9	90-120	105	4739,882	8095,097	14537,766
10	120-180	150	13427,667	13213,291	16506,982
11	180-240	210	15141,098	19699,973	23674,104
12	240-360	300	40548,429	48177,673	64204,391
		sum	83449,625	99467,811	132883,778

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
130,706	134,869	133,027	132,867	1,703

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,614	0,630	0,636
1,932	1,940	2,211
3,851	3,836	4,443
4,704	4,787	5,310
16,928	17,679	20,274
44,160	48,753	54,495
59,909	66,571	74,200
73,973	84,121	98,846
179,162	207,222	247,525
216,627	250,146	292,201
529,348	620,358	715,453

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
1131,208	1306,042	1515,592

Average AUC0-360 (µg/ml.min)	1317,614
STDEV	192,453

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,363	1,399	1,413
5	1,499	1,475	1,862
10	1,925	1,934	2,087
15	2,257	2,321	2,633

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,122	0,125	0,143	0,130	0,009

Table 112: Table containing the AUC, DRi and MDT values and information regarding the commercial product (Lasix®) evaluated in the pH 1.2 environment using 0.1M HCl buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	2,008	320,795	1,704	273,013	2,160	348,766
3	5	4,462	712,861	3,785	606,546	4,171	673,414
4	10	8,506	1358,923	8,626	1382,433	9,137	1475,244
5	15	13,005	2077,779	13,097	2098,906	14,100	2276,499
6	30	18,500	2955,655	18,120	2903,939	22,272	3595,912
7	60	24,042	3841,078	20,689	3315,687	23,607	3811,605
8	90	28,310	4522,931	27,016	4329,670	27,801	4488,732
9	120	30,017	4795,619	30,036	4813,618	30,516	4927,054
10	180	33,527	5356,494	32,693	5239,402	33,800	5457,191
11	240	36,227	5787,860	35,715	5723,657	36,554	5901,872
12	360	38,539	6157,207	39,035	6255,743	38,839	6270,887

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
15976,478	16026,132	16145,762

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	320,795	273,013	348,766
3	5	2-5	712,861	606,546	673,414
4	10	5-10	1358,923	1382,433	1475,244
5	15	10-15	2077,779	2098,906	2276,499
6	30	15-30	2955,655	2903,939	3595,912
7	60	30-60	3841,078	3315,687	3811,605
8	90	60-90	4522,931	4329,670	4488,732
9	120	90-120	4795,619	4813,618	4927,054
10	180	120-180	5356,494	5239,402	5457,191
11	240	180-240	5787,860	5723,657	5901,872
12	360	240-360	6157,207	6255,743	6270,887

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	320,795	273,013	348,766
3	2-5	3,5	392,066	333,533	324,648
4	5-10	7,5	646,062	775,887	801,831
5	10-15	12,5	718,855	716,473	801,255
6	15-30	22,5	877,876	805,033	1319,413
7	30-60	45	885,424	411,748	215,693
8	60-90	75	681,852	1013,983	677,127
9	90-120	105	272,688	483,947	438,322
10	120-180	150	560,876	425,785	530,137
11	180-240	210	431,365	484,254	444,681
12	240-360	300	369,347	532,086	369,015
		sum	6157,207	6255,743	6270,887

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	320,795	273,013	348,766
3	2-5	3,5	1372,231	1167,366	1136,268
4	5-10	7,5	4845,468	5819,153	6013,729
5	10-15	12,5	8985,692	8955,912	10015,691
6	15-30	22,5	19752,206	18113,237	29686,783
7	30-60	45	39844,063	18528,668	9706,199
8	60-90	75	51138,933	76048,740	50784,536
9	90-120	105	28632,245	50814,478	46023,820
10	120-180	150	84131,330	63867,685	79520,499
11	180-240	210	90586,717	101693,413	93382,987
12	240-360	300	110804,072	159625,867	110704,422
		sum	440413,754	504907,531	437323,700

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
71,528	80,711	69,739	73,993	4,806

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,904	0,767	0,972
4,367	3,705	4,273
14,589	13,962	14,971
24,200	24,438	26,141
106,330	105,357	122,753
287,159	261,963	309,683
353,376	322,013	347,009
393,705	385,103	393,642
857,846	846,840	868,261
941,689	923,500	949,768
2018,698	2018,227	2035,608

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
5002,863	4905,875	5073,084

Average AUC0-360 (µg/ml.min)		4993,940
	STDEV	83,961

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	2,008	1,704	2,160
5	4,462	3,785	4,171
10	8,506	8,626	9,137
15	13,005	13,097	14,100

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,854	0,877	0,930	0,887	0,032

Table 113: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.5 mm bead size) evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	0,890	153,917	1,166	176,656	1,232	240,207
3	5	1,461	252,572	1,790	271,066	1,907	371,752
4	10	2,894	500,334	1,000	151,463	3,388	660,485
5	15	4,189	724,319	4,307	652,416	5,073	988,880
6	30	6,258	1082,030	6,183	936,507	7,583	1478,170
7	60	9,882	1708,561	9,497	1438,390	12,090	2356,581
8	90	14,273	2467,777	13,129	1988,524	16,998	3313,336
9	120	17,563	3036,494	16,409	2485,372	20,701	4035,130
10	180	21,896	3785,734	19,927	3018,171	26,399	5145,692
11	240	27,115	4688,073	24,033	3640,146	32,434	6322,158
12	360	34,251	5921,776	29,882	4525,983	39,817	7761,227

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
17289,515	15146,336	19492,185

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	153,917	176,656	240,207
3	5	2-5	252,572	271,066	371,752
4	10	5-10	500,334	151,463	660,485
5	15	10-15	724,319	652,416	988,880
6	30	15-30	1082,030	936,507	1478,170
7	60	30-60	1708,561	1438,390	2356,581
8	90	60-90	2467,777	1988,524	3313,336
9	120	90-120	3036,494	2485,372	4035,130
10	180	120-180	3785,734	3018,171	5145,692
11	240	180-240	4688,073	3640,146	6322,158
12	360	240-360	5921,776	4525,983	7761,227

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	153,917	176,656	240,207
3	2-5	3,5	98,654	94,409	131,545
4	5-10	7,5	247,762	-119,602	288,734
5	10-15	12,5	223,985	500,952	328,395
6	15-30	22,5	357,711	284,092	489,290
7	30-60	45	626,531	501,883	878,411
8	60-90	75	759,216	550,134	956,755
9	90-120	105	568,717	496,847	721,794
10	120-180	150	749,239	532,800	1110,562
11	180-240	210	902,339	621,974	1176,466
12	240-360	300	1233,703	885,837	1439,069
		sum	5921,776	4525,983	7761,227

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	153,917	176,656	240,207
3	2-5	3,5	345,290	330,433	460,407
4	5-10	7,5	1858,215	-897,017	2165,503
5	10-15	12,5	2799,812	6261,902	4104,935
6	15-30	22,5	8048,502	6392,060	11009,015
7	30-60	45	28193,902	22584,717	39528,510
8	60-90	75	56941,204	41260,082	71756,617
9	90-120	105	59715,288	52168,980	75788,393
10	120-180	150	112385,923	79919,958	166584,237
11	180-240	210	189491,262	130614,627	247057,864
12	240-360	300	370110,888	265751,056	431720,611
		sum	830044,204	604563,456	1050416,300

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
140,168	133,576	135,342	136,362	2,786

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,401	0,525	0,555
1,587	1,995	2,119
4,899	5,320	5,958
7,969	8,152	9,519
35,261	35,405	42,716
108,947	105,838	132,795
163,048	152,721	196,345
214,892	199,380	254,472
532,693	490,533	635,850
661,652	593,459	794,246
1656,877	1455,702	1950,789

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
3388,226	3049,030	4025,364

Average AUC0-360 (µg/ml.min)		3487,540
	STDEV	495,686

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	0,890	1,166	1,232
5	1,461	1,790	1,907
10	2,894	2,939	3,388
15	4,189	4,307	5,073

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,271	0,268	0,320	0,286	0,024

Table 114: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.75 mm bead size) evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,061	157,837	1,263	197,499	0,970	132,224
3	5	1,831	272,284	1,945	304,084	1,588	216,517
4	10	3,278	487,515	1,000	156,336	3,012	410,729
5	15	5,446	809,895	4,722	738,200	4,034	550,004
6	30	7,056	1049,325	6,884	1076,215	5,947	810,879
7	60	10,888	1619,358	10,592	1655,908	9,215	1256,468
8	90	14,829	2205,346	14,141	2210,787	12,603	1718,465
9	120	17,738	2638,108	17,020	2660,897	15,184	2070,419
10	180	21,992	3270,706	21,546	3368,424	18,829	2567,521
11	240	26,574	3952,208	26,045	4071,801	22,542	3073,750
12	360	32,197	4788,425	32,419	5068,286	27,823	3793,908

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
14872,327	15633,615	13635,642

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	157,837	197,499	132,224
3	5	2-5	272,284	304,084	216,517
4	10	5-10	487,515	156,336	410,729
5	15	10-15	809,895	738,200	550,004
6	30	15-30	1049,325	1076,215	810,879
7	60	30-60	1619,358	1655,908	1256,468
8	90	60-90	2205,346	2210,787	1718,465
9	120	90-120	2638,108	2660,897	2070,419
10	180	120-180	3270,706	3368,424	2567,521
11	240	180-240	3952,208	4071,801	3073,750
12	360	240-360	4788,425	5068,286	3793,908

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	157,837	197,499	132,224
3	2-5	3,5	114,447	106,585	84,293
4	5-10	7,5	215,231	-147,748	194,212

5	10-15	12,5	322,380	581,864	139,274
6	15-30	22,5	239,431	338,015	260,876
7	30-60	45	570,032	579,693	445,588
8	60-90	75	585,989	554,879	461,998
9	90-120	105	432,762	450,110	351,954
10	120-180	150	632,597	707,526	497,102
11	180-240	210	681,502	703,377	506,230
12	240-360	300	836,218	996,485	720,158
		sum	4788,425	5068,286	3793,908

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	157,837	197,499	132,224
3	2-5	3,5	400,566	373,046	295,026
4	5-10	7,5	1614,232	-1108,109	1456,588
5	10-15	12,5	4029,744	7273,301	1740,929
6	15-30	22,5	5387,188	7605,333	5869,708
7	30-60	45	25651,460	26086,187	20051,465
8	60-90	75	43949,146	41615,947	34649,836
9	90-120	105	45440,001	47261,559	36955,131
10	120-180	150	94889,621	106128,911	74565,233
11	180-240	210	143115,421	147709,168	106308,243
12	240-360	300	250865,281	298945,603	216047,342
		sum	615500,495	682088,445	498071,725

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
128,539	134,580	131,282	131,467	2,469

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,478	0,568	0,436
1,952	2,166	1,726
5,747	5,960	5,175
9,814	9,084	7,926
42,192	39,170	33,684
121,122	117,963	102,339
173,589	166,949	147,267
219,827	210,341	187,560
536,358	520,646	459,180
655,643	642,481	558,515
1586,820	1578,537	1359,868

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
3353,542	3293,864	2863,678

Average AUC0-360 (µg/ml.min)		3170,361
	STDEV	267,267

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,061	1,263	0,970
5	1,831	1,945	1,588
10	3,278	3,352	3,012
15	5,446	4,722	4,034

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,345	0,298	0,262	0,301	0,034

Table 115: Table containing the AUC, DRi and MDT values and information regarding the control formulation (1 mm bead size) evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	1,055	185,025	1,116	193,770	1,207	234,175
3	5	1,976	346,738	2,020	350,517	2,482	481,672
4	10	3,342	586,381	1,000	173,552	4,860	943,023
5	15	5,055	886,896	5,952	1032,936	7,272	1411,106
6	30	7,554	1325,411	8,895	1543,756	10,753	2086,667
7	60	11,619	2038,557	13,154	2282,943	15,989	3102,827
8	90	15,704	2755,392	17,462	3030,633	20,907	4057,142
9	120	18,878	3312,155	19,425	3371,261	21,970	4263,441
10	180	23,362	4099,016	27,457	4765,286	31,712	6153,893
11	240	27,896	4894,404	31,304	5432,780	35,779	6943,177
12	360	33,901	5948,113	38,008	6596,329	42,986	8341,699

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
17545,433	17355,158	19405,648

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	185,025	193,770	234,175
3	5	2-5	346,738	350,517	481,672
4	10	5-10	586,381	173,552	943,023
5	15	10-15	886,896	1032,936	1411,106
6	30	15-30	1325,411	1543,756	2086,667
7	60	30-60	2038,557	2282,943	3102,827
8	90	60-90	2755,392	3030,633	4057,142
9	120	90-120	3312,155	3371,261	4263,441
10	180	120-180	4099,016	4765,286	6153,893
11	240	180-240	4894,404	5432,780	6943,177
12	360	240-360	5948,113	6596,329	8341,699

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	185,025	193,770	234,175
3	2-5	3,5	161,713	156,747	247,498
4	5-10	7,5	239,643	-176,965	461,351
5	10-15	12,5	300,515	859,385	468,083
6	15-30	22,5	438,515	510,819	675,560
7	30-60	45	713,147	739,187	1016,160
8	60-90	75	716,834	747,690	954,315
9	90-120	105	556,763	340,629	206,298
10	120-180	150	786,861	1394,025	1890,453
11	180-240	210	795,388	667,494	789,284
12	240-360	300	1053,709	1163,549	1398,522
		sum	5948,113	6596,329	8341,699

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	185,025	193,770	234,175
3	2-5	3,5	565,997	548,615	866,243
4	5-10	7,5	1797,324	-1327,241	3460,129
5	10-15	12,5	3756,433	10742,310	5851,043
6	15-30	22,5	9866,589	11493,438	15200,111
7	30-60	45	32091,602	33263,409	45727,222
8	60-90	75	53762,575	56076,735	71573,629
9	90-120	105	58460,143	35766,000	21661,299
10	120-180	150	118029,174	209103,743	283567,924
11	180-240	210	167031,423	140173,693	165749,546
12	240-360	300	316112,784	349064,615	419556,654
		sum	761659,067	845099,086	1033447,975

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
128,051	128,117	123,889	126,686	1,977

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
0,475	0,502	0,543
2,046	2,117	2,490
5,983	6,719	8,259
9,447	11,143	13,648
42,555	50,108	60,833
129,417	148,833	180,510
184,431	206,663	249,050
233,428	248,991	289,421
570,238	632,915	724,707
691,982	793,274	911,129
1668,514	1871,409	2126,657

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
3538,515	3972,673	4567,246

Average AUC0-360 (µg/ml.min)	4026,145
STDEV	516,446

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	1,055	1,116	1,207
5	1,976	2,020	2,482
10	3,342	3,953	4,860
15	5,055	5,952	7,272

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
0,322	0,387	0,478	0,395	0,064

Table 116: Table containing the AUC, DRi and MDT values and information regarding the commercial product (Lasix®) evaluated in the pH 4.6 environment using a citric acid buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	7,418	2936,461	3,731	1465,601	9,294	3719,660
3	5	19,410	7683,208	10,330	4058,385	22,250	8904,514
4	10	32,716	12950,448	18,607	7309,976	44,091	17645,838
5	15	42,254	16726,243	32,673	12835,585	57,134	22865,640
6	30	46,242	18304,817	46,467	18254,636	67,013	26819,218
7	60	66,807	26445,379	62,883	24703,928	69,967	28001,492
8	90	76,651	30342,143	75,310	29585,860	83,244	33315,050
9	120	81,751	32360,759	79,471	31220,637	87,356	34960,800
10	180	88,078	34865,222	86,193	33861,478	92,199	36898,744
11	240	90,034	35639,834	87,862	34517,119	97,235	38914,319
12	360	96,769	38305,506	95,965	37700,238	97,659	39084,200

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
39584,652	39285,506	40020,979

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2936,461	1465,601	3719,660
3	5	2-5	7683,208	4058,385	8904,514
4	10	5-10	12950,448	7309,976	17645,838
5	15	10-15	16726,243	12835,585	22865,640
6	30	15-30	18304,817	18254,636	26819,218
7	60	30-60	26445,379	24703,928	28001,492
8	90	60-90	30342,143	29585,860	33315,050
9	120	90-120	32360,759	31220,637	34960,800
10	180	120-180	34865,222	33861,478	36898,744
11	240	180-240	35639,834	34517,119	38914,319
12	360	240-360	38305,506	37700,238	39084,200

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2936,461	1465,601	3719,660
3	2-5	3,5	4746,746	2592,785	5184,853
4	5-10	7,5	5267,241	3251,591	8741,324
5	10-15	12,5	3775,795	5525,609	5219,802
6	15-30	22,5	1578,573	5419,051	3953,579
7	30-60	45	8140,562	6449,293	1182,273
8	60-90	75	3896,765	4881,932	5313,558
9	90-120	105	2018,616	1634,777	1645,750
10	120-180	150	2504,463	2640,841	1937,944
11	180-240	210	774,612	655,640	2015,575
12	240-360	300	2665,672	3183,120	169,882
		sum	38305,506	37700,238	39084,200

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2936,461	1465,601	3719,660
3	2-5	3,5	16613,612	9074,746	18146,987
4	5-10	7,5	39504,305	24386,930	65559,933
5	10-15	12,5	47197,440	69070,107	65247,521
6	15-30	22,5	35517,895	121928,653	88955,519
7	30-60	45	366325,295	290218,171	53202,299
8	60-90	75	292257,347	366144,885	398516,869
9	90-120	105	211954,662	171651,559	172803,759
10	120-180	150	375669,450	396126,207	290691,548
11	180-240	210	162668,572	137684,455	423270,765
12	240-360	300	799701,481	954935,856	50964,538
		sum	2350346,519	2542687,170	1631079,398

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
61,358	67,445	41,732	56,845	10,971

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
3,338	1,679	4,182
18,109	9,491	21,292
58,641	32,555	74,634
84,341	57,690	113,879
298,676	267,095	418,996
763,083	738,110	924,615
968,344	932,802	1034,174
1069,214	1044,772	1151,551
2292,683	2236,470	2423,988
2404,513	2349,750	2557,350
5043,683	4963,328	5262,140

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13004,626	12633,742	13986,801

Average AUC0-360 (µg/ml.min)		13208,390
	STDEV	699,165

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	7,418	3,731	9,294
5	19,410	10,330	22,250
10	32,716	18,607	44,091
15	42,254	32,673	57,134

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
2,824	2,125	3,874	2,941	0,719

Table 117: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.5 mm bead size) evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	3,895	1614,404	1,796	806,709	5,548	2234,038
3	5	25,809	10697,766	15,762	7081,377	20,205	8135,681
4	10	40,233	16676,432	1,000	449,281	39,957	16089,334
5	15	51,807	21473,966	56,139	25222,282	52,607	21182,981
6	30	64,097	26568,456	71,765	32242,864	64,225	25861,211
7	60	73,490	30461,836	86,991	39083,367	73,852	29737,392
8	90	79,700	33035,517	95,534	42921,761	81,727	32908,338
9	120	84,240	34917,620	103,251	46388,922	87,988	35429,669
10	180	92,149	38195,768	105,216	47271,550	97,458	39242,998
11	240	98,075	40652,257	110,934	49840,328	99,423	40034,101
12	360	102,346	42422,434	109,275	49095,287	94,378	38002,621

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
41450,073	44928,090	40266,377

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1614,404	806,709	2234,038
3	5	2-5	10697,766	7081,377	8135,681
4	10	5-10	16676,432	449,281	16089,334
5	15	10-15	21473,966	25222,282	21182,981
6	30	15-30	26568,456	32242,864	25861,211
7	60	30-60	30461,836	39083,367	29737,392
8	90	60-90	33035,517	42921,761	32908,338
9	120	90-120	34917,620	46388,922	35429,669
10	180	120-180	38195,768	47271,550	39242,998
11	240	180-240	40652,257	49840,328	40034,101
12	360	240-360	42422,434	49095,287	38002,621

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1614,404	806,709	2234,038
3	2-5	3,5	9083,362	6274,668	5901,642
4	5-10	7,5	5978,666	-6632,096	7953,653
5	10-15	12,5	4797,534	24773,001	5093,647
6	15-30	22,5	5094,490	7020,582	4678,230
7	30-60	45	3893,380	6840,503	3876,181
8	60-90	75	2573,681	3838,393	3170,946
9	90-120	105	1882,103	3467,162	2521,331
10	120-180	150	3278,148	882,628	3813,329
11	180-240	210	2456,488	2568,777	791,103
12	240-360	300	1770,177	-745,041	-2031,480
		sum	42422,434	49095,287	38002,621

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1614,404	806,709	2234,038
3	2-5	3,5	31791,768	21961,338	20655,748
4	5-10	7,5	44839,998	-49740,720	59652,400
5	10-15	12,5	59969,173	309662,515	63670,587
6	15-30	22,5	114626,033	157963,088	105260,186
7	30-60	45	175202,091	307822,645	174428,127
8	60-90	75	193026,083	287879,510	237820,926
9	90-120	105	197620,798	364051,980	264739,794
10	120-180	150	491722,220	132394,207	571999,291
11	180-240	210	515862,538	539443,257	166131,713
12	240-360	300	531053,222	-223512,256	-609444,039
		sum	2357328,328	1848732,273	1057148,772

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
55,568	37,656	27,818	40,347	11,488

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
1,753	0,808	2,497
20,050	11,851	17,383
74,297	61,381	67,682
103,544	106,806	104,135
391,177	431,678	394,310
928,718	1071,606	932,020
1034,032	1232,046	1050,153
1106,593	1341,804	1145,575
2381,252	2814,311	2503,530
2568,025	2918,019	2657,902
5411,370	5945,638	5232,632

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14020,811	15935,949	14107,819

Average AUC0-360 (µg/ml.min)		14688,193
	STDEV	1081,464

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	3,895	1,796	5,548
5	25,809	15,762	20,205
10	40,233	38,799	39,957
15	51,807	56,139	52,607

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,600	3,971	3,643	3,738	0,166

Table 118: Table containing the AUC, DRi and MDT values and information regarding the control formulation (0.75 mm bead size) evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	4,828	1806,727	7,441	3005,256	5,780	2196,458
3	5	19,040	7124,562	22,761	9192,381	18,292	6950,596
4	10	37,060	13867,882	1,000	403,874	33,558	12751,525
5	15	48,544	18164,895	55,789	22531,849	44,524	16918,194
6	30	60,425	22610,847	70,780	28586,151	56,368	21418,773
7	60	69,900	26156,165	83,004	33522,975	67,940	25815,904
8	90	78,257	29283,553	89,755	36249,687	77,925	29609,912
9	120	82,745	30962,992	92,703	37440,309	83,474	31718,533
10	180	90,444	33843,772	95,739	38666,369	89,521	34016,066
11	240	90,929	34025,251	99,722	40275,065	93,822	35650,403
12	360	90,588	33897,791	98,352	39721,774	87,717	33330,782

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
37419,667	40387,376	37997,912

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	1806,727	3005,256	2196,458
3	5	2-5	7124,562	9192,381	6950,596
4	10	5-10	13867,882	403,874	12751,525
5	15	10-15	18164,895	22531,849	16918,194
6	30	15-30	22610,847	28586,151	21418,773
7	60	30-60	26156,165	33522,975	25815,904
8	90	60-90	29283,553	36249,687	29609,912
9	120	90-120	30962,992	37440,309	31718,533
10	180	120-180	33843,772	38666,369	34016,066
11	240	180-240	34025,251	40275,065	35650,403
12	360	240-360	33897,791	39721,774	33330,782

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	1806,727	3005,256	2196,458
3	2-5	3,5	5317,834	6187,125	4754,137
4	5-10	7,5	6743,321	-8788,508	5800,929
5	10-15	12,5	4297,012	22127,976	4166,669
6	15-30	22,5	4445,952	6054,302	4500,579
7	30-60	45	3545,318	4936,824	4397,130
8	60-90	75	3127,388	2726,711	3794,008
9	90-120	105	1679,439	1190,622	2108,621
10	120-180	150	2880,780	1226,060	2297,533
11	180-240	210	181,479	1608,696	1634,337
12	240-360	300	-127,459	-553,290	-2319,621
		sum	33897,791	39721,774	33330,782

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	1806,727	3005,256	2196,458
3	2-5	3,5	18612,420	21654,939	16639,480
4	5-10	7,5	50574,905	-65913,806	43506,970
5	10-15	12,5	53712,656	276599,697	52083,367
6	15-30	22,5	100033,919	136221,791	101263,028
7	30-60	45	159539,316	222157,084	197870,865
8	60-90	75	234554,114	204503,358	284550,627
9	90-120	105	176341,082	125015,337	221405,219
10	120-180	150	432116,935	183908,970	344629,975
11	180-240	210	38110,608	337826,120	343210,704
12	240-360	300	-38237,776	-165987,128	-695886,342
		sum	1227164,907	1278991,616	911470,352

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
36,202	32,199	27,346	31,916	3,621

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,173	3,348	2,601
16,111	20,386	16,249
63,113	73,287	58,332
96,305	110,444	87,843
367,770	427,171	340,512
879,691	1038,039	839,083
1000,057	1166,121	984,592
1086,766	1231,591	1089,447
2338,052	2543,964	2335,436
2448,530	2638,719	2475,129
4900,958	5347,995	4901,564

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
13199,524	14601,064	13130,787

Average AUC0-360 (µg/ml.min)		13643,792
	STDEV	829,734

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	4,828	7,441	5,780
5	19,040	22,761	18,292
10	37,060	42,383	33,558
15	48,544	55,789	44,524

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
3,371	3,805	3,034	3,404	0,316

Table 119: Table containing the AUC, DRi and MDT values and information regarding the control formulation (1 mm bead size) evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	5,790	2317,976	6,000	2453,271	4,622	1841,566
3	5	22,785	9121,948	25,340	10360,872	21,701	8646,059
4	10	46,656	18678,474	1,000	408,879	47,360	18868,802
5	15	66,122	26471,826	67,768	27708,706	68,453	27272,706
6	30	82,595	33066,690	82,858	33878,890	85,976	34254,085
7	60	93,115	37278,583	94,857	38785,111	93,358	37195,359
8	90	94,151	37693,249	97,123	39711,377	95,521	38057,097
9	120	96,360	38577,646	97,415	39831,014	95,996	38246,395
10	180	97,721	39122,357	100,657	41156,656	95,907	38210,769
11	240	95,201	38113,374	100,942	41273,121	98,374	39193,850
12	360	97,933	39207,468	100,649	41153,315	97,537	38860,176

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
40034,833	40887,855	39841,573

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	2317,976	2453,271	1841,566
3	5	2-5	9121,948	10360,872	8646,059
4	10	5-10	18678,474	408,879	18868,802
5	15	10-15	26471,826	27708,706	27272,706
6	30	15-30	33066,690	33878,890	34254,085
7	60	30-60	37278,583	38785,111	37195,359
8	90	60-90	37693,249	39711,377	38057,097
9	120	90-120	38577,646	39831,014	38246,395
10	180	120-180	39122,357	41156,656	38210,769
11	240	180-240	38113,374	41273,121	39193,850
12	360	240-360	39207,468	41153,315	38860,176

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	2317,976	2453,271	1841,566
3	2-5	3,5	6803,972	7907,601	6804,493
4	5-10	7,5	9556,526	-9951,994	10222,742
5	10-15	12,5	7793,352	27299,828	8403,904
6	15-30	22,5	6594,865	6170,184	6981,379
7	30-60	45	4211,892	4906,221	2941,274
8	60-90	75	414,667	926,265	861,738
9	90-120	105	884,397	119,638	189,299
10	120-180	150	544,710	1325,641	-35,626
11	180-240	210	-1008,983	116,465	983,081
12	240-360	300	1094,094	-119,806	-333,674
		sum	39207,468	41153,315	38860,176

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	2317,976	2453,271	1841,566
3	2-5	3,5	23813,901	27676,603	23815,727
4	5-10	7,5	71673,944	-74639,952	76670,568
5	10-15	12,5	97416,896	341247,847	105048,798
6	15-30	22,5	148384,459	138829,134	157081,035
7	30-60	45	189535,146	220779,959	132357,327
8	60-90	75	31100,011	69469,887	64630,320
9	90-120	105	92861,672	12561,979	19876,384
10	120-180	150	81706,557	198846,218	-5343,958
11	180-240	210	-211886,355	24457,729	206446,957
12	240-360	300	328228,120	-35941,847	-100102,063
		sum	855152,327	925740,829	682322,659

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
21,811	22,495	17,558	20,621	2,184

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
2,605	2,700	2,080
19,288	21,154	17,768
78,121	85,498	77,693
126,875	133,230	130,289
501,919	508,362	521,197
1186,044	1199,579	1210,504
1264,049	1295,865	1274,935
1285,952	1313,131	1292,742
2620,093	2673,981	2590,690
2604,438	2721,595	2622,794
5214,616	5442,970	5289,597

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
14903,999	15398,065	15030,289

Average AUC0-360 (µg/ml.min)		15110,784
	STDEV	256,681

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	5,790	6,000	4,622
5	22,785	25,340	21,701
10	46,656	50,659	47,360
15	66,122	67,768	68,453

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
4,553	4,714	4,748	4,672	0,085

Table 120: Table containing the AUC, DRi and MDT values and information regarding the commercial product (Lasix®) evaluated in the pH 7.4 environment using a phosphate buffer solution.

MDT							
Sample nr	Time (min)	Tablet 1		Tablet 2		Tablet 3	
		% Dissolved	Mass diss.	% Dissolved	Mass diss.	% Dissolved	Mass diss.
1	0	0	0	0	0	0	0
2	2	78,465	34229,501	81,967	35732,820	78,521	34501,478
3	5	98,540	42986,949	98,591	42979,560	95,735	42064,690
4	10	100,532	43855,702	103,169	44975,423	108,491	47669,808
5	15	107,672	46970,557	107,639	46924,230	103,859	45634,677
6	30	104,807	45720,909	105,881	46157,716	104,197	45783,086
7	60	107,713	46988,556	105,695	46076,570	103,234	45360,061
8	90	101,728	44377,737	101,030	44043,162	101,888	44768,622
9	120	102,018	44504,157	103,712	45212,054	104,658	45985,429
10	180	101,459	44260,291	102,384	44633,335	104,836	46063,955
11	240	102,587	44752,453	104,208	45428,280	104,468	45902,010
12	360	101,511	44283,097	104,993	45770,372	103,580	45511,934

Total drug per sample 1 (µg)	Total drug per sample 2 (µg)	Total drug per sample 3 (µg)
43623,807	43593,937	43938,903

Sample nr	Time (min)	Time range	Tablet 1	Tablet 2	Tablet 3
			Mass diss.	Mass diss.	Mass diss.
1	0	0	0	0	0
2	2	0-2	34229,501	35732,820	34501,478
3	5	2-5	42986,949	42979,560	42064,690
4	10	5-10	43855,702	44975,423	47669,808
5	15	10-15	46970,557	46924,230	45634,677
6	30	15-30	45720,909	46157,716	45783,086
7	60	30-60	46988,556	46076,570	45360,061
8	90	60-90	44377,737	44043,162	44768,622
9	120	90-120	44504,157	45212,054	45985,429
10	180	120-180	44260,291	44633,335	46063,955
11	240	180-240	44752,453	45428,280	45902,010
12	360	240-360	44283,097	45770,372	45511,934

Sample nr	Time range	Tmid	DXd Tablet 1	DXd Tablet 2	DXd Tablet 3
1	0	0	0	0	0
2	0-2	1	34229,501	35732,820	34501,478
3	2-5	3,5	8757,449	7246,740	7563,212
4	5-10	7,5	868,753	1995,863	5605,118
5	10-15	12,5	3114,855	1948,807	-2035,131
6	15-30	22,5	-1249,648	-766,514	148,409
7	30-60	45	1267,647	-81,146	-423,025
8	60-90	75	-2610,818	-2033,408	-591,439
9	90-120	105	126,419	1168,892	1216,807
10	120-180	150	-243,866	-578,719	78,526
11	180-240	210	492,163	794,945	-161,945
12	240-360	300	-469,356	342,092	-390,076
		sum	44283,097	45770,372	45511,934

Sample nr	Time range	Tmid	Tmid x DXd	Tmid x DXd	Tmid x DXd
1	0	0	0	0	0
2	0-2	1	34229,501	35732,820	34501,478
3	2-5	3,5	30651,070	25363,591	26471,244
4	5-10	7,5	6515,646	14968,974	42038,383
5	10-15	12,5	38935,684	24360,086	-25439,133
6	15-30	22,5	-28117,078	-17246,569	3339,194
7	30-60	45	57044,105	-3651,557	-19036,123
8	60-90	75	-195811,380	-152505,584	-44357,950
9	90-120	105	13274,024	122733,616	127764,784
10	120-180	150	-36579,908	-86807,906	11778,881
11	180-240	210	103354,169	166938,513	-34008,386
12	240-360	300	-140806,877	102627,662	-117022,861
		sum	-117311,044	232513,645	6029,510

MDT Tablet 1	MDT Tablet 2	MDT Tablet 3	Average MDT	STDEV MDT
-2,649	5,080	0,132	0,854	3,196

AUC		
Sample 1	Sample 2	Sample 3
0	0	0
35,309	36,885	35,335
119,479	121,877	117,623
223,956	226,980	229,754
234,229	237,159	238,894
717,117	720,631	702,191
1434,512	1428,138	1400,163
1413,729	1395,396	1384,579
1375,288	1382,010	1394,186
2746,941	2782,297	2828,170
2754,624	2788,993	2825,607
5510,660	5648,408	5617,292

AUC0-360 (µg/ml.min)		
Sample 1	Sample 2	Sample 3
16565,844	16768,775	16773,792

Average AUC0-360 (µg/ml.min)		16702,803
	STDEV	118,637

Dri			
Withdrawal times	Vessel 1 % Dissolution	Vessel 2 % Dissolution	Vessel 3 % Dissolution
0	0	0	0
2	78,465	81,967	78,521
5	98,540	98,591	95,735
10	100,532	103,169	108,491
15	107,672	107,639	103,859

Dri				
Vessel 1	Vessel 2	Vessel 3	Average Dri	SD
5,393	5,351	5,390	5,378	0,019

Annexure I

% transport and apparent permeability results

In this Annexure the % transport and apparent permeability results are provided for all formulations. These evaluations were done on eight formulations in three different pH environments (1.2, 4.6 and 7.4).

Table 1: Table containing the percentage transport and apparent permeability results of formulation 1B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,152	0,152	0,152	2,930	8,382
	40	0,179	0,190	0,205	3,953	11,310
	60	0,217	0,231	0,249	4,797	13,725
	80	0,238	0,254	0,275	5,294	15,148
	100	0,252	0,270	0,292	5,623	16,086
	120	0,268	0,287	0,310	5,967	17,072
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,115	0,115	0,115	2,209	6,321
	40	0,134	0,143	0,154	2,966	8,485
	60	0,162	0,172	0,186	3,586	10,258
	80	0,187	0,199	0,216	4,149	11,870
	100	0,222	0,236	0,255	4,908	14,041
	120	0,244	0,260	0,281	5,413	15,487
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,072	0,072	0,072	1,393	3,986
	40	0,094	0,099	0,094	1,805	5,163
	60	0,115	0,122	0,116	2,225	6,366
	80	0,128	0,137	0,129	2,490	7,124
	100	0,148	0,158	0,149	2,874	8,222
	120	0,153	0,164	0,155	2,991	8,558

	Slope	1/A.60.100	Papp
Chamber 1	0,126	3,29968E-05	4,15186E-06
Chamber 2	0,117	3,29968E-05	3,84677E-06
Chamber 3	0,064	3,29968E-05	2,12746E-06

Mean Papp	STDEV
3,37536E-06	8,91149E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	6,230	1,796
40	8,319	2,512
60	10,116	3,006
80	11,381	3,294
100	12,783	3,332
120	13,706	3,697

Table 2: Table containing the percentage transport and apparent permeability results of formulation 2B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,057	0,057	0,057	1,090	3,119
	40	0,076	0,080	0,086	1,663	4,759
	60	0,089	0,094	0,102	1,966	5,623
	80	0,100	0,106	0,115	2,212	6,328
	100	0,107	0,114	0,123	2,374	6,793
	120	0,114	0,122	0,132	2,547	7,288
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,054	0,054	0,054	1,031	2,951
	40	0,086	0,090	0,097	1,863	5,331
	60	0,105	0,111	0,120	2,310	6,608
	80	0,115	0,123	0,133	2,563	7,333
	100	0,116	0,124	0,134	2,585	7,396
	120	0,117	0,125	0,135	2,606	7,456
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,069	0,069	0,069	1,321	3,780
	40	0,096	0,101	0,096	1,846	5,281
	60	0,116	0,124	0,117	2,249	6,433
	80	0,130	0,139	0,132	2,533	7,246
	100	0,128	0,138	0,131	2,514	7,194
	120	0,141	0,151	0,143	2,749	7,866

	Slope	1/A.60.100	Papp
Chamber 1	0,055	3,29968E-05	1,81373E-06
Chamber 2	0,059	3,29968E-05	1,95972E-06
Chamber 3	0,058	3,29968E-05	1,90851E-06

Mean Papp	STDEV
1,89398E-06	6,04766E-08

Time (min)	Mean Transport	STDEV-P
0	0	0
20	3,283	0,358
40	5,124	0,259
60	6,221	0,429
80	6,969	0,455
100	7,127	0,251
120	7,537	0,242

Table 3: Table containing the percentage transport and apparent permeability results of formulation 3B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,085	0,085	0,085	1,640	4,691
	40	0,101	0,107	0,116	2,236	6,398
	60	0,114	0,122	0,132	2,532	7,243
	80	0,128	0,137	0,148	2,845	8,140
	100	0,137	0,147	0,158	3,049	8,724
	120	0,160	0,170	0,184	3,543	10,138
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,091	0,091	0,091	1,757	5,027
	40	0,110	0,117	0,127	2,437	6,973
	60	0,122	0,130	0,140	2,702	7,730
	80	0,140	0,149	0,162	3,109	8,894
	100	0,157	0,167	0,181	3,483	9,965
	120	0,171	0,183	0,198	3,809	10,896
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,089	0,089	0,089	1,707	4,884
	40	0,110	0,116	0,110	2,116	6,055
	60	0,111	0,120	0,113	2,176	6,225
	80	0,131	0,139	0,132	2,535	7,252
	100	0,152	0,161	0,153	2,938	8,407
	120	0,169	0,180	0,170	3,278	9,378

	Slope	1/A.60.100	Papp
Chamber 1	0,072	3,29968E-05	2,36992E-06
Chamber 2	0,079	3,29968E-05	2,62129E-06
Chamber 3	0,065	3,29968E-05	2,14353E-06

Mean Papp	STDEV
2,37825E-06	1,95134E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	4,867	0,138
40	6,475	0,379
60	7,066	0,627
80	8,095	0,671
100	9,032	0,672
120	10,137	0,620

Table 4: Table containing the percentage transport and apparent permeability results of formulation 4B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,039	0,039	0,039	0,751	2,150
	40	0,059	0,062	0,067	1,280	3,662
	60	0,069	0,074	0,080	1,536	4,395
	80	0,082	0,087	0,094	1,805	5,164
	100	0,084	0,090	0,098	1,877	5,370
	120	0,094	0,101	0,109	2,095	5,994
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,047	0,047	0,047	0,907	2,596
	40	0,070	0,074	0,080	1,535	4,392
	60	0,084	0,089	0,097	1,857	5,313
	80	0,094	0,100	0,108	2,080	5,952
	100	0,101	0,108	0,117	2,255	6,451
	120	0,105	0,113	0,122	2,351	6,726
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,080	0,080	0,080	1,531	4,380
	40	0,118	0,124	0,117	2,249	6,435
	60	0,124	0,133	0,126	2,416	6,912
	80	0,132	0,141	0,134	2,572	7,359
	100	0,134	0,144	0,136	2,613	7,476
	120	0,141	0,151	0,142	2,742	7,845

	Slope	1/A.60.100	Papp
Chamber 1	0,046	3,29968E-05	1,52751E-06
Chamber 2	0,053	3,29968E-05	1,73514E-06
Chamber 3	0,055	3,29968E-05	1,80598E-06

Mean Papp	STDEV
1,68955E-06	1,18168E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,042	0,963
40	4,830	1,174
60	5,540	1,040
80	6,158	0,908
100	6,432	0,860
120	6,855	0,761

Table 5: Table containing the percentage transport and apparent permeability results of formulation 5B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,038	0,038	0,038	0,725	2,076
	40	0,057	0,060	0,065	1,246	3,564
	60	0,067	0,072	0,077	1,491	4,266
	80	0,074	0,079	0,085	1,641	4,694
	100	0,081	0,086	0,093	1,794	5,133
	120	0,087	0,093	0,100	1,930	5,521
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,068	0,068	0,068	1,304	3,730
	40	0,081	0,086	0,093	1,789	5,118
	60	0,088	0,094	0,101	1,953	5,587
	80	0,098	0,105	0,113	2,179	6,234
	100	0,101	0,109	0,117	2,260	6,465
	120	0,113	0,120	0,130	2,498	7,148
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,052	0,052	0,052	1,003	2,868
	40	0,066	0,070	0,066	1,275	3,649
	60	0,077	0,082	0,078	1,498	4,287
	80	0,083	0,089	0,084	1,617	4,625
	100	0,090	0,096	0,091	1,752	5,011
	120	0,094	0,101	0,096	1,842	5,271

	Slope	1/A.60.100	Papp
Chamber 1	0,043	3,29968E-05	1,40272E-06
Chamber 2	0,050	3,29968E-05	1,65159E-06
Chamber 3	0,038	3,29968E-05	1,24174E-06

Mean Papp	STDEV
1,43201E-06	1,68597E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	2,891	0,676
40	4,110	0,713
60	4,713	0,618
80	5,184	0,743
100	5,536	0,658
120	5,980	0,832

Table 6: Table containing the percentage transport and apparent permeability results of formulation 6B in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,054	0,054	0,054	1,041	2,979
	40	0,086	0,091	0,098	1,883	5,387
	60	0,105	0,112	0,121	2,326	6,653
	80	0,123	0,131	0,142	2,731	7,812
	100	0,150	0,159	0,172	3,315	9,485
	120	0,145	0,156	0,168	3,241	9,274
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,058	0,058	0,058	1,109	3,174
	40	0,090	0,094	0,101	1,953	5,587
	60	0,116	0,123	0,133	2,560	7,325
	80	0,131	0,140	0,151	2,913	8,335
	100	0,151	0,161	0,174	3,353	9,592
	120	0,140	0,152	0,164	3,158	9,035
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,051	0,051	0,051	0,977	2,794
	40	0,077	0,081	0,076	1,469	4,203
	60	0,088	0,094	0,089	1,715	4,907
	80	0,111	0,117	0,111	2,136	6,111
	100	0,136	0,144	0,136	2,625	7,510
	120	0,123	0,133	0,126	2,416	6,913

	Slope	1/A.60.100	Papp
Chamber 1	0,077	3,29968E-05	2,54892E-06
Chamber 2	0,076	3,29968E-05	2,51528E-06
Chamber 3	0,057	3,29968E-05	1,89023E-06

Mean Papp	STDEV
2,31815E-06	3,02894E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	2,982	0,155
40	5,059	0,611
60	6,295	1,019
80	7,419	0,949
100	8,862	0,957
120	8,407	1,061

Table 7: Table containing the percentage transport and apparent permeability results of the commercial product (Lasix®) in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,048	0,048	0,048	0,917	2,623
	40	0,070	0,073	0,079	1,525	4,364
	60	0,084	0,089	0,096	1,849	5,290
	80	0,091	0,098	0,106	2,032	5,814
	100	0,101	0,108	0,117	2,244	6,420
	120	0,103	0,111	0,120	2,303	6,587
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,039	0,039	0,039	0,755	2,161
	40	0,056	0,059	0,064	1,226	3,508
	60	0,066	0,070	0,076	1,457	4,169
	80	0,070	0,075	0,081	1,551	4,437
	100	0,076	0,082	0,088	1,698	4,858
	120	0,087	0,093	0,100	1,926	5,510
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,046	0,046	0,046	0,889	2,544
	40	0,074	0,077	0,073	1,404	4,016
	60	0,082	0,088	0,083	1,599	4,574
	80	0,093	0,099	0,094	1,809	5,175
	100	0,101	0,108	0,102	1,961	5,611
	120	0,103	0,110	0,104	2,003	5,732

	Slope	1/A.60.100	Papp
Chamber 1	0,051	3,29968E-05	1,69722E-06
Chamber 2	0,041	3,29968E-05	1,34661E-06
Chamber 3	0,044	3,29968E-05	1,44301E-06

Mean Papp	STDEV
1,49561E-06	1,4789E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	2,443	0,202
40	3,963	0,351
60	4,678	0,463
80	5,142	0,563
100	5,630	0,638
120	5,943	0,464

Table 8: Table containing the percentage transport and apparent permeability results of the control formulation (C) in the pH 1.2 environment performed using the pyloric antrum region of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,037	0,037	0,037	0,709	2,029
	40	0,051	0,054	0,058	1,125	3,218
	60	0,067	0,071	0,077	1,482	4,241
	80	0,074	0,079	0,085	1,643	4,699
	100	0,080	0,086	0,093	1,788	5,115
	120	0,084	0,090	0,097	1,871	5,353
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,050	0,050	0,050	0,964	2,758
	40	0,067	0,071	0,077	1,476	4,223
	60	0,080	0,085	0,092	1,767	5,056
	80	0,090	0,096	0,104	2,005	5,737
	100	0,096	0,102	0,111	2,131	6,097
	120	0,099	0,107	0,115	2,217	6,343
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,046	0,046	0,046	0,876	2,505
	40	0,063	0,067	0,063	1,216	3,480
	60	0,071	0,076	0,072	1,383	3,956
	80	0,078	0,083	0,079	1,512	4,325
	100	0,083	0,089	0,084	1,625	4,650
	120	0,085	0,091	0,086	1,659	4,748

	Slope	1/A.60.100	Papp
Chamber 1	0,042	3,29968E-05	1,39723E-06
Chamber 2	0,049	3,29968E-05	1,60393E-06
Chamber 3	0,035	3,29968E-05	1,14176E-06

Mean Papp	STDEV
1,38097E-06	1,8903E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	2,431	0,302
40	3,640	0,426
60	4,417	0,466
80	4,921	0,597
100	5,287	0,603
120	5,481	0,658

Table 9: Table containing the percentage transport and apparent permeability results of formulation 1B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,061	0,061	0,061	1,170	3,347
	40	0,105	0,110	0,119	2,288	6,545
	60	0,117	0,124	0,134	2,588	7,405
	80	0,133	0,141	0,153	2,941	8,416
	100	0,145	0,155	0,168	3,227	9,232
	120	0,152	0,163	0,176	3,382	9,677
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,058	0,058	0,058	1,118	3,199
	40	0,082	0,086	0,093	1,798	5,143
	60	0,098	0,104	0,113	2,167	6,199
	80	0,115	0,122	0,132	2,547	7,288
	100	0,126	0,134	0,145	2,797	8,002
	120	0,126	0,135	0,146	2,807	8,031
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,056	0,056	0,056	1,072	3,067
	40	0,086	0,090	0,085	1,634	4,676
	60	0,099	0,106	0,100	1,925	5,509
	80	0,112	0,120	0,113	2,177	6,229
	100	0,130	0,138	0,131	2,515	7,196
	120	0,135	0,144	0,137	2,628	7,520

	Slope	1/A.60.100	Papp
Chamber 1	0,076	3,29968E-05	2,51429E-06
Chamber 2	0,064	3,29968E-05	2,1121E-06
Chamber 3	0,058	3,29968E-05	1,90731E-06

Mean Papp	STDEV
2,1779E-06	2,52129E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,204	0,115
40	5,455	0,794
60	6,371	0,784
80	7,311	0,893
100	8,143	0,837
120	8,409	0,921

Table 10: Table containing the percentage transport and apparent permeability results of formulation 2B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,047	0,047	0,047	0,906	2,593
	40	0,070	0,073	0,079	1,523	4,356
	60	0,087	0,093	0,100	1,925	5,507
	80	0,108	0,114	0,124	2,379	6,806
	100	0,118	0,126	0,137	2,628	7,520
	120	0,127	0,136	0,147	2,833	8,105
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,056	0,056	0,056	1,085	3,105
	40	0,078	0,082	0,089	1,714	4,903
	60	0,096	0,102	0,110	2,113	6,045
	80	0,113	0,120	0,130	2,494	7,135
	100	0,124	0,133	0,143	2,757	7,887
	120	0,135	0,144	0,156	2,996	8,571
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,047	0,047	0,047	0,905	2,590
	40	0,072	0,075	0,071	1,366	3,908
	60	0,098	0,103	0,098	1,883	5,388
	80	0,122	0,129	0,122	2,347	6,714
	100	0,135	0,144	0,136	2,616	7,485
	120	0,149	0,159	0,150	2,893	8,278

	Slope	1/A.60.100	Papp
Chamber 1	0,065	3,29968E-05	2,15762E-06
Chamber 2	0,067	3,29968E-05	2,21011E-06
Chamber 3	0,067	3,29968E-05	2,20542E-06

Mean Papp	STDEV
2,19105E-06	2,37168E-08

Time (min)	Mean Transport	STDEV
0	0	0
20	2,763	0,242
40	4,389	0,407
60	5,647	0,286
80	6,885	0,181
100	7,630	0,182
120	8,318	0,192

Table 11: Table containing the percentage transport and apparent permeability results of formulation 3B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,056	0,056	0,056	1,083	3,100
	40	0,080	0,084	0,091	1,750	5,007
	60	0,113	0,119	0,129	2,476	7,083
	80	0,144	0,152	0,164	3,164	9,052
	100	0,204	0,214	0,232	4,460	12,760
	120	0,228	0,243	0,263	5,053	14,456
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,053	0,053	0,053	1,012	2,896
	40	0,076	0,080	0,086	1,655	4,735
	60	0,107	0,113	0,122	2,342	6,700
	80	0,124	0,132	0,142	2,738	7,834
	100	0,199	0,208	0,225	4,325	12,373
	120	0,201	0,216	0,234	4,498	12,868
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,055	0,055	0,055	1,051	3,006
	40	0,076	0,080	0,076	1,463	4,187
	60	0,110	0,116	0,109	2,105	6,022
	80	0,135	0,143	0,135	2,600	7,439
	100	0,199	0,210	0,198	3,814	10,912
	120	0,215	0,230	0,217	4,184	11,971

	Slope	1/A.60.100	Papp
Chamber 1	0,119	3,29968E-05	3,93203E-06
Chamber 2	0,108	3,29968E-05	3,57409E-06
Chamber 3	0,098	3,29968E-05	3,23947E-06

Mean Papp	STDEV
3,58186E-06	2,82791E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,001	0,083
40	4,643	0,341
60	6,602	0,439
80	8,108	0,686
100	12,015	0,795
120	13,098	1,027

Table 12: Table containing the percentage transport and apparent permeability results of formulation 4B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,068	0,068	0,068	1,305	3,733
	40	0,098	0,103	0,111	2,136	6,112
	60	0,145	0,152	0,165	3,169	9,066
	80	0,201	0,211	0,229	4,398	12,581
	100	0,268	0,283	0,306	5,882	16,829
	120	0,329	0,349	0,377	7,260	20,772
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,067	0,067	0,067	1,296	3,708
	40	0,086	0,091	0,098	1,889	5,405
	60	0,105	0,111	0,120	2,310	6,609
	80	0,130	0,138	0,149	2,872	8,217
	100	0,161	0,170	0,184	3,545	10,143
	120	0,193	0,205	0,221	4,262	12,193
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,063	0,063	0,063	1,206	3,449
	40	0,086	0,090	0,086	1,647	4,713
	60	0,103	0,109	0,103	1,984	5,676
	80	0,130	0,137	0,130	2,497	7,145
	100	0,165	0,175	0,166	3,188	9,120
	120	0,202	0,215	0,203	3,907	11,177

	Slope	1/A.60.100	Papp
Chamber 1	0,170	3,29968E-05	5,59624E-06
Chamber 2	0,093	3,29968E-05	3,07935E-06
Chamber 3	0,084	3,29968E-05	2,78726E-06

Mean Papp	STDEV
3,82095E-06	1,26097E-06

Time (min)	Mean Transport	STDEV
0	0	0
20	3,630	0,128
40	5,410	0,571
60	7,117	1,430
80	9,314	2,351
100	12,031	3,418
120	14,714	4,304

Table 13: Table containing the percentage transport and apparent permeability results of formulation 5B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,047	0,047	0,047	0,907	2,596
	40	0,070	0,074	0,080	1,538	4,401
	60	0,088	0,094	0,101	1,947	5,570
	80	0,101	0,107	0,116	2,234	6,391
	100	0,110	0,118	0,127	2,453	7,018
	120	0,118	0,126	0,136	2,626	7,513
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,048	0,048	0,048	0,929	2,659
	40	0,073	0,076	0,083	1,590	4,549
	60	0,094	0,099	0,107	2,059	5,890
	80	0,107	0,114	0,124	2,378	6,804
	100	0,117	0,125	0,135	2,598	7,434
	120	0,125	0,133	0,144	2,776	7,941
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,045	0,045	0,045	0,857	2,453
	40	0,070	0,073	0,069	1,327	3,796
	60	0,093	0,098	0,093	1,789	5,118
	80	0,102	0,109	0,103	1,984	5,676
	100	0,112	0,120	0,114	2,184	6,250
	120	0,120	0,128	0,121	2,335	6,681

	Slope	1/A.60.100	Papp
Chamber 1	0,060	3,29968E-05	1,96646E-06
Chamber 2	0,064	3,29968E-05	2,09928E-06
Chamber 3	0,053	3,29968E-05	1,73914E-06

Mean Papp	STDEV
1,93496E-06	1,48704E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	2,569	0,086
40	4,249	0,326
60	5,526	0,317
80	6,290	0,466
100	6,901	0,491
120	7,378	0,523

Table 14: Table containing the percentage transport and apparent permeability results of formulation 6B in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,080	0,080	0,080	1,545	4,421
	40	0,130	0,136	0,147	2,819	8,066
	60	0,141	0,150	0,163	3,128	8,950
	80	0,147	0,157	0,170	3,277	9,374
	100	0,155	0,166	0,179	3,446	9,858
	120	0,155	0,166	0,180	3,459	9,895
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,070	0,070	0,070	1,343	3,843
	40	0,103	0,109	0,117	2,261	6,469
	60	0,124	0,131	0,142	2,732	7,816
	80	0,151	0,161	0,174	3,342	9,560
	100	0,155	0,166	0,179	3,451	9,875
	120	0,156	0,168	0,182	3,495	9,999
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,062	0,062	0,062	1,186	3,394
	40	0,082	0,086	0,082	1,573	4,501
	60	0,093	0,099	0,094	1,811	5,181
	80	0,109	0,116	0,110	2,115	6,052
	100	0,120	0,128	0,121	2,325	6,653
	120	0,124	0,133	0,126	2,419	6,920

	Slope	1/A.60.100	Papp
Chamber 1	0,075	3,29968E-05	2,46692E-06
Chamber 2	0,081	3,29968E-05	2,66044E-06
Chamber 3	0,051	3,29968E-05	1,69859E-06

Mean Papp	STDEV
2,27532E-06	4,15392E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,886	0,420
40	6,346	1,458
60	7,316	1,579
80	8,329	1,612
100	8,795	1,515
120	8,938	1,428

Table 15: Table containing the percentage transport and apparent permeability results of the commercial product (Lasix®) in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,068	0,068	0,068	1,308	3,741
	40	0,082	0,087	0,094	1,817	5,199
	60	0,098	0,104	0,113	2,165	6,194
	80	0,115	0,122	0,132	2,535	7,252
	100	0,117	0,125	0,136	2,610	7,466
	120	0,134	0,143	0,155	2,976	8,515
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,051	0,051	0,051	0,974	2,786
	40	0,074	0,077	0,084	1,610	4,607
	60	0,093	0,098	0,106	2,044	5,849
	80	0,107	0,114	0,123	2,370	6,780
	100	0,117	0,125	0,135	2,593	7,418
	120	0,119	0,128	0,138	2,665	7,624
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,052	0,052	0,052	1,008	2,885
	40	0,079	0,083	0,078	1,503	4,301
	60	0,096	0,102	0,096	1,849	5,289
	80	0,104	0,111	0,105	2,023	5,787
	100	0,115	0,123	0,117	2,244	6,419
	120	0,122	0,131	0,124	2,385	6,823

	Slope	1/A.60.100	Papp
Chamber 1	0,063	3,29968E-05	2,0652E-06
Chamber 2	0,061	3,29968E-05	2,02162E-06
Chamber 3	0,052	3,29968E-05	1,71014E-06

Mean Papp	STDEV
1,93232E-06	1,58111E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,137	0,429
40	4,702	0,373
60	5,777	0,373
80	6,606	0,610
100	7,101	0,483
120	7,654	0,691

Table 16: Table containing the percentage transport and apparent permeability results of the control formulation(C) in the pH 4.6 environment performed using the ascending duodenum segment of porcine tissue.

	Time (min)	Peak	Correction 1	Correction 2	Concentration (mg/ml)	% Transport
Chamber 1	0	1,816	1,816	1,816	34,953	0
	20	0,063	0,063	0,063	1,205	3,447
	40	0,106	0,110	0,119	2,298	6,574
	60	0,102	0,110	0,118	2,279	6,519
	80	0,109	0,117	0,127	2,435	6,965
	100	0,110	0,118	0,127	2,453	7,018
	120	0,103	0,112	0,121	2,321	6,641
Chamber 2	0	1,816	1,816	1,816	34,953	0
	20	0,056	0,056	0,056	1,072	3,067
	40	0,079	0,083	0,090	1,723	4,930
	60	0,097	0,103	0,112	2,149	6,148
	80	0,105	0,112	0,121	2,334	6,679
	100	0,118	0,125	0,136	2,608	7,462
	120	0,110	0,119	0,129	2,478	7,090
Chamber 3	0	1,816	1,816	1,816	34,953	0
	20	0,049	0,049	0,049	0,946	2,706
	40	0,072	0,076	0,072	1,383	3,957
	60	0,095	0,101	0,095	1,833	5,243
	80	0,103	0,110	0,104	2,010	5,752
	100	0,110	0,118	0,112	2,146	6,140
	120	0,104	0,112	0,106	2,038	5,831

	Slope	1/A.60.100	Papp
Chamber 1	0,049	3,29968E-05	1,61787E-06
Chamber 2	0,057	3,29968E-05	1,87424E-06
Chamber 3	0,047	3,29968E-05	1,54119E-06

Mean Papp	STDEV
1,67777E-06	1,4241E-07

Time (min)	Mean Transport	STDEV
0	0	0
20	3,073	0,302
40	5,154	1,080
60	5,970	0,536
80	6,465	0,518
100	6,873	0,549
120	6,521	0,521

Annexure J

Difference factor results

In this Annexure the difference factor results are provided for all formulations. These evaluations were done on all formulations (36) in three different pH environments (1.2, 4.6 and 7.4).

Table 1: Table containing the difference factor values regarding formula 1A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,724	1,674	14,778	6,392
3	5	14,437	8,898	27,637	16,991
4	10	30,610	15,420	30,461	25,497
5	15	48,237	19,200	38,127	35,188
6	30	65,070	33,139	48,067	48,759
7	60	81,396	41,720	49,282	57,466
8	90	83,539	46,808	58,313	62,887
9	120	87,814	52,865	61,154	67,278
10	180	87,628	54,904	62,509	68,347
11	240	89,495	54,188	61,261	68,314
12	360	88,907	55,443	64,060	69,470
13	375	85,013	55,369	63,546	67,976
	SUM	764,871	439,628	579,193	594,564

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
1281,398	692,033	1031,166		1001,532	295,798

Table 2: Table containing the difference factor values regarding formula 1B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	4,111	6,193	5,109	5,138
3	5	11,993	11,482	8,905	10,793
4	10	19,431	18,669	13,458	17,186
5	15	25,061	26,720	24,581	25,454
6	30	35,137	31,385	27,649	31,390
7	60	38,961	41,300	37,272	39,178
8	90	47,874	51,449	50,030	49,784
9	120	58,070	49,531	57,288	54,963
10	180	59,819	58,823	58,166	58,936
11	240	62,026	61,168	61,671	61,622
12	360	60,234	65,647	66,041	63,974
13	375	67,339	63,862	59,884	63,695
	SUM	490,056	486,230	470,054	482,113

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
820,997	765,391	836,860		807,749	37,531

Table 3: Table containing the difference factor values regarding formula 1C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,576	0,039	0,073	0,229
3	5	5,459	1,703	2,925	3,362
4	10	6,981	7,438	10,301	8,240
5	15	12,196	16,105	20,019	16,106
6	30	18,835	26,814	29,214	24,954
7	60	26,624	33,253	36,301	32,060
8	90	31,840	37,465	39,184	36,163
9	120	35,209	41,125	43,757	40,030
10	180	37,974	40,951	45,373	41,433
11	240	38,329	45,371	49,317	44,339
12	360	40,872	45,830	48,446	45,049
13	375	45,274	47,763	48,610	47,216
	SUM	300,168	343,857	373,520	339,182

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
446,179	523,697	588,779		519,552	71,390

Table 4: Table containing the difference factor values regarding formula 1D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,210	0,402	0,668	0,427
3	5	0,887	1,560	3,176	1,874
4	10	5,149	5,567	7,272	5,996
5	15	12,818	13,807	14,994	13,873
6	30	23,607	24,777	25,384	24,589
7	60	33,010	37,021	31,750	33,927
8	90	42,607	46,564	39,349	42,840
9	120	49,570	55,264	52,714	52,516
10	180	55,308	60,250	57,264	57,608
11	240	59,470	66,095	63,421	62,995
12	360	61,354	63,093	64,632	63,026
13	375	62,863	62,187	63,319	62,790
	SUM	406,851	436,589	423,944	422,461

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
604,757	664,928	668,262		645,982	35,741

Table 5: Table containing the difference factor values regarding formula 1E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,475	1,968	1,736	2,060
3	5	5,935	7,109	9,260	7,435
4	10	10,470	14,362	17,083	13,971
5	15	19,931	24,515	24,176	22,874
6	30	27,544	32,342	31,152	30,346
7	60	31,162	37,732	36,193	35,029
8	90	36,329	40,477	39,825	38,877
9	120	40,795	42,498	41,580	41,624
10	180	40,447	42,398	42,699	41,848
11	240	41,539	43,258	43,904	42,900
12	360	42,716	43,659	43,411	43,262
13	375	44,085	45,655	43,609	44,450
	SUM	343,429	375,974	374,628	364,677

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
520,871	519,582	446,957		495,803	42,307

Table 6: Table containing the difference factor values regarding formula 1F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,806	0,166	0,343	0,438
3	5	0,950	1,670	3,682	2,101
4	10	3,835	4,265	10,248	6,116
5	15	10,409	13,541	21,789	15,246
6	30	23,493	27,072	31,201	27,255
7	60	37,054	41,899	40,993	39,982
8	90	47,551	52,834	50,271	50,219
9	120	57,651	62,534	56,890	59,025
10	180	52,975	60,239	60,050	57,754
11	240	58,234	60,753	61,857	60,281
12	360	59,897	60,915	61,651	60,821
13	375	62,903	62,941	64,013	63,286
	SUM	415,757	448,830	462,989	442,525

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
630,569	620,266	552,378		601,071	42,483

Table 7: Table containing the difference factor values regarding formula 2A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,048	3,834	1,791	1,891
3	5	8,215	4,506	2,560	5,094
4	10	8,377	6,109	7,115	7,200
5	15	12,114	11,578	13,397	12,363
6	30	17,933	19,072	20,596	19,200
7	60	37,676	35,643	27,087	33,469
8	90	29,391	43,377	38,456	37,075
9	120	42,146	48,068	49,395	46,536
10	180	48,320	36,026	49,000	44,449
11	240	53,337	38,479	50,126	47,314
12	360	55,320	49,488	54,215	53,008
13	375	52,718	51,623	53,286	52,542
	SUM	365,595	347,804	367,023	360,141

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
612,487	547,489	653,429		604,468	53,423

Table 8: Table containing the difference factor values regarding formula 2B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,199	2,458	3,393	3,017
3	5	6,043	7,725	6,923	6,897
4	10	8,788	10,264	10,962	10,005
5	15	16,295	19,747	19,143	18,395
6	30	28,021	27,878	38,360	31,420
7	60	42,028	41,752	43,619	42,466
8	90	37,472	50,992	54,322	47,595
9	120	57,055	58,676	48,604	54,779
10	180	60,300	61,982	53,278	58,520
11	240	63,766	64,405	60,028	62,733
12	360	38,666	65,916	67,311	57,297
13	375	55,853	61,763	62,473	60,030
	SUM	417,486	473,557	468,416	453,153

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
699,420	745,442	833,944		759,602	68,371

Table 9: Table containing the difference factor values regarding formula 2C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,480	0,758	0,335	0,524
3	5	3,073	4,480	3,178	3,577
4	10	8,935	11,081	9,382	9,799
5	15	16,064	18,288	17,245	17,199
6	30	22,088	25,276	23,462	23,609
7	60	29,211	31,706	31,103	30,673
8	90	35,628	40,594	39,048	38,423
9	120	43,278	46,843	45,333	45,151
10	180	47,824	51,764	49,375	49,654
11	240	51,276	54,444	54,169	53,296
12	360	53,333	57,630	55,589	55,517
13	375	58,026	60,036	57,741	58,601
	SUM	369,216	402,900	385,960	386,025

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
548,814	613,620	608,388		590,274	36,001

Table 10: Table containing the difference factor values regarding formula 2D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,144	0,273	0,368	0,262
3	5	1,701	1,882	2,755	2,113
4	10	6,090	5,702	8,908	6,900
5	15	13,182	12,214	17,312	14,236
6	30	23,203	20,931	26,076	23,403
7	60	37,074	34,992	39,864	37,310
8	90	49,735	47,787	51,383	49,635
9	120	58,214	55,052	60,405	57,890
10	180	61,245	58,903	63,597	61,248
11	240	63,432	62,517	65,686	63,878
12	360	65,375	63,276	66,221	64,957
13	375	66,420	65,089	68,477	66,662
	SUM	445,815	428,618	471,051	448,495

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
662,673	652,789	742,517		685,993	49,200

Table 11: Table containing the difference factor values regarding formula 2E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,174	0,231	0,061	0,155
3	5	0,509	0,633	0,026	0,389
4	10	2,243	2,480	1,923	2,215
5	15	6,917	6,443	5,795	6,385
6	30	13,388	12,634	12,191	12,738
7	60	21,399	20,779	21,000	21,060
8	90	29,662	27,507	28,252	28,474
9	120	34,758	30,873	32,341	32,657
10	180	38,576	33,728	33,803	35,369
11	240	39,840	34,247	36,112	36,733
12	360	42,327	34,751	36,046	37,708
13	375	39,089	36,383	37,255	37,576
	SUM	268,882	240,690	244,807	251,460

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
407,807	332,624	292,071		344,168	58,725

Table 12: Table containing the difference factor values regarding formula 2F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,023	0,236	0,050	0,103
3	5	0,603	1,869	0,570	1,014
4	10	3,457	6,386	3,987	4,610
5	15	10,364	14,525	10,848	11,912
6	30	19,802	24,963	20,331	21,699
7	60	34,183	40,196	33,855	36,078
8	90	47,770	51,779	44,401	47,983
9	120	53,324	56,837	52,837	54,333
10	180	57,503	60,591	54,818	57,637
11	240	59,719	62,980	58,078	60,259
12	360	62,293	63,788	58,008	61,363
13	375	60,954	65,062	56,603	60,873
	SUM	409,995	449,213	394,385	417,864

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
621,830	620,795	470,530		571,051	87,056

Table 13: Table containing the difference factor values regarding formula 3A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,475	1,092	1,763	1,110
3	5	4,832	6,300	7,313	6,148
4	10	12,622	16,521	16,999	15,381
5	15	21,957	26,899	25,924	24,927
6	30	30,270	48,884	33,387	37,514
7	60	36,422	39,753	38,517	38,230
8	90	42,722	43,299	43,634	43,218
9	120	45,403	46,391	45,627	45,807
10	180	47,730	48,103	47,424	47,752
11	240	49,673	48,479	48,014	48,722
12	360	49,326	48,706	49,342	49,125
13	375	46,779	47,127	47,283	47,063
	SUM	388,211	421,553	405,225	404,997

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
650,375	663,580	721,443		678,466	37,800

Table 14: Table containing the difference factor values regarding formula 3B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,117	0,865	1,245	1,409
3	5	9,349	6,611	6,329	7,430
4	10	18,714	15,493	15,374	16,527
5	15	26,356	24,677	24,837	25,290
6	30	33,929	32,041	30,405	32,125
7	60	42,015	37,735	38,328	39,359
8	90	48,589	47,153	48,761	48,168
9	120	54,315	51,877	58,627	54,940
10	180	57,849	55,946	62,279	58,691
11	240	64,293	62,400	65,497	64,063
12	360	67,916	65,163	69,099	67,393
13	375	65,936	64,387	67,241	65,855
	SUM	491,380	464,348	488,022	481,250

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
823,215	730,945	868,850		807,670	70,254

Table 15: Table containing the difference factor values regarding formula 3C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,853	0,955	1,797	1,535
3	5	8,924	6,392	10,092	8,469
4	10	21,810	17,607	23,079	20,832
5	15	32,036	27,664	32,502	30,734
6	30	38,635	35,119	37,763	37,172
7	60	42,915	40,134	42,224	41,758
8	90	47,888	43,511	47,847	46,416
9	120	45,605	46,940	47,689	46,745
10	180	44,326	46,520	48,119	46,322
11	240	54,481	48,050	48,388	50,307
12	360	53,952	48,646	49,926	50,842
13	375	47,883	46,265	46,072	46,740
	SUM	440,308	407,804	435,497	427,870

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
654,488	621,089	686,474		654,017	32,695

Table 16: Table containing the difference factor values regarding formula 3D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,332	0,404	0,222	0,319
3	5	2,240	3,697	1,537	2,491
4	10	7,616	11,156	6,282	8,351
5	15	15,508	20,602	13,369	16,493
6	30	22,925	27,778	20,131	23,612
7	60	32,467	38,853	27,670	32,997
8	90	40,182	50,879	35,556	42,206
9	120	48,034	56,761	46,240	50,345
10	180	54,076	62,123	52,871	56,357
11	240	57,175	64,380	58,600	60,052
12	360	62,626	66,838	61,024	63,496
13	375	58,464	60,629	57,368	58,820
	SUM	401,646	464,099	380,869	415,538

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
597,019	706,827	600,363		634,737	62,455

Table 17: Table containing the difference factor values regarding formula 3E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,140	0,095	0,009	0,081
3	5	1,024	1,755	0,425	1,068
4	10	4,679	6,410	4,159	5,083
5	15	12,142	14,034	11,761	12,646
6	30	20,476	21,075	22,322	21,291
7	60	26,557	25,644	32,364	28,188
8	90	30,837	28,601	37,073	32,170
9	120	32,840	30,331	38,491	33,887
10	180	33,649	31,451	39,217	34,772
11	240	33,995	31,164	38,545	34,568
12	360	33,012	31,150	35,772	33,312
13	375	32,460	30,794	34,139	32,465
	SUM	261,810	252,505	294,278	269,531

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
397,081	348,952	351,094		365,709	27,190

Table 18: Table containing the difference factor values regarding formula 3F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,089	1,115	1,349	0,851
3	5	0,744	6,215	4,099	3,686
4	10	3,758	15,224	12,290	10,424
5	15	9,709	24,305	21,126	18,380
6	30	17,278	32,613	28,581	26,157
7	60	26,371	39,253	34,751	33,458
8	90	33,526	36,710	40,360	36,866
9	120	38,155	52,184	48,163	46,167
10	180	42,790	53,654	49,915	48,786
11	240	48,458	57,416	53,875	53,250
12	360	51,422	59,522	56,072	55,672
13	375	54,509	59,183	54,782	56,158
	SUM	326,810	437,394	405,365	389,856

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
495,665	604,461	483,629		527,918	66,561

Table 19: Table containing the difference factor values regarding formula 4A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,262	0,165	0,710	0,379
3	5	3,054	2,638	3,132	2,941
4	10	9,005	7,825	9,199	8,676
5	15	16,077	14,613	16,319	15,670
6	30	23,414	21,834	23,713	22,987
7	60	28,821	28,804	29,431	29,019
8	90	35,814	34,246	34,960	35,007
9	120	37,703	35,728	36,018	36,483
10	180	40,284	38,758	38,621	39,221
11	240	43,382	40,730	39,601	41,238
12	360	43,469	39,931	40,690	41,363
13	375	42,761	41,464	42,016	42,080
	SUM	324,048	306,736	314,408	315,064

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
542,882	482,842	559,756		528,494	40,426

Table 20: Table containing the difference factor values regarding formula 4B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,519	0,112	0,964	0,532
3	5	2,963	2,585	4,950	3,499
4	10	9,430	9,412	13,702	10,848
5	15	18,500	19,474	25,221	21,065
6	30	29,883	30,601	35,103	31,863
7	60	37,677	43,760	47,915	43,117
8	90	53,611	52,700	59,844	55,385
9	120	56,520	56,837	62,980	58,779
10	180	57,379	59,215	69,624	62,073
11	240	63,129	63,212	66,826	64,389
12	360	63,459	64,011	68,073	65,181
13	375	65,026	65,644	65,734	65,468
	SUM	458,096	467,562	520,936	482,198

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
767,454	736,004	927,448		810,302	102,663

Table 21: Table containing the difference factor values regarding formula 4C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,109	0,163	0,197	0,156
3	5	1,431	0,984	1,132	1,182
4	10	5,739	3,994	4,025	4,586
5	15	11,650	9,298	10,012	10,320
6	30	17,841	16,238	17,276	17,118
7	60	25,570	23,928	23,867	24,455
8	90	30,910	30,031	30,475	30,472
9	120	34,180	33,741	33,591	33,837
10	180	37,409	37,067	36,671	37,049
11	240	38,703	39,938	39,580	39,407
12	360	39,817	39,860	40,399	40,025
13	375	42,136	42,402	41,946	42,161
	SUM	285,494	277,642	279,170	280,769

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
424,367	422,851	440,056		429,091	9,526

Table 22: Table containing the difference factor values regarding formula 4D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,363	0,113	0,144	0,207
3	5	3,074	1,593	2,358	2,341
4	10	10,208	7,531	8,667	8,802
5	15	20,997	17,421	18,129	18,849
6	30	32,786	28,473	29,457	30,239
7	60	43,735	40,746	41,581	42,021
8	90	53,484	52,685	52,557	52,909
9	120	59,325	58,621	59,831	59,259
10	180	64,636	65,329	65,027	64,997
11	240	69,788	69,202	67,052	68,681
12	360	68,886	69,349	68,971	69,069
13	375	72,190	72,692	71,957	72,280
	SUM	499,473	483,755	485,731	489,653

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
742,433	736,763	765,657		748,284	15,310

Table 23: Table containing the difference factor values regarding formula 4E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,045	0,012	0,087	0,048
3	5	0,845	0,983	1,583	1,137
4	10	5,021	5,094	7,805	5,973
5	15	12,554	13,109	15,982	13,882
6	30	21,124	20,903	23,646	21,891
7	60	29,195	29,757	30,676	29,876
8	90	36,805	36,731	37,010	36,849
9	120	42,766	42,542	41,520	42,276
10	180	45,261	45,120	44,486	44,956
11	240	48,035	48,481	46,786	47,767
12	360	49,394	49,106	47,596	48,698
13	375	49,530	49,530	48,589	49,216
	SUM	340,575	341,367	345,765	342,569

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
516,543	471,757	412,522		466,941	52,177

Table 24: Table containing the difference factor values regarding formula 4F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,781	0,489	0,006	0,425
3	5	4,031	2,924	0,731	2,562
4	10	12,495	10,416	5,473	9,461
5	15	23,098	21,240	14,927	19,755
6	30	34,501	32,479	25,753	30,911
7	60	44,842	44,259	39,067	42,723
8	90	52,740	52,255	47,049	50,681
9	120	56,632	56,098	52,298	55,009
10	180	58,846	59,065	55,220	57,711
11	240	62,702	61,094	56,365	60,054
12	360	59,084	60,127	55,085	58,099
13	375	59,347	61,027	54,664	58,346
	SUM	469,098	461,473	406,639	445,737

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
711,471	637,738	485,149		611,452	115,428

Table 25: Table containing the difference factor values regarding formula 5A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,317	0,517	0,728	0,521
3	5	2,477	1,658	1,927	2,021
4	10	5,870	10,699	6,026	7,532
5	15	14,281	17,004	11,897	14,394
6	30	21,169	25,174	18,541	21,628
7	60	27,533	33,739	26,378	29,217
8	90	33,772	39,892	32,687	35,451
9	120	38,573	45,296	36,948	40,272
10	180	41,774	47,934	40,994	43,567
11	240	43,584	49,576	42,526	45,228
12	360	44,305	50,742	45,683	46,910
13	375	43,330	45,843	40,704	43,292
	SUM	316,984	368,074	305,039	330,032

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
531,048	579,397	543,076		551,174	25,171

Table 26: Table containing the difference factor values regarding formula 5B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,141	0,025	0,955	0,374
3	5	1,552	4,037	3,785	3,125
4	10	5,443	10,860	9,713	8,672
5	15	12,781	20,191	17,151	16,708
6	30	22,502	28,509	25,057	25,356
7	60	33,018	37,381	34,869	35,089
8	90	42,880	47,087	43,386	44,451
9	120	50,270	53,466	50,972	51,569
10	180	55,322	60,285	57,372	57,660
11	240	58,058	63,639	59,908	60,535
12	360	59,186	65,715	63,108	62,670
13	375	55,462	57,658	56,447	56,522
	SUM	396,617	448,852	422,725	422,731

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
664,457	706,553	752,598		707,869	44,085

Table 27: Table containing the difference factor values regarding formula 5C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,236	0,407	0,565	0,403
3	5	1,414	2,667	3,427	2,503
4	10	5,101	7,712	9,293	7,369
5	15	11,027	14,403	15,278	13,569
6	30	18,160	21,296	23,238	20,898
7	60	26,555	28,377	30,183	28,372
8	90	32,158	35,335	36,901	34,798
9	120	36,208	39,134	43,036	39,459
10	180	35,839	43,306	40,032	39,726
11	240	42,445	45,152	44,279	43,959
12	360	43,219	46,970	45,918	45,369
13	375	42,756	43,862	42,504	43,041
	SUM	295,121	328,622	334,653	319,465

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
438,677	500,493	527,513		488,895	45,540

Table 28: Table containing the difference factor values regarding formula 5D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,370	0,183	0,082	0,212
3	5	1,311	1,018	0,834	1,055
4	10	3,584	3,358	3,491	3,478
5	15	8,297	8,020	8,151	8,156
6	30	17,073	17,942	17,678	17,565
7	60	32,141	33,939	31,395	32,492
8	90	43,467	46,831	42,939	44,412
9	120	50,094	53,687	52,962	52,248
10	180	55,843	60,217	57,058	57,706
11	240	59,464	61,095	60,126	60,228
12	360	61,042	63,735	61,670	62,149
13	375	54,586	55,858	54,300	54,914
	SUM	387,271	405,882	390,687	394,613

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
575,652	618,162	615,839		603,218	23,901

Table 29: Table containing the difference factor values regarding formula 5E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,242	0,203	0,309	0,252
3	5	2,099	2,450	2,396	2,315
4	10	7,956	8,593	8,218	8,256
5	15	16,346	16,211	15,313	15,957
6	30	24,800	24,128	22,568	23,832
7	60	28,500	29,870	27,946	28,772
8	90	33,998	34,179	32,533	33,570
9	120	39,412	37,145	35,213	37,257
10	180	42,902	39,500	37,459	39,954
11	240	44,231	41,396	39,661	41,763
12	360	44,460	42,072	40,626	42,386
13	375	40,507	40,389	37,360	39,419
	SUM	325,453	316,136	299,602	313,730

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
493,607	436,888	357,447		429,314	68,396

Table 30: Table containing the difference factor values regarding formula 5F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,185	0,702	0,582	0,490
3	5	0,728	3,122	2,348	2,066
4	10	2,897	10,685	11,898	8,493
5	15	9,586	22,393	26,344	19,441
6	30	21,227	35,917	36,512	31,218
7	60	37,384	46,627	46,151	43,387
8	90	48,856	55,819	58,081	54,252
9	120	51,044	59,791	61,035	57,290
10	180	62,168	63,290	64,197	63,218
11	240	62,207	64,344	65,158	63,903
12	360	66,762	66,158	65,203	66,041
13	375	61,088	62,378	60,620	61,362
	SUM	424,129	491,226	498,128	471,161

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
643,267	678,855	594,302		638,808	42,453

Table 31: Table containing the difference factor values regarding formula 6A evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,146	0,213	0,359	0,239
3	5	1,799	0,845	2,176	1,607
4	10	5,283	2,850	7,058	5,064
5	15	9,816	5,625	13,383	9,608
6	30	17,950	10,120	23,351	17,140
7	60	29,671	16,560	35,349	27,193
8	90	39,809	24,299	45,554	36,554
9	120	46,521	31,336	51,915	43,257
10	180	51,325	37,628	56,217	48,390
11	240	55,135	42,757	57,672	51,855
12	360	56,789	48,168	61,330	55,429
13	375	53,228	48,856	58,002	53,362
	SUM	367,472	269,256	412,367	349,698

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
615,631	423,844	734,157		591,211	156,591

Table 32: Table containing the difference factor values regarding formula 6B evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,062	0,014	0,227	0,101
3	5	0,430	1,328	0,509	0,756
4	10	1,550	5,140	2,773	3,154
5	15	4,421	11,203	6,692	7,439
6	30	10,702	20,410	13,638	14,917
7	60	20,290	33,139	23,315	25,581
8	90	29,274	44,156	31,622	35,017
9	120	36,067	51,149	42,735	43,317
10	180	40,166	55,499	43,509	46,391
11	240	46,725	58,427	47,270	50,807
12	360	51,681	58,659	53,513	54,618
13	375	53,626	57,121	55,397	55,381
	SUM	294,993	396,246	321,200	337,480

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
494,205	623,743	571,849		563,266	65,194

Table 33: Table containing the difference factor values regarding formula 6C evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,478	0,054	0,283	0,272
3	5	0,566	0,894	1,087	0,849
4	10	1,775	3,652	3,249	2,892
5	15	5,544	9,212	7,877	7,544
6	30	14,055	17,768	15,701	15,841
7	60	23,297	28,830	26,427	26,185
8	90	32,543	36,995	34,092	34,543
9	120	37,836	42,949	39,550	40,112
10	180	43,834	46,939	42,418	44,397
11	240	46,168	50,578	46,403	47,716
12	360	48,842	53,664	48,271	50,259
13	375	53,189	56,135	51,767	53,697
	SUM	308,127	347,672	317,124	324,308

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
458,009	529,507	499,882		495,800	35,924

Table 34: Table containing the difference factor values regarding formula 6D evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,272	0,188	0,290	0,250
3	5	0,745	0,843	0,777	0,788
4	10	3,883	17,554	3,741	8,393
5	15	11,739	11,904	12,346	11,996
6	30	25,333	24,935	25,030	25,099
7	60	42,508	42,260	43,107	42,625
8	90	53,928	54,895	53,383	54,068
9	120	60,143	60,739	61,586	60,823
10	180	64,130	63,775	64,268	64,058
11	240	65,022	65,064	65,949	65,345
12	360	66,068	65,753	65,712	65,844
13	375	66,750	66,531	67,415	66,899
	SUM	460,522	474,440	463,603	466,188

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
684,535	722,576	730,777		712,629	24,674

Table 35: Table containing the difference factor values regarding formula 6E evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,354	0,444	0,353	0,384
3	5	2,925	2,330	1,546	2,267
4	10	9,823	7,513	6,286	7,874
5	15	18,532	14,738	12,759	15,343
6	30	25,570	21,591	19,805	22,322
7	60	32,898	28,611	28,187	29,899
8	90	39,885	36,014	34,373	36,757
9	120	45,420	39,979	38,014	41,138
10	180	49,224	42,684	41,484	44,464
11	240	52,345	45,069	44,482	47,299
12	360	53,271	46,003	44,603	47,959
13	375	48,451	46,717	44,092	46,420
	SUM	378,699	331,695	315,983	342,126

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
574,364	458,390	376,990		469,915	99,190

Table 36: Table containing the difference factor values regarding formula 6F evaluated in the pH 1.2 environment using a 0.1M HCl buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,196	0,165	0,101	0,154
3	5	1,301	1,099	0,170	0,857
4	10	5,361	3,969	2,966	4,099
5	15	12,725	9,461	7,863	10,017
6	30	23,317	18,912	15,122	19,117
7	60	37,883	33,627	27,459	32,990
8	90	49,348	45,161	38,597	44,368
9	120	56,777	53,049	46,063	51,963
10	180	58,374	56,455	50,023	54,951
11	240	61,774	58,750	54,738	58,420
12	360	62,549	59,510	54,005	58,688
13	375	57,415	57,859	52,746	56,007
	SUM	427,020	398,016	349,853	391,629

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
647,651	550,042	417,399		538,364	115,569

Table 37: Table containing the difference factor values regarding formula 1A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	14,493	14,194	16,698	15,128
3	5	43,957	41,884	45,706	43,849
4	10	70,458	71,553	70,481	70,830
5	15	80,634	82,947	78,520	80,700
6	30	81,664	84,432	82,411	82,836
7	60	82,114	83,999	86,264	84,126
8	90	82,861	78,247	81,198	80,768
9	120	79,347	76,945	77,872	78,055
10	180	72,843	71,521	73,107	72,490
11	240	68,832	68,475	65,469	67,592
12	360	65,464	63,715	61,208	63,462
13	375	55,817	54,969	54,003	54,930
	SUM	798,483	792,881	792,938	794,767

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
435,467	475,748	367,521		426,245	54,699

Table 38: Table containing the difference factor values regarding formula 1B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	20,202	10,079	19,223	16,501
3	5	57,401	46,424	58,584	54,136
4	10	84,972	80,063	90,657	85,231
5	15	92,553	93,235	94,627	93,472
6	30	87,478	88,652	93,113	89,748
7	60	87,066	92,086	92,818	90,657
8	90	82,008	85,440	83,852	83,767
9	120	79,136	81,493	81,523	80,717
10	180	74,381	76,124	78,568	76,358
11	240	70,055	79,815	69,920	73,263
12	360	69,175	74,338	57,872	67,129
13	375	61,526	66,970	58,595	62,364
	SUM	865,954	874,719	879,351	873,341

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
472,263	524,853	407,573		468,230	58,744

Table 39: Table containing the difference factor values regarding formula 1C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	11,714	10,528	9,904	10,716
3	5	34,188	31,261	35,531	33,660
4	10	66,377	62,680	71,035	66,697
5	15	87,791	83,035	88,983	86,603
6	30	99,450	93,002	89,709	94,053
7	60	92,964	96,695	89,099	92,920
8	90	86,957	87,060	82,169	85,395
9	120	94,227	94,472	87,705	92,135
10	180	83,679	83,726	83,001	83,468
11	240	77,286	76,485	74,366	76,046
12	360	69,657	72,647	69,653	70,652
13	375	63,623	63,573	66,164	64,453
	SUM	867,914	855,164	847,320	856,799

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
483,218	478,997	545,200		502,472	37,064

Table 40: Table containing the difference factor values regarding formula 1D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	4,139	7,976	5,929	6,014
3	5	20,811	28,151	27,079	25,347
4	10	49,914	59,116	60,593	56,541
5	15	71,375	79,212	81,223	77,270
6	30	89,267	86,352	88,973	88,197
7	60	79,100	88,238	82,171	83,170
8	90	78,204	81,583	83,212	81,000
9	120	76,908	79,373	84,112	80,131
10	180	72,017	75,556	81,383	76,318
11	240	67,044	71,952	73,574	70,857
12	360	60,318	64,338	66,461	63,705
13	375	59,279	55,990	64,609	59,959
	SUM	728,375	777,836	799,319	768,510

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
405,528	435,684	514,314		451,842	56,164

Table 41: Table containing the difference factor values regarding formula 1E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,902	1,005	0,492	0,800
3	5	49,201	16,321	42,227	35,916
4	10	84,096	40,238	75,229	66,521
5	15	93,853	58,861	83,833	78,849
6	30	89,150	67,561	83,804	80,172
7	60	84,797	68,473	77,784	77,018
8	90	87,354	64,351	77,655	76,453
9	120	86,006	64,791	80,456	77,084
10	180	82,317	57,449	70,763	70,177
11	240	79,035	52,337	63,235	64,869
12	360	62,808	44,005	52,928	53,247
13	375	49,789	36,745	50,969	45,834
	SUM	849,310	572,137	759,374	726,940

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
438,549	270,388	311,434		340,124	87,675

Table 42: Table containing the difference factor values regarding formula 1F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,075	0,527	5,445	2,349
3	5	10,277	4,574	29,897	14,916
4	10	31,586	18,664	64,360	38,204
5	15	50,101	36,225	80,907	55,744
6	30	69,579	56,363	84,323	70,088
7	60	72,593	62,650	85,950	73,731
8	90	69,681	60,125	76,057	68,621
9	120	71,711	59,885	79,422	70,339
10	180	68,653	50,959	70,862	63,491
11	240	59,668	49,819	63,803	57,763
12	360	50,463	38,524	61,562	50,183
13	375	44,877	33,999	56,297	45,057
	SUM	600,264	472,314	758,884	610,487

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
309,952	223,212	311,233		281,466	50,453

Table 43: Table containing the difference factor values regarding formula 2A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	4,405	3,290	4,582	4,092
3	5	18,251	15,050	21,970	18,424
4	10	40,033	34,696	48,234	40,987
5	15	57,438	50,481	68,126	58,682
6	30	70,996	63,412	75,390	69,933
7	60	77,073	68,386	78,631	74,697
8	90	73,067	69,041	81,103	74,404
9	120	74,704	67,778	75,794	72,759
10	180	77,516	68,377	68,509	71,468
11	240	66,260	63,189	61,261	63,570
12	360	64,458	57,186	58,293	59,979
13	375	50,234	49,114	47,582	48,977
	SUM	674,436	609,999	689,476	657,970

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
367,815	366,014	319,567		351,132	27,351

Table 44: Table containing the difference factor values regarding formula 2B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	14,306	14,308	14,625	14,413
3	5	37,760	36,741	42,147	38,883
4	10	59,912	57,621	65,633	61,055
5	15	75,988	72,518	79,976	76,161
6	30	77,450	73,718	80,099	77,089
7	60	75,303	73,354	81,664	76,774
8	90	73,717	70,166	75,112	72,998
9	120	69,409	68,442	71,540	69,797
10	180	72,729	64,597	70,939	69,422
11	240	60,196	60,353	61,164	60,571
12	360	53,627	55,588	55,340	54,852
13	375	44,773	47,747	43,816	45,445
	SUM	715,170	695,154	742,055	717,460

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
390,030	417,110	343,937		383,692	36,996

Table 45: Table containing the difference factor values regarding formula 2C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	9,859	11,855	13,512	11,742
3	5	34,965	40,345	42,920	39,410
4	10	63,858	70,691	71,648	68,732
5	15	74,672	82,494	83,454	80,207
6	30	81,094	86,109	90,276	85,827
7	60	83,599	84,795	87,764	85,386
8	90	79,342	83,241	85,379	82,654
9	120	74,938	77,908	82,524	78,456
10	180	76,247	78,425	81,380	78,684
11	240	72,093	77,174	78,039	75,769
12	360	70,598	70,411	72,586	71,199
13	375	68,398	66,003	72,268	68,890
	SUM	789,663	829,450	861,750	826,954

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
439,651	464,594	554,485		486,243	60,401

Table 46: Table containing the difference factor values regarding formula 2D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	7,366	2,668	6,551	5,528
3	5	29,262	22,602	24,413	25,426
4	10	57,320	53,585	50,017	53,641
5	15	74,134	74,553	68,255	72,314
6	30	85,325	83,244	77,357	81,976
7	60	84,633	81,852	80,037	82,174
8	90	80,497	79,272	76,775	78,848
9	120	76,162	80,155	80,060	78,792
10	180	73,799	69,290	71,996	71,695
11	240	69,569	67,949	67,990	68,502
12	360	66,851	65,056	66,055	65,987
13	375	60,189	58,720	61,258	60,056
	SUM	765,108	738,946	730,763	744,939

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
425,979	413,901	470,203		436,694	29,641

Table 47: Table containing the difference factor values regarding formula 2E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,601	0,870	1,376	0,949
3	5	5,474	8,635	10,529	8,213
4	10	19,340	24,647	28,264	24,084
5	15	34,944	40,821	45,187	40,317
6	30	55,546	59,455	61,215	58,739
7	60	59,015	64,385	63,764	62,388
8	90	67,116	66,574	64,216	65,969
9	120	60,369	65,043	64,491	63,301
10	180	55,989	58,888	54,702	56,527
11	240	52,559	55,915	52,788	53,754
12	360	49,212	50,987	46,073	48,757
13	375	44,758	46,069	44,110	44,979
	SUM	504,925	542,290	536,713	527,976

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
260,722	256,282	220,116		245,707	22,273

Table 48: Table containing the difference factor values regarding formula 2F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	4,597	3,972	4,065	4,211
3	5	18,769	15,451	15,707	16,642
4	10	40,074	34,723	33,032	35,943
5	15	59,556	51,303	48,808	53,223
6	30	69,238	63,642	57,526	63,469
7	60	67,251	67,054	64,403	66,236
8	90	65,496	61,627	58,150	61,758
9	120	62,858	58,894	58,303	60,019
10	180	59,512	53,801	49,587	54,300
11	240	54,248	51,604	47,393	51,082
12	360	48,849	43,645	39,985	44,160
13	375	38,747	39,045	34,540	37,444
	SUM	589,196	544,762	511,501	548,486

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
304,237	257,450	209,776		257,154	47,231

Table 49: Table containing the difference factor values regarding formula 3A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	24,290	17,347	23,670	21,769
3	5	59,094	48,212	59,548	55,618
4	10	81,089	76,562	81,295	79,649
5	15	86,393	84,792	88,655	86,613
6	30	86,790	86,629	88,344	87,254
7	60	81,254	77,758	78,906	79,306
8	90	75,656	76,874	72,279	74,936
9	120	74,434	73,251	70,847	72,844
10	180	72,326	70,829	66,979	70,045
11	240	66,690	66,181	62,058	64,976
12	360	61,055	61,367	57,214	59,879
13	375	52,151	55,656	47,336	51,715
	SUM	821,220	795,457	797,133	804,603

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
447,867	477,294	369,465		431,542	55,737

Table 50: Table containing the difference factor values regarding formula 3B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	40,578	23,076	33,380	32,345
3	5	81,653	49,779	76,619	69,351
4	10	95,027	74,746	94,170	87,981
5	15	95,945	82,944	95,728	91,539
6	30	95,253	81,778	91,641	89,557
7	60	90,876	78,372	86,721	85,323
8	90	88,762	69,538	82,003	80,101
9	120	81,436	72,960	74,484	76,294
10	180	79,107	66,041	73,837	72,995
11	240	75,552	63,736	64,424	67,904
12	360	67,382	60,361	61,723	63,155
13	375	57,148	54,555	54,583	55,429
	SUM	948,719	777,886	889,312	871,972

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
517,400	466,751	412,190		465,447	52,617

Table 51: Table containing the difference factor values regarding formula 3C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	8,866	1,665	8,517	6,349
3	5	36,923	12,658	31,220	26,934
4	10	72,436	35,939	63,011	57,129
5	15	78,270	50,176	71,247	66,564
6	30	83,220	54,217	74,625	70,687
7	60	86,612	56,302	74,958	72,624
8	90	83,553	60,936	78,059	74,183
9	120	81,656	64,061	78,336	74,684
10	180	77,625	64,681	79,227	73,844
11	240	74,776	59,229	70,076	68,027
12	360	67,299	56,905	72,437	65,547
13	375	58,897	50,655	59,920	56,491
	SUM	810,133	567,425	761,634	713,064

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
451,047	317,828	490,066		419,647	90,311

Table 52: Table containing the difference factor values regarding formula 3D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	6,226	4,710	9,355	6,764
3	5	34,540	29,030	40,121	34,563
4	10	70,453	60,502	70,797	67,251
5	15	78,231	78,986	84,385	80,534
6	30	83,184	84,658	88,111	85,317
7	60	83,125	84,722	89,356	85,734
8	90	82,273	85,024	93,628	86,975
9	120	85,904	88,200	90,336	88,147
10	180	82,608	83,508	86,097	84,071
11	240	77,847	75,136	77,181	76,721
12	360	71,989	72,693	76,895	73,859
13	375	67,029	63,981	72,098	67,703
	SUM	823,407	811,149	878,359	837,638

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
458,438	454,343	565,172		492,651	62,838

Table 53: Table containing the difference factor values regarding formula 3E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,318	3,333	0,284	1,312
3	5	4,504	19,119	5,658	9,760
4	10	21,279	52,188	22,350	31,939
5	15	37,209	76,477	42,487	52,058
6	30	54,865	87,005	58,601	66,824
7	60	59,806	91,535	72,839	74,727
8	90	58,294	77,721	58,107	64,707
9	120	58,210	83,215	59,735	67,053
10	180	53,947	72,625	51,509	59,360
11	240	53,186	72,515	47,156	57,619
12	360	45,159	64,723	40,556	50,146
13	375	35,799	33,225	35,330	34,784
	SUM	482,576	733,679	494,612	570,289

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
249,182	346,731	202,850		266,255	73,444

Table 54: Table containing the difference factor values regarding formula 3F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,887	7,230	6,731	5,949
3	5	26,313	27,709	34,187	29,403
4	10	63,644	25,877	70,556	53,359
5	15	82,899	45,621	82,843	70,454
6	30	82,614	64,398	84,112	77,041
7	60	84,425	64,687	81,380	76,831
8	90	84,400	66,036	77,503	75,980
9	120	77,024	62,443	74,989	71,485
10	180	71,940	54,611	69,434	65,328
11	240	72,085	50,017	77,742	66,615
12	360	62,250	42,830	55,728	53,603
13	375	45,413	35,827	45,471	42,237
	SUM	756,894	547,287	760,675	688,286

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
390,829	258,644	311,968		320,480	66,503

Table 55: Table containing the difference factor values regarding formula 4A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,230	2,294	1,752	1,758
3	5	6,955	11,741	13,084	10,593
4	10	20,744	33,932	33,911	29,529
5	15	37,641	48,597	50,824	45,687
6	30	54,585	65,654	67,823	62,687
7	60	65,324	71,656	75,635	70,872
8	90	63,884	70,708	72,491	69,028
9	120	65,082	68,047	70,776	67,968
10	180	59,942	67,059	64,833	63,945
11	240	54,845	67,636	61,982	61,488
12	360	48,294	59,904	52,528	53,575
13	375	46,458	53,839	43,752	48,016
	SUM	524,984	621,066	609,392	585,147

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
286,309	372,655	282,449		313,804	51,003

Table 56: Table containing the difference factor values regarding formula 4B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	7,692	11,351	7,173	8,738
3	5	29,816	41,201	26,354	32,457
4	10	58,577	76,949	51,569	62,365
5	15	77,771	87,862	68,772	78,135
6	30	88,773	93,367	77,635	86,592
7	60	90,459	92,277	80,323	87,686
8	90	83,934	87,892	78,989	83,605
9	120	82,811	84,172	77,390	81,458
10	180	78,291	79,337	70,979	76,202
11	240	71,668	76,058	67,881	71,869
12	360	67,280	72,961	61,939	67,394
13	375	57,977	65,948	51,812	58,579
	SUM	795,051	869,374	720,817	795,081

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
433,595	521,646	334,093		429,778	93,834

Table 57: Table containing the difference factor values regarding formula 4C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,781	3,982	0,997	1,920
3	5	7,778	22,881	7,453	12,704
4	10	27,159	52,528	29,403	36,363
5	15	47,575	76,103	51,661	58,446
6	30	66,640	84,191	66,698	72,510
7	60	72,900	82,693	69,691	75,095
8	90	70,852	87,151	68,757	75,587
9	120	69,289	84,216	70,363	74,623
10	180	65,467	76,711	69,300	70,492
11	240	62,341	71,699	61,636	65,225
12	360	56,865	66,561	57,216	60,214
13	375	58,030	63,049	63,888	61,656
	SUM	605,677	771,766	617,063	664,835

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
337,215	432,284	397,043		388,848	48,061

Table 58: Table containing the difference factor values regarding formula 4D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	11,172	5,900	3,351	6,808
3	5	43,087	25,623	17,352	28,687
4	10	67,436	52,648	43,218	54,434
5	15	80,178	72,053	62,986	71,739
6	30	83,118	79,672	72,149	78,313
7	60	80,948	79,057	71,761	77,255
8	90	83,677	81,874	69,736	78,429
9	120	77,076	75,574	67,898	73,516
10	180	67,884	76,033	67,539	70,485
11	240	73,161	72,670	63,308	69,713
12	360	61,833	60,065	56,710	59,536
13	375	57,326	52,322	51,781	53,810
	SUM	786,897	733,493	647,787	722,726

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
438,111	410,846	416,812		421,923	14,333

Table 59: Table containing the difference factor values regarding formula 4E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,607	0,333	3,199	1,380
3	5	7,770	9,055	23,748	13,525
4	10	29,812	27,399	52,845	36,685
5	15	51,056	47,738	73,017	57,271
6	30	70,062	68,177	83,501	73,914
7	60	74,430	69,780	75,360	73,190
8	90	71,015	68,208	78,247	72,490
9	120	71,115	74,166	80,373	75,218
10	180	67,580	64,113	67,897	66,530
11	240	65,501	62,280	67,599	65,127
12	360	58,994	53,654	59,128	57,259
13	375	45,752	42,623	44,354	44,243
	SUM	613,696	587,527	709,269	636,831

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
316,887	277,661	290,885		295,144	19,957

Table 60: Table containing the difference factor values regarding formula 4F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	9,399	6,066	0,897	5,454
3	5	34,429	28,339	12,864	25,211
4	10	66,856	59,165	37,016	54,346
5	15	81,696	76,964	57,711	72,124
6	30	90,615	88,355	71,846	83,605
7	60	82,152	87,331	75,308	81,597
8	90	81,742	83,289	70,741	78,591
9	120	75,311	83,693	74,542	77,849
10	180	79,918	76,227	59,844	71,996
11	240	75,560	72,969	60,755	69,761
12	360	69,243	57,891	54,356	60,497
13	375	54,595	54,315	43,350	50,753
	SUM	801,518	774,604	619,231	731,784

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
413,871	366,072	253,958		344,634	82,084

Table 61: Table containing the difference factor values regarding formula 5A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	13,375	3,154	10,466	8,998
3	5	20,325	16,633	22,274	19,744
4	10	40,080	39,166	40,986	40,077
5	15	39,020	38,028	39,544	38,864
6	30	74,987	70,527	70,849	72,121
7	60	75,393	73,252	73,680	74,108
8	90	71,234	71,532	74,279	72,348
9	120	73,755	69,550	65,046	69,450
10	180	74,653	67,186	61,886	67,908
11	240	57,326	56,815	56,884	57,008
12	360	62,754	59,847	52,560	58,387
13	375	52,123	57,134	44,746	51,334
	SUM	655,024	622,823	613,199	630,349

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
357,229	373,709	284,213		338,384	47,631

Table 62: Table containing the difference factor values regarding formula 5B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	11,678	7,999	12,640	10,772
3	5	24,864	23,735	32,830	27,143
4	10	31,558	43,860	60,922	45,446
5	15	60,996	60,004	76,304	65,768
6	30	68,051	67,119	81,433	72,201
7	60	64,833	64,205	77,412	68,817
8	90	67,726	67,987	81,504	72,406
9	120	66,144	67,323	73,116	68,861
10	180	61,226	66,486	69,074	65,596
11	240	57,688	61,652	60,560	59,967
12	360	55,644	61,646	54,590	57,293
13	375	51,969	54,059	49,271	51,766
	SUM	622,376	646,074	729,655	666,035

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
339,424	387,660	338,190		355,091	28,212

Table 63: Table containing the difference factor values regarding formula 5C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,7131	7,2512	6,9266	5,96364
3	5	17,965	23,127	23,342	21,4782
4	10	35,956	46,857	47,94	43,5844
5	15	60,213	64,423	66,093	63,5761
6	30	72,579	73,834	84,051	76,8213
7	60	70,079	77,867	75,895	74,6137
8	90	68,321	77,188	73,333	72,9476
9	120	67,081	73,323	75,944	72,1159
10	180	64,856	72,488	69,893	69,0789
11	240	60,845	70,748	68,993	66,8619
12	360	56,203	56,733	60,415	57,7838
13	375	51,637	51,743	53,853	52,4109
	SUM	629,45	695,58	706,68	677,236

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
350,4509924	389,61	454,71		398,26	52,6621

Table 64: Table containing the difference factor values regarding formula 5D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	5,494	1,659	1,199	2,784
3	5	20,545	11,468	11,880	14,631
4	10	49,774	28,892	32,952	37,206
5	15	69,767	44,082	51,717	55,189
6	30	71,490	60,382	67,375	66,416
7	60	83,058	68,263	74,666	75,329
8	90	77,479	70,053	78,167	75,233
9	120	78,811	73,586	78,973	77,123
10	180	73,393	72,440	81,996	75,943
11	240	75,709	64,787	71,595	70,697
12	360	61,329	53,314	63,554	59,399
13	375	56,879	49,570	59,449	55,299
	SUM	723,728	598,494	673,523	665,248

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
402,941	335,230	433,372		390,514	50,237

Table 65: Table containing the difference factor values regarding formula 5E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,114	0,734	1,516	1,121
3	5	8,778	9,090	10,108	9,325
4	10	27,019	27,374	28,206	27,533
5	15	46,994	44,833	46,291	46,039
6	30	61,154	59,736	60,321	60,404
7	60	65,762	64,031	62,556	64,116
8	90	65,086	64,870	59,492	63,149
9	120	66,664	67,306	62,201	65,390
10	180	67,567	64,014	56,040	62,540
11	240	62,755	58,768	49,741	57,088
12	360	58,414	57,044	43,033	52,830
13	375	45,779	46,439	38,401	43,539
	SUM	577,086	564,238	517,905	553,076

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
297,984	266,655	212,403		259,014	43,299

Table 66: Table containing the difference factor values regarding formula 5F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,436	3,084	0,044	1,188
3	5	3,522	14,682	3,701	7,302
4	10	14,659	37,297	14,279	22,078
5	15	28,501	56,662	28,807	37,990
6	30	47,767	68,917	48,088	54,924
7	60	60,720	79,116	60,654	66,830
8	90	63,906	77,453	63,626	68,329
9	120	58,617	80,327	68,134	69,026
10	180	64,801	83,610	59,979	69,464
11	240	56,953	67,087	56,235	60,092
12	360	53,313	61,576	49,955	54,948
13	375	49,674	55,963	43,123	49,587
	SUM	502,870	685,776	496,625	561,757

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
259,661	324,093	203,676		262,477	60,258

Table 67: Table containing the difference factor values regarding formula 6A evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,529	4,593	7,662	4,594
3	5	12,570	20,486	25,379	19,478
4	10	38,408	44,813	49,061	44,094
5	15	60,729	63,637	65,909	63,425
6	30	73,528	74,849	78,233	75,537
7	60	80,318	80,473	80,317	80,369
8	90	76,079	76,139	78,733	76,984
9	120	73,579	74,283	68,648	72,170
10	180	68,497	66,839	63,882	66,406
11	240	70,481	63,469	58,728	64,226
12	360	58,272	54,189	53,206	55,222
13	375	47,722	45,362	49,137	47,407
	SUM	661,710	669,132	678,894	669,912

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
341,680	316,227	278,428		312,111	31,826

Table 68: Table containing the difference factor values regarding formula 6B evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,244	1,106	2,488	1,613
3	5	7,798	10,320	14,950	11,023
4	10	21,494	29,356	40,842	30,564
5	15	42,584	50,176	62,320	51,694
6	30	63,045	68,731	73,095	68,290
7	60	70,791	74,413	80,846	75,350
8	90	68,819	73,857	74,005	72,227
9	120	66,644	71,391	67,917	68,651
10	180	61,281	70,224	61,670	64,392
11	240	58,467	63,586	58,707	60,253
12	360	56,320	61,018	55,891	57,743
13	375	50,125	56,618	46,572	51,105
	SUM	568,612	630,797	639,302	612,904

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
310,103	378,494	296,312		328,303	44,010

Table 69: Table containing the difference factor values regarding formula 6C evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,215	0,131	0,471	0,273
3	5	7,258	6,535	4,311	6,035
4	10	23,957	23,997	19,920	22,624
5	15	40,880	42,961	43,691	42,511
6	30	59,939	61,158	60,683	60,593
7	60	69,432	72,529	75,475	72,478
8	90	67,311	71,959	73,735	71,002
9	120	74,054	82,020	78,039	78,038
10	180	77,386	78,891	78,607	78,295
11	240	67,854	70,565	76,023	71,481
12	360	55,691	67,294	65,908	62,964
13	375	50,132	50,700	54,032	51,622
	SUM	594,108	628,740	630,897	617,915

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
330,774	352,172	405,945		362,963	38,730

Table 70: Table containing the difference factor values regarding formula 6D evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,506	0,321	0,403	0,410
3	5	6,181	5,765	2,839	4,928
4	10	20,756	21,113	12,441	18,103
5	15	38,617	40,283	27,321	35,407
6	30	58,093	59,570	50,032	55,898
7	60	71,751	69,007	63,073	67,943
8	90	69,671	69,307	64,818	67,932
9	120	75,379	74,357	68,142	72,626
10	180	67,992	66,919	64,272	66,394
11	240	63,482	60,892	62,777	62,384
12	360	55,541	59,421	56,780	57,247
13	375	42,988	42,142	44,335	43,155
	SUM	570,957	569,096	517,231	552,428

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
317,885	318,764	332,807		323,152	8,373

Table 71: Table containing the difference factor values regarding formula 6E evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	6,556	3,067	4,022	4,548
3	5	24,102	13,924	13,947	17,324
4	10	48,578	31,367	30,079	36,675
5	15	65,531	47,255	46,522	53,103
6	30	74,780	61,177	58,842	64,933
7	60	77,004	68,933	66,111	70,683
8	90	76,006	69,763	65,596	70,455
9	120	76,512	69,739	66,653	70,968
10	180	72,741	61,396	60,242	64,793
11	240	69,968	58,524	52,702	60,398
12	360	61,948	54,733	49,327	55,336
13	375	40,966	38,843	34,897	38,236
	SUM	694,694	578,722	548,939	607,451

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
358,711	273,500	225,131		285,781	67,632

Table 72: Table containing the difference factor values regarding formula 6F evaluated in the pH 4.6 environment using a citric acid buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,529	4,593	7,662	4,594
3	5	12,570	20,486	25,379	19,478
4	10	38,408	44,813	49,061	44,094
5	15	60,729	63,637	65,909	63,425
6	30	73,528	74,849	78,233	75,537
7	60	80,318	80,473	80,317	80,369
8	90	76,079	76,139	78,733	76,984
9	120	73,579	74,283	68,648	72,170
10	180	68,497	66,839	63,882	66,406
11	240	70,481	63,469	58,728	64,226
12	360	58,272	54,189	53,206	55,222
13	375	47,722	45,362	49,137	47,407
	SUM	661,710	669,132	678,894	669,912

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
341,680	316,227	278,428		312,111	31,826

Table 73: Table containing the difference factor values regarding formula 1A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	24,844	28,557	41,987	31,796
3	5	24,945	34,415	44,373	34,578
4	10	20,594	20,183	32,047	24,275
5	15	18,645	10,068	26,743	18,485
6	30	6,738	5,199	15,556	9,164
7	60	4,837	15,107	11,205	10,383
8	90	5,565	16,244	10,199	10,669
9	120	10,553	23,316	5,800	13,223
10	180	8,263	19,218	10,748	12,743
11	240	6,184	19,611	1,361	9,052
12	360	1,788	18,726	7,389	9,301
13	375	7,234	19,614	0,769	9,206
	SUM	140,192	230,259	208,176	192,876

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
17,142	25,450	25,639		22,743	4,852

Table 74: Table containing the difference factor values regarding formula 1B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	34,135	61,785	46,766	47,562
3	5	6,196	62,860	59,298	42,785
4	10	32,847	44,784	53,249	43,627
5	15	26,176	33,472	44,645	34,764
6	30	14,310	18,333	33,556	22,066
7	60	9,712	9,738	22,584	14,011
8	90	11,740	10,796	22,397	14,978
9	120	14,130	2,265	10,152	8,849
10	180	9,001	1,138	4,696	4,945
11	240	2,908	6,300	3,501	4,236
12	360	0,376	7,884	10,264	6,175
13	375	0,111	3,582	7,185	3,626
	SUM	161,642	262,937	318,293	247,624

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
19,764	29,062	39,201		29,342	9,721

Table 75: Table containing the difference factor values regarding formula 1C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	7,707	0,522	1,180	3,136
3	5	19,468	2,081	4,632	8,727
4	10	26,579	8,151	11,005	15,245
5	15	33,663	18,841	22,969	25,158
6	30	29,354	8,413	13,179	16,982
7	60	33,321	10,544	18,361	20,742
8	90	23,098	0,003	16,469	13,190
9	120	32,393	2,014	12,848	15,752
10	180	35,613	7,962	8,103	17,226
11	240	6,975	19,385	6,386	10,915
12	360	1,268	7,497	2,544	3,770
13	375	4,029	7,771	2,805	4,868
	SUM	253,467	93,183	120,480	155,710

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
33,126	10,874	16,128		20,043	11,631

Table 76: Table containing the difference factor values regarding formula 1D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,256	1,813	4,711	2,260
3	5	9,954	8,130	22,482	13,522
4	10	12,623	7,847	39,074	19,848
5	15	27,125	14,989	46,234	29,449
6	30	22,364	4,767	33,905	20,346
7	60	25,378	1,980	47,476	24,945
8	90	23,789	0,657	38,873	21,106
9	120	15,605	7,901	25,762	16,423
10	180	5,871	12,789	4,585	7,748
11	240	4,440	15,115	1,398	6,985
12	360	4,911	12,994	10,327	9,411
13	375	1,676	17,348	4,464	7,829
	SUM	153,992	106,332	279,292	179,872

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
20,126	12,408	37,387		23,307	12,790

Table 77: Table containing the difference factor values regarding formula 1E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	5,638	5,889	3,908	5,145
3	5	46,824	38,122	10,505	31,817
4	10	53,634	42,632	19,761	38,676
5	15	36,416	33,246	17,448	29,036
6	30	24,683	25,800	8,743	19,742
7	60	14,722	13,627	5,777	11,376
8	90	14,054	10,260	0,067	8,127
9	120	7,829	10,616	6,364	8,270
10	180	0,958	4,728	6,533	4,073
11	240	4,196	9,201	5,557	6,318
12	360	14,169	17,041	13,964	15,058
13	375	7,952	6,602	10,710	8,421
	SUM	231,073	217,764	109,337	186,058

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
25,753	23,536	12,115		20,468	7,318

Table 78: Table containing the difference factor values regarding formula 1F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,888	2,797	0,896	2,194
3	5	13,280	9,007	8,435	10,241
4	10	17,270	6,100	10,706	11,359
5	15	19,312	0,535	10,401	10,083
6	30	6,563	8,672	5,701	6,979
7	60	7,065	3,254	3,727	4,682
8	90	7,294	4,195	6,153	5,880
9	120	24,374	16,471	21,808	20,884
10	180	23,715	15,427	13,704	17,615
11	240	21,011	25,109	25,305	23,809
12	360	27,702	25,389	27,764	26,952
13	375	25,938	30,506	22,113	26,186
	SUM	196,411	147,464	156,714	166,863

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
21,890	15,938	17,365		18,398	3,107

Table 79: Table containing the difference factor values regarding formula 2A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,599	3,889	1,053	2,514
3	5	1,989	4,836	3,675	3,500
4	10	1,516	0,629	3,419	1,855
5	15	5,181	5,066	9,057	6,435
6	30	9,112	3,516	3,941	5,523
7	60	0,146	16,852	1,934	6,311
8	90	3,940	15,829	1,955	7,241
9	120	6,706	9,872	0,248	5,608
10	180	8,856	23,896	16,463	16,405
11	240	11,115	18,138	0,292	9,848
12	360	14,421	20,144	1,196	11,920
13	375	9,927	15,496	0,423	8,615
	SUM	75,506	138,163	43,657	85,775

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
9,232	15,271	5,377		9,960	4,987

Table 80: Table containing the difference factor values regarding formula 2B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	15,160	20,969	9,319	15,149
3	5	17,426	33,722	18,981	23,377
4	10	27,875	47,992	21,627	32,498
5	15	34,933	34,324	29,792	33,016
6	30	28,251	38,397	29,055	31,901
7	60	20,441	0,234	8,436	9,704
8	90	29,057	10,703	16,345	18,702
9	120	0,250	10,422	1,797	4,156
10	180	3,896	15,237	4,995	8,043
11	240	0,816	9,183	6,743	5,581
12	360	3,490	33,368	2,773	13,210
13	375	17,862	25,106	19,075	20,681
	SUM	199,457	279,657	168,936	216,017

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
24,388	30,910	20,806		25,368	5,123

Table 81: Table containing the difference factor values regarding formula 2C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	11,388	17,103	13,417	13,969
3	5	29,239	33,618	24,618	29,158
4	10	35,266	39,116	41,077	38,486
5	15	26,113	27,619	34,624	29,452
6	30	26,585	23,160	32,449	27,398
7	60	36,185	10,378	16,594	21,052
8	90	26,296	3,189	11,966	13,817
9	120	13,359	1,823	8,927	8,036
10	180	12,534	5,947	2,389	6,957
11	240	5,684	4,640	1,634	3,986
12	360	0,914	3,770	2,018	2,234
13	375	1,949	2,216	4,089	2,751
	SUM	225,512	172,579	193,802	197,298

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
29,473	20,139	25,943		25,185	4,713

Table 82: Table containing the difference factor values regarding formula 2D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	14,370	5,279	16,811	12,153
3	5	28,265	16,237	40,865	28,455
4	10	47,304	23,635	29,949	33,629
5	15	40,281	23,644	45,880	36,602
6	30	30,864	16,244	34,692	27,267
7	60	24,141	2,933	23,267	16,780
8	90	14,477	2,616	11,148	9,414
9	120	12,143	9,144	23,103	14,797
10	180	5,234	2,369	10,399	6,001
11	240	1,797	10,573	0,959	4,443
12	360	4,272	8,279	17,143	9,898
13	375	0,603	8,956	2,243	3,934
	SUM	223,751	129,907	256,460	203,373

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
29,243	15,159	34,330		26,244	9,931

Table 83: Table containing the difference factor values regarding formula 2E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	5,079	4,579	3,911	4,523
3	5	14,512	13,239	11,823	13,192
4	10	20,185	19,845	17,869	19,300
5	15	20,451	19,812	18,402	19,555
6	30	13,903	12,594	15,809	14,102
7	60	12,369	17,620	11,776	13,922
8	90	9,711	15,618	9,146	11,492
9	120	15,007	9,463	6,969	10,480
10	180	7,150	3,876	13,264	8,097
11	240	12,175	17,943	13,883	14,667
12	360	13,378	20,313	15,629	16,440
13	375	17,291	18,103	14,197	16,531
	SUM	161,211	173,005	152,679	162,298

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
17,967	18,699	16,918		17,861	0,895

Table 84: Table containing the difference factor values regarding formula 2F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,655	4,433	2,859	3,649
3	5	11,374	15,560	9,365	12,100
4	10	15,850	20,787	13,375	16,671
5	15	16,512	18,496	12,564	15,857
6	30	13,102	13,596	17,268	14,655
7	60	13,599	10,650	16,638	13,629
8	90	10,009	14,637	11,235	11,960
9	120	17,944	17,009	15,171	16,708
10	180	10,745	15,551	19,165	15,154
11	240	10,404	17,664	18,878	15,649
12	360	20,083	21,355	10,075	17,171
13	375	20,670	21,618	19,145	20,478
	SUM	163,948	191,356	165,739	173,681

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
18,272	20,682	18,365		19,106	1,365

Table 85: Table containing the difference factor values regarding formula 3A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	9,456	11,000	16,065	12,174
3	5	10,752	18,713	36,193	21,886
4	10	32,316	18,335	38,853	29,835
5	15	35,486	11,949	39,203	28,879
6	30	25,240	1,790	24,344	17,125
7	60	14,769	5,836	27,059	15,888
8	90	22,828	7,337	14,704	14,957
9	120	9,242	15,938	3,345	9,508
10	180	13,883	18,630	3,201	11,904
11	240	8,453	19,367	0,829	9,550
12	360	5,417	2,697	17,693	8,602
13	375	10,948	3,982	17,978	10,969
	SUM	198,790	135,573	239,469	191,278

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
24,307	14,984	29,493		22,928	7,352

Table 86: Table containing the difference factor values regarding formula 3B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	18,516	21,009	33,308	24,278
3	5	25,953	35,923	54,939	38,938
4	10	33,670	38,175	61,242	44,362
5	15	40,691	36,479	50,289	42,486
6	30	24,428	14,800	44,756	27,995
7	60	23,225	2,703	32,925	19,618
8	90	18,298	6,959	28,154	17,803
9	120	14,659	12,707	5,543	10,970
10	180	3,192	10,044	14,690	9,309
11	240	0,621	17,996	11,170	9,929
12	360	10,672	15,012	18,425	14,703
13	375	3,479	13,295	18,540	11,771
	SUM	217,404	225,102	373,982	272,163

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
26,582	24,880	46,059		32,507	11,767

Table 87: Table containing the difference factor values regarding formula 3C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,921	4,889	0,688	2,833
3	5	10,791	20,046	6,002	12,280
4	10	30,360	47,398	21,947	33,235
5	15	31,143	30,129	27,184	29,486
6	30	41,590	29,519	25,285	32,131
7	60	28,108	0,388	14,084	14,193
8	90	22,687	12,936	8,753	14,792
9	120	18,089	5,678	6,183	9,983
10	180	14,813	4,198	0,776	6,596
11	240	4,755	15,996	8,535	9,762
12	360	0,358	9,879	1,696	3,978
13	375	0,001	4,390	7,511	3,967
	SUM	205,615	185,447	128,644	173,235

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
26,872	21,641	17,221		21,911	4,832

Table 88: Table containing the difference factor values regarding formula 3D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,0861	3,4707	4,3716	2,97612
3	5	4,5017	2,9391	2,1252	3,18864
4	10	16,07	15,707	12,348	14,7082
5	15	29,797	20,368	28,439	26,2013
6	30	25,63	17,483	28,177	23,7637
7	60	18,227	11,209	19,624	16,3533
8	90	16,864	14,694	12,374	14,6443
9	120	8,8167	2,0393	11,005	7,28711
10	180	0,0627	8,1252	8,1159	5,43458
11	240	0,4444	2,8602	5,9155	3,07336
12	360	7,6811	10,568	0,1674	6,13879
13	375	8,0101	13,36	8,981	10,1171
	SUM	137,19	122,82	141,64	133,886

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
17,92986775	14,333	18,961		17,075	2,42967

Table 89: Table containing the difference factor values regarding formula 3E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	5,0788	5,2889	2,7141	4,36058
3	5	13,412	18,223	9,3937	13,676
4	10	14,806	26,509	9,7982	17,0377
5	15	13,343	23,886	8,7834	15,3375
6	30	13,492	25,294	18,757	19,1807
7	60	22,763	36,23	15,66	24,8842
8	90	20,673	26,731	12,67	20,0248
9	120	17,957	25,188	18,235	20,4599
10	180	20,015	23,72	11,289	18,3415
11	240	12,531	31,275	16,973	20,2595
12	360	7,4653	29,885	14,112	17,1541
13	375	4,2077	25,891	13,84	14,6464
	SUM	165,74	298,12	152,23	205,363

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
18,4716965	32,221	16,868		22,52	8,43959

Table 90: Table containing the difference factor values regarding formula 3F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,969	1,846	3,911	2,575
3	5	5,983	2,417	14,103	7,501
4	10	22,513	14,706	17,329	18,183
5	15	15,639	17,545	16,557	16,581
6	30	4,661	1,782	12,733	6,392
7	60	4,553	9,209	17,047	10,270
8	90	2,508	7,956	17,783	9,416
9	120	3,378	3,101	26,673	11,051
10	180	12,517	2,998	19,799	11,771
11	240	3,691	11,647	17,847	11,062
12	360	6,457	7,051	30,312	14,607
13	375	18,434	22,209	33,383	24,675
	SUM	102,303	102,468	227,476	144,082

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
11,401	11,075	25,206		15,894	8,066

Table 91: Table containing the difference factor values regarding formula 4A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,147	3,824	1,126	2,366
3	5	0,898	5,491	4,223	3,537
4	10	15,819	6,348	13,156	11,774
5	15	14,192	5,854	16,408	12,151
6	30	26,564	20,345	31,700	26,203
7	60	2,091	3,117	2,571	2,593
8	90	2,701	8,110	3,627	4,813
9	120	1,026	5,936	1,513	2,825
10	180	16,690	29,367	18,344	21,467
11	240	7,679	30,073	20,777	19,510
12	360	22,511	26,448	14,174	21,044
13	375	15,649	15,565	11,200	14,138
	SUM	127,966	160,477	138,817	142,420

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
15,647	17,737	17,097		16,827	1,071

Table 92: Table containing the difference factor values regarding formula 4B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	6,850	8,681	6,849	7,460
3	5	6,911	18,312	18,857	14,693
4	10	16,944	20,600	27,067	21,537
5	15	25,828	23,120	32,987	27,311
6	30	26,918	27,546	39,536	31,333
7	60	20,844	0,707	6,451	9,334
8	90	10,723	22,341	2,606	11,890
9	120	4,943	6,435	23,655	11,678
10	180	17,240	18,256	9,712	15,069
11	240	21,719	29,456	23,979	25,051
12	360	19,748	34,758	4,665	19,724
13	375	18,545	32,502	4,163	18,403
	SUM	197,214	242,714	200,527	213,485

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
24,114	26,826	24,697		25,212	1,428

Table 93: Table containing the difference factor values regarding formula 4C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,948	4,466	3,641	3,685
3	5	4,415	4,304	3,932	4,217
4	10	3,494	4,383	5,109	4,329
5	15	10,423	23,842	23,155	19,140
6	30	17,917	10,952	19,816	16,228
7	60	15,702	4,234	16,875	12,270
8	90	30,798	1,234	8,286	13,439
9	120	2,071	13,530	6,249	7,283
10	180	3,746	1,998	5,181	3,642
11	240	3,736	3,186	1,462	2,795
12	360	9,544	7,005	7,108	7,886
13	375	2,564	4,387	6,119	4,357
	SUM	107,358	83,522	106,933	99,271

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
14,031	9,747	14,314		12,697	2,559

Table 94: Table containing the difference factor values regarding formula 4D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,320	3,726	1,955	3,000
3	5	12,990	0,006	4,005	5,667
4	10	22,371	9,722	17,030	16,374
5	15	34,399	13,104	18,824	22,109
6	30	28,610	33,771	39,295	33,892
7	60	36,671	19,865	30,201	28,913
8	90	16,952	1,250	11,217	9,806
9	120	8,507	5,385	3,813	5,902
10	180	3,487	2,046	0,753	2,095
11	240	7,432	15,067	6,389	9,629
12	360	6,012	3,779	18,006	9,266
13	375	7,977	13,140	2,005	7,708
	SUM	188,729	120,861	153,495	154,362

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
24,666	14,104	20,547		19,772	5,323

Table 95: Table containing the difference factor values regarding formula 4E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,584	0,253	1,081	1,640
3	5	7,820	3,807	2,139	4,588
4	10	5,226	12,999	2,659	6,961
5	15	0,923	12,337	8,751	7,337
6	30	6,650	2,271	5,466	4,795
7	60	19,071	17,844	14,066	16,994
8	90	17,549	7,016	15,313	13,293
9	120	14,087	4,453	1,497	6,679
10	180	1,289	4,090	4,783	3,387
11	240	4,711	14,448	3,140	7,433
12	360	17,186	3,602	10,269	10,352
13	375	6,956	2,134	10,847	6,646
	SUM	105,051	85,255	80,011	90,106

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
11,708	9,214	8,866		9,929	1,550

Table 96: Table containing the difference factor values regarding formula 4F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,126	1,951	3,021	1,699
3	5	6,114	2,976	9,259	6,116
4	10	18,346	0,277	11,451	10,025
5	15	24,468	14,192	11,857	16,839
6	30	9,253	5,184	8,369	7,602
7	60	8,947	10,846	14,791	11,528
8	90	1,189	4,078	11,986	5,751
9	120	9,716	20,143	11,431	13,763
10	180	6,310	4,635	2,146	4,364
11	240	7,119	8,837	14,644	10,200
12	360	4,605	10,328	0,247	5,060
13	375	2,353	1,315	0,818	1,495
	SUM	98,546	84,761	100,020	94,442

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
10,983	9,161	11,083		10,409	1,082

Table 97: Table containing the difference factor values regarding formula 5A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,535	3,684	1,975	3,065
3	5	1,929	3,130	4,718	3,259
4	10	15,753	3,011	6,036	8,267
5	15	17,255	8,969	4,515	10,247
6	30	27,620	10,660	1,245	13,175
7	60	11,072	14,300	6,938	10,770
8	90	22,456	14,437	0,862	12,585
9	120	8,162	12,230	1,977	7,456
10	180	3,575	17,149	12,604	11,109
11	240	4,687	15,892	13,190	11,257
12	360	18,993	11,660	0,846	10,500
13	375	13,553	17,513	2,636	11,234
	SUM	148,591	132,636	57,542	112,923

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
18,169	14,660	7,087		13,305	5,664

Table 98: Table containing the difference factor values regarding formula 5B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	12,707	15,446	12,498	13,550
3	5	12,173	23,950	24,991	20,371
4	10	22,802	25,990	42,165	30,319
5	15	20,296	15,387	57,761	31,148
6	30	23,205	8,239	46,094	25,846
7	60	16,656	0,977	37,460	18,364
8	90	17,227	7,363	26,645	17,078
9	120	25,008	1,436	16,247	14,230
10	180	1,064	13,464	1,629	5,386
11	240	12,477	1,269	5,332	6,360
12	360	1,313	12,515	12,329	8,719
13	375	2,537	4,446	8,430	5,138
	SUM	167,464	130,482	291,581	196,509

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
20,476	14,422	35,911		23,603	11,081

Table 99: Table containing the difference factor values regarding formula 5C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,901	0,787	4,569	2,419
3	5	5,450	8,884	17,567	10,634
4	10	12,917	19,611	31,332	21,286
5	15	17,348	26,264	35,355	26,322
6	30	21,010	15,998	29,513	22,174
7	60	4,299	0,156	17,068	7,175
8	90	0,499	0,696	3,755	1,650
9	120	8,135	10,929	17,973	12,346
10	180	3,927	12,782	0,899	5,869
11	240	13,944	20,119	10,873	14,979
12	360	8,721	12,359	4,615	8,565
13	375	7,259	23,430	9,119	13,269
	SUM	105,409	152,016	182,638	146,688

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
13,776	17,739	24,449		18,655	5,395

Table 100: Table containing the difference factor values regarding formula 5D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,799	4,730	3,425	3,318
3	5	4,326	7,668	3,428	5,141
4	10	2,008	1,473	2,148	1,876
5	15	17,251	9,961	9,817	12,343
6	30	33,056	24,040	27,611	28,236
7	60	27,687	13,112	20,152	20,317
8	90	18,261	9,330	6,251	11,281
9	120	18,016	4,702	9,113	10,610
10	180	5,479	5,214	5,735	5,476
11	240	0,768	18,394	18,714	12,625
12	360	7,744	15,180	15,588	12,837
13	375	5,347	8,589	7,556	7,164
	SUM	141,741	122,394	129,538	131,224

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
18,525	14,283	17,340		16,716	2,189

Table 101: Table containing the difference factor values regarding formula 5E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	2,846	2,690	2,369	2,635
3	5	5,624	12,765	6,838	8,409
4	10	5,207	20,328	10,775	12,103
5	15	10,181	22,665	5,645	12,831
6	30	3,887	20,238	3,126	9,084
7	60	9,123	22,450	0,433	10,669
8	90	13,341	14,820	0,688	9,616
9	120	5,280	3,654	8,922	5,952
10	180	20,652	24,862	10,958	18,824
11	240	2,409	7,654	8,193	6,085
12	360	0,683	9,605	3,642	4,644
13	375	5,094	13,142	3,862	7,366
	SUM	84,328	174,875	65,450	108,218

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
9,398	18,901	7,252		11,850	6,199

Table 102: Table containing the difference factor values regarding formula 5F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	5,079	4,671	3,911	4,554
3	5	17,293	10,559	16,848	14,900
4	10	26,999	15,799	29,520	24,106
5	15	29,439	16,040	35,360	26,947
6	30	19,695	15,139	23,136	19,324
7	60	19,053	10,118	17,212	15,461
8	90	17,611	14,093	4,063	11,922
9	120	13,553	11,818	12,425	12,598
10	180	26,889	14,927	19,435	20,417
11	240	3,027	3,120	8,720	4,956
12	360	1,336	11,166	2,779	5,094
13	375	0,979	3,847	3,303	2,710
	SUM	180,953	131,298	176,714	162,988

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
20,167	14,191	19,581		17,980	3,294

Table 103: Table containing the difference factor values regarding formula 6A evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	0,813	7,843	1,850	3,502
3	5	5,464	17,489	2,713	8,555
4	10	8,142	23,866	2,048	11,352
5	15	6,974	39,620	2,471	16,355
6	30	11,301	29,863	0,774	13,979
7	60	14,712	14,267	11,422	13,467
8	90	8,006	6,614	1,128	5,249
9	120	14,374	1,306	18,041	11,240
10	180	6,110	3,022	32,403	13,845
11	240	1,446	3,843	17,038	7,442
12	360	4,909	5,095	4,958	4,988
13	375	0,471	0,671	3,129	1,424
	SUM	82,722	153,502	97,974	111,399

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
10,115	16,966	12,066		13,049	3,530

Table 104: Table containing the difference factor values regarding formula 6B evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,671	1,907	0,530	1,369
3	5	7,237	2,141	2,535	3,971
4	10	2,425	2,793	12,162	5,793
5	15	2,802	5,700	17,296	8,599
6	30	11,167	0,760	16,508	9,478
7	60	7,173	5,660	13,810	8,881
8	90	4,682	15,772	7,454	9,303
9	120	8,329	30,402	1,879	13,537
10	180	8,416	27,421	13,901	16,579
11	240	8,715	33,589	6,105	16,136
12	360	8,577	26,845	0,578	12,000
13	375	10,714	21,124	2,829	11,556
	SUM	81,908	174,113	95,589	117,203

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
10,015	19,244	11,773		13,677	4,900

Table 105: Table containing the difference factor values regarding formula 6C evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,261	5,514	4,296	4,357
3	5	8,216	12,758	8,428	9,801
4	10	8,564	9,513	4,272	7,450
5	15	4,135	10,107	8,312	7,518
6	30	0,474	3,321	20,571	8,122
7	60	8,879	10,935	13,993	11,269
8	90	2,754	6,145	13,454	7,451
9	120	4,116	13,666	25,924	14,569
10	180	9,986	11,813	21,689	14,496
11	240	3,088	1,623	16,084	6,932
12	360	3,798	5,442	20,137	9,792
13	375	7,170	3,203	16,462	8,945
	SUM	64,440	94,041	173,621	110,700

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
8,422	10,974	23,241		14,212	7,923

Table 106: Table containing the difference factor values regarding formula 6D evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	3,261	5,514	4,296	4,357
3	5	8,216	12,758	8,428	9,801
4	10	8,564	9,513	4,278	7,452
5	15	4,135	10,107	8,312	7,518
6	30	0,474	3,321	20,571	8,122
7	60	8,879	10,935	13,993	11,269
8	90	2,754	6,145	13,454	7,451
9	120	4,116	13,666	25,924	14,569
10	180	9,986	11,813	21,689	14,496
11	240	3,088	1,623	18,488	7,733
12	360	5,602	6,380	23,900	11,961
13	375	10,961	8,199	16,851	12,004
	SUM	70,036	99,975	180,184	116,732

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
9,153	11,666	24,120		14,980	8,015

Table 107: Table containing the difference factor values regarding formula 6E evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,058	5,474	6,486	4,339
3	5	3,246	9,538	5,217	6,000
4	10	3,167	8,152	9,057	6,792
5	15	5,253	24,467	15,473	15,064
6	30	1,712	5,053	16,918	7,895
7	60	3,808	6,845	13,268	7,974
8	90	6,363	0,664	12,370	6,466
9	120	10,642	8,462	13,461	10,855
10	180	8,835	20,231	7,497	12,188
11	240	2,034	23,985	1,149	9,056
12	360	8,807	24,169	5,254	12,744
13	375	3,229	22,157	6,118	10,501
	SUM	58,154	159,197	112,269	109,873

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
6,481	17,206	12,440		12,043	5,374

Table 108: Table containing the difference factor values regarding formula 6F evaluated in the pH 7.4 environment using a phosphate buffer solution.

Absolute value of Difference between Reference (Ri) and Test fomulation (Ti)					
Sample nr	Time	Tablet 1	Tablet 2	Tablet 3	Average
1	0	0	0	0	0
2	2	1,963	1,957	15,548	6,489
3	5	5,077	3,649	24,811	11,179
4	10	4,289	8,024	18,001	10,105
5	15	5,446	23,410	4,979	11,278
6	30	1,803	24,292	3,837	9,977
7	60	5,057	2,150	18,106	8,438
8	90	13,395	4,585	23,376	13,785
9	120	16,050	10,987	18,310	15,116
10	180	5,173	3,731	14,802	7,902
11	240	10,330	4,194	22,357	12,294
12	360	1,656	7,725	5,806	5,063
13	375	4,333	10,926	3,576	6,278
	SUM	74,573	105,631	173,509	117,904

Difference factor (f1)					
Tablet 1	Tablet 2	Tablet 3		AVG	SD
f1	f1	f1		f1	f1
8,311	11,417	19,226		12,985	5,624

Annexure K

Assays

In this Annexure the assay results for all formulations are provided.

Table 1: Table consisting of the assays done on formulations 1A-1F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml		m	54,876
		c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**1A**	**1B**	**1C**	**1D**	**1E**	**1F**
	0,813	0,807	0,810	0,840	0,819	0,785
	0,813	0,807	0,808	0,835	0,822	0,790
	0,810	0,807	0,811	0,838	0,813	0,795
	0,809	0,805	0,813	0,831	0,823	0,786
Average	0,811	0,806	0,811	0,836	0,819	0,789
	0,015	0,015	0,015	0,016	0,015	0,015
	0,507	0,504	0,507	0,522	0,512	0,494
Assay percentage	**101,850**	**101,244**	**101,753**	**104,840**	**102,795**	**99,113**

Table 2: Table consisting of the assays done on formulations 2A-2F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml			

m	54,876
c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**2A**	**2B**	**2C**	**2D**	**2E**	**2F**
	0,815	0,830	0,816	0,792	0,788	0,793
	0,810	0,829	0,817	0,791	0,788	0,784
	0,811	0,825	0,817	0,794	0,793	0,791
	0,816	0,827	0,817	0,801	0,790	0,793
Average	0,813	0,828	0,817	0,794	0,790	0,790
	0,015	0,016	0,015	0,015	0,015	0,015
	0,509	0,517	0,511	0,497	0,494	0,495
Assay percentage	**102,073**	**103,828**	**102,499**	**99,777**	**99,238**	**99,281**

Table 3: Table consisting of the assays done on formulations 3A-3F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml			

m	54,876
c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**3A**	**3B**	**3C**	**3D**	**3E**	**3F**
	0,836	0,830	0,827	0,829	0,813	0,820
	0,834	0,833	0,816	0,838	0,813	0,814
	0,835	0,827	0,817	0,838	0,808	0,813
	0,819	0,820	0,822	0,831	0,815	0,818
Average	0,831	0,828	0,820	0,834	0,812	0,816
	0,016	0,016	0,015	0,016	0,015	0,015
	0,519	0,517	0,513	0,521	0,508	0,510
Assay percentage	**104,249**	**103,828**	**102,957**	**104,593**	**101,936**	**102,466**

Table 4: Table consisting of the assays done on formulations 4A-4F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml			

m	54,876
c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**4A**	**4B**	**4C**	**4D**	**4E**	**4F**
	0,804	0,816	0,790	0,812	0,812	0,813
	0,797	0,818	0,791	0,826	0,818	0,811
	0,794	0,816	0,796	0,826	0,814	0,817
	0,798	0,818	0,798	0,826	0,815	0,814
Average	0,798	0,817	0,793	0,823	0,815	0,814
	0,015	0,015	0,015	0,015	0,015	0,015
	0,499	0,511	0,497	0,514	0,509	0,509
Assay percentage	**100,253**	**102,527**	**99,662**	**103,222**	**102,246**	**102,134**

Table 5: Table consisting of the assays done on formulations 5A-5F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml			

m	54,876
c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**5A**	**5B**	**5C**	**5D**	**5E**	**5F**
	0,815	0,819	0,805	0,825	0,799	0,806
	0,821	0,822	0,795	0,817	0,796	0,812
	0,822	0,828	0,804	0,818	0,795	0,812
	0,822	0,826	0,801	0,820	0,792	0,809
Average	0,820	0,824	0,801	0,820	0,796	0,810
	0,015	0,015	0,015	0,015	0,015	0,015
	0,513	0,515	0,501	0,513	0,498	0,506
Assay percentage	**102,890**	**103,338**	**100,582**	**102,920**	**99,921**	**101,661**

Table 6: Table consisting of the assays done on formulations 6A-6F. This assay was performed using 0.1M NaOH.

50mg/100ml - 500µg/ml			
Dilute in 100ml 0.1M NaOH			
Dilution done by taking 3ml of the mother solution and diluting it in 100ml of distilled water	$x = \frac{y - c}{m}$	y = 54.876x - 0.024	x = y-(-0.024)/54.876
Concentration then being 15µg/ml			

m	54,876
c	0,024

Theoretical average absorbance value at 273nm		
0,796	**0,015**	**0,498**

Formula	**6A**	**6B**	**6C**	**6D**	**6E**	**6F**
	0,810	0,798	0,801	0,788	0,799	0,809
	0,798	0,792	0,804	0,786	0,800	0,808
	0,801	0,794	0,804	0,790	0,797	0,806
	0,803	0,790	0,805	0,790	0,796	0,804
Average	0,803	0,794	0,803	0,789	0,798	0,807
	0,015	0,015	0,015	0,015	0,015	0,015
	0,502	0,497	0,503	0,494	0,499	0,505
Assay percentage	**100,835**	**99,680**	**100,872**	**99,073**	**100,189**	**101,277**

Annexure L

MDPI: Instructions for Authors

This Annexure contains the instructions to authors for the publication of articles and manuscripts within the journal entitled “Pharmaceutics from MDPI (Multidisciplinary Digital Publishing Institute)”.

Instructions for Authors

Shortcuts

- **Manuscript Submission Overview**
- **Manuscript Preparation**
- **Preparing Figures, Schemes and Tables**
- **Supplementary Materials, Data Deposit and Software Source Code**
- **Research and Publication Ethics**
- **Reviewer Suggestions**
- **English Corrections**
- **Preprints and Conference Papers**
- **Authorship**
- **Conflict of Interests**
- **Editorial Procedures and Peer-Review**

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2. use the **Microsoft Word template** or **LaTeX template** to prepare your manuscript;
3. make sure that issues about **publication ethics**, **copyright**, **authorship**, **figure formats**, **data** and **references format** have been appropriately considered;
4. Ensure that all authors have approved the content of the submitted manuscript.
5. Authors are encouraged to add a **biography** (optional) to the submission and publish it.

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- *Reviews:* These provide concise and precise updates on the latest progress made in a given area of research. Systematic reviews should follow the PRISMA **guidelines.**

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1. Authors' full names followed by current positions;
2. Education background including institution information and year of graduation (type and level of degree received);
3. Work experience;
4. Current and previous research interests;
5. Memberships of professional societies and awards received.

Manuscript Preparation

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- **Research manuscripts** should comprise:
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    - **Research manuscript sections**: Introduction, Materials and Methods, Results, Discussion, Conclusions (optional).
    - **Back matter**: Supplementary Materials, Acknowledgments, Author Contributions, Conflicts of Interest, **References**.
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  A graphical abstract (GA) is an image that appears alongside the text abstract in the Table of Contents. In addition to summarizing content, it should represent the topic of the article in an attention-grabbing way.

  The GA should be a high-quality illustration or diagram in any of the following formats: PNG, JPEG, EPS, SVG, PSD or AI. Written text in a GA should be clear and easy to read, using one of the following fonts: Times, Arial, Courier, Helvetica, Ubuntu or Calibri.

  The minimum required size for the GA is 560 × 1100 pixels (height × width). When submitting larger images, please make sure to keep to the same ratio.
- **Abbreviations** should be defined in parentheses the first time they appear in the abstract, main text, and in figure or table captions and used consistently thereafter.
- **SI Units** (International System of Units) should be used. Imperial, US customary and other units should be converted to SI units whenever possible.
- **Equations:** If you are using Word, please use either the Microsoft Equation Editor or the MathType add-on. Equations should be editable by the editorial office and not appear in a picture format.
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Front Matter

These sections should appear in all manuscript types

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- **Abstract:** The abstract should be a total of about 200 words maximum. The abstract should be a single paragraph and should follow the style of structured abstracts, but without headings: 1) Background: Place the question addressed in a broad context and highlight the purpose of the study; 2) Methods: Describe briefly the main methods or treatments applied. Include any relevant preregistration numbers, and species and strains of any animals used. 3) Results: Summarize the article's main findings; and 4) Conclusion: Indicate the main conclusions or interpretations. The abstract should be an objective representation of the article: it must not contain results which are not presented and substantiated in the main text and should not exaggerate the main conclusions.
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Research Manuscript Sections

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- **Discussion:** Authors should discuss the results and how they can be interpreted in perspective of previous studies and of the working hypotheses. The findings and their implications should be discussed in the broadest context possible and limitations of the work highlighted. Future research directions may also be mentioned. This section may be combined with Results.
- **Conclusions:** This section is not mandatory, but can be added to the manuscript if the discussion is unusually long or complex.
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Back Matter

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  For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, X.X. and Y.Y.; Methodology, X.X.; Software, X.X.; Validation, X.X., Y.Y. and Z.Z.; Formal Analysis, X.X.; Investigation, X.X.; Resources, X.X.; Data Curation, X.X.; Writing – Original Draft Preparation, X.X.; Writing – Review & Editing, X.X.; Visualization, X.X.; Supervision, X.X.; Project Administration, X.X.; Funding Acquisition, Y.Y.", please turn to the **CRediT taxonomy** for the term explanation. For more background on CRediT, see **here**. "**Authorship must include and be limited to those who have contributed substantially to the work. Please read the section concerning the criteria to qualify for authorship carefully**".

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- **References:** References must be numbered in order of appearance in the text (including table captions and figure legends) and listed individually at the end of the manuscript. We recommend preparing the references with a bibliography software package, such as **EndNote**, **ReferenceManager** or **Zotero** to avoid typing mistakes and duplicated references. We encourage citations to data, computer code and other citable research material. If available online, you may use reference style 9. below.

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In the text, reference numbers should be placed in square brackets [ ], and placed before the punctuation; for example [1], [1–3] or [1,3]. For embedded citations in the text with pagination, use both parentheses and brackets to indicate the reference number and page numbers; for example [5] (p. 10). or [6] (pp. 101–105).

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 Journal Articles:
1. Author 1, A.B.; Author 2, C.D. Title of the article. *Abbreviated Journal Name* **Year**, *Volume*, page range.
 Books and Book Chapters:
2. Author 1, A.; Author 2, B. *Book Title*, 3rd ed.; Publisher: Publisher Location, Country, Year; pp. 154–196.
3. Author 1, A.; Author 2, B. Title of the chapter. In *Book Title*, 2nd ed.; Editor 1, A., Editor 2, B., Eds.; Publisher: Publisher Location, Country, Year; Volume 3, pp. 154–196.
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- Data available in a publicly accessible repository that does not issue DOIs
  Publicly available datasets were analyzed in this study. This data can be found here: [link/accession number]
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  No new data were created or analyzed in this study. Data sharing is not applicable to this article.
- Data is contained within the article or supplementary material
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Research and Publication Ethics

Research Ethics

Research Involving Human Subjects

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The journal operates optional open peer-review: *Authors are given the option for all review reports and editorial decisions to be published alongside their manuscript. In addition, reviewers can sign their review, i.e., identify themselves in the published review reports.* Authors can alter their choice for open review at any time before publication, but once the paper has been published changes will only be made at the discretion of the *Publisher* and *Editor-in-Chief*. We encourage authors to take advantage of this opportunity as proof of the rigorous process employed in publishing their research. To guarantee impartial refereeing, the names of referees will be revealed only if the referees agree to do so, and after a paper has been accepted for publication.

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- *Reject and Encourage Resubmission*:
  If additional experiments are needed to support the conclusions, the manuscript will be rejected and the authors will be encouraged to re-submit the paper once further experiments have been conducted.

- *Reject*:
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Production and Publication

Once accepted, the manuscript will undergo professional copy-editing, English editing, proofreading by the authors, final corrections, pagination, and, publication on the **www.mdpi.com** website.

Annexure M

Pharmaceutical Development and Technology: Instructions for Authors

This Annexure contains the instructions to authors for the publication of articles and manuscripts within the Taylor & Francis publishers' journal Pharmaceutical Development and Technology.

Instructions for authors

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As a result of the significant disruption that is being caused by the COVID-19 pandemic we understand that many authors and peer reviewers will be making adjustments to their professional and personal lives. As a result they may have difficulty in meeting the timelines associated with our peer review process. Please let the journal editorial office know if you need additional time. Our systems will continue to remind you of the original timelines but we intend to be flexible.

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Updated 22-09-2020

Annexure N

Ethics approval document

This Annexure contains the document supplied by the NWU-Potchefstroom providing ethics approval for the use of porcine tissue.

Private Bag X1290, Potchefstroom
South Africa 2520

Tel: 086 016 9698
Web: http://www.nwu.ac.za/

North-West University Animal Care, Health and Safety Research Ethics Committee (NWU-AnimCareREC)

Tel: 018 299-1208
Email: Ethics-AnimCare@nwu.ac.za (for animal studies)

3 June 2020

ETHICS APPROVAL LETTER OF STUDY

Based on approval by the North-West University Animal Care, Health and Safety Research Ethics Committee (NWU-AnimCareREC) on 03/06/2020, the NWU-AnimCareREC hereby approves your study as indicated below. This implies that the NWU-AnimCareREC grants its permission that, provided the general conditions specified below are met and pending any other authorisation that may be necessary, the study may be initiated, using the ethics number below.

Study title: Improvement of the pharmaceutical availability and membrane permeability of furosemide by formulation design
Principal Investigator/Study Supervisor/Researcher: Prof JH Steenekamp
Student: CJ van der Merwe – 22111247

Ethics number: N W U - 0 0 5 0 4 - 2 0 - A 5

Application Type: Single study
Commencement date: 03/06/2020
Expiry date: 30/06/2021

Risk: Category 0

Approval of the study is provided for a year, after which continuation of the study is dependent on receipt and review of an annual monitoring report and the concomitant issuing of a letter of continuation. A monitoring report is required at the end of June annually until completion.

General conditions:

While this ethics approval is subject to all declarations, undertakings and agreements incorporated and signed in the application form, the following general terms and conditions will apply:

- *The principal investigator/study supervisor/researcher must report in the prescribed format to the NWU-AnimCareREC:*
  - *Annually on the monitoring of the study, whereby a letter of continuation will be provided annually, and upon completion of the study; and*
  - *without any delay in case of any adverse event or incident (or any matter that interrupts sound ethical principles) during the course of the study.*
- *The approval applies strictly to the proposal as stipulated in the application form. Should any amendments to the proposal be deemed necessary during the course of the study, the principal investigator/study supervisor/researcher must apply for approval of these amendments at the NWU-AnimCareREC, prior to implementation. Should there be any deviations from the study proposal without the necessary approval of such amendments, the ethics approval is immediately and automatically forfeited.*

- *Annually a number of studies may be randomly selected for active monitoring.*
- *The date of approval indicates the first date that the study may be started.*
- *In the interest of ethical responsibility, the NWU-AnimCareREC reserves the right to:*
  - *request access to any information or data at any time during the course or after completion of the study;*
  - *to ask further questions, seek additional information, require further modification or monitor the conduct of your research or the informed consent process;*
  - *withdraw or postpone approval if:*
    - *any unethical principles or practices of the study are revealed or suspected;*
    - *it becomes apparent that any relevant information was withheld from the NWU-AnimCareREC or that information has been false or misrepresented;*
    - *submission of the annual monitoring report, the required amendments, or reporting of adverse events or incidents was not done in a timely manner and accurately; and/or*
    - *new institutional rules, national legislation or international conventions deem it necessary.*
- *NWU-AnimCareREC can be contacted for further information via Ethics-AnimCare@nwu.ac.za or 018 299 1208*

Special COVID-19 arrangements:

There may be certain changes that you may need to make to your study, after it has been approved, due to the impact of the COVID-19 pandemic or the lockdown e.g.:

a. Changing the ages of the animals to be used in the research study
b. Changing the approved methodology to use data collection methods that ensure physical distancing from farmers and owners
c. The implementation of risk-mitigating strategies to prevent infection during data collection
d. Changes in time schedules etc.

Please note that any 1) amendments, 2) request for extensions or 3) any other kind of modification to the proposal or other associated documentation must be submitted for review by the NWU-AnimCareREC, Faculty of Health Sciences, and must be approved, prior to these changes being implemented.

These amendment requests will be handled via the *expedited process*.

Process to be followed:

a. Ensure all your amendments are indicated in yellow highlight in the amended documents.
b. Submit your request to Ethics-AnimCare@nwu.ac.za with a *cover letter* with a specific subject title indicating, "Amendment request (COVID-19): NWU-XXXXX-XX-XX". The letter should include the title of the approved study, the names of the researchers involved, the nature of the amendment/s being made (indicating what changes have been made as well as where they have been made), which documents have been attached and any further explanation to clarify the amendment request being submitted.
c. Name the emails, to which you attach the documents that you send, with a *specific subject line* indicating that it is an amendment request e.g. "Amendment request (COVID-19): NWU-XXXXX-XX-XX". This e-mail should indicate the nature of the amendment.
d. Send a short email to Prof Wayne Towers and Prof Tiaan Brink indicating to them that you have submitted an amendment request due to the COVID-19 impact.

NWU-AnimCareREC would like to remain at your service and wishes you well with your study. Please do not hesitate to contact the NWU-AnimCareREC for any further enquiries or requests for assistance.

Yours sincerely,

Digitally signed by Prof Christiaan B Brink (Tiaan)
Date: 2020.06.03 14:38:42 +02'00'

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