# THE EVALUATION AND COMPARISON OF VARIOUS TABLET DISINTEGRANTS

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"When you saw only one set of footprints,
it was then that I carried you."

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## AIM AND OBJECTIVES OF THE STUDY

The aim of the study was to evaluate and compare the mechanism of action and efficiency of various disintegrants in pure disintegrant compacts and tablet formulations and to determine the primary factors affecting their efficiency.

Disintegration is the first step in the process of assuring the bioavailability of orally administered drugs from a solid oral dosage form. Disintegrants are pharmaceutical excipients that promote the break up of an orally ingested tablet into smaller fragments (disintegrate) in an aqueous environment in order to release the active ingredient from the tablet and cause a physiological effect in the body. The more efficient the disintegrant, the faster disintegration of the tablet can occur and thus the faster the active ingredient can become available for absorption in the gastro-intestinal tract.

Independent of the actual mechanism of action of most disintegrants, their efficiency is primarily dependent on contact with an aqueous environment. Various factors are known to affect the efficiency of disintegrants, including formulation factors such as disintegrant type and concentration, solubility, hydrophobicity and hygroscopicity of the formulation and process factors, such as tablet porosity (compression force).

This study involved the evaluation of disintegrants based on disintegration time, water uptake and swelling of tablets and it necessitated the following investigations:

- A literature study on the mechanism of action of disintegrants and determination of factors influencing disintegrant efficiency.

- Preparing compacts of the various pure disintegrants and evaluating these compacts in terms of compact hardness, disintegration time, extent and rate of water uptake and swelling.

- Selecting of various formulations where the determinants of the efficiency of disintegrants are varied, using fraction experimental design.

- Preparing tablets of selected formulations and evaluating the efficiency of two super disintegrants in terms of disintegration times, water uptake and swelling of tablets.

- Determining an area inside the experimental design where the formulation is optimum in terms of disintegrant efficiency and disintegration of the tablets for both soluble and insoluble formulations.

# ABSTRACT

The aim of the tablet formulator is to formulate a tablet, which when ingested, disintegrates to give the same system or powder blend as before compression. The faster this disintegration can occur, the faster the absorption of the active ingredient, and thus the faster a physiological effect can be expected. There is no single mechanism of action for disintegrants, but rather a combination of mechanisms which causes disintegration, including water uptake (capillary action), swelling, gas production, deformation and particle repulsion.

Compacts of various pure disintegrants were prepared and evaluated in terms of their disintegration efficiency and their mechanism of action, including potato starch, sodium starch glycolate, Explotab®, Avicel® PH 200, Ac-Di-Sol® and Kollidon® CL. The compact hardness, disintegration time, water uptake and swelling of each pure disintegrant were evaluated at different compression forces. Order of disintegration time of the pure compacts seemed to be: Kollidon® CL ≈ SSG ≈ Potato starch < Explotab® << Ac-Di-Sol® <<<< Avicel®, for water uptake: SSG > Kollidon® CL >> Avicel® >>> Explotab® > Potato starch > Ac-Di-Sol®, and for swelling: SSG >> Avicel® ≈ Kollidon® CL >> Potato starch > Explotab® ≈ Ac-Di-Sol®. The best swelling and water uptake profiles were found for the super disintegrants, namely Kollidon® CL, sodium starch glycolate (Explotab®) and Ac-Di-Sol®.

The super disintegrants are known to be more efficient because of their rate and extent of swelling, despite small concentrations needed in a formulation. Various factors affecting the efficiency of the disintegrants were used to conduct a fractional factorial design. Two super disintegrants (Explotab® and Ac-Di-Sol®) were formulated in different concentrations (0.5% and 1.0%) in a soluble (Tablettose®) and insoluble (Emcompress®) formulation, with different types (magnesium stearate and Pruv®) and concentrations (0.5% and 1.0%) of lubricant and tabletted at two different compression forces (setting 1 and 7). Results were statistically analysed and the main effects of each factor on the responses were calculated.

Formulations with Ac-Di-Sol® as disintegrant showed better disintegration profiles in terms of disintegration time, swelling and water uptake, than the formulations with Explotab® as disintegrant. A concentration of 1.0% super disintegrant was more effective than 0.5%. The hydrophobic nature of magnesium stearate as lubricant in a formulation probably prevented liquid penetration and thus increased disintegration times, with 1.0% having a greater detrimental effect than 0.5%. Formulations with Pruv® as lubricant did not exhibit this disadvantages. The two compression forces used during tabletting did not seem to have any

significant effect on the efficiency of the disintegrants. The fractional factorial design made it possible to predict a formulation for optimum disintegration in tablets.

**Keywords:** Disintegration, disintegrants, Explotab®, Ac-Di-Sol®, Kollidon® CL, potato starch, Avicel® PH 200, sodium starch glycolate,water uptake, swelling

# UITTREKSEL

Die oogmerk tydens tabletformulering is om 'n tablet te lewer wat disintegreer nadat dit ingeneem is om dieselfde sisteem of poeiermengsel te lewer as wat dit voor samepersing was. Hoe vinniger disintegrasie van 'n tablet plaasvind, hoe vinniger kan 'n fisiologiese effek verkry word omdat absorpsie van die aktiewe bestanddeel vinniger kan plaasvind. Die werking van disintegreermiddels kan nie aan 'n enkele meganisme toegeskryf word nie, maar vind gewoonlik plaas as gevolg van 'n kombinasie van meganismes, insluitend water-opname (kapillêre werking), swelling, gasproduksie, deformasie en deeltjie-afstoting.

Kompakte van verskillende suiwer disintegreermiddels is berei en geëvalueer in terme van hul effektiwiteit en meganisme van werking, insluitend aartappelstysel, natriumstyselglikolaat, Explotab®, Avicel® PH 200, Ac-Di-Sol® en Kollidon® CL. Die hardheid, disintegrasietyd, water-opname en swelling van die suiwer kompakte, wat by verskillende drukke saamgepers is, is geëvalueer. Die volgorde van disintegrasietyd van die suiwer kompakte is: Kollidon® CL ≈ natriumstyselglikolaat ≈ aartappelstysel < Explotab® << Ac-Di-Sol® <<<< Avicel®, vir water opname: natriumstyselglikolaat > Kollidon® CL >> Avicel® >>> Explotab® > aartappelstysel > Ac-Di-Sol® en vir swelling: natriumstyselglikolaat >> Avicel® ≈ Kollidon® CL >> aartappelstysel > Explotab® ≈ Ac-Di-Sol®. Die superdisintegreermiddels, naamlik Kollidon® CL, natriumstyselglikolaat (Explotab®) en Ac-Di-Sol® het die beste swelling en water-opname getoon.

Die superdisintegreermiddels is bekend vir hul goeie effektiwiteit a.g.v. die vinnige water-opname en swelling in tablette, ten spyte van die lae konsentrasies waarin hulle in tablette voorkom (1 – 2%). 'n Deelfaktoriaalontwerp is opgestel deur gebruik te maak van faktore wat die effektiwiteit van disintegreermiddels beïnvloed. Twee superdisintegreermiddels (Explotab® en Ac-Di-Sol®) is in verskillende konsentrasies (0.5% en1.0%) in oplosbare (Tablettose®) en onoplosbare (Emcompress®) tablette geformuleer, met verskillende tipes (magnesiumstearaat en Pruv®) en verskillende konsentrasies (0.5% en 1.0%) smeermiddel, en getabletteer by twee verskillende persdrukke (verstelling 1 en 7). Resultate is statisties geanaliseer en die hoofeffekte van elke veranderlike op die responsies is bereken.

Formules met Ac-Di-Sol® as disintegreermiddel het 'n beter disintegrasieprofiel, in terme van disintegrasietyd, swelling en water-opname getoon as die formules wat Explotab® bevat het. 'n Konsentrasie van 1.0% disintegreermiddel was meer effektief as 0.5%. Die hidrofobiese eienskappe van magnesiumstearaat as smeermiddel, het die opname van water deur die tablet vertraag en langer disintegrasie tye veroorsaak en 1.0% smeermiddel het 'n groter

negatiewe effek gehad as 0.5%. Formules met Pruv® as smeermiddel het nie hierdie nadele vertoon nie. Die twee persdrukke wat ondersoek is, het geen effek op die effektiwiteit van die disintegreermiddels gehad nie. Die deelfaktoriaal het dit moontlik gemaak om 'n formule vir optimale disintegrasie van tablette te voorspel.

**Sleutelwoorde:** Disintegreermiddels, Explotab®, Ac-Di-Sol®, Kollidon® CL, aartappelstysel, Avicel® PH 200, natriumstyselglikolaat, wateropname, swelling

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# CHAPTER 1

# DISINTEGRANTS

## 1.1 INTRODUCTION

The aim of the tablet formulator is to produce a hard tablet which, when ingested, disintegrates to give a particulate system of similar size distribution to the original powder blend before processing.

The rate, at which a physiological effect is produced from a drug taken orally, is dependent upon the rate of absorption from the gastro-intestinal tract. Before a drug in tablet form may be absorbed, it must first be released from the tablet by disintegration of the tablet. The usefulness of a tablet arises wholly from its ability to disintegrate upon contact with fluid.

## 1.2 DISINTEGRANTS AND THEIR IMPORTANCE IN DRUG FORMULATIONS

The release of an active ingredient from a tablet involves two distinct processes: disintegration of the tablet and dissolution of the active ingredient. Although both processes commence when the tablet encounters an aqueous environment, the bulk of the active ingredient cannot dissolve until disintegration has occurred. The two processes are sequential and occur simultaneously until the tablet has disintegrated completely (Nelson & Wang, 1977:1758). Disintegration is the first step in the process of drugs becoming bio-available from tablets (Jonas *et al.*, 1996:605). Kanig and Rudnic (1984:50) suggested that the absorption of a drug into the bloodstream from an intact solid dosage form follows a fairly well-defined sequence of events (Figure 1.1)

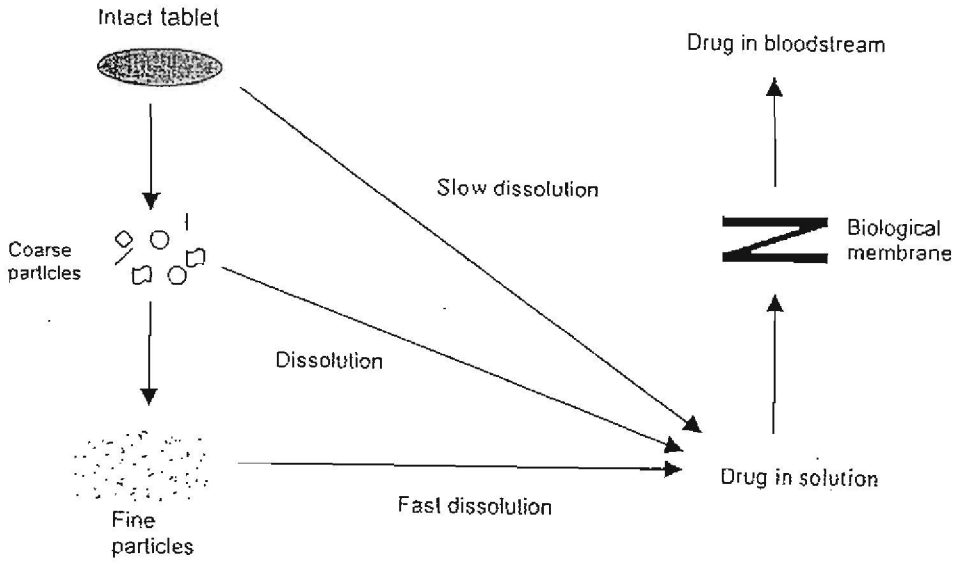



**Figure 1.1:** *The absorption of a drug into the bloodstream from an intact dosage form.*

Disintegrants are agents added to formulations to promote the break-up of the tablet into smaller fragments (disintegration) in an aqueous environment, thereby increasing the surface area of tablet particles, and thus increasing the rate of absorption of the active ingredient. The function of the disintegrant is to counteract the action of the tablet binder and the compression forces used to form the tablet. The stronger the effect of the binder, the more efficient the disrupting effect required of the disintegrant in order to release the active ingredient into the gastro-intestinal fluid (Visavarungroj & Remon, 1990:125).

## 1.3 MECHANISM OF ACTION OF DISINTEGRANTS

According to Kanig and Rudnic (1984:52) no single mechanism of disintegrant action is applicable to all disintegrants. In some instances, a combination of mechanisms may be operative. Caramella *et al.* (1987:2111-2112) stated that: to obtain a rapid disintegration, a disintegration force must develop inside the tablet, capable of weakening and breaking the inter particle bonds. The authors stressed the concept that force is not a mechanism by itself, but the outcome of a series of events beginning with water penetration and leading to the activation of one of the mechanisms proposed for disintegrant action.

Proposed mechanisms of disintegrant action include:

- Swelling
- Capillary action
- Heat of immersion and wettability

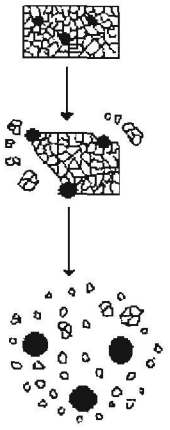
- Gas production
- Deformation
- Particle repulsion.

### 1.3.1 Swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegrants is swelling; primarily because almost all disintegrants swell to some extent (Kanig & Rudnic 1984:54). According to Bolhuis *et al.* (1982:114) swelling is the dominant factor in the process of disintegration when the tablets contain strongly swelling disintegrants. In strongly swelling disintegrants the swelling of particles play a decisive role in force development: only when a significant swelling of disintegrant particles is present does an efficient force develop inside the tablet for disintegration (Bolhuis *et al.*, 1982:114; Caramella *et al.*, 1987:2111-2112).

When particles of a swelling disintegrant and particles of other substances or excipients are compressed to form a tablet, the disintegrant, which are usually low in concentration in the formula, are found under compressive stresses exerted by the rest of the tablet when the tablet is placed in an aqueous environment for disintegration. This happens through a combination of processes, such as porous diffusion and capillarity. The phenomenon of disintegrant swelling is observed, which leads to the application of a certain pressure on the particles of the rest of the substance inside the tablet. This pressure then causes the tablet to disrupt or disintegrate (Caramella *et al.*, 1986:182).

Swelling of the disintegrant occurs since the disintegrant particles are hydrophilic polymers (Kanig & Rudnic, 1984:54). It is important to understand that, as particles swell, there must be little or no accommodation by the tablet matrix for that swelling. If the matrix yields elastically to the swelling, little or no force will be expanded on the system and disintegration will not take place. If the matrix is rigid, and does not accommodate swelling, disintegration or deaggregation will occur (Kanig & Rudnic, 1984:54). Figure 1.2 illustrates swelling as a mechanism of action of disintegrants (Kanig & Rudnic, 1984:56).



**Swelling**

Particles swell and break up the matrix from within; swelling sets up localized stresses that spread throughout the matrix.

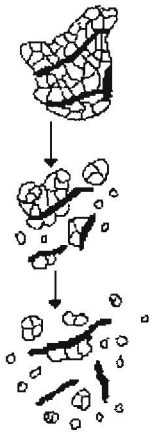
**Figure 1.2:** *Swelling as disintegrating mechanism.*

### 1.3.2 Capillary action ("wicking")

Water uptake has been implicated as an important mechanism of action for tablet disintegrants (Khan & Rhodes, 1975:447). According to the authors the ability of particles to draw up water into the porous network of a tablet (wicking) is essential for efficient disintegration. Water is pulled into the porous network of the tablet, by the disintegrant particles, and reduces the physical bonding forces between particles.

It is thus important that disintegrants in this group must be able to maintain a porous structure in the compressed tablet and show a low interfacial tension towards aqueous fluids. Rapid penetration by water throughout the entire tablet matrix to facilitate its break-up is thus achieved. Concentrations of disintegrant that ensure a continuous matrix of disintegrant are desirable and levels of between 5 and 20% are common (Kottke & Rudnic, 2002:298). Bolhuis *et al.* (1982:112) concluded that if wetting of the disintegrant particles was slowed, disintegration of the tablet also slowed: the authors have demonstrated that the rate of water uptake is of critical importance for a number of tablet disintegrants.

For instance, Cross-linked PVP swells very little, although it takes water up into its network quite rapidly, it is concluded that the mechanism of action for this disintegrant is wicking. Figure 1.3 illustrates "wicking" as a mechanism of action of disintegrants (Kanig & Rudnic, 1984:56).



**Wicking**

Water is pulled into pores by the disintegrant and reduces the physical bonding forces between particles.

**Figure 1.3:** *"Wicking" as disintegrating mechanism.*

### 1.3.3 Heat of immersion and wettability

According to Kanig and Rudnic (1984:56) the heat generated by the wetting of ingredients that occurs when the tablet is immersed in a fluid has been suggested as a method of tablet disintegration. The heat presumably causes the air in the tablet to expand pushing the tablet apart.

According to Lowenthal (1973:591) it is doubtful if the amount of heat produced by wetting can cause sufficient increase in the volume of air to cause enough pressure to break tablets apart. The author states that if production of heat were an important mechanism of action of disintegrants, then why wouldn't the heat produced during compression and ejection of the tablet from the die cause an expansion of air and tablet disintegration?

### 1.3.4 Gas production

According to Lowenthal (1973:589) there is no uncertainty about the mechanism of action of disintegrants that generate a gas; such as carbon dioxide ($CO_2$) or oxygen, when moistened. The tablet is disrupted by the pressure of the gas formed. The gas generation is accomplished by the reaction of citric and tartaric acids with sodium bicarbonate to give $CO_2$, or the decomposition of peroxides to give oxygen.

### 1.3.5 Deformation

The existence of plastic deformation under the stress of tabletting has been reported for many years. Evidence that disintegrant particles, such as potato starch, deform during tablet compression was demonstrated by Erdös and Bezegh (1977:1130) with the aid of

microscopic observations. The deformed particles tend to regenerate i.e. strive to regain their original shape if wetted, causing tablet break-up. Figure 1.4 illustrates deformation as mechanism of action of disintegrants (Kanig & Rudnic, 1984:56).

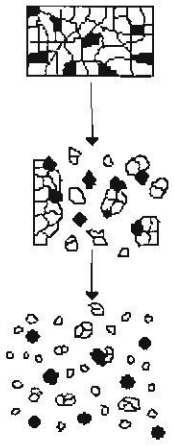
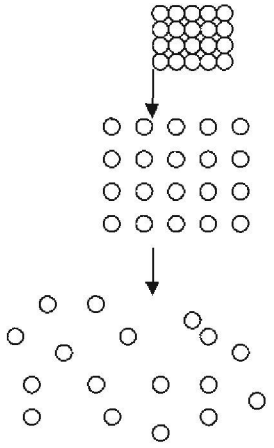



**Figure 1.4:** *Deformation as disintegrating mechanism.*

Studies by Lowenthal (1972:455) on the basis of electron microscopic examinations, definitely pointed out that starch granules, deformed by compression, did not regain their original shape. Wetting of the granules did show less distortion; consequently certain regeneration took place.

### 1.3.6 Particle repulsion

Another theory of tablet disintegration attempts to explain the swelling of tablets made with "non-swellable" starch. Ringard and Guyot-Hermann (1981:155) have proposed a particle repulsion theory based upon the observation that particles that do not seem to swell may still disintegrate tablets. It is suggested that water is drawn into pores and particles repulse each other because of the resulting electrical force. According to Kanig and Rudnic (1984:56) this theory is not supported by adequate data. Figure 1.5 illustrates particle repulsion as a mechanism of disintegrant action (Kanig & Rudnic, 1984:56).



**Repulsion**

Water is drawn into pores, and particles repulse each other because of the resulting electrical force.

**Figure 1.5:** *Particle repulsion as disintegrating mechanism.*

## 1.4 FACTORS AFFECTING DISINTEGRATION AND DISINTEGRANT EFFICIENCY

### 1.4.1 Hygroscopicity

According to Gordon and Chowhan (1987:907-909) hygroscopic ingredients in tablet formulations decrease the effectiveness of superdisintegrants in promoting dissolution. The study examined the effect of overall tablet solubility and hygroscopicity in influencing the effectiveness of super disintegrants. The greater the overall tablet hygroscopicity, the larger the decrease in disintegrant efficiency. This may be due to a competitive inhibition of disintegrant by the other tablet components competing for locally available water. The water is then unavailable for disintegrant uptake and swelling. The amount of super disintegrant inhibition will increase as the composite hygroscopicity of the formulation increases. Lactose monohydrate (Tablettose®) and calcium phosphate monohydrate (Emcompress®) are both nonhygroscopic.

### 1.4.2 Solubility

The solubility of the major component in tablet formulation affects both the rate and mechanism of tablet disintegration. Since the dissolution of a soluble system takes place by erosion at the outer surface, swelling of disintegrant particles is not expected to play a major role. Water soluble materials tend to dissolve rather than disintegrate, while insoluble materials will produce a rapidly disintegrating tablet if an appropriate amount of disintegrant is included in the formulation. It now seems obvious that tablets prepared from Emcompress® (insoluble) would be expected to show a different behaviour from that shown by tablets prepared from Tablettose® (soluble) (Johnson *et al.*, 1991:469).

In hydrophobic and/or water insoluble base formulations, the disintegrant (which is always needed to promote disintegration), is capable of developing its maximum swelling force, besides drawing water inside the compact. Therefore, highly hydrophilic and strongly swelling disintegrants are to be preferred. On the other hand, in hydrophilic and water soluble formulations, the disintegrant, when needed, assists in the drawing of water inside the compact, but is not always able to develop its maximum swelling force. This suggests that limited swelling disintegrants should work as well as, and even better than strongly swelling materials in water soluble formulations (Caramella *et al.*, 1986:1764). However, according to Gordon and Chowhan (1987:907) overall tablet solubility did not appear to have any influence on the effectiveness of super disintegrants.

### 1.4.3 Compression force

According to Higuchi *et al.*, (1953:199) there appears to be a good exponential relationship between disintegration time and compression force in some formulations.

The role of compression forces on the tablet disintegration was evaluated by Sheen and Kim (1989:403). According to the authors tablet porosity decreases as compression force increases; this may hinder penetration of fluid into tablets, and slow down disintegration.

It has been hypothesized that, high porosity tablets, due to low compression force, have too much void space, so that when disintegrants swell, too little pressure is exerted and disintegration is slow. Medium force allows swelling and sufficient pressure to cause tablet disintegration. High force results in tablets of low porosity and decrease the ability of fluid to enter the tablets, so that disintegration time increases. This would seem to indicate that there is an optimum compression force for tablet disintegration (Lowenthal, 1973:595). Nevertheless, Sheen and Kim (1989:403) suggested that some newer super disintegrants such as croscarmellose sodium and sodium starch glycolate, were fairly insensitive to increases in compression force.

The concentration of a disintegrant influences the relationship between compression force and disintegration time. According to Ferrero *et al.*, (1997:17) disintegration time decreases when Ac-Di-Sol® concentration increases. However, they observed a slight increase in disintegration time at a concentration level near 10%. The effect of applied pressure is important at low proportions of disintegrant (the disintegration time increases when applied pressure rises), but this effect diminishes at concentration near 10%.

Khan and Rooke (1976:634) found that the well-known supposition, "harder tablets take longer to disintegrate", is not applicable to all systems. It is evident that the effect of compression force on disintegration time is largely dependent upon the type and concentration of the disintegrant and also the type of excipients used in the formulation.

### 1.4.4 Hydrophobic excipients

The negative effect of hydrophobic excipients, especially magnesium stearate (lubricant) on tablet properties have been investigated by Bolhuis *et al.* (1975:317) and it was found that magnesium stearate as lubricant can greatly reduce the strengths of tablets. The phenomenon is caused by the formation of a lubricant film upon the substrate as a result of the adhesion to the substrate surface of magnesium stearate molecules which are sheared off from the magnesium stearate crystals during the mixing process. Van Kamp *et al.,* (1983:167) stated that the hydrophobic film affects the disintegration time by increasing it.

It was found by Bolhuis *et al.* (1975:322) that starch products, which deform plastically under compression, exhibit almost maximum reduction in crushing strength of tablets. In contrast they found that the binding properties of dicalcium phosphate dihydrate (Emcompress®) are completely unaffected by the presence of Magnesium stearate®. A reduction in crushing strength is thus found to be dependent upon the physical nature of the base material.

Hydrophobic surfaces are those tablet surfaces on which water will not spread. The hydrophobicity or water repellence of a surface, when measured by contact angle, affects the capillary action involved in pore penetration. Hydrophobic excipients are known to increase disintegration time by forming the hydrophobic film, which inhibits water penetration into the original pores (Bolhuis *et al.,* 1982:111). In tablets containing strongly swelling disintegrants, like sodium starch glycolate or croscarmellose sodium, the authors observed that the swelling properties were hardly affected by the presence of a hydrophobic lubricant. It was also suggested that in the case of tablets containing a slightly swelling but hydrophilic disintegrant, tablet disintegration is strongly affected by the presence of a hydrophobic lubricant.

## 1.5 BASIC CATEGORIES OF DISINTEGRANTS

Seven basic categories of disintegrants have been described by Peck et al., (1989:108-110): (1) Starches, (2) Celluloses, (3) Pyrrolidones, (4) Clays, (5) Algins, (6) Gums and (7) Miscellaneous. Table 1.1 summarizes the different categories of disintegrants.

**Table 1.1:** *Categories of disintegrants*

| Category | Chemical name | Trade name |
|---|---|---|
| Starches | Corn starch<br>Sodium starch glycolate<br><br>Pregelatinized starch | *<br>Explotab®<br>Primojel®<br>Starch 1500® |
| Celluloses | Microcrystalline cellulose<br><br>Carboxymethylcellulose<br>Croscarmellose sodium | Avicel ®<br>Emcocell®<br>*<br>Ac-Di-Sol® |
| Pyrrolidones | Crospovidone | Polyplasdone® XL<br>Kollidon® CL |
| Alginates | Alginic acid<br>Sodium alginates | |
| Clays | Magnesium aluminium silicate | Veegum® |
| Gums | | Agar<br>Guar<br>Karaya<br>Pectin |

### 1.5.1 Starches

Starch is the most common disintegrating agent available. It was once assumed that the function of starch as a disintegrant depended on its swelling when in contact with a liquid (Visavarungroj & Remon, 1990:125).

The swelling of starch grains observed by Ingram and Lowenthal (1966:614) does not seem to the authors to be a large enough change to cause tablets to rupture. They have attributed the activity of starch as disintegrant to intermolecular hydrogen bonding, which is formed during compression and is suddenly released in the presence of excess moisture.

Starches show a great affinity for water through capillary action, resulting in the expansion and subsequent disintegration of the compressed tablet. Formerly accepted theories of the mechanism of action of starches as disintegrants have been generally discounted. Lowenthal and Wood (1973:287) showed that the rupture of the surface of a tablet employing starch as a disintegrant occurred where starch agglomerates were found. The conditions best suited for rapid tablet disintegration are a sufficient number of starch agglomerates, low compression force, and the presence of water.

Starch shows a number of disadvantages when used in direct compression formulations. Visavarungroj and Remon (1990:125-127) showed that in general, higher levels of starch result in more rapid disintegration times. These high levels required and the lack of

compressibility often weakens tablet structure and results in a loss of bonding, cohesion and hardness in tablets (Lowenthal, 1972:1703). Therefore the development of new disintegrants that are effective at lower levels is of great importance in formulations for direct compression.

*Pregelatinized starch* is produced by the hydrolyzing and rupturing of the starch grain. It is directly compressible and its optimum concentration is 5 – 10%. The main mechanism of action is through swelling (Bandelin, 1989:174).

*Modified starch* – to have high swelling properties and faster disintegration, starch is modified by carboxymethylation followed by cross linking, giving cross-linked starch. Sodium starch glycolate (a low substituted carboxymethyl starch) is a modified starch with dramatic disintegrating properties, and is available as Explotab® and Primojel® (Peck *et al.*, 1989:109). One surprising fact about sodium starch glycolate is the range of permitted impurities. Since sodium starch glycolate may contain significant levels of other materials, it can be considered to be a "composite excipient" (Edge *et al.*, 2002:68).

While natural pre-dried starches swell in water to the extent of 10 – 25%, these modified starches increase in volume by 200 – 300% in water (Bolhuis *et al.*, 1982:112). Sodium starch glycolate has also been classified as a superdisintegrant (Marais *et al.*, 2003:125), it has outstanding water wicking capacity and good swelling properties. The mechanism by which action takes place involves rapid absorption of water leading to an enormous increase in volume of the disintegrant particles. The increase in volume results in rapid and uniform disintegration (Bandelin, 1989:175).

### 1.5.2 Celluloses

Celluloses, such as purified cellulose, methylcellulose, and carboxymethylcellulose are disintegrants to some extent, depending on their ability to swell in contact with water (Bandelin, 1989:177).

In September 1962 the preparation of cellulose in a microcrystalline form, called Avicel, which possesses many unique properties, was reported (Fox *et al.*, 1963:161). Along with the characteristic inertness and absorbent properties exhibited by most cellulose compounds, it is nonfibrous, free-flowing and possesses an extremely high surface area. *Microcrystalline cellulose* exhibits very good disintegrant properties when present at a level as low as 10%. It functions by allowing water to enter the tablet matrix by means of capillary

pores, which breaks the hydrogen bonding between adjacent bundles of cellulose micro crystals (Fox *et al,*. 1963:161).

*Croscarmellose sodium* (Ac-Di-Sol®) is a cross linked form of sodium carboxymethylcellulose (Ferrero *et al.*, 1997:18) unlike sodium carboxymethylcellulose, Ac-Di-Sol is essentially water insoluble, allowing the material to swell and absorb as many times its weight of water. It has a high affinity for water which results in rapid tablet disintegration (Peck *et al.*, 1989:109). Croscarmellose sodium has also been classified as a super disintegrant (Marais *et al.*, 2003:125).

### 1.5.3 Pyrrolidones

Cross-linked polyvinylpyrrolidone (Crospovidone) is a cross-linked polymer of vinylpyrrolidone formed under the influence of a special catalytic environment; It is highly insoluble in water (Kornblum & Stoopak, 1973:43-44). The authors have reported that the mechanism of action of cross-linked PVP depends greatly upon capillary effect in the presence of water, with a secondary swelling effect.

The interesting properties of cross-linked PVP stem from its ability at low concentrations (2 – 5 %) to bring about acceptable tablet disintegration as well as its inherent ability to function as a tablet binder. The tablets resulting from its use possess low percent friability characteristics (Kornblum & Stoopak, 1973:47). Cross-linked PVP also falls under the classification of super disintegrants (Marais *et al.*, 2003:125).

### 1.5.4 Alginates

Alginates are hydrophilic colloidal substances extracted from certain species of kelp. They demonstrate a great affinity for water, which may even exceed that of corn starch, as well as significant expansion and swelling properties. Alginic acid is commonly used at levels 1 – 5%, while sodium alginate is used between 2.5 – 10%. Unlike starch, microcrystalline cellulose and alginic acid, sodium alginate does not retard flow (Khan & Rhodes, 1972:48-49).

### 1.5.5 Clays

Clays such as Veegum® HV (magnesium aluminium silicate) have been used as disintegrants at levels ranging from 2 – 10%. The use of clays in white tablets is limited because of the tendency for tablets to be slightly discoloured. In general, clays do not offer

many advantages over the more common disintegrants, such as starches and celluloses (Peck *et al.*, 1989:109).

### 1.5.6 Gums

Gums have been used as disintegrants because of their tendency to swell in water. Common gums used as disintegrants include agar, guar, locust bean, Karaya, pectin and tragacanth. Available as natural and synthetic gums (Peck *et al.*, 1989:110).

### 1.5.7 Miscellaneous

Miscellaneous disintegrants include surfactants, natural sponge resins and effervescent mixtures (Peck *et al.*, 1989:110).

### 1.5.8 Super disintegrants

Super disintegrants is the name of a group of excipients known to be effective as disintegrants at very low levels (2 – 4%). The mechanism of action of these disintegrants is that of water uptake (liquid penetration) into the table, which causes the disintegrant particles to swell. This swelling results in a significant disintegrating force inside the tablet, causing rupture of the tablet structure (Bolhuis *et al.*, 1982:114) (Caramella *et al.*, 1987:2129).

According to Marais *et al.* (2003:125) disintegrants belonging to this group includes: (1) Croscarmellose sodium, type A (Ac-Di-Sol®), (2) Sodium starch glycolate (Explotab®) and (3) Cross-linked PVP (Kollidon® CL).

# CHAPTER 2

# 2 EXPERIMENTAL METHODS

This chapter deals with the choice of excipients used in this study. Experimental methods used throughout the study are explained and apparatus are described.

## 2.1 MATERIALS

The materials used in this study are represented in table 2.1.

**Table 2.1:** *Materials used in this study*

| Material | Lot number | Manufacturer |
|---|---|---|
| Avicel® PH 200 | M939C | FMC International, Wallingstown, Ireland |
| Ac-Di-Sol® | T017C | FMC |
| Explotab® | E8857X | Penwest Pharmaceuticals Co., Patterson, NY |
| Kollidon® CL | 30-1411 | BASF, Ludwigshafen, Germany |
| Sodium starch glycolate | SSGP0601 | Mirren (PTY)LTD |
| Potato starch | N91PSV | LABCHEM, Bardene, Boksburg |
| Emcompress® | C06D Pallet H | Penwest Pharmaceuticals Co., Mendell, UK |
| Tablettose® | 0116 | Meggle GmbH, Wasserberg, Germany |
| Magnesium stearate | ART5876 | Merck, Darmstadt, Germany |
| Pruv® | 30003103 | Penwest Pharmaceuticals Co., Mendell, UK |

## 2.2 METHODS AND APPARATUS

### 2.2.1 Mixture preparation

The composition of various mixtures used in this study is presented in table 2.2. Each formulation was prepared in a 250 $cm^3$ glass honey jar and mixed in a Turbula®-mixer, model T2C (W.A. Bachofen, Basel, Switzerland) for 5 minutes at 69 rpm.

**Table 2.2:** *Formulation components.*

| Component | Function | Amount per mixture |
|---|---|---|
| Emcompress® | Filler | 150mg |
| Tablettose® | Filler | 150mg |
| Ac-Di-Sol® | Disintegrant | 0.5 – 1.0 % |
| Explotab® | Disintegrant | 0.5 – 1.0 % |
| Magnesium Stearate® | Lubricant | 0.5 – 1.0 % |
| Pruv® | Lubricant | 0.5 – 1.0 % |

In order to compare the swelling, disintegration and water uptake of different disintegrants, tablets of each of the following materials were compressed: Avicel® PH 200, Kollidon® CL, sodium starch glycolate, potato starch, Ac-Di-Sol® and Explotab®.

### 2.2.2 Compression of compacts and tablets

Two different tablet presses were used in this study:

1. A modified IR press (Marais, 2000:66).
2. A Cadmach® single station press.

#### 2.2.2.1 Modified IR press

For compacts compressed on the modified IR press, compression forces ranging from 15 – 21 bars were used. The compression unit consisted of a top plunger, a metal pellet, an 8 mm steel die and a round metal base plate (figure 2.1).

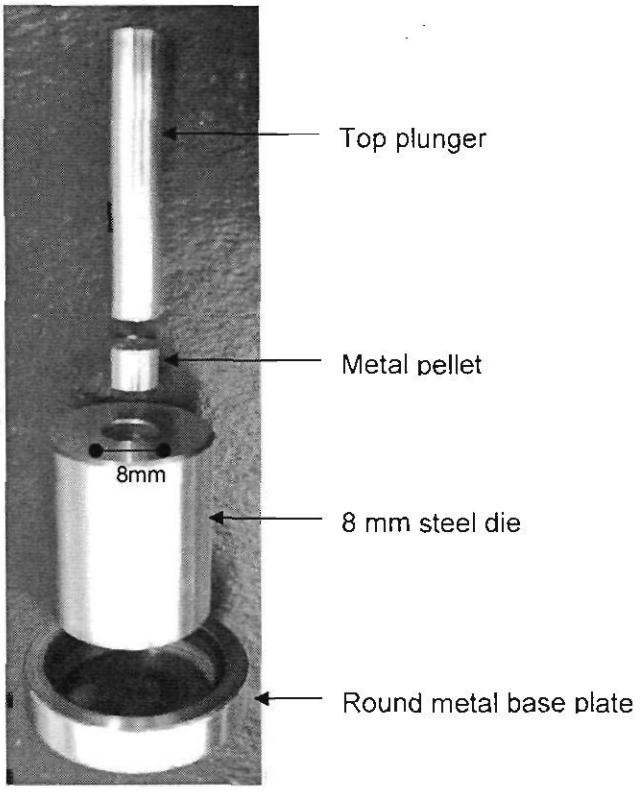



**Figure 2.1:** *The different parts of the compression unit.*

Flat faced compacts with a diameter of 8 mm were prepared on the IR press according to the following procedure (Marais, 2000:66).

A steel die with an opening of 8 mm were used for compression. The die was inserted into a round metal base plate to secure the die and ensure that no movement of the die was allowed during compression. The bottom opening of the die was then sealed by inserting a metal pellet into the die. A weight of 200 mg of each of the pure disintegrants was transferred to the die for each compact compressed.

The top plunger was inserted into the top opening of the die and slightly pressed down into the die. The unit was then placed on the base of the IR press and the plunger screw was then adjusted to touch the top plunger (Figure 2.2).

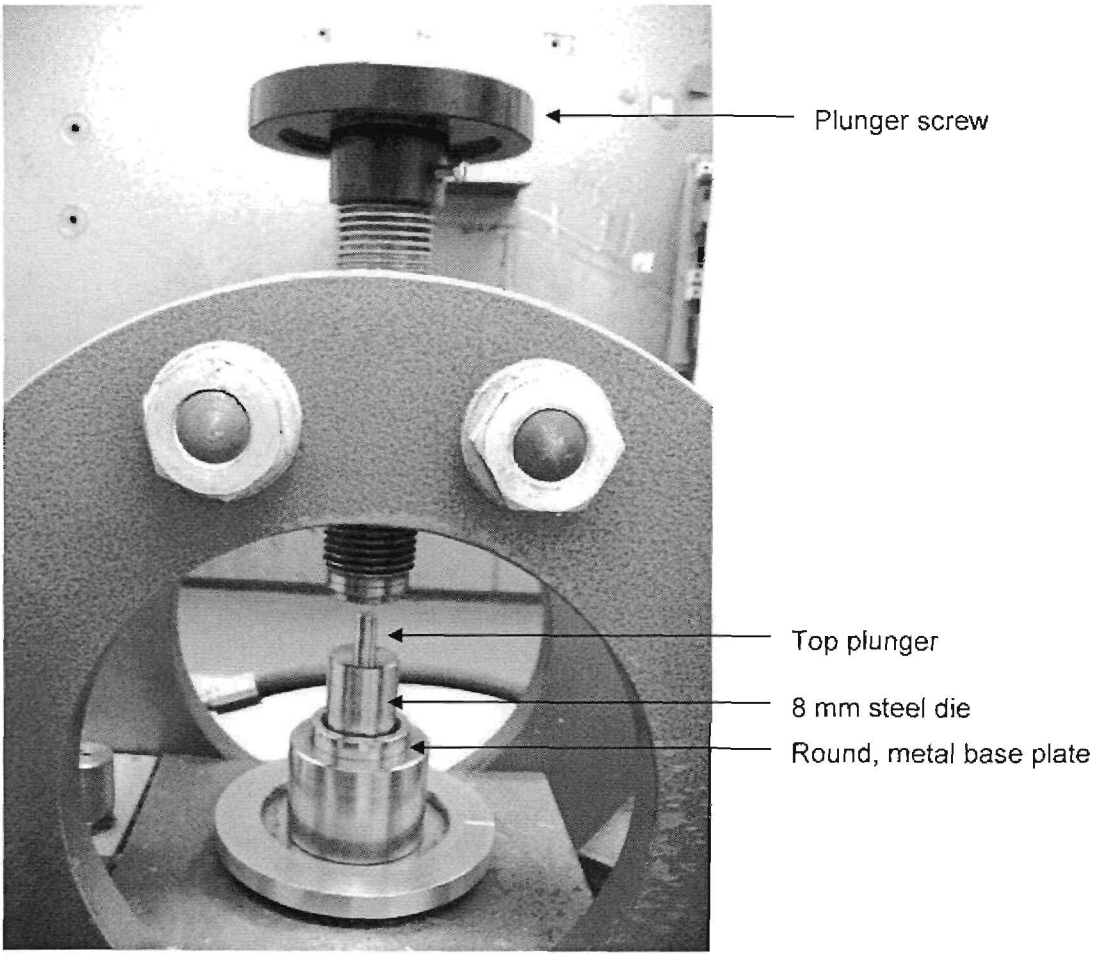



**Figure 2.2:** *The compression unit.*

The pressure exerted was manually adjusted to the required pressure by turning the knob of the hydraulic unit. A compression process was initiated from the computer. The pressure exerted onto the powder inside the die increased to the set compression force, and was kept at set compression force for 30 seconds, after which pressure dropped to zero and compression stopped.

During compression the forces exerted on the powder was measured continuously and were logged on the computer. This data was used to calculate the average compression force exerted on each tablet. The compression forces for different disintegrants varied according to the compressibility of the disintegrant. A summary of compression forces used for different disintegrants are given in table 2.3.

**Table 2.3:** *Compression forces used to prepare disks of each pure disintegrant.*

| Disintegrant | Average compression forces | | | | | | |
|---|---|---|---|---|---|---|---|
| | 15 | 16 | 17 | 18 | 19 | 20 | 21 |
| Avicel PH200® | X | X | X | X | | | |
| Ac-Di-Sol® | X | X | X | X | | | |
| Explotab® | | | | X | X | X | X |
| Kollidon CL® | | X | X | X | X | | |
| Sodium starch glycolate | | | | X | X | X | X |
| Potato Starch | | X | X | X | X | | |

The compact was then manually pushed from the die using the plunger. Tablets were stored at room temperature inside a glass honey jar for a minimum of 24 hours before testing.

#### 2.2.2.2 Cadmach® single station press

Mixtures from the various formulations including a filler, disintegrant (0.5 and 1.0%) and lubricant (0.5 and 1.0%), were compressed on a Cadmach® single station press. Flat faced punches with a diameter of 8 mm were used. For all tablet formulations the filling volume of the die were kept constant. Two compression settings were used to evaluate the effect of compression force on tablet disintegration and crushing strength. Compression force was manipulated by changing the depth of movement of the upper punch into the die during the compression cycle. Since the filling volume of the die was kept constant during compression, the deeper movement of the punch into the die represents a higher compression force exerted. The movement of the upper punch is regulated by a scale ranging from 0 – 35, with the setting on 35 presenting the deepest movement into the die during compression. Settings used to compare tablets were 1 (the smallest setting where acceptable tablets were obtained) and 7 (the highest setting where acceptable tablets were obtained).

The first five tablets of each compressed batch were not included in the testing of tablets. Tablets were stored in glass honey jars at room temperature for a minimum of 24 hours before testing.

## 2.3 EVALUATION OF TABLET PROPERTIES

### 2.3.1 Crushing strength

The average crushing strength for each formulation as well as for pure disintegrant compacts was determined by testing 10 tablets of each. Apparatus used was a Pharma Test® tablet testing unit (model PTB-311, Hainburg, West-Germany).

### 2.3.2 Disintegration time

The disintegration time of six tablets of each formulation as well as tablets compressed from disintegrants only, was determined using a 3 station Erweka ZT503 disintegration apparatus (Erweka Apparatbau GmBH, Hausenstamm, Germany). The disintegration medium was distilled water, and the temperature was kept at 37 ± 0.5 °C. The times at which all particles of the tablet were able to move through the sieve at the bottom of each test tube, were noted. A limit of 15 minutes (900 seconds) was employed.

### 2.3.3 Swelling and water uptake

A device (see figure 2.3 and 2.4) was developed to measure the amount of water absorbed by tablets and the subsequent swelling of the particular tablet (Buys, 2006:60).

The tablet with an 8 mm diameter is placed into the 8 mm wide cylindrical shaft with the gauge, measuring the depth of the plunger, fitted on top. A chamber holding water with a membrane fixed on top of the chamber was connected to a glass tube leading into a glass container on an electronic balance. The glass container on the balance was filled with water, allowing capillary uptake of water through the membrane of the water chamber. The device holding the tablet was then placed on top of the water holding chamber with a film between the membrane and tablet, avoiding water uptake until the experiment starts. The plunger was lowered to touch the top of the tablet, with the gauge reading a value of 0 mm. At time (t = 5 sec) the film between the tablet and the water chamber membrane was removed. The weight of water absorbed by the tablet was measured by the balance and recorded onto the computer every second.

The swelling of the tablet was measured by recording the gauge movement on a video camera. The video was then played back in slow motion on the video editing programme Studio Launcher, and the swelling (in mm) was recorded for every second.

The total swelling (mm) of each tablet and the total amount of water (ml) absorbed by the tablet was used to compare formulations and disintegrants.

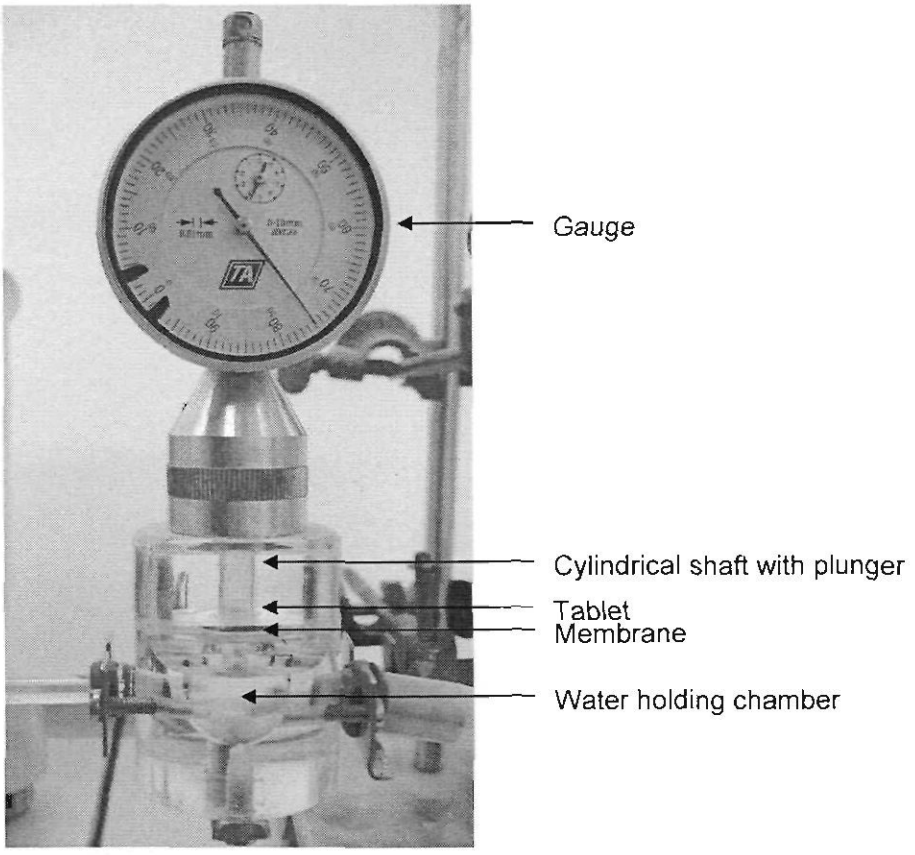



**Figure 2.3:** *The measuring device used to determine swelling and water uptake.*

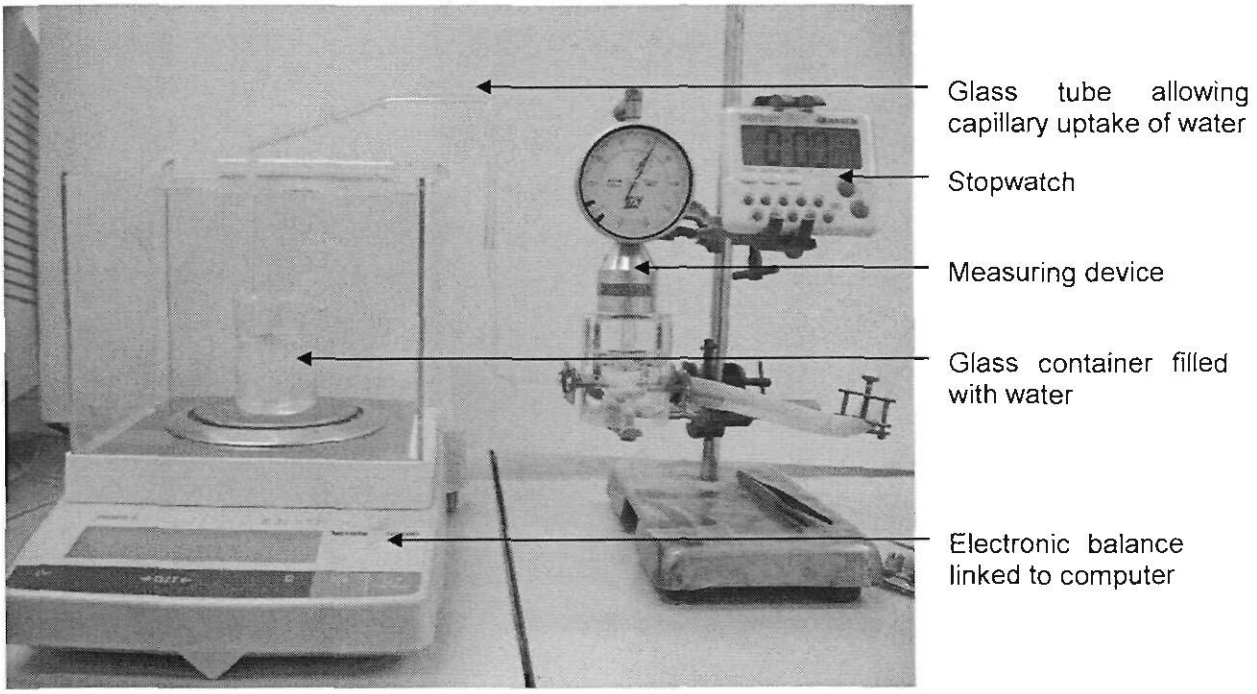


**Figure 2.4:** The setup used for determining swelling and water uptake.

## 2.4 CALCULATIONS

### 2.4.1 Theoretical porosity

The porosity of a powder is defined as the proportion of a powder bed that is occupied by pores. Therefore, the porosity could be considered as the packing efficiency of a powder inside the compact (Martin, A. 1993:444). The theoretical porosity of each compact was calculated by means of the following equation:

$$\varepsilon = \left(1 - \frac{\rho_C}{\rho_T}\right) \times 100$$

Where:

$\epsilon$ = Porosity (%), $\rho_C$ = Compact density ($g.cm^{-3}$) and $\rho_T$ = True density ($g.cm^{-3}$).

The density of compacts was calculated by means of the following equation:

$$\rho_C = \frac{w}{v_C}$$

Where:

$\rho_C$ = Compact density ($g.cm^{-3}$), $W$ = weight (g) and $V_C$ = Compact volume ($cm^{-3}$).

### 2.4.2 Statistical processing of data

Statistical analysis was done using StatSoft, Inc. (2007). STATISTICA (data analysis software system), version 8.0. www.statsoft.com. A 6-way variance analysis with main effects based on a fraction factorial design with 16 combinations was used.

### 2.4.3 General calculations

All of the calculations were done using the Microsoft® Office Excel® XP package for Windows® XP (Microsoft Corporation, Seattle, Washington, USA).

# CHAPTER 3

## 3 PROPERTIES OF PURE DISINTEGRANT COMPACTS

### 3.1 INTRODUCTION

The most common mechanism of action of disintegrants is considered to be swelling upon contact with liquid molecules (Kanig & Rudnic 1984:54). In order to confirm and assess this mechanism and to compare the disintegration efficiency of various disintegrants in pharmaceutical formulations, the disintegration properties of the pure disintegrants have to be confirmed and quantified.

This chapter discusses the disintegration properties of the various disintegrants used in this study, especially in terms of their ability to absorb water (both the rate and extent), swell and disintegrate.

### 3.2 PROPERTIES OF PURE POTATO STARCH COMPACTS

Compacts of pure potato starch were prepared at different compression forces as described in section 2.2.2.1 and analysed as described in section 2.3. The results are presented in table 3.1 and the data in annexure A.1. At each compression force 5, swelling and water uptake "time points" have been identified, namely after 10, 20, 30, 40 and 50 seconds (noted as $T_{10}$, $T_{20}$, $T_{30}$, $T_{40}$ and $T_{50}$ respectively). The theoretical porosity of the compacts at the various compression forces was calculated as described in section 2.4.1.

**Table 3.1:** *Properties of pure potato starch compacts prepared at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression force (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **15.8 (0.90)** | | **16.7 (0.98)** | | **18.0 (0.89)** | | **19.1 (0.95)** | |
| Hardness (N) | 6.40 (26.4) | | 20.34 (11.72) | | 28.52 (18.66) | | 66.34 (33.70) | |
| Disintegration time (sec) | 25.14 (14.48) | | 14.61 (17.18) | | 36.52 (2.68) | | 170.22 (8.05) | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_{10}$ | 0.53 | 0.032 | 0.50 | 0.022 | 0.50 | 0.024 | 0.01 | 0.011 |
| $T_{20}$ | 0.66 | 0.042 | 0.67 | 0.035 | 0.66 | 0.038 | 0.05 | 0.014 |
| $T_{30}$ | 0.72 | 0.047 | 0.76 | 0.042 | 0.76 | 0.045 | 0.09 | 0.017 |
| $T_{40}$ | 0.75 | 0.050 | 0.82 | 0.046 | 0.81 | 0.050 | 0.11 | 0.019 |
| $T_{50}$ | 0.75 | 0.051 | 0.87 | 0.049 | 0.86 | 0.053 | 0.13 | 0.019 |
| Initial compact thickness (mm) | 3.56 (2.06) | | 3.19 (2.11) | | 3.03 (1.18) | | 2.96 (1.73) | |
| Total swelling (%) | 11.09% | | 27.76% | | 28.62% | | 4.31% | |
| Porosity (%) | 25.6 (5.58) | | 17.3 (6.94) | | 13.1 (8.15) | | 10.1 (14.8) | |

The data showed an expected increase in compact hardness as a function of compression force which sharply increased above 18 N and which was accompanied by a marked increase in disintegration time above this compression force (figure 3.1).

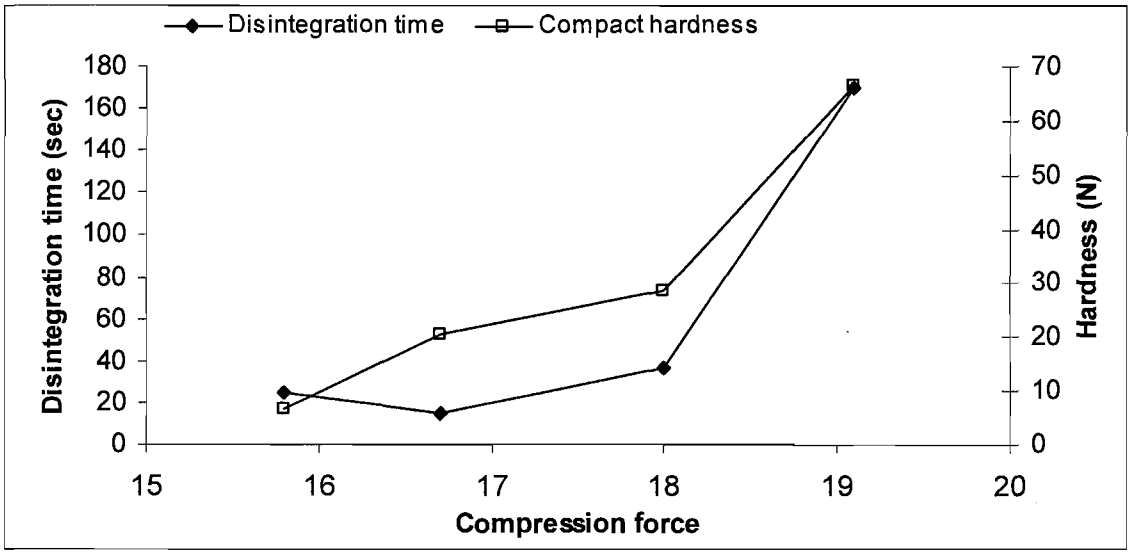



**Figure 3.1:** *The disintegration time and hardness of potato starch compacts at various compression forces.*

The initial decrease in the disintegration time may be explained in terms of the effective uptake of water into the porous network of the compact, by capillary action. The porosity of compacts compressed at 15.8 N (25.6%) might not have been sufficient for capillary action inside the compact. Compacts compressed at 16.7 N possessed a lower porosity (17.3%),

thus resulting in better uptake of water by capillary action. At compression forces higher than 16.7 N, the reduced porosity inside the compacts markedly reduced both the rate and extent of water uptake. This could also be concluded from the data in table 3.1 which indicates that at a compression force of 16.7 N swelling was at a maximum of 0.87 mm compared to 0.75 mm at 15.8 N. As the compression force increased, the penetration rate of water into the compact decreased due to a further decrease in compact porosity. Consequently, the swelling rate and the development of an effective disintegration force were retarded, resulting in an increase in the disintegration time of the compacts. These results confirmed that the efficacy of a moderate swelling disintegrant, like potato starch, is highly dependent on contact with aqueous media.

Figures 3.2 and 3.3 show the time course of water uptake and swelling of potato starch compacts at different compression forces respectively. The graphs clearly show an initial rapid water uptake and swelling over the first 10 to 15 seconds, followed by a gradual levelling off until a plateau was reached at approximately 50 seconds. For compacts compressed at 19.1 N both the water uptake and swelling were markedly lower compared to the results obtained at lower compression forces. This illustrated the negative effect of an increase in compression force on both water uptake and swelling, especially above a "critical" compression force (in this case 18.0 N). For instance, at 19.1 N the water uptake was only 37.25% compared to the uptake achieved at 15.8 N, whilst the swelling was only 17.33% (0.13 mm compared to 0.75 mm). These results confirmed the dependency of water uptake on compression force. With an increase in compression force, particles were compressed more tightly, thus reducing inter-particular voids (compact porosity), which decreased the extent and rate of water uptake, resulting in less and slower swelling.

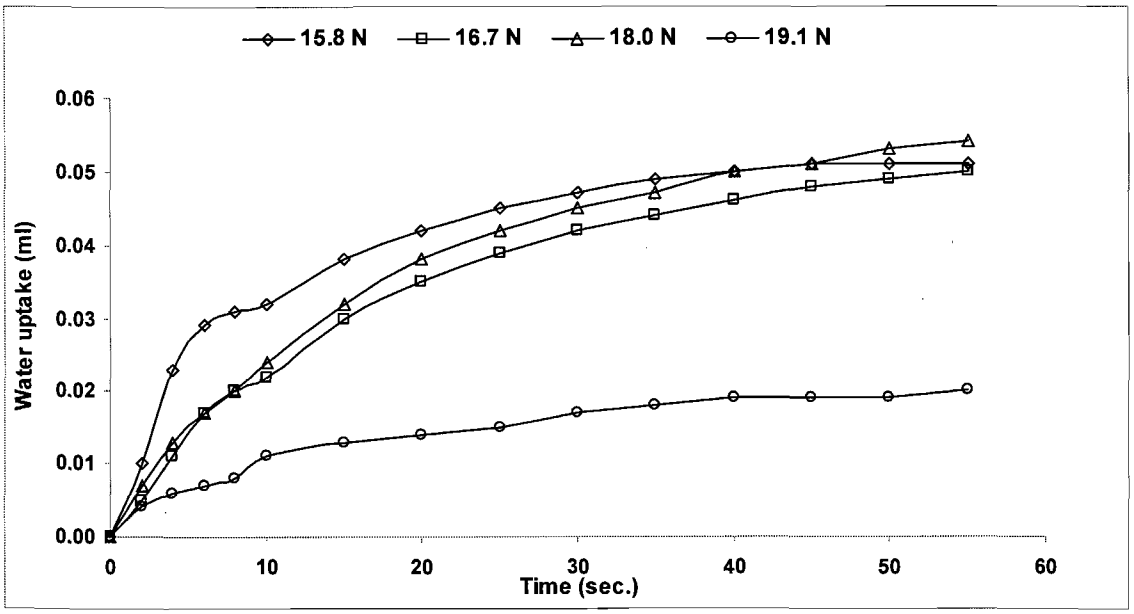



**Figure 3.2:** *The water uptake of pure potato starch compacts at various compression forces.*

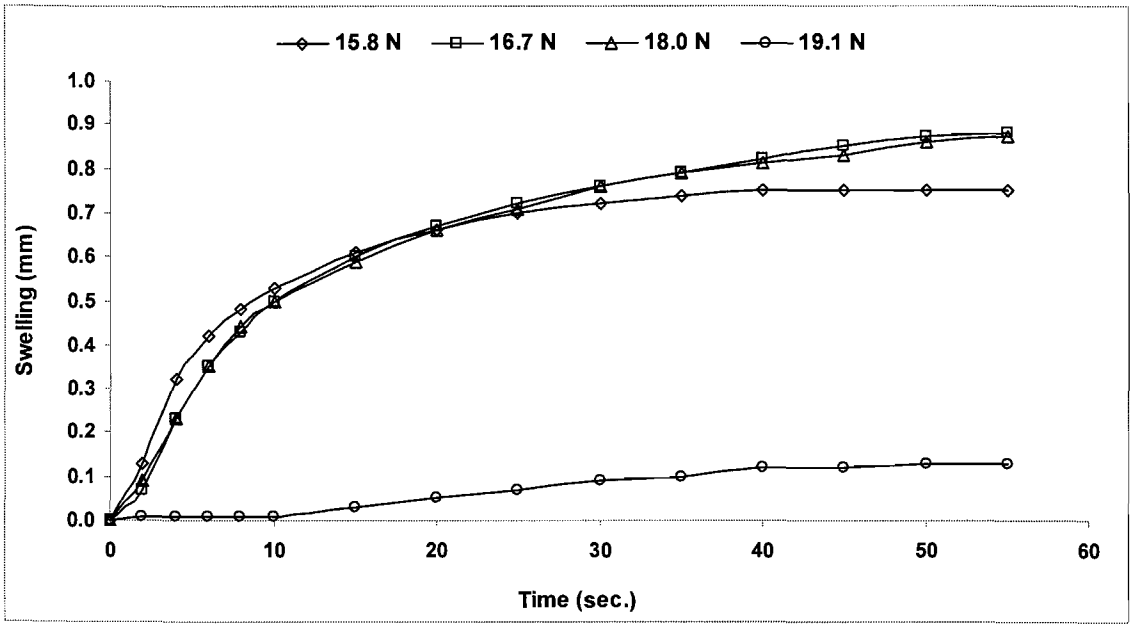



**Figure 3.3:** *The swelling of pure potato starch compacts at various compression forces.*

Careful consideration of the data suggested a definite relationship between swelling and water uptake over the compression force range employed. Figure 3.4 presents a clear picture of the relationship. The correlation coefficient of the lines between $T_{10}$ and $T_{50}$ at each compression force ($r^2$ >0.993) confirmed the direct proportionality between swelling and water uptake. Forcing the lines through the origin (at $T_0$) reduced the linearity, but provided a better estimate of the real slope of the lines, which corresponded to the rate constant of the

process. It was evident that the rate constants at compression forces up to 18 N were of the same magnitude (15-18 $mm.ml^{-1}$), but significantly decreased at 19 N (5.4 $mm.ml^{-1}$) due to prevention of water penetration into the compact at this compression force as a result of the decrease in the porosity of the compact.

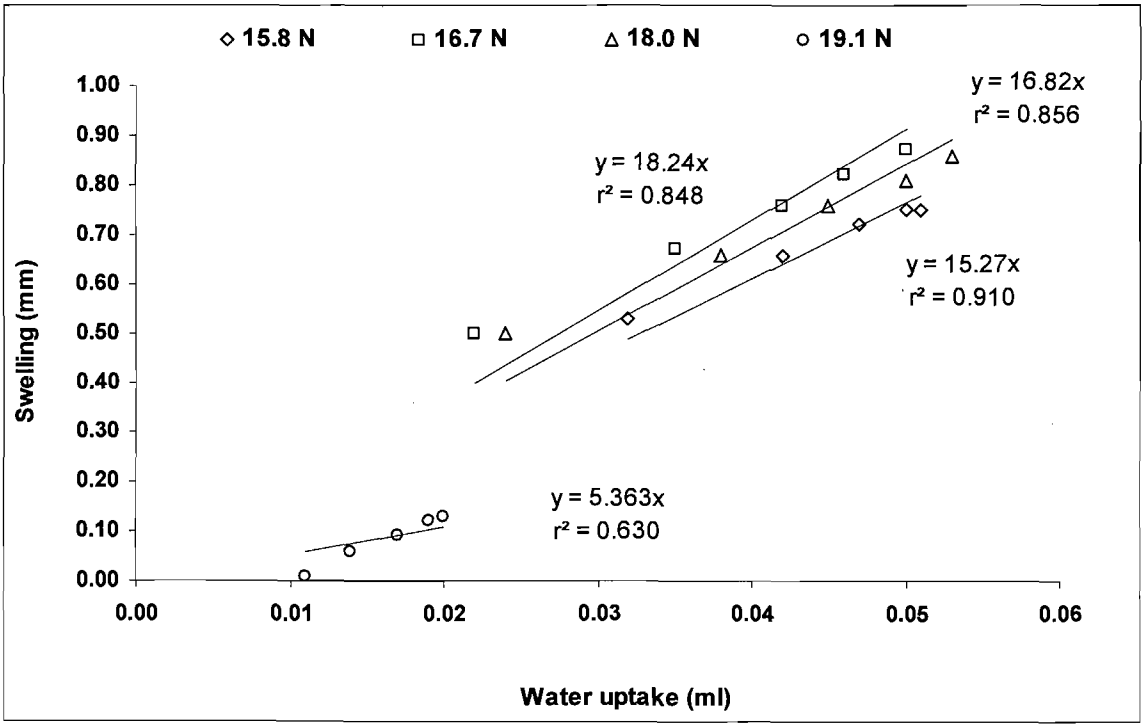



**Figure 3.4:** *The relationship between swelling and water uptake in potato starch compacts at various compression forces.*

To further explore this relationship, a factor relating swelling to water uptake, and noted as SWU, was determined using the time points ($T_{10}$ to $T_{50}$) in table 3.1. The values are presented in table 3.2.

**Table 3.2:** *Swelling-Water uptake factors (mm/ml) for potato starch at various compression forces.*

| Time point | Compression force (N) | | | |
|---|---|---|---|---|
| | 15.8 | 16.7 | 18.0 | 19.1 |
| $T_{10}$ | 16.56 | 22.73 | 20.83 | 0.91 |
| $T_{20}$ | 15.71 | 19.14 | 17.37 | 4.14 |
| $T_{30}$ | 15.32 | 18.10 | 16.89 | 5.29 |
| $T_{40}$ | 15.00 | 17.83 | 16.20 | 6.32 |
| $T_{50}$ | 14.71 | 17.40 | 16.23 | 6.50 |

The magnitude of the SWU factor indicates the swelling (mm) of a compact per unit volume (ml) of liquid, and the higher the value the more efficient the swelling behaviour of the material. The detrimental effect of compression force on the SWU factor is clearly visible

from the data. At 19.1 N the factor only reached a maximum of approximately 6, compared to the values at the other compression forces in the range of 14 to 17. At compression forces between 15 and 18.0 N the factor gradually decreased with time, which indicates a reduction in swelling compared to water uptake. Conversely, at 19.1 N swelling increased compared to water uptake with time resulting in an increase in the SWU factor. This could possibly be due to the capillary effect of water inside the compact structure.

Considering the results obtained for compacts of potato starch, it is unlikely that the disintegrating action of potato starch can be attributed to swelling alone. Although swelling did occur to some extent, it did not seem to be a large enough change to cause tablets to rupture as stated by Ingram and Lowenthal (1966:614). The authors have attributed the activity of starch as disintegrant to intermolecular hydrogen bonding which is formed during compression and is suddenly released in the presence of excess moisture. These statements were confirmed by the low percentage of swelling of compacts, considering the low disintegration times. It is unlikely that a swelling of only 11.09 % could lead to the disintegration of a compact within 25 seconds at a compression force of 15.8 N, considering the high porosity (26.3 %) of the compact.

The results clearly showed that the efficacy of starch as disintegrant is largely dependent on contact with water molecules, and that any factor which reduced / retarded this contact (like compression force) could be detrimental to its action. The efficiency of the material as a disintegrant could, however, only be judged and ranked when the properties of the other materials used in this study were carefully examined and studied.

## 3.3 PROPERTIES OF PURE SODIUM STARCH GLYCOLATE COMPACTS

Sodium starch glycolate (SSG) is a cross-linked starch with superior disintegration properties compared to the natural starches (Peck *et al.*, 1989:109). It is available on the market under its general name, sodium starch glycolate, or under various trade names, including Explotab® (Penwest Pharmaceuticals Co.)

Compacts of pure SSG and Explotab® were prepared at different compression forces as described in section 2.2.2.1 and analysed for hardness, disintegration time, water uptake and swelling as described in section 2.3. The results are presented in table 3.3 and 3.4 and the data in annexure A.2 and A.3 respectively.

**Table 3.3:** *Properties of pure sodium starch glycolate compacts prepared at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression force (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **17.9 (1.03)** | | **18.9 (0.75)** | | **19.9 (0.58)** | | **21.0 (0.46)** | |
| Hardness (N) | - | | 14.22 (39.70) | | 28.58 (17.29) | | 30.5 (14.64) | |
| Disintegration time (sec) | 29.71 (17.35) | | 32.87 (18.44) | | 166.76 (13.11) | | 130.43 (6.92) | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_{10}$ | 1.50 | 0.119 | 1.78 | 0.115 | 1.67 | 0.093 | 1.90 | 0.095 |
| $T_{20}$ | 2.08 | 0.169 | 2.44 | 0.159 | 2.60 | 0.153 | 3.09 | 0.167 |
| $T_{30}$ | 2.33 | 0.193 | 2.61 | 0.180 | 2.73 | 0.173 | 3.14 | 0.181 |
| $T_{40}$ | 2.36 | 0.219 | 2.61 | 0.203 | 2.78 | 0.195 | 3.14 | 0.201 |
| $T_{50}$ | 2.42 | 0.242 | 2.61 | 0.222 | 2.84 | 0.217 | 3.14 | 0.220 |
| Initial compact thickness (mm) | 3.02 | | 2.91 | | 2.84 | | 2.83 | |
| Total swelling (%) | 80.43% | | 89.50% | | 108.45% | | 110.91% | |
| Porosity (%) | 15.0 (20.09) | | 6.0 (10.10) | | 0.6 (91.87) | | 2.1 (15.07) | |

**Table 3.4:** *Properties of pure Explotab® compacts at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression force (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **17.8 (0.58)** | | **18.8 (0.56)** | | **20.0 (0.92)** | | **20.9 (0.48)** | |
| Hardness (N) | 16.42 (24.79) | | 33.02 (51.46) | | 61.44 (22.16) | | 94.08 (27.17) | |
| Disintegration time (sec) | 50.73 (11.48) | | 57.82 (7.86) | | 87.53 (6.12) | | 135.75 (3.55) | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_{10}$ | 0.43 | 0.039 | 0.50 | 0.036 | 0.93 | 0.057 | 0.42 | 0.041 |
| $T_{20}$ | 0.56 | 0.055 | 0.75 | 0.053 | 1.07 | 0.070 | 0.46 | 0.053 |
| $T_{30}$ | 0.54 | 0.064 | 0.87 | 0.064 | 1.13 | 0.079 | 0.47 | 0.061 |
| $T_{40}$ | 0.55 | 0.071 | 0.96 | 0.071 | 1.17 | 0.084 | 0.47 | 0.066 |
| $T_{50}$ | 0.55 | 0.076 | 1.03 | 0.077 | 1.19 | 0.087 | 0.47 | 0.068 |
| Initial compact thickness (mm) | 3.42 | | 3.25 | | 3.15 | | 2.92 | |
| Total swelling (%) | 16.00% | | 34.50% | | 38.04% | | 16.07% | |
| Porosity (%) | 25.6 (4.96) | | 20.8 (8.37) | | 16.0 (6.43) | | 12.6 (10.50) | |

Both materials showed an expected increase in compact hardness with an increase in compression force, but the compressibility of SSG was much lower compared to that of Explotab®. Explotab® showed a much higher sensitivity to compression force compared to the SSG in terms of compact hardness. The hardness of Explotab® compacts increased almost 3-fold over a compression force range of 19 to 21 N, whereas the increase in the hardness of SSG compacts were only 2-fold. Compared to natural potato starch, however,

the hardness of the compacts of both materials were significantly lower at comparable compression forces, namely 18 and 19 N (compare values from table 3.1, 3.3 and 3.4).

Comparison of the physical properties of compacts of pure sodium starch glycolate and Explotab® showed marked differences. These differences could be attributed to the fact that sodium starch glycolate may contain significant levels of other materials (impurities) and it can be considered to be a "composite excipient" (Edge *et al.*, 2002:67). This potential range of impurities makes a direct comparison between sodium starch glycolates difficult due to the potential inter-batch and inter-brand variations. According to Bolhuis *et al.* (1984:25) swelling and water uptake are mainly controlled by the degree of substitution and the degree of cross linking and thus the molecular structure of sodium starch glycolate will determine its efficiency as a disintegrant. The water uptake capacity of carboxymethylated starches was strongly increased at low levels of cross-linking followed by a decrease at higher cross-linking. In addition, the degree of purity (sodium chloride content) may be expected to have an effect as well, the presence of sodium chloride seemed to reduce the swelling capacity. The difference in disintegrant behaviour between pure sodium starch glycolate and Explotab® might thus be attributed to the difference in molecular structure as observed by Rudnic *et al.*, (1985:647). Several workers have also described the importance of particle size distribution on the efficiency of some tablet disintegrants. Shah and Augsburger (2002:345) stated that the extent of liquid uptake and settling volume of sodium starch glycolate were observed to be higher for the smaller sieve fraction. Determining the average particle size for both sodium starch glycolate and Explotab® failed to show a significant difference between the materials.

A comparison of the disintegration times and theoretical porosity of compacts of the two materials at the different compression forces revealed marked differences in behaviour (figure 3.5). Explotab® compacts showed a gradual increase in disintegration time with an increase in compression force which was accompanied by a similar decrease in compact porosity. SSG compacts exhibited a sharp increase in disintegration time above 19 N, followed by a decrease at 21 N to a value comparable to that of the Explotab® compacts, whilst the porosity of the compacts gradually increase and then levelled off at 19 N. The disintegration profile of the Explotab® compacts coincided with that of the compression profile of the material, but the SSG compacts showed little comparison between disintegration time and compact hardness.

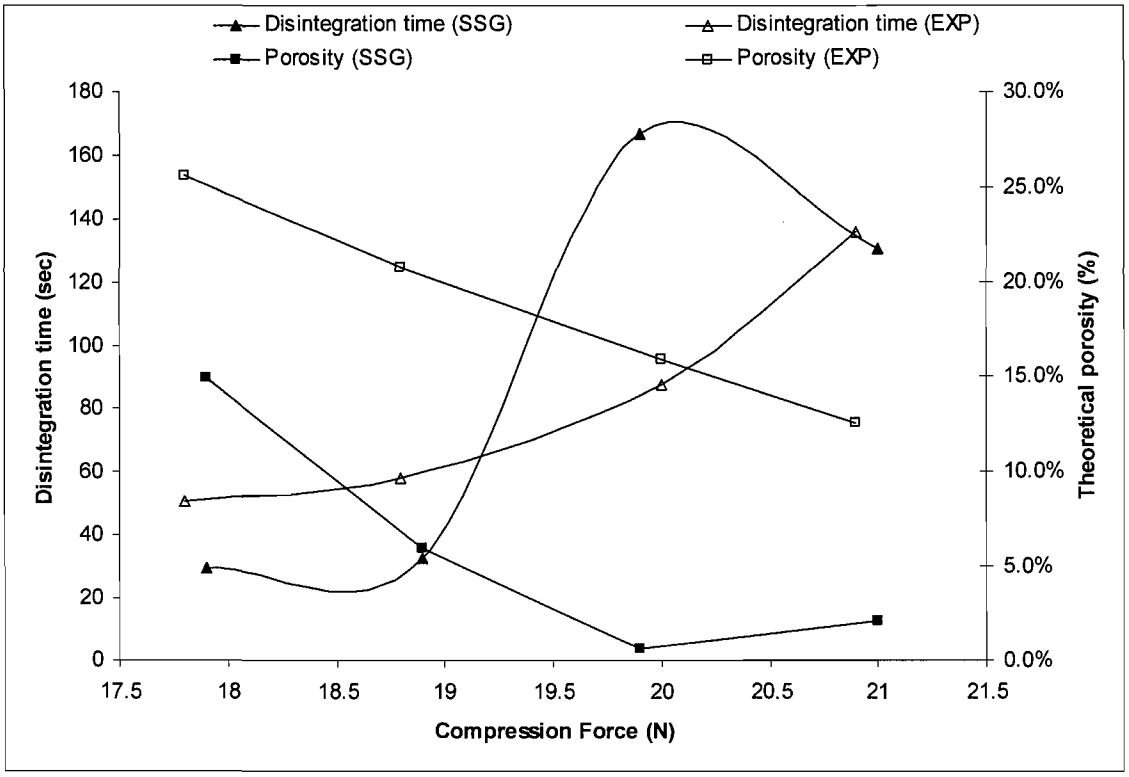



**Figure 3.5:** *The disintegration time and theoretical porosity of pure sodium starch glycolate and Explotab® compacts compressed at various compression forces.*

The water uptake and swelling behaviour of the two materials are presented in figure 3.6 and 3.7 respectively. From these graphs and the time points identified in table 3.3 it is obvious that the SSG compacts exhibited both significantly higher water uptake (figure 3.6) and swelling properties (figure 3.7) compared to the Explotab® compacts at each time point at every compression force. For a specific material, however, there were no significant differences between either the water uptake or the swelling at the different compression forces. On average the water uptake and swelling of the SSG compacts were respectively ±290 % and ±175 % higher compared to that of the Explotab® compacts.

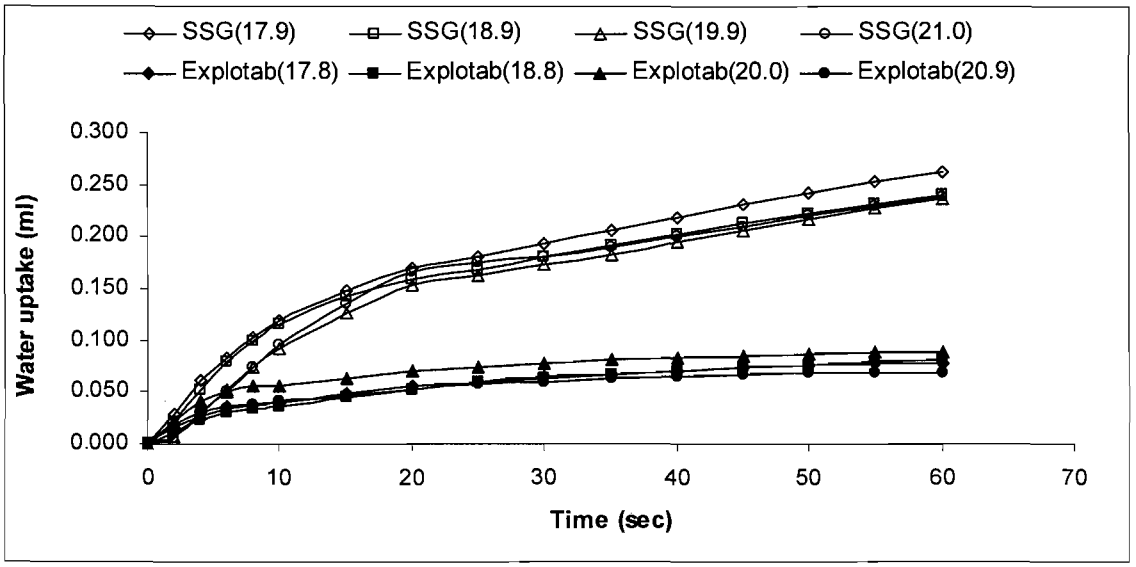



**Figure 3.6:** *The water uptake of pure sodium starch glycolate and Explotab® compacts at various compression forces.*

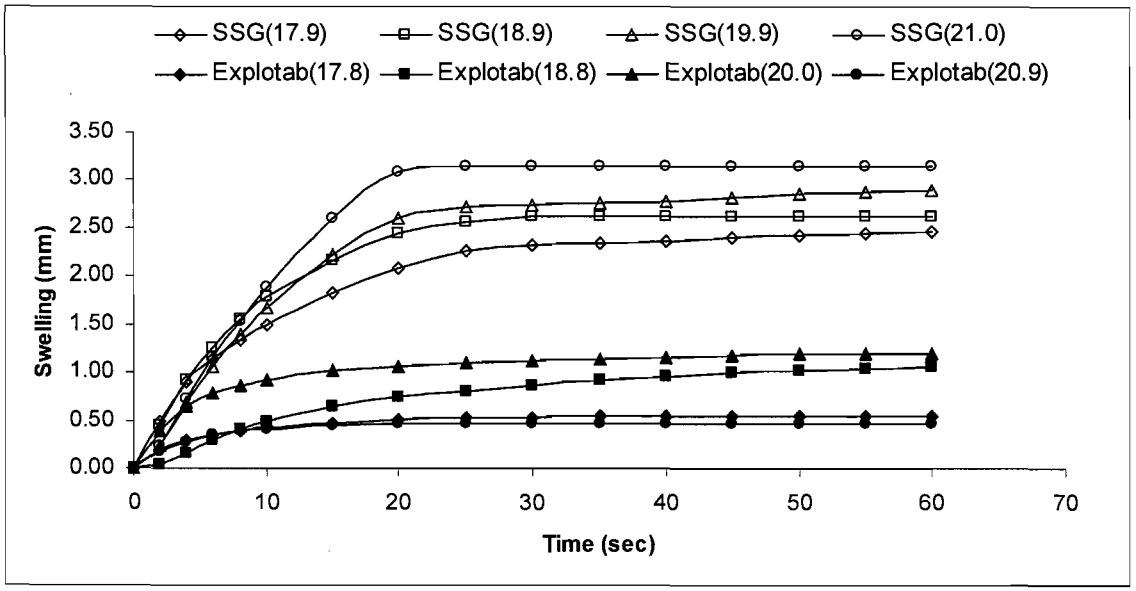



**Figure 3.7:** *The swelling of pure sodium starch glycolate and Explotab® at various compression forces.*

The data failed to demonstrate any clear relationship between water uptake and compression force or between swelling and compression force for either material, except in the case of the swelling of the SSG compacts where swelling increased as the compression force increased.

As in the case of potato starch, the relationship between water uptake and swelling of each material at a specific compression force was examined. The results are presented in figure

3.8 and 3.9 for SSG and Explotab® respectively. Comparison of the swelling of the compacts as a function of water uptake showed a noticeable difference in behaviour between SSG and Explotab®.

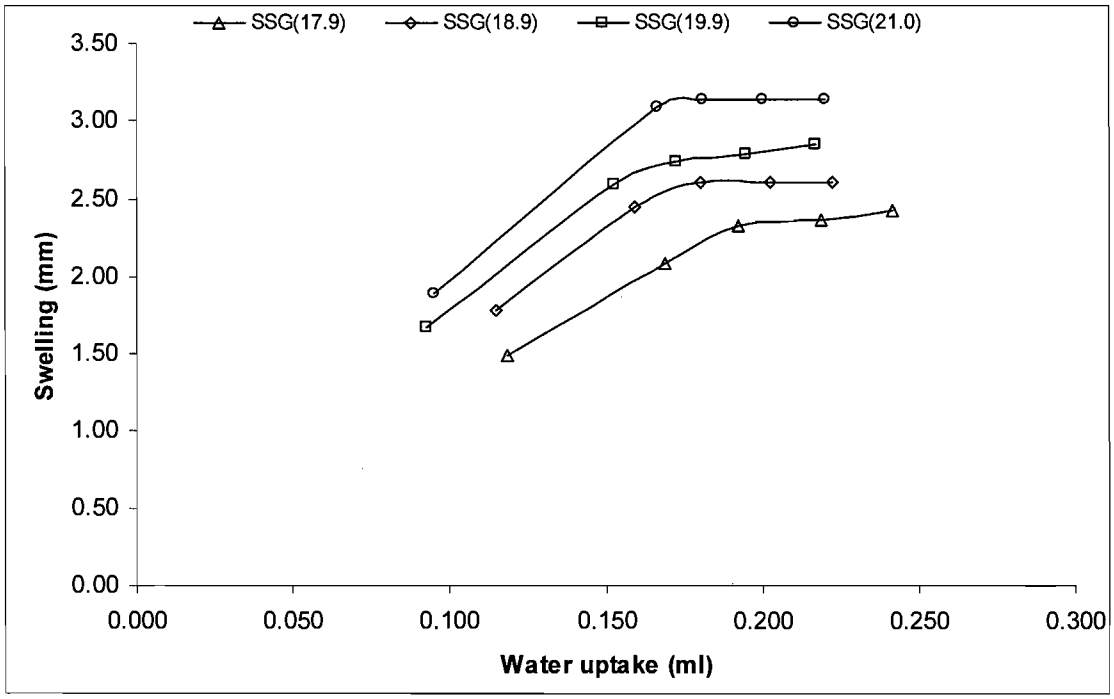



**Figure 3.8:** *The relationship between swelling and water uptake in pure sodium starch glycolate compacts at various compression forces.*

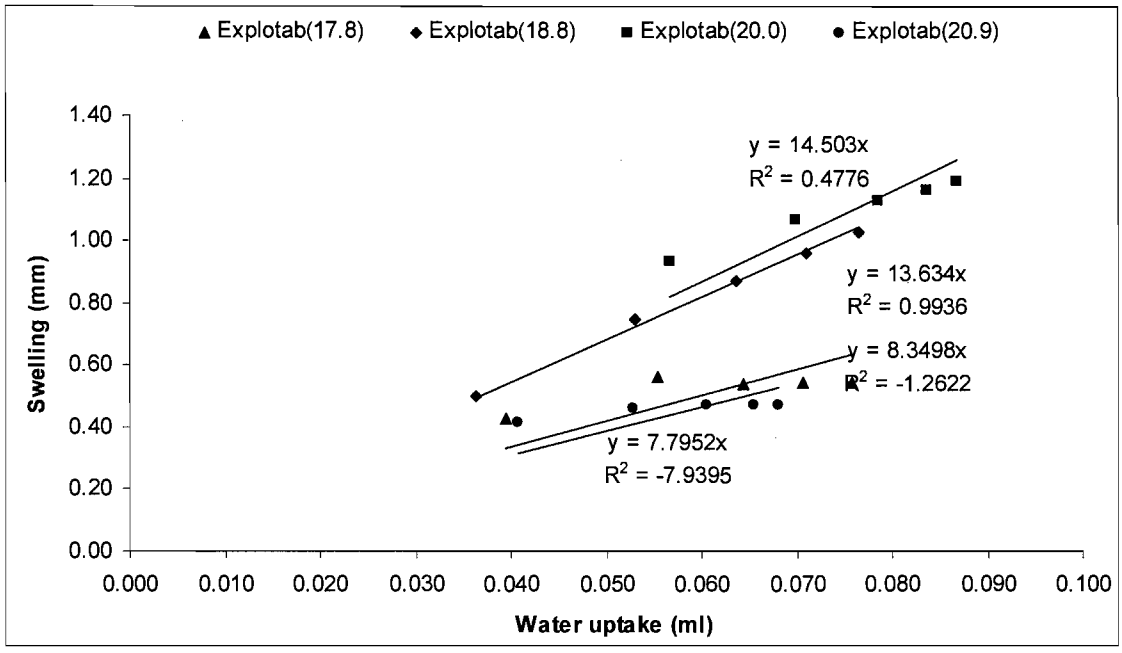



**Figure 3.9:** *The relationship between swelling and water uptake in Explotab® compacts at various compression forces.*

In contradiction with the behaviour of potato starch (figure 3.4) and Explotab® (figure 3.9), no direct relationship between water uptake and swelling could be established for SSG. The SSG compacts, however, exhibited a similar trend at all compression forces, with an initial increase in swelling with water uptake, which led to a plateau where swelling remained constant although water uptake continued (figure 3.8). As compression force increased, the location of the plots shifted upwards, which indicated a higher degree of swelling with the same amount of water uptake. There seems to be no indication of a direct relationship between swelling and water uptake of Explotab® compacts at compression forces of 17.8 and 20.9 N, however, for compacts compressed at a compression force of 18.8 and 20.0 N swelling seems to be directly proportionate to water uptake with correlation coefficients of 0.9956 and 0.9909 respectively (figure 3.9), when lines were not forced through the origin (at $T_0$). Linearity was reduced when the lines were forced through the origin, but a better estimate of the rate constant of the process could be established.

The SWU-factor was determined for pure sodium starch glycolate and Explotab®. The values are presented in table 3.5. The results clearly showed that the factor gradually decreased with time, which indicates that swelling slowed down compared to water uptake. Explotab® compacts showed an increase in the factor as compression force increased to 20.0 N, after which void space within the compact is reduced as compression force increases and swelling and water uptake are impaired.

**Table 3.5:** *Swelling-Water uptake factors (mm/ml) for sodium starch glycolate and Explotab® at various compression forces.*

| Time points (sec.) | Average compression force (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **17.9** | **18.9** | **19.9** | **21.0** | **17.8** | **18.8** | **20.0** | **20.9** |
| | **Sodium starch glycolate** | | | | **Explotab®** | | | |
| $T_{10}$ | 12.62 | 15.51 | 17.99 | 19.95 | 10.81 | 13.68 | 16.47 | 10.29 |
| $T_{20}$ | 12.29 | 15.35 | 16.96 | 18.53 | 10.11 | 14.15 | 15.32 | 8.77 |
| $T_{30}$ | 12.1 | 14.47 | 15.83 | 17.31 | 8.39 | 13.71 | 14.39 | 7.77 |
| $T_{40}$ | 10.8 | 12.86 | 14.29 | 15.64 | 7.76 | 13.52 | 13.94 | 7.18 |
| $T_{50}$ | 10 | 11.74 | 13.1 | 14.27 | 7.23 | 13.42 | 13.74 | 6.91 |

Although both sodium starch glycolate and Explotab® satisfy the pharmacopoeial description of SSG, it could be stated that their disintegrant efficiency differed markedly. It could be stated that the mechanism of disintegrant action of sodium starch glycolate in general, is through the development of a disintegrating force as a result of water uptake followed by particle swelling. The observed differences in the water uptake and swelling behaviour of the

two materials could be attributed to the difference between their composition and particle size, but this needs further studies to substantiate.

## 3.4 PROPERTIES OF PURE MICROCRYSTALLINE CELLULOSE COMPACTS

Avicel® is prepared from cellulose in a microcrystalline form. Compacts of pure microcrystalline cellulose were prepared at different compression forces as described in section 2.2.2.1 and analysed as described in section 2.3. The results are presented in table 3.6 and the data in annexure A.4. An extra time point ($T_5$) has been identified, (namely after 5 seconds) for Avicel® compacts at each compression force due to the fact that after only 10 seconds the compacts have reached their maximum swelling.

**Table 3.6:** *Properties of pure Avicel® prepared at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression force (N) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **15.0 (0.79)** | | **16.1 (0.44)** | | **17.1 (0.79)** | | **18.0 (0.55)** | |
| Hardness (N) | 51.66 (5.96) | | 132.78 (5.25) | | 214.26 (10.73) | | 292.9 (5.97) | |
| Disintegration time (sec) | 13.73 (22.86) | | 149.85 (17.14) | | 900.00 | | 900.00 | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_5$ | 2.45 | 0.159 | 1.43 | 0.092 | 0.798 | 0.057 | 0.63 | 0.041 |
| $T_{10}$ | 3.03 | 0.240 | 2.13 | 0.133 | 1.12 | 0.078 | 0.89 | 0.055 |
| $T_{20}$ | 3.03 | 0.242 | 2.74 | 0.176 | 1.57 | 0.097 | 1.22 | 0.070 |
| $T_{30}$ | 3.03 | 0.242 | 2.75 | 0.179 | 1.82 | 0.117 | 1.46 | 0.086 |
| $T_{40}$ | 3.03 | 0.242 | 2.75 | 0.179 | 1.89 | 0.128 | 1.65 | 0.097 |
| $T_{50}$ | 3.03 | 0.242 | 2.75 | 0.179 | 1.92 | 0.132 | 1.78 | 0.107 |
| Initial compact thickness (mm) | 4.98 | | 3.82 | | 3.38 | | 3.15 | |
| Total swelling (%) | 60.87% | | 72.03% | | 57.46% | | 57.64% | |
| Porosity (%) | 48.2 (1.28) | | 31.8 (2.57) | | 23.1 (4.47) | | 16.3 (7.13) | |

Avicel® compacts exhibited an excellent compression profile with a linear increase in hardness with an increase in compression force ($R^2$>0.9999). The increase in disintegration time corresponded with an increase in compression force (and tablet hardness), which coincided with a decrease in tablet porosity (figure 3.10). At a compression force of 17 N and higher the disintegration times exceeded the set limit of 15 minutes (900 sec). According to Fox et al. (1963:161) the disintegration of microcrystalline cellulose tablets has been attributed to the entrance of water into the tablet matrix by means of capillary pores and the subsequent breaking of the hydrogen bonding between adjacent bundles of cellulose micro crystals. When compression force increased capillary porosity became smaller and disintegration time increased. Upon pressure the matchstick like bundles of micro crystals appear to line themselves up into layers. This arrangement decreases the bond distance between particles and further increases the inter-particle forces. At compression forces of 17 N and higher the tablet porosity has decreased to such an extent (less than 24%) that entrance of water into the compact matrix was noticeably reduced. Breaking of the strong H-bonds between individual particles were thus impeded which led to a subsequent reduction in particle swelling and disintegration time.

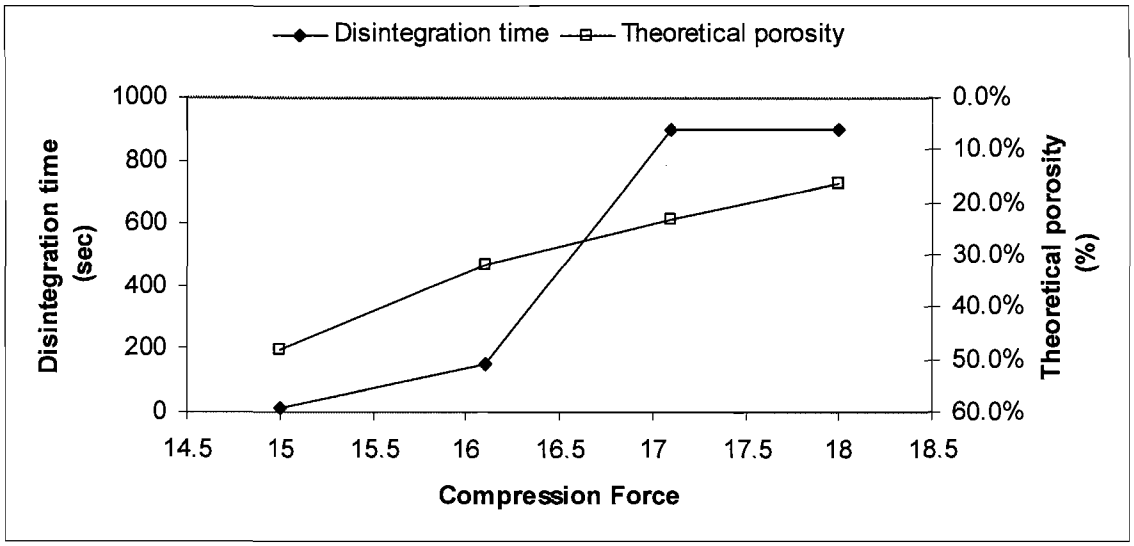



**Figure 3.10:** *The effect of compression force on the disintegration time and porosity of pure Avicel® compacts.*

Figure 3.11 and 3.12 show the water uptake and swelling of compacts of Avicel® at the different compression forces, respectively. Once again, a definite relationship between the two parameters was observed. When water uptake of a compact was low, swelling was proportionately retarded. At low compression forces water uptake was more sufficient, resulting in an increase in swelling of the compact. As compression force increased to 18 N, water uptake (of the compacts) was retarded by low porosity, and swelling subsequently decreased.

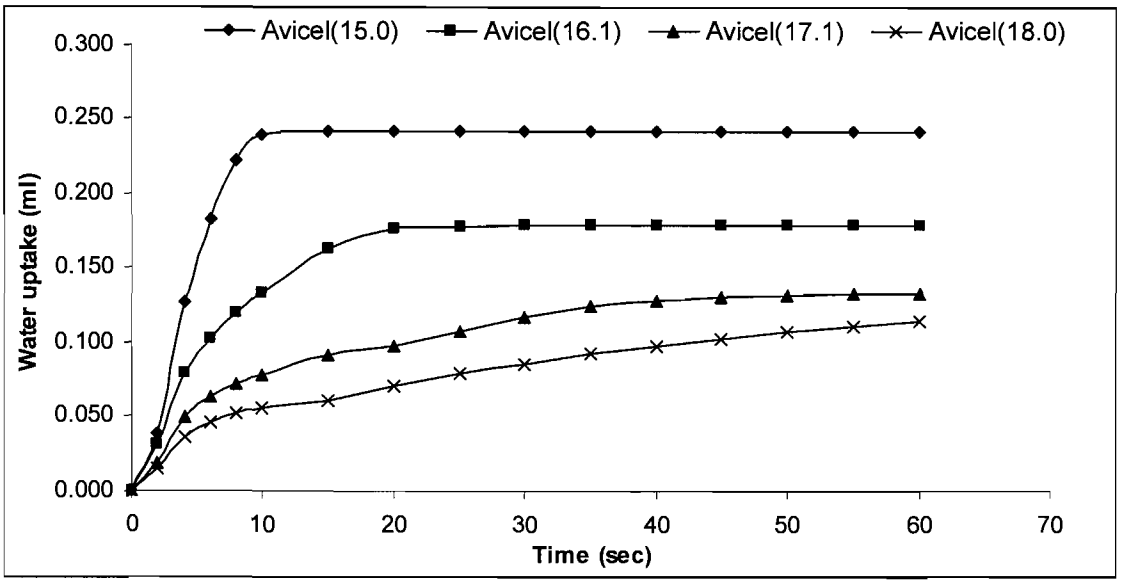



**Figure 3.11:** *The water uptake of compacts of pure* Avicel® *prepared at different compression forces.*

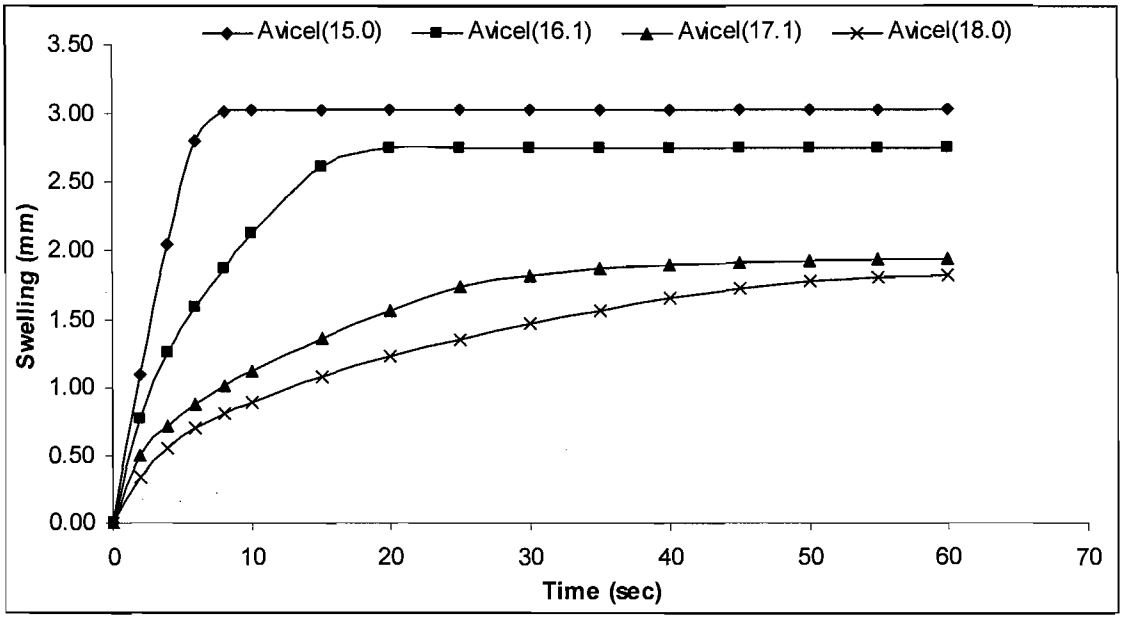



**Figure 3.12:** *The swelling of compacts of pure Avicel® prepared at different compression forces.*

The relationship between water uptake and swelling of the compacts is illustrated in figure 3.13. There seemed to be a direct proportionality between water uptake and swelling at each compression force indicated by $R^2$-values higher than 0.9779. The rate constant at the various compression forces (indicated by the slope of the line when forced through the origin) showed a slight increase with compression force, (from 12.7 to 16.8mm/ml). This result suggested that although the water uptake and subsequent swelling decreased with an increase in compression force, a higher compression force allowed for more effective swelling in terms of water uptake, although to a markedly lesser extent.

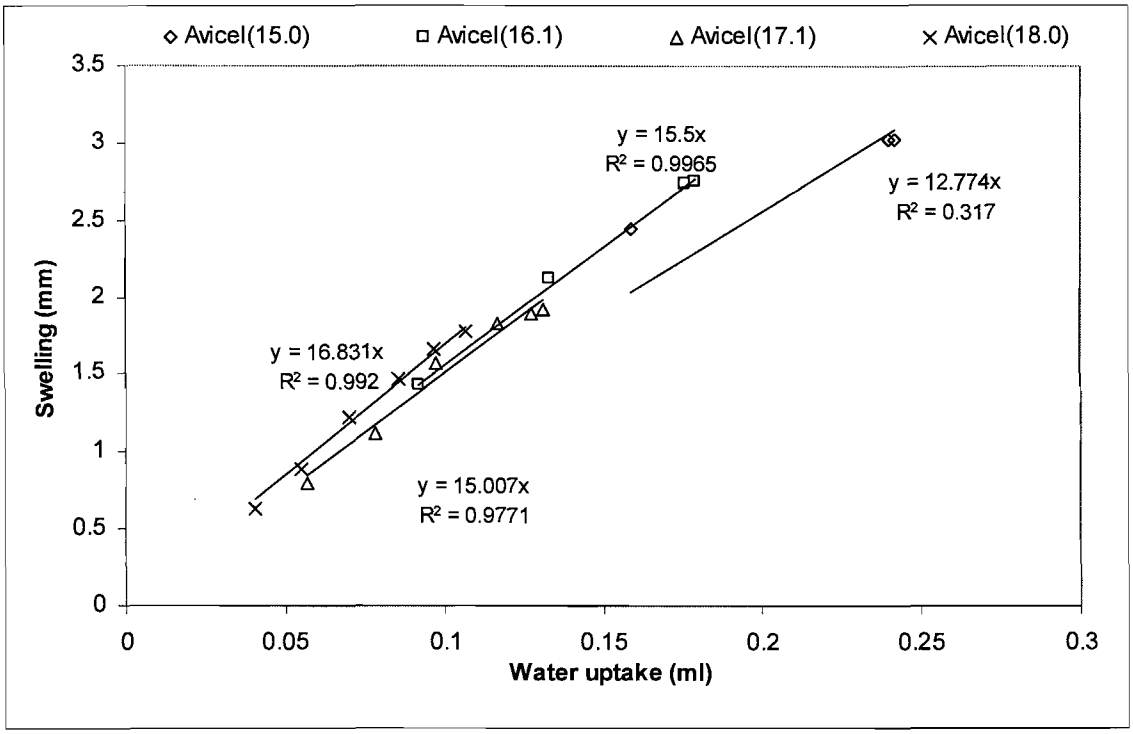



**Figure 3.13:** *The relationship between swelling and water uptake in pure Avicel® compacts at various compression forces.*

On conclusion the results confirmed that the disintegrating mechanism of microcrystalline cellulose can be attributed to the development of a force inside the compact which is linked to the swelling of the material (Caramella *et al.,* 1984:137). It was also clear that the swelling of particles were dependent upon water uptake of the compact, and the detrimental effect of compression force on disintegration time was evident.

## 3.5 PROPERTIES OF PURE CROSCARMELLOSE SODIUM COMPACTS

Croscarmellose sodium marketed as Ac-Di-Sol®, is a cross linked form of sodium carboxymethylcellulose. The fibrous structure of Ac-Di-Sol® provides many sites for fluid uptake and water wicking capabilities. Cross-linking creates an insoluble hydrophilic, highly absorbent excipient resulting in good swelling properties (Peck *et al.*, 1989:109). Compacts of pure croscarmellose sodium (Ac-Di-Sol®) were prepared at various compression forces as described in section 2.2.2.1 and analyzed as described in section 2.3. The results are presented in table 3.7 and the data in annexure A.5.

**Table 3.7:** *Properties of pure Ac-Di-Sol® prepared at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression Force | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **15.0 (0.38)** | | **16.1 (0.39)** | | **16.9 (0.78)** | | **18.0 (0.59)** | |
| Hardness (N) | 20.92 (9.30) | | 85.96 (21.50) | | 175.3 (10.43) | | 255.06 (4.71) | |
| Disintegration time (sec) | 430.57 (15.29) | | 496.80 (6.30) | | 326.38 (5.23) | | 346.10 (6.16) | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_{10}$ | 0.61 | 0.035 | 0.13 | 0.017 | 0.11 | 0.012 | 0.12 | 0.008 |
| $T_{20}$ | 0.77 | 0.047 | 0.20 | 0.025 | 0.17 | 0.019 | 0.17 | 0.019 |
| $T_{30}$ | 0.89 | 0.055 | 0.22 | 0.029 | 0.19 | 0.024 | 0.28 | 0.024 |
| $T_{40}$ | 0.99 | 0.061 | 0.25 | 0.032 | 0.20 | 0.027 | 0.31 | 0.028 |
| $T_{50}$ | 1.08 | 0.066 | 0.26 | 0.034 | 0.21 | 0.027 | 0.32 | 0.030 |
| Initial compact thickness (mm) | 4.64 | | 3.70 | | 3.18 | | 2.97 | |
| Total swelling (%) | 27.78% | | 6.97% | | 6.55% | | 10.73% | |
| Porosity (%) | 46.1 (1.13) | | 31.6 (8.31) | | 20.9 (6.96) | | 13.9 (2.95) | |

The results failed to demonstrate a correlation between the compression force and the disintegration time for the Ac-Di-Sol® compacts. Disintegration time initially increased with an increase in compression force, but sharply decreased as a higher compression force (at 16.9 N) was exerted on the compacts. Figure 3.14 illustrates this relationship. The slight increase in the disintegration time after 16.9 N is so small that it might seem that the disintegration time was no longer influenced by an increase in the compression force exerted at 16.9 N and higher. It was suggested by Bolhuis *et al.,* (1982:113) that croscarmellose sodium possesses two disintegration mechanisms; swelling and capillary action. The observed total swelling of the compacts did not seem sufficient to cause disintegration of the compacts. Ferrero *et al.,* (1997:18) stated that when the percent of super disintegrant increases to a level higher than 7.6 %, the swelling process is not the predominant mechanism. Although this study was conducted on tablet formulations containing Ac-Di-Sol® as disintegrant in various concentrations, it might be applicable to pure Ac-Di-Sol® compacts.

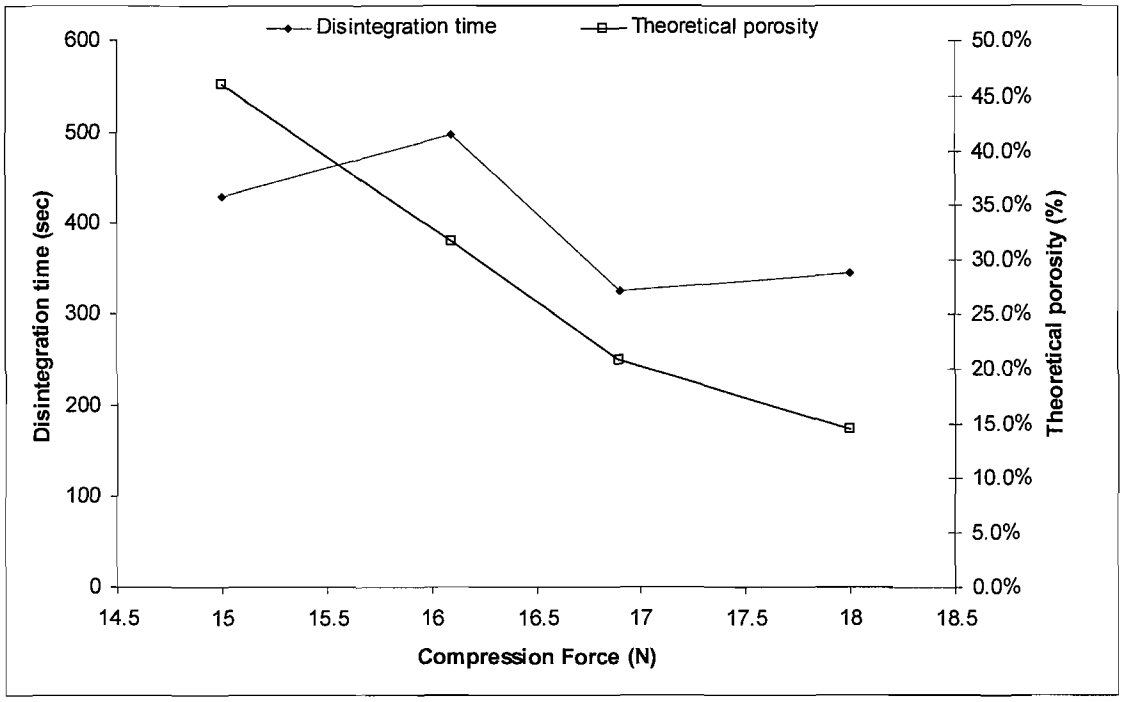



**Figure 3.14:** *Plot of the disintegration times of pure Ac-Di-Sol® compacts prepared at different compression forces.*

Capillary action inside a compact is influenced by the total porosity of the compact. If capillary action is considered to be the disintegration mechanism for pure Ac-Di-Sol® compacts, the decrease in porosity with an increase in the compression force (figure 3.14), might explain the variation in disintegration times at different compression forces. A compression force of 16.9 N seems to be the "optimum" compression force for the disintegration mechanism of Ac-Di-Sol®. At this compression force the porous network of the compact accommodates higher water uptake and thus faster disintegration of the compact. Increasing the compression force from 16.9 N to 18.0 N caused a further decrease in porosity of 6.9% (table 3.7), which might have caused a loss of the porous network inside the compact, hindering water uptake and capillary action within the compact.

Figure 3.15 and 3.16 illustrate the swelling and water uptake of pure Ac-Di-Sol® compacts at different compression forces. The small extent of swelling of Ac-Di-Sol® compacts illustrated that swelling did not seem to be the predominant disintegration mechanism for pure croscarmellose sodium. The results showed that the disintegration of pure Ac-Di-Sol® compacts was dependent upon the ability of the compact to draw water into the porous network. The compression force exerted on the compacts negatively influenced water uptake into the compact and thus the disintegration time of compacts.

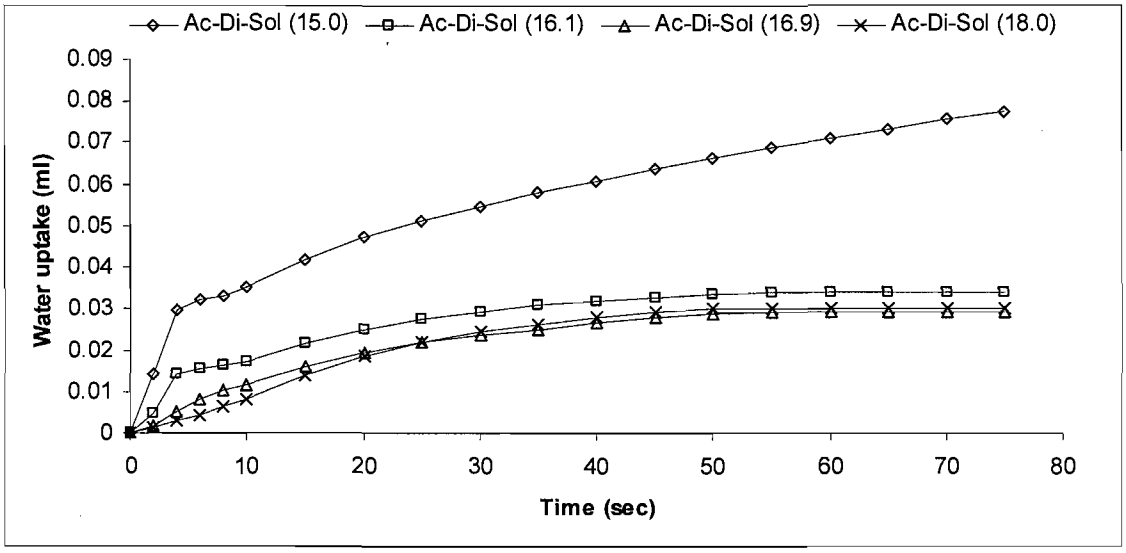



**Figure 3.15:** *The water uptake of pure Ac-Di-Sol® compacts at different compression forces.*

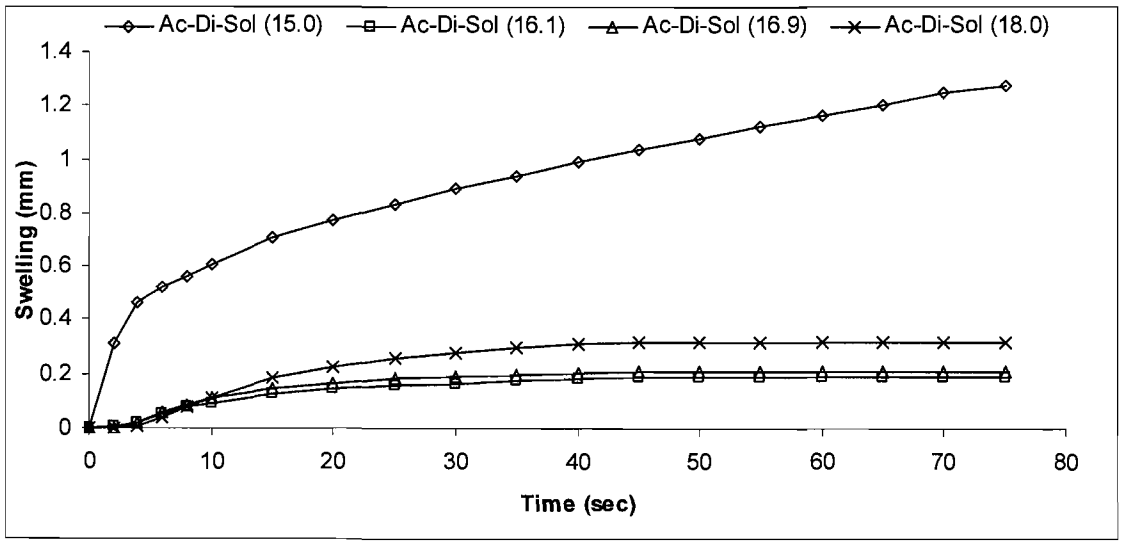



**Figure 3.16:** *The swelling of pure Ac-Di-Sol® compacts at different compression forces.*

The relationship between the swelling and water uptake of pure Ac-Di-Sol® compacts was found to be linear for all four compression forces exerted. The linearity is illustrated by figure 3.17, where $R^2$>0.8866 for lines forced through the origin. The rate constant of the process, given by the slope of the lines, showed a high rate of swelling compared to water uptake for compacts compressed at a compression force of 15.0 N, followed by a decrease in the SWU factor as compression forces increased, and again an increase for compacts compressed at 18.0 N. These results failed to correlate with the disintegration times of compacts, which emphasized the suggestion that the disintegrating action of Ac-Di-Sol® could not be attributed to the swelling of the compact alone.

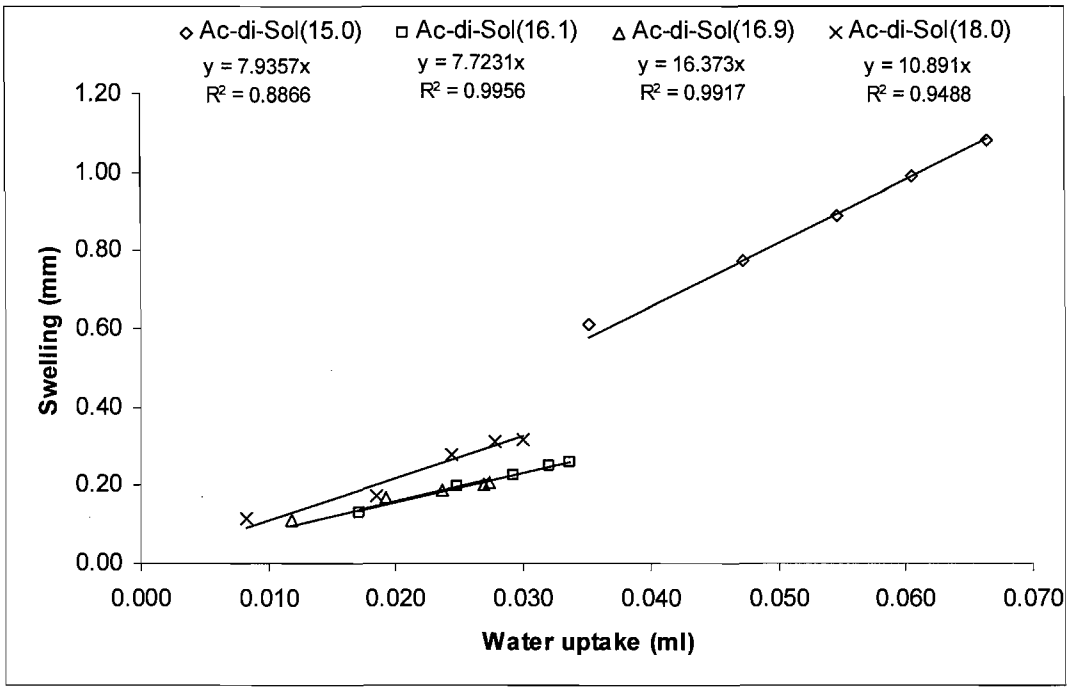



**Figure 3.17:** *The relationship between water uptake and swelling of pure Ac-Di-Sol® compacts at different compression forces.*

Although Ac-Di-Sol® is classified as a strongly swelling disintegrant (Bolhuis *et al.*, 1982:114) it seems that the swelling characteristics of this disintegrant is highly dependent upon the concentration of disintegrant present. Although super disintegrants (including Ac-Di-Sol®) are known to be effective as swelling disintegrants in low concentrations; it seemed as if capillary action might be the predominant disintegrant mechanism in pure Ac-Di-Sol® compacts. When Ac-Di-Sol® is added to tablet formulations at a high concentration, its absorption of water might cause an increase in viscosity of the liquid within the tablet, and further water penetration would be delayed by a gel barrier formed within the tablet matrix (Bi *et al.*, 1999:571).

## 3.6 PROPERTIES OF PURE POLYVINYLPYRROLIDONE (CROSPOVIDONE) COMPACTS

Insoluble polyvinylpyrrolidone (crospovidone) is manufactured by a polymerization process that produces a mainly physically cross-linked popcorn polymer, (Kornblum & Stoopak, 1973:43-44) and is available on the market as Kollidon® CL (BASF) and Polyplasdone® XL (ISP Investments Inc.). Compacts of pure Kollidon® CL were compressed at different compression forces (section 2.2.2.1) and evaluated as described in section 2.3. Two extra time points, namely after 2 seconds ($T_2$) and after 5 seconds ($T_5$) have been identified due to the fact that maximum swelling of some compacts was reached within the first five seconds of evaluation. The results are presented in table 3.8 and the data in Annexure A.6.

**Table 3.8:** *Properties of pure Kollidon® CL prepared at different compression forces. Percentage relative standard deviation is indicated in brackets.*

| Property | Average compression Force | | | | | |
|---|---|---|---|---|---|---|
| | **17.0 (0.43)** | | **17.9 (0.69)** | | **18.9 (0.53)** | |
| Hardness (N) | 209.48 (3.13) | | 286.42 (12.39) | | 301.62 (4.61) | |
| Disintegration time (sec) | 20.65 (5.63) | | 23.62 (0.65) | | 28.3 (3.62) | |
| Swelling (mm) and water uptake (ml) | Swelling | Water uptake | Swelling | Water uptake | Swelling | Water uptake |
| $T_2$ | 1.08 | 0.029 | 0.72 | 0.016 | 0.27 | 0.015 |
| $T_5$ | 1.66 | 0.111 | 1.67 | 0.093 | 0.84 | 0.053 |
| $T_{10}$ | 1.66 | 0.145 | 1.86 | 0.130 | 1.58 | 0.099 |
| $T_{20}$ | 1.66 | 0.195 | 1.89 | 0.149 | 2.52 | 0.158 |
| $T_{30}$ | 1.66 | 0.235 | 2.01 | 0.180 | 2.65 | 0.171 |
| $T_{40}$ | 1.66 | 0.266 | 2.07 | 0.215 | 2.65 | 0.180 |
| $T_{50}$ | 1.66 | 0.294 | 2.07 | 0.241 | 2.65 | 0.181 |
| Initial compact thickness (mm) | 4.13 (0.044) | | 3.95 (0.060) | | 3.94 (0.043) | |
| Total swelling (%) | 40.13% | | 52.49% | | 67.20% | |
| Porosity (%) | 20.6 (1.51) | | 16.6 (8.70) | | 15.3 (2.91) | |

The Kollidon® compacts exhibited an excellent hardness-compression force profile reaching a compact hardness in excess of 300 N at a compression force of 19 N, which was comparable to that of microcrystalline cellulose (compare table 3.6). The disintegration time of the compacts was rapid (less than 30 seconds) and remained relatively constant with an increase in compression force. Only a slight decrease (5%) in compact porosity occurred across the compression range applied (figure 3.18).

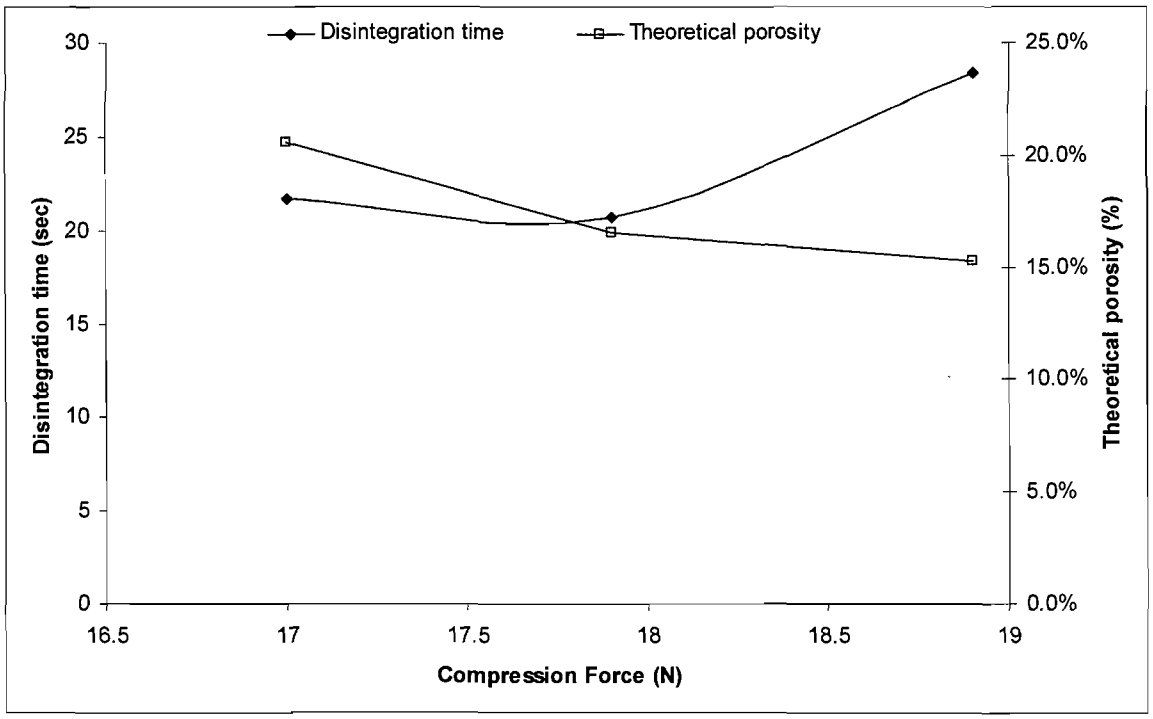



**Figure 3.18:** *Plot of disintegration time and compact hardness of pure Kollidon® CL compacts as a function of compression force.*

The observed increase in the percentage swelling of the compacts (from 40 to 67%) with an increase in compression force coincided with a decrease in water uptake (0.294 to 0.181) suggested a compact structure which could effectively convert particle swelling to a disintegrating force able to rapidly break interparticle bonds, despite the fact that less water was available. The extent of swelling of Kollidon® CL particles seemed sufficient to produce a significant force inside the compact to cause rapid disintegration. The disintegration mechanism of Kollidon® CL might thus be predominantly attributed to particle swelling.

The relationship between swelling and the porosity of the compacts at the various compression forces is illustrated by figure 3.19. The extent of swelling was observed to be significant (67%) at a low compact porosity (15%) at high compression forces (19 N), despite the decrease in water uptake which accompanied an increase in compression force. This phenomenon might be attributed to the fact that at high compact (40%) at low compression forces (17 N) the compact structure did not delay the uptake of water into the compact, but the porosity was too low for particles to develop a sufficient disintegrating force inside the compact. At high compression forces water uptake were retarded by the low porosity inside the compact, but the disintegrant particles were closer together, enabling particles to create a sufficient swelling or disintegrating force inside the compact to facilitate rapid compact disintegration.

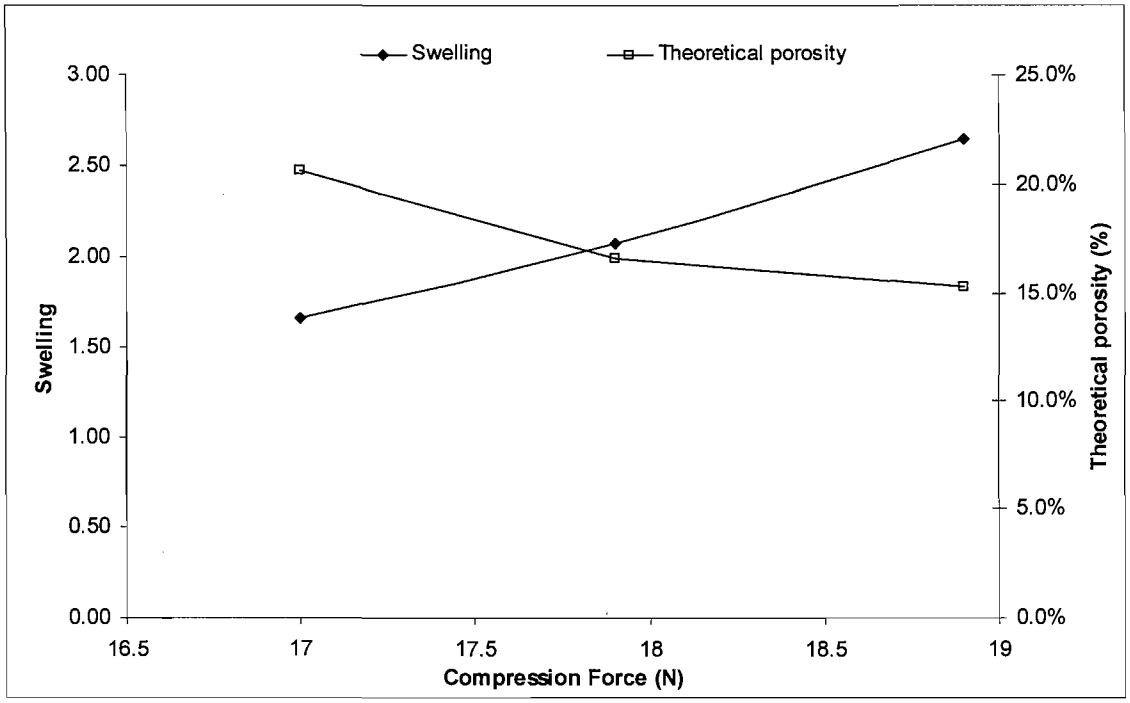



**Figure 3.19:** *The swelling and theoretical porosity of pure Kollidon® CL compacts at different compression forces.*

The water uptake and swelling of pure Kollidon® CL compacts as a function of time at different compression force are presented in figure 3.20 and 3.21 respectively. It is clear from figure 3.20 and 3.21 that the extent and rate of water uptake were retarded at high compression forces (18 N), accompanied by better swelling of compacts.

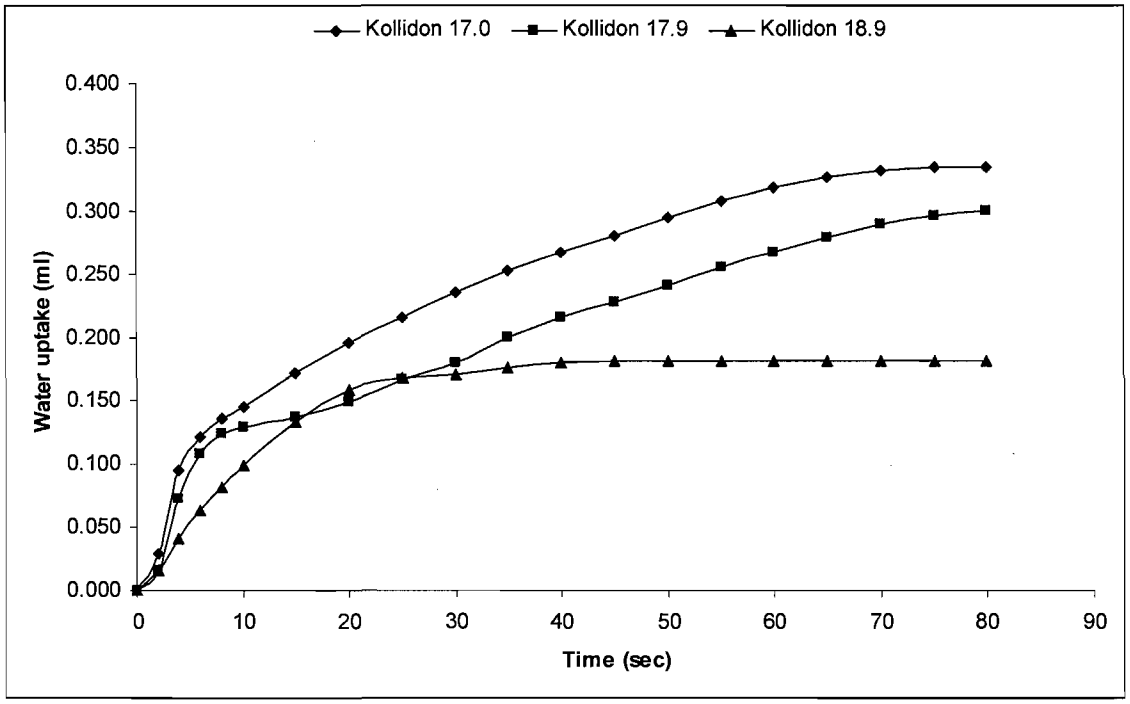



**Figure 3.20:** *The water uptake of pure Kollidon® CL compacts at different compression forces.*

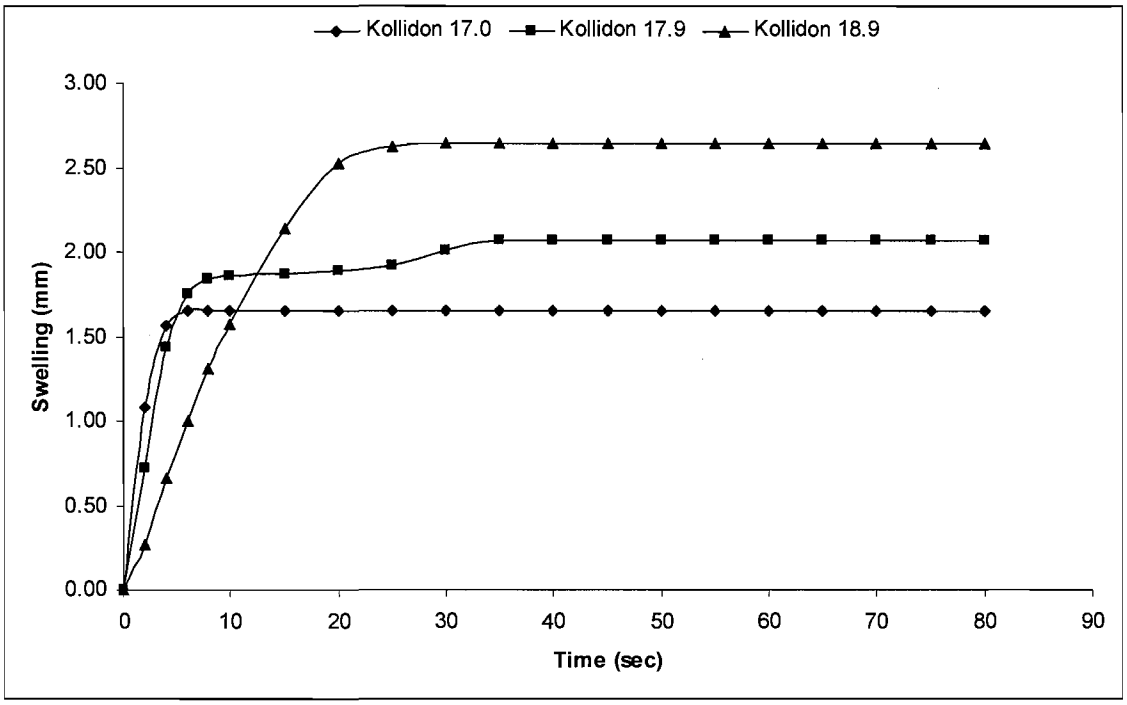



**Figure 3.21:** *The swelling of pure Kollidon® CL compacts at different compression forces.*

Figure 3.22 further illustrates that the Kollidon® compacts prepared at various compression forces followed the same trend, characterized by a significant initial swelling in terms of water uptake, reaching a plateau where swelling reached a maximum, while water uptake

continued. The results showed that the best swelling of compacts was obtained at a compression force of 18.9 N, regardless of the small extent of water uptake at this compression force. For Kollidon® CL no linear relationship between water uptake and swelling could be established (as was the case for potato starch, Explotab® and Avicel®).

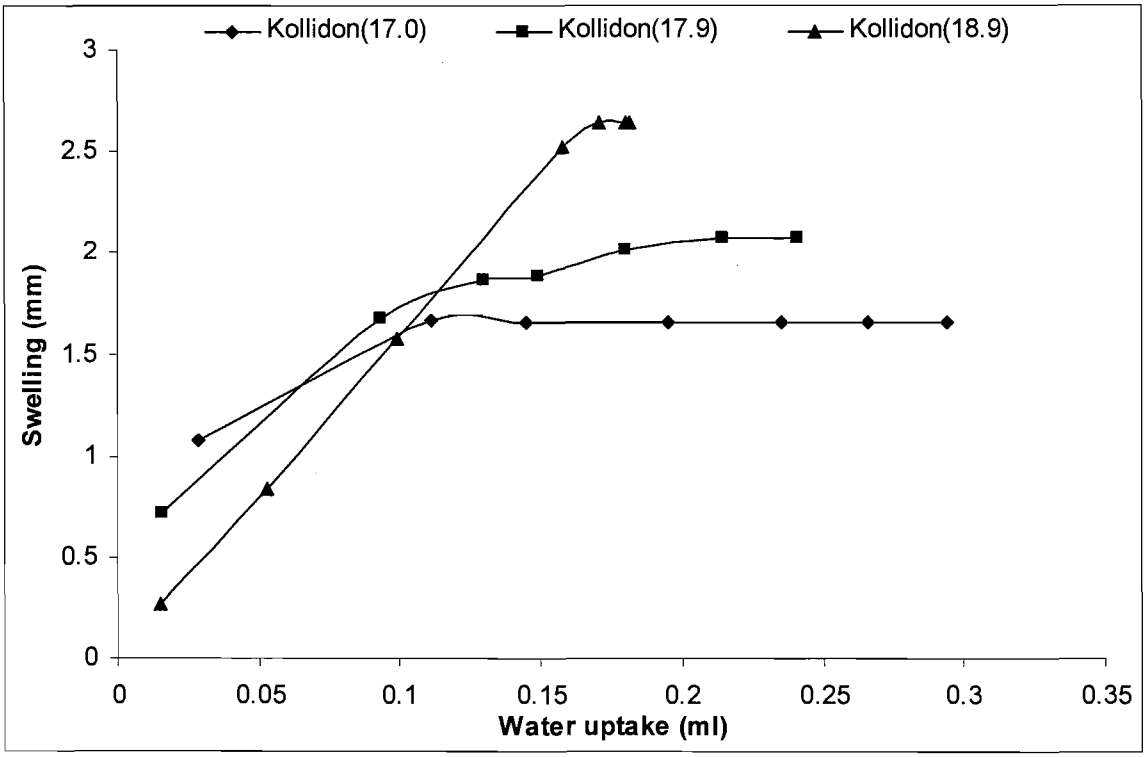



**Figure 3.22:** *The swelling behaviour of Kollidon® CL compacts at different compression forces as a function of the water uptake.*

It is clear from the results obtained that the disintegrating action of Kollidon® CL could be attributed to the development of a sufficient force inside the compact, caused by swelling of the particles. Swelling was dependent upon the ability of the compact to draw water into the porous network, thus the capillary effect of the compact seemed to influence the disintegration of the compacts.

## 3.7 COMPARISON OF THE PROPERTIES OF PURE DISINTEGRANTS COMPRESSED AT THE SAME AVERAGE COMPRESSION FORCE.

The compression forces employed to produce compacts of the various pure disintegrants varied according to the compressibility of each disintegrant as illustrated in section 2.2.2. A compression force of approximately 18 N was, however, applicable to all disintegrants. This compression force was therefore used to compare their behaviour.

From the previous sections where the properties and disintegration behaviour of the individual disintegrants were discussed it became obvious that various (and different) factors and properties of the materials are involved (and interconnected) in their overall behaviour. In order to compare the behaviour of the various disintegrants, and to determine the respective disintegration efficiency, these factors and properties must be analysed, related and connected.

Compacts of pure potato starch, sodium starch glycolate and Explotab® exhibited markedly lower hardness compared to Avicel®, Ac-Di-Sol® and Kollidon® CL (figure 3.23) with the hardness of the sodium starch glycolate so low that it could not be measured. These results confirmed the poor compressibility properties of the starches (Lowenthal, 1972:1703). The high compact hardness exhibited by compacts containing pure Avicel® and Ac-Di-Sol® respectively, confirmed the excellent compressibility of these cellulose materials which produce strong bonds under compaction due to hydrogen bonding. Cross-linked PVP has been proven to be directly compressible in pure form, and this phenomenon relates to the low percent friability exhibited with its tablet formulations (Kornblum & Stoopak, 1973:43). Kollidon® has been reported in the literature to have an excellent adhesive ability and thus provides good compressibility and high compact hardness.

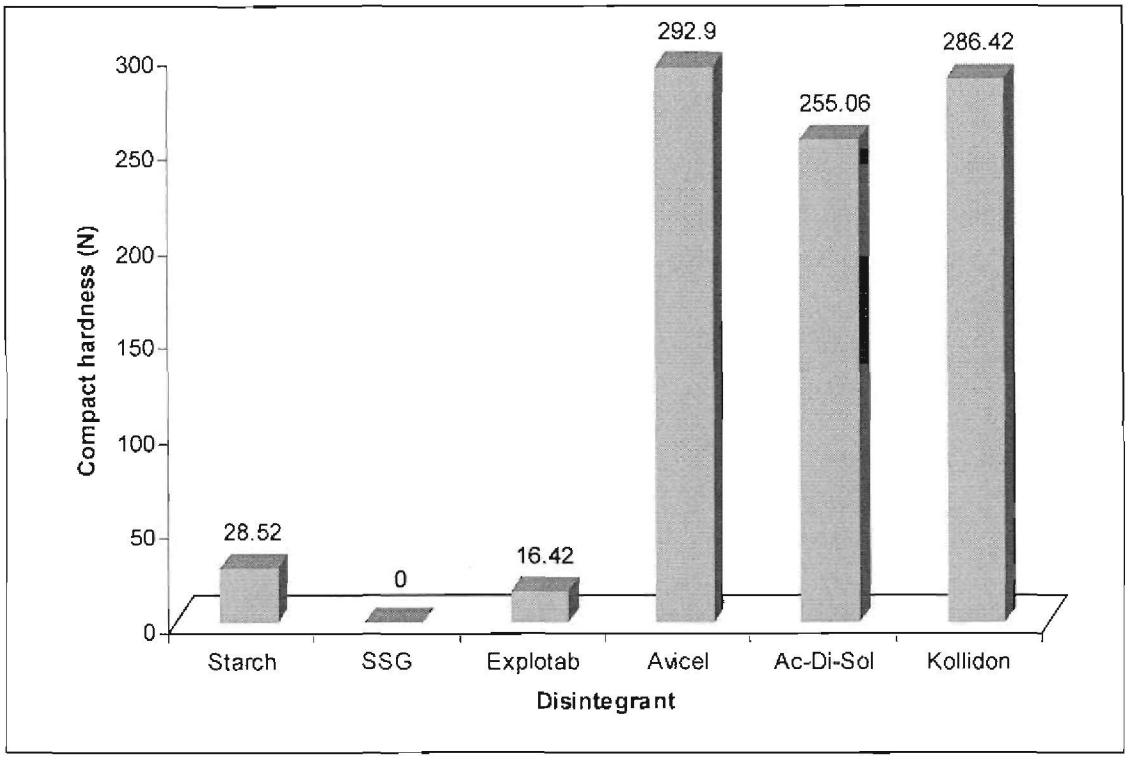



**Figure 3.23:** *Compact hardness of the different disintegrants obtained at a compression force of ±18 N.*

The low compact hardness of the starch-containing disintegrants (i.e. potato starch, SSG and Explotab®) correlated with their disintegration times (figure 3.24). It could, however, be argued that these rapid disintegration times (< 60 seconds) could rather be contributed to partial dissolution of the materials in the disintegration medium (i.e. water), rather than to disintegration. The poor disintegration performance of Avicel® compacts (no disintegration within 15 minutes) could possibly be attributed to the strength of the interparticulate hydrogen bonds which produced a compact hardness in excess of 290 N. This was despite the high SWU factor (16.88 $mm.ml^{-1}$) of the material, which was a measurement of the swelling efficiency per unite volume (ml) of water uptake. The relative poor disintegration performance of Ac-Di-Sol® (average disintegration time ≈ 6 minutes) was somewhat surprisingly considering literature reports which rate it as one of the most effective "super disintegrants" with a high affinity for water producing rapid disintegration (Peck *et al.*, 1989:109). From the water uptake and swelling profiles (figure 3.25 and 3.26), however, it was obvious that the pure compacts exhibited the poorest water uptake (0.029 ml) and swelling (0.31 mm) of all the disintegrants. Kollidon® CL showed superior disintegration properties (averaging 20 seconds) considering the hardness of the compacts (> 280 N). This could probably be related to the excellent water uptake and swelling behaviour of this material (figure 3.25 and 3.26).

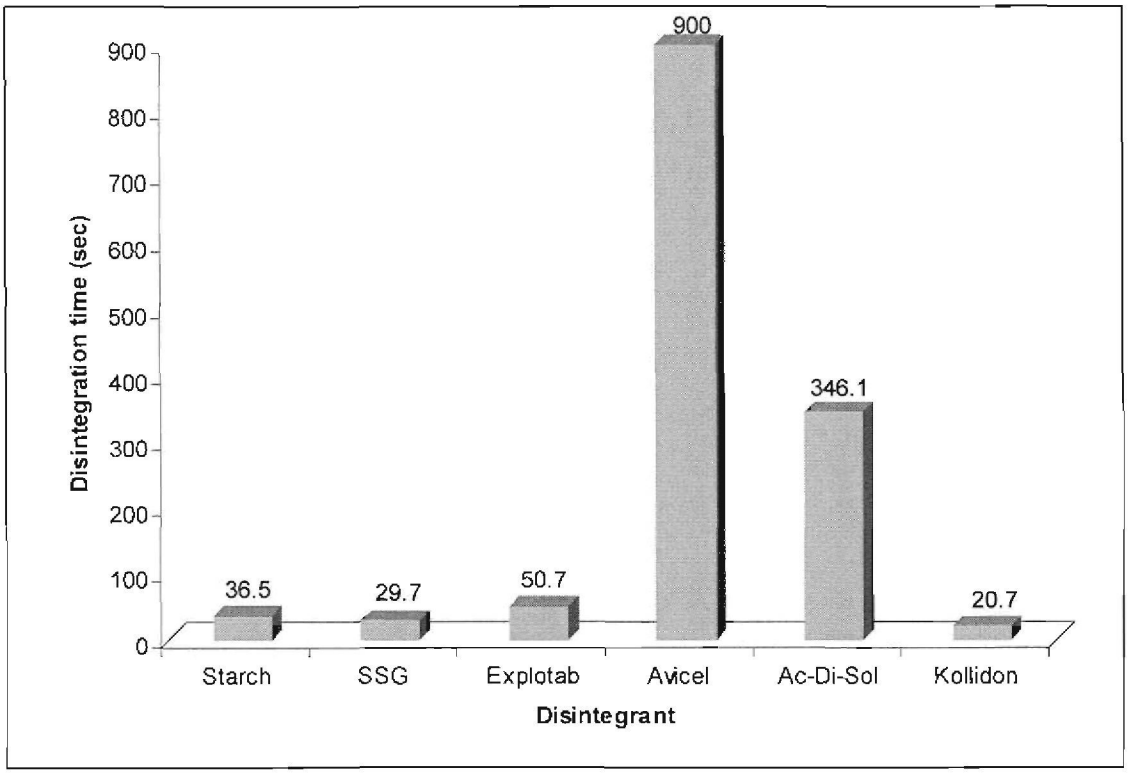



**Figure 3.24:** *Disintegration times of the pure disintegrant compacts exhibited at a compression force of ±18 N.*

From the profiles in figure 3.25 and 3.26 it can be deducted that not only the extent of water uptake (and swelling as result thereof), but also (and possibly even more so) the rate of the process, determined their disintegration efficiency. Both SSG and Kollidon® CL significantly outperformed the other disintegrants in both the rate and extent of water uptake and swelling, which was reflected in their rapid disintegration times.

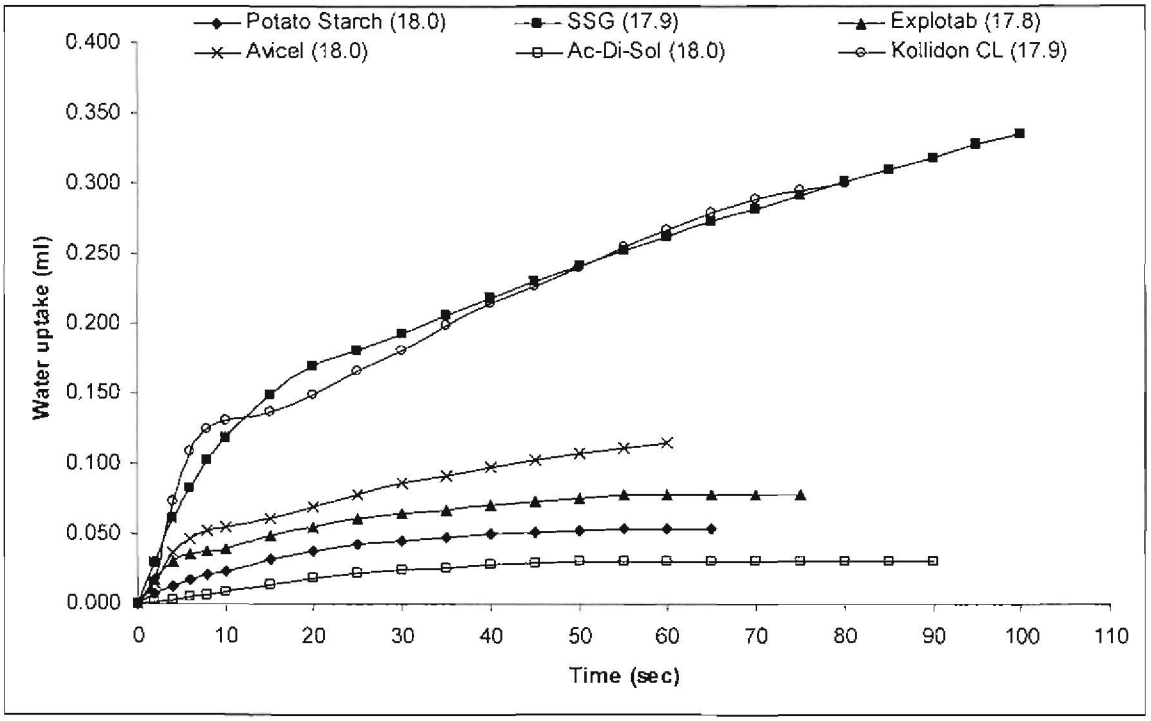



**Figure 3.25:** *The water uptake of compacts of pure disintegrants compressed at the same average compression force.*

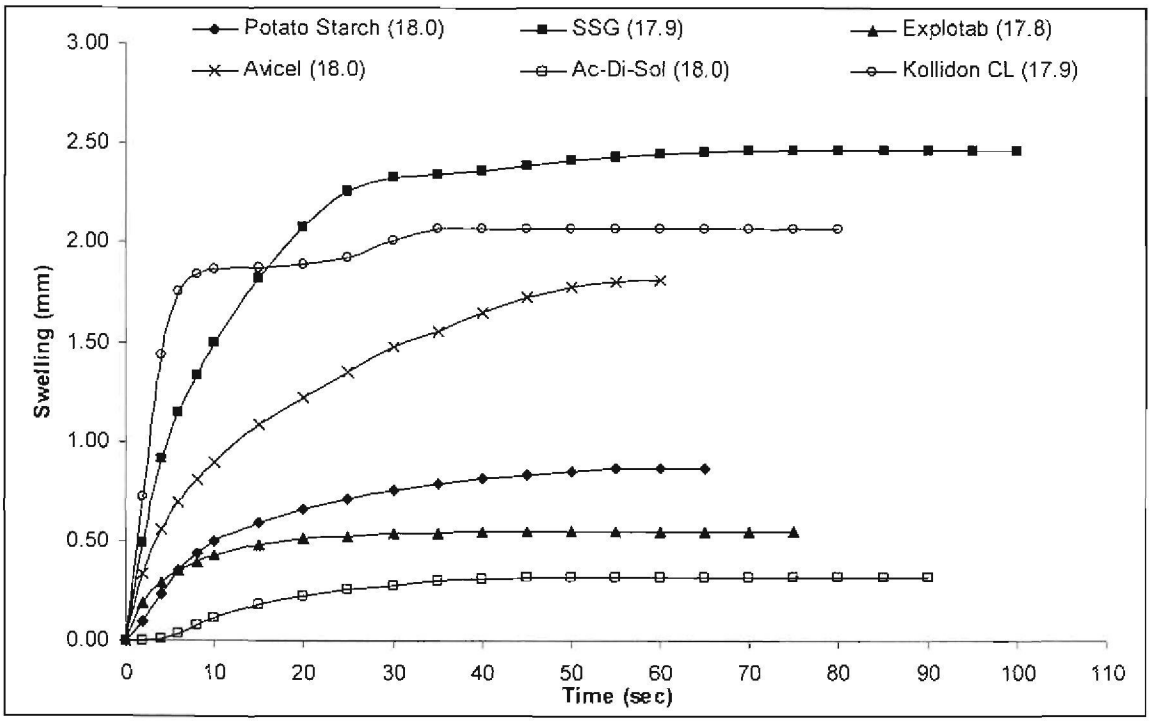



**Figure 3.26:** *The swelling of compacts of pure disintegrants compressed at the same average compression force.*

Figure 3.27 shows the overall average percentage swelling of the various disintegrant compacts (determined from the initial thickness of the compacts).

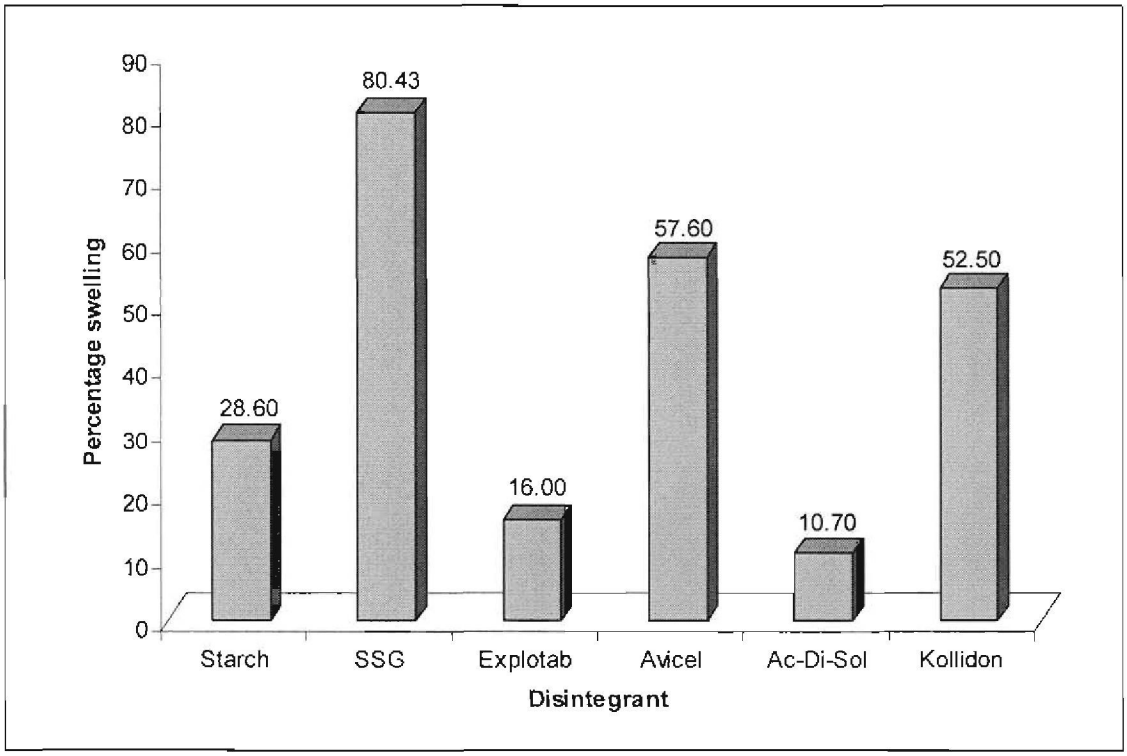



**Figure 3.27:** *Percentage swelling of compacts of the different pure disintegrants at a compression force of ±18 N.*

Table 3.9 presents a rank order between the various disintegrants in terms of the water uptake, swelling and disintegration time. The results did suggest some correlation between the three parameters for a particular disintegrant, especially for SSG and Kollidon® which ranked in the top three for each of the parameters.

**Table 3.9:** *Rank order for the water uptake, swelling and disintegration time of compacts from different disintegrants at a compression force of ±18 N.*

| | |
|---|---|
| Water uptake (ml) | **SSG > Kollidon® CL >> Avicel® >>> Explotab® > Potato starch > Ac-Di-Sol®** |
| Swelling (%) | **SSG >> Avicel® ≈ Kollidon® CL >> Potato starch > Explotab® ≈ Ac-Di-Sol®** |
| Disintegration time (sec.) | **Kollidon® CL ≈ SSG ≈ Potato starch < Explotab® << Ac-Di-Sol® <<<< Avicel®** |

This absence of a clear correlation between water uptake and / or swelling and disintegration time confirmed the difference in the mechanism of action of the various disintegrants. It became obvious that not all of the disintegrants brought about disintegration through water uptake followed by particle swelling, and that the extent of water uptake and swelling were

affected by compact properties such as hardness, porosity, as well as the inherent chemical structure of the various materials. The results, however, did clearly demonstrate that contact between disintegrant particles and water molecules was in most cases a prerequisite for initiation of the disintegration process, and that pure disintegrant compacts disintegration efficiency was negatively affected when this contact was impeded, especially by an increase in compression force. An increase in compression force reduced water penetration into the compacts due to a decrease in compact porosity, which led to a decrease in both the rate and the extent of water uptake and swelling.

## 3.8 CONCLUSION

The results on the properties and disintegration behaviour of pure disintegrant compacts clearly indicated that contact of disintegrant particles with water molecules played an important role in their disintegration efficiency, regardless of the actual disintegration mechanism of the disintegrant. The results further confirmed differences in the specific mechanism of action by which the various disintegrants facilitate disintegration. Marked differences in the physical properties of the compacts, affected by the compressibility of the compound, however, made it difficult to compare their individual disintegration efficiency.

Proper comments on and conclusion about disintegrant efficiency could probably only be made in systems (compacts) with comparable physical properties. The following chapter, will, therefore deal with a comparison of two of the disintegrants, namely Ac-Di-Sol® and Explotab®, in pharmaceutical tablets containing fillers with different properties which would assist in determining the factors that affect the disintegration efficiency of the disintegrants.

# CHAPTER 4

# 4 DETERMINATION OF DISINTEGRANT EFFICIENCY IN TABLET FORMULATIONS USING A FACTORIAL DESIGN

## 4.1 INTRODUCTION

The results in chapter 3 on the behaviour and action of various disintegrants indicated that, despite their mechanism of action, most disintegrants require some contact with an aqueous environment to function optimally. Any factor or process, therefore, which reduces or prevents this contact between disintegrant particles and water molecules would inhibit / suppress both the rate and extent of their efficiency.

Factors which have been identified as determinants in the efficiency of disintegrants include:

- **formulation factors** such as type and concentration, hydrophobicity and solubility and hygroscopicity of the formulation (depending on the properties and concentrations of the excipients included in the formulation), and
- **process factors** such as method of manufacturing and porosity of the tablet matrix (compression force).

In order to determine the major factor(s) which affect the efficiency of disintegrants in direct compressible tablet formulations, two disintegrants were selected from those tested in chapter 3, namely Explotab® and Ac-Di-Sol®. The selection was made based on the following:

- both are described in the literature as "super disintegrants" due to their efficiency at relative low concentrations;
- the similarity in their water uptake and swelling behaviour, and
- the difference in the disintegration times they produced as pure compacts.

The factors decided on to evaluate disintegration efficiency were:

- a soluble and an insoluble tablet filler;
- disintegrant type;

- disintegrant concentration;
- a hydrophobic and a hydrophilic lubricant;
- lubricant concentration;
- compression force;

## 4.2 FACTORIAL DESIGN

The factorial design was set up with six variables (A to F) each at two levels (0 and 1), which produce 64 possible combinations (if *n* is the amount of variables in a formula, the amount of formulas needed for a 2-level study is $2^n$ (Bolton, 1983:362). Table 4.1 presents the different variables and their respective levels. The six factors selected as variables were those most liable to affect the disintegrant action.

**Table 4.1:** *The different variables and their respective levels used in the factorial design.*

| Variable letter | Variable | Code | Level |
|---|---|---|---|
| A | Filler | $A_0$ | Tablettose® (water soluble) |
| | | $A_1$ | Emcompress® (insoluble) |
| B | Disintegrant | $B_0$ | Explotab® |
| | | $B_1$ | Ac-Di-Sol® |
| C | Disintegrant concentration | $C_0$ | 0.5% w/w |
| | | $C_1$ | 1.0% w/w |
| D | Lubricant | $D_0$ | Magnesium stearate |
| | | $D_1$ | Pruv® |
| E | Lubricant concentration | $E_0$ | 0.5% w/w |
| | | $E_1$ | 1.0% w/w |
| F | Upper punch setting (reflecting compression force) | $F_0$ | 1 |
| | | $F_1$ | 7 |

### 4.2.1 Fractional factorial design

In an experiment with a large number of factors and / or a large number of levels of factors, the number of experiments needed to complete a factorial design may be inordinately large. If the cost and time considerations make the implementation of a full

factorial design impractical, a fractional factorial design is used. Reduction in the number of experiments can be achieved by only running a fraction (e.g. ½, ¼, etc.) of the original number of experiments (Bolton & Bon 2003:281). One of the prerequisites for a sound partial factorial design is that it must be balanced. A balanced design implicates that each variable are presented equally in the chosen combinations. It was decided to do a ¼ factorial design, which meant that 16 of the possible 64 combinations were to be selected. Figure 4.2 presents the chosen combinations for this experiment and table 4.2 presents the composition of each combination. These 16 formulations were prepared and tablets compressed as described in section 2.2 and tested as described in section 2.3. The results are presented in table 4.3 and the data in annexure B.1 to B.16.

**Figure 4.1:** *Lay-out of the partial factorial design with indication of the combinations used in this study. Each of the chosen combinations was designated a number as shown in brackets.*

| | | | $A_0$ | | | | $A_1$ | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | $B_0$ | | $B_1$ | | $B_0$ | | $B_1$ | |
| | | | $C_0$ | $C_1$ | $C_0$ | $C_1$ | $C_0$ | $C_1$ | $C_0$ | $C_1$ |
| $D_0$ | $E_0$ | $F_0$ | x [1] | | | | | | | x [9] |
| | | $F_1$ | | x [2] | | | | | x [10] | |
| | $E_1$ | $F_0$ | | | x [3] | | | x [11] | | |
| | | $F_1$ | | | | x [4] | x [12] | | | |
| $D_1$ | $E_0$ | $F_0$ | | | | x [5] | x [13] | | | |
| | | $F_1$ | | | x [6] | | | x [14] | | |
| | $E_1$ | $F_0$ | | x [7] | | | | | x [15] | |
| | | $F_1$ | x [8] | | | | | | | x [16] |

### 4.2.2 Choice of responses

The aim of this part of the study was to determine (i) the efficiency of the disintegrants and (ii) factors which affect their efficiency. The responses chosen to be measured were based on the disintegration phenomenon of tablets, and were:

- Tablet hardness;
- Disintegration time;
- Swelling of the tablet after 5 and 10 minutes; and
- Water uptake of the tablet after 5 and 10 minutes.

**Table 4.2:** *Composition of the combinations chosen in the fractional design.*

| Number | Combination | Filler (A) | Disintegrant | | Lubricant | | Upper punch setting (F) |
|---|---|---|---|---|---|---|---|
| | | | Name (B) | Concentration (C) | Name (D) | Concentration (E) | |
| 1 | $A_0B_0C_0D_0E_0F_0$ | Tablettose | Ac-Di-Sol | 0.5% w/w | Mg-St | 0.5% w/w | 1 |
| 2 | $A_0B_0C_1D_0E_0F_1$ | Tablettose | Ac-Di-Sol | 1.0% w/w | Mg-St | 0.5% w/w | 7 |
| 3 | $A_0B_1C_0D_0E_1F_0$ | Tablettose | Explotab | 0.5% w/w | Mg-St | 1.0% w/w | 1 |
| 4 | $A_0B_1C_1D_0E_1F_1$ | Tablettose | Explotab | 1.0% w/w | Mg-St | 1.0% w/w | 7 |
| 5 | $A_0B_1C_1D_1E_0F_0$ | Tablettose | Explotab | 1.0% w/w | Pruv | 0.5% w/w | 1 |
| 6 | $A_0B_1C_0D_1E_0F_1$ | Tablettose | Explotab | 0.5% w/w | Pruv | 0.5% w/w | 7 |
| 7 | $A_0B_0C_1D_1E_1F_0$ | Tablettose | Ac-Di-Sol | 1.0% w/w | Pruv | 1.0% w/w | 1 |
| 8 | $A_0B_0C_0D_1E_1F_1$ | Tablettose | Ac-Di-Sol | 0.5% w/w | Pruv | 1.0% w/w | 7 |
| 9 | $A_1B_1C_1D_0E_0F_0$ | Emcompress | Explotab | 1.0% w/w | Mg-St | 0.5% w/w | 1 |
| 10 | $A_1B_1C_0D_0E_0F_1$ | Emcompress | Explotab | 0.5% w/w | Mg-St | 0.5% w/w | 7 |
| 11 | $A_1B_0C_1D_0E_1F_0$ | Emcompress | Ac-Di-Sol | 1.0% w/w | Mg-St | 1.0% w/w | 1 |
| 12 | $A_1B_0C_0D_0E_1F_1$ | Emcompress | Ac-Di-Sol | 0.5% w/w | Mg-St | 1.0% w/w | 7 |
| 13 | $A_1B_0C_0D_1E_0F_0$ | Emcompress | Ac-Di-Sol | 0.5% w/w | Pruv | 0.5% w/w | 1 |
| 14 | $A_1B_0C_1D_1E_0F_1$ | Emcompress | Ac-Di-Sol | 1.0% w/w | Pruv | 0.5% w/w | 7 |
| 15 | $A_1B_1C_0D_1E_1F_0$ | Emcompress | Explotab | 0.5% w/w | Pruv | 1.0% w/w | 1 |
| 16 | $A_1B_1C_1D_1E_1F_1$ | Emcompress | Explotab | 1.0% w/w | Pruv | 1.0% w/w | 7 |

## 4.3 THE EFFECT OF FORMULATION AND PROCESS VARIABLES ON RESPONSES

Table 4.3 presents the results of the responses measured for each combination.

**Table 4.3:** *Results obtained for the different responses for each combination.*

| Formu-lation nr. | Tablet hardness (N) | Disintegration time (sec.) | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|---|---|
| | | | 5 min | 10 min | 5 min | 10 min |
| 1 | 68.3 ± 4.06 | 46.8 ± 8.38 | 0.108 ± 0.010 | 0.118 ± 0.010 | 1.654 ± 0.232 | 1.656 ± 0.233 |
| 2 | 60.4 ± 2.64 | 41.0 ± 5.29 | 0.132 ± 0.010 | 0.144 ± 0.011 | 1.950 ± 0.048 | 1.950 ± 0.048 |
| 3 | 52.0 ± 4.11 | 145.8 ± 8.73 | 0.000 ± 0.00 | 0.000 ± 0.00 | 0.558 ± 0.103 | 0.672 ± 0.086 |
| 4 | 52.5 ± 1.76 | 116.2 ± 2.86 | 0.000 ± 0.00 | 0.000 ± 0.00 | 1.236 ± 0.079 | 1.478 ± 0.083 |
| 5 | 87.5 ± 3.97 | 37.2 ± 8.13 | 0.099 ± 0.006 | 0.112 ± 0.005 | 1.428 ± 0.111 | 1.468 ± 0.116 |
| 6 | 102.4 ± 6.63 | 65.3 ± 11.38 | 0.069 ± 0.006 | 0.084 ± 0.006 | 0.864 ± 0.065 | 0.918 ± 0.066 |
| 7 | 64.6 ± 2.69 | 32.0 ± 1.17 | 0.129 ± 0.006 | 0.143 ± 0.006 | 1.824 ± 0.024 | 1.824 ± 0.024 |
| 8 | 76.8 ± 3.18 | 42.0 ± 1.79 | 0.113 ± 0.006 | 0.128 ± 0.005 | 1.648 ± 0.151 | 1.658 ± 0.147 |
| 9 | 163.2 ± 10.05 | 900 ± 0.00 | 0.090 ± 0.010 | 0.098 ± 0.010 | 1.166 ± 0.083 | 1.168 ± 0.081 |
| 10 | 176.4 ± 6.41 | 900 ± 0.00 | 0.000 ± 0.00 | 0.000 ± 0.00 | 0.004 ± 0.006 | 0.024 ± 0.036 |
| 11 | 162.2 ± 13.75 | 48.5 ± 2.26 | 0.134 ± 0.016 | 0.139 ± 0.018 | 2.118 ± 0.193 | 2.122 ± 0.797 |
| 12 | 132.0 ± 5.82 | 900 ± 0.00 | 0.000 ± 0.00 | 0.000 ± 0.00 | 0.000 ± 0.00 | 0.004 ± 0.004 |
| 13 | 170.0 ± 9.36 | 213.3 ± 39.37 | 0.024 ± .004 | 0.032 ± 0.006 | 0.786 ± 0.164 | 0.800 ± 0.165 |
| 14 | 186.5 ± 10.58 | 68.3 ± 4.63 | 0.136 ± 0.002 | 0.142 ± 0.002 | 2.394 ± 0.033 | 2.394 ± 0.033 |
| 15 | 145.7 ± 8.86 | 900 ± 0.00 | 0.000 ± 0.00 | 0.000 ± 0.00 | 0.028 ± 0.026 | 0.078 ± 0.087 |
| 16 | 113.6 ± 6.10 | 201.2 ± 41.69 | 0.039 ± 0.010 | 0.087 ± 0.022 | 0.482 ± 0.147 | 1.102 ± 0.378 |

It has been proved by Gordon & Chowhan (1987:907) that overall tablet hygroscopicity negatively influences the efficiency of super disintegrants by competing for water with disintegrant particles. Emcompress® and Tablettose®, however, is both non-hygroscopic excipients, which are not expected to influence the efficiency of Ac-Di-Sol® or Explotab® when formulated with these super disintegrants in tablets. A comparison of the disintegration behaviour of tablets, compressed from different filler-binders, showed that the disintegration time was also dependent on the nature of the bonds. Tablets compressed from Tablettose® (1 – 8) showed an overall lower disintegration time (65.8 seconds) compared to the Emcompress® tablets (9 – 16) with an average disintegration time of 516.4 seconds). This might be attributed to a result of rapid liquid uptake into hydrophilic pores and a fast release of the bonds, or the lower overall tablet hardness observed for Tablettose® formulations. For Emcompress® tablets, from which the bonds are not loosened when they come in contact with water, a disintegrant are needed both to stimulate water uptake and to push the filler-binder particles apart. It is suggested that for tablets compressed from Tablettose®, the incorporation of a disintegrant in the tablet formulation is only needed to overcome the negative effect of a hydrophobic lubricant e.g. magnesium stearate, to promote water penetration into the tablet (Van Kamp *et al.,* 1986:218).

Magnesium stearate is a boundary lubricant and is strongly hydrophobic, if its concentration in a tablet is sufficiently high, penetration of water into the tablet is retarded, inhibiting disintegration of the tablet (Ganderton, 1969:9S). The average water uptake of tablets after ten minutes, decreased from 0.090 ml to 0.035 ml when the concentration of magnesium stearate in the formula were increased from 0.5% to 1.0% w/w. The decrease in water uptake also seemed to cause a decrease or inhibition in the swelling of the disintegrant inside the tablet from 1.20 mm to 1.07 mm after ten minutes. The incorporation of magnesium stearate in a formulation was proved to cause a decrease in the crushing strength of tablets compressed from Tablettose® (Van Kamp *et al.*, 1986:221). The results showed that Tablettose® formulations containing magnesium stearate (1 – 4) and Pruv® (5 – 8) yielded lower tablet hardness for the tablets containing magnesium stearate (58.3 N and 82.8 N respectively).

Pruv® is a sodium stearyl fumarate lubricant and is more hydrophilic than magnesium stearate, which resulted in faster disintegration times and harder tablets (Rizk *et al.*, 1995:61). This was confirmed by the results obtained in table 4.4 where formulations containing Pruv® (5 – 8 and 13 – 16) showed a higher average crushing strength (118.4 N) and lower disintegration time (194.9 seconds) compared to formulations with magnesium stearate (1 – 4 and 9 – 12) with an average crushing strength of 108.4 N and an average disintegration time of 387.3 seconds. Pruv® as lubricant in a tablet formulation did not seem to inhibit the water uptake into the tablet, as was seen for magnesium stearate formulations. Higher swelling was also observed for the tablets containing Pruv® in the formulation.

According to Khan & Rooke (1976:633) Explotab® as super disintegrant is more effective in soluble directly compressed tablets and Paronen *et al.*, (1985:405) found that Ac-Di-Sol® seemed to be more effective in a totally insoluble direct compression formulation. Later studies by Gordon & Chowhan (1987:907) showed that the overall tablet solubility did not appear to have any influence on the effectiveness of the tablet disintegrant. The results obtained seemed to show that the efficiency of the super disintegrants were affected by solubility of the formulation, but it is important to see that the overall disintegration times for all Tablettose® formulations were lower than for Emcompress® formulations, (65.8 seconds and 516.4 seconds respectively) due to the difference in properties of Tablettose® and Emcompress®.

Visavarungroj *et al.*, (1990:129) found that difference in tablet hardness for tablets containing Ac-Di-Sol® or Explotab® as a disintegrant did not reveal any influence on their disintegration time. The results showed no evidence that the difference in compression force tested had any effect on the efficiency of the disintegrants. Formulations containing 0.5% and 1.0% Ac-Di-Sol® showed an average disintegration time of 300.5 and 47.5 seconds respectively, while 0.5% and 1.0% Explotab® formulations showed average disintegration times of 502.8 and 313.7 seconds respectively. When the effect of compression force on the disintegrant efficiency is accepted to be unimportant, it was clear from the results that an increase in disintegrant concentration showed a decrease

in disintegration time for tablets containing both Explotab® and Ac-Di-Sol® (compare disintegration times for formulations 1 and 2, 3 and 4 etc.).

## 4.4 THE MAIN EFFECT OF A VARIABLE

The main effect of a variable is the difference in response (e.g. disintegration time) caused by the change in the level of a variable (for example, the concentration of a disintegrant) averaged over all levels of the other variables. The main effect of a variable (X) is determined as the average of all results at the high level of X ($X_1$) minus the average of all results at the low level of X ($X_0$). Thus, all the results (values) of a specific response (e.g. tablet hardness) are used to calculate each main effect of a particular variable. The following equation was used to determine the main effects of each variable (Bolton, 1983:363):

$$\text{Main effect of variable X} = \frac{\sum X_1 - \sum X_0}{\text{number of values}}$$

Statistical analysis of the results obtained showed the main effects of each variable on the different responses chosen and are presented in table 4.4. Variables which had a significant effect ($p < 0.05$) on the specific response are highlighted in the table.

**Table 4.4**: *The main effects of each variable on the responses chosen.*

| Variable | Main effects | | | | | |
|---|---|---|---|---|---|---|
| | Hardness (N) | Disintegration time (sec) | Water uptake 5min | Water uptake 10 min | Swelling 5 min | Swelling 10 min |
| A | 85.66 | 450.52 | -0.0286 | -0.0287 | -0.5230 | -0.4915 |
| B | -3.41 | 234.10 | -0.0596 | -0.0584 | -0.8260 | -0.6875 |
| C | -4.15 | -221.02 | 0.0557 | 0.0632 | 0.8820 | 0.9620 |
| D | 10.02 | -192.27 | 0.0182 | 0.0290 | 0.0960 | 0.1460 |
| E | -26.90 | 14.31 | -0.0303 | -0.0294 | -0.2940 | -0.1800 |
| F | -1.63 | 1.19 | -0.0120 | -0.0068 | -0.1230 | -0.0325 |

The values of the effect of the variables on the responses were only an indication of the magnitude of the change from a high level of the variable to a low level of the variable and were not an indication of the direction of the change that occurred. It is clear from the results that factor A (filler) had an effect on all responses, and particularly significant

effects on the hardness and disintegration times of tablets. When the filler in the formulation was changed from Emcompress ($A_1$) to Tablettose ($A_0$) the hardness and disintegration times of tablets decreased significantly, accompanied by an increase in the water uptake and swelling of tablets.

Changing the type of super disintegrant in the formulation did not have an effect on the hardness of tablets, but significant effects were seen for disintegration times, water uptake and swelling of tablets when changing the formula from Explotab® as disintegrant to Ac-Di-Sol®. Both the average water uptake and the swelling of tablets were higher for formulations with Ac-Di-Sol® as disintegrant, with an accompanied decrease in disintegration times.

The concentration of disintegrant in a formulation showed to have a significant effect on the disintegration times and both water uptake and swelling of tablets. Increasing the concentration of super disintegrant from 0.5% to 1.0% caused a significant increase in both water uptake (from 0.045 ml to 0.109 ml after ten minutes) and swelling (from 0.726 mm to 1.688 mm after ten minutes) of tablets, accompanied by an expected decrease in the disintegration time of tablets (from 401.7 seconds to 180.6 seconds). The disintegration mechanism of super disintegrants were proved to be that of water uptake into the tablet causing particles to swell to a significant extent, which leads to a disintegrating force inside the tablets, causing disintegration (Bolhuis *et al.,* 1982:114), thus, better water uptake and swelling led to faster disintegration of tablets. The hardness of tablets was not affected by a change in super disintegrant concentration.

As previously mentioned, changing the lubricant of a formulation from a hydrophilic lubricant (Pruv®) to a hydrophobic lubricant (magnesium stearate), caused a decrease in the crushing strength of tablets (from 118.4 N to 108.4 N). The disintegration times of magnesium stearate tablets were higher compared to Pruv® tablets (387.3 seconds and 194.9 seconds respectively), which might be attributed to the decrease in water uptake due to the hydrophobic nature of magnesium stearate, inhibiting water penetration into the tablet.

A change in the concentration of lubricant used in a formula, seemed to have a significant effect on tablet hardness and the water uptake and swelling of tablets. An increase from 0.5% to 1.0% lubricant in the formula caused a decrease in the average crushing strength of tablets (from 126.8 N to 99.9 N), but disintegration times were not affected by the change in concentration. The higher concentration lubricant caused a prevention of water penetrating the tablet, and both water uptake and swelling were affected, but to a lesser extent than the effect of other factors.

No significant effect on the responses where $p < 0.05$ could be found when changing the compression force. As previously mentioned, the efficiency of the super disintegrants has been proved not to be influenced at all by compression force (Visavarungroj *et al.*, 1990:129).

Ahlneck & Waltersson (1986:139) stated that an underestimation of effects can occur in factorial experiments when a dominating factor covers a smaller, but still significant effect of another factor. This might be the case when both a soluble and insoluble filler are being used in a formulation. In the case of Tablettose® and Emcompress® tablets, the average disintegration times for Tablettose® formulas were faster (65.8 seconds) compared to Emcompress® formulas (516.4 seconds). It has been stated that for Tablettose® (soluble) formulations, a disintegrant is only added to overcome the negative effects of the lubricant used in the formulation. Emcompress® formulations, on the other hand are all insoluble and the incorporation of a disintegrant is required for disintegration of tablets in aqueous medium. When ignoring the filler as a factor and looking only at Emcompress® formulations, a better estimation could be made about the influence of different factors on the efficiency of the disintegrant and thus the disintegration of tablets.

Table 4.5 shows the main effects of variables B to F on the responses for Emcompress® formulations only. It is clear from the results that disintegration time, water uptake and swelling were significantly influenced by the type of super disintegrant used and the concentration of the super disintegrant in the formulation. The only factor showing a mentionable influence on the hardness of tablets was once again the concentration of lubricant present in the formula. Disintegration times were substantially influenced by

the type of disintegrant, disintegrant concentration and the type of lubricant used. When the super disintegrant in the formulation were changed from Explotab® to Ac-Di-Sol® a significant decrease in disintegration time (from 307.5 seconds to 725.3 seconds) were observed. Increasing the concentration of disintegrant from 0.5% to 1.0% also caused a tremendous decrease in the disintegration time of tablets (from 728.3 seconds to 304.5 seconds). The other factor that had a noteworthy influence on the disintegration time was the type of lubricant used in the formula, formulations with Pruv® as lubricant showed faster disintegration (345.7 seconds) compared to the magnesium stearate formulations (687.1 seconds).

**Table 4.5:** *The main effects of variables on the responses of Emcompress® formulations.*

| Variable | Main effect | | | | | |
|---|---|---|---|---|---|---|
| | **Hardness (N)** | **Disintegration time (sec)** | **Water uptake 5 min** | **Water uptake 10 min** | **Swelling 5 min** | **Swelling 10 min** |
| **B** | -12.95 | 417.78 | -0.041 | 0.010 | -0.905 | -0.737 |
| **C** | 0.35 | -423.83 | 0.094 | 0.109 | 1.336 | 1.470 |
| **D** | -4.50 | -341.43 | -0.006 | 0.007 | 0.101 | 0.264 |
| **E** | -35.65 | -7.98 | -0.019 | -0.012 | -0.431 | -0.270 |
| **F** | -8.15 | 1.93 | -0.018 | -0.010 | -0.305 | -0.161 |

The water uptake and swelling of tablets were mainly influenced by the type of disintegrant used and the concentration of the disintegrant in the formulation. Ac-Di-Sol® as disintegrant in the Emcompress® formulations showed better swelling than Explotab®, these results might confirm the statement by Paronen *et al.,* (1985:405) that Ac-Di-Sol® seemed to be more effective in an insoluble formulation. The concentration of super disintegrant used seemed to have a significant effect on the water uptake and swelling of tablets. Formulations with 1.0% super disintegrant showed a swelling of almost seven times the swelling of formulations with only 0.5% super disintegrant. A Higher concentration of disintegrant also showed a greater extent and rate of water uptake, with consequential faster disintegration times.

## 4.5 PREDICTION OF AN OPTIMUM FORMULATION

The advantage of a fractional factorial design is the possibility to predict an optimum combination for a specific response, without testing all the possible combinations.

### 4.5.1 Determining an optimum combination in terms of responses

The combination of factors producing the fastest disintegration time (lowest value) would be an optimum formulation for disintegration of a tablet. For variable A (fillers), $A_0$ showed an average disintegration time of 65.8 seconds (for all formulations with Tablettose® as filler) compared to 516.4 seconds for $A_1$ (for all formulations with Emcompress® as filler). Therefore factor A should be present on the lower level ($A_0$ = Tablettose®) in the formulation for optimum disintegration time. The same method was used to determine the level of factors B to F, which showed optimum values for the responses. For water uptake and swelling the optimum combination should show the highest extent and rate for both responses, therefore the highest value would be the optimum. Table 4.6 shows which level of each variable yielded an optimum response for the specific variables.

**Table 4.6:** *Level of each variable which showed an optimum for a specific response.*

| Variable | Response | | | | |
|---|---|---|---|---|---|
| | **Disintegration time (sec)** | **Water uptake 5 min** | **Water uptake 10 min** | **Swelling 5 min** | **Swelling 10 min** |
| **Filler** | $A_0$ | $A_0$ | $A_0$ | $A_0$ | $A_0$ |
| **Disintegrant** | $B_0$ | $B_0$ | $B_0$ | $B_0$ | $B_0$ |
| **Disintegrant concentration** | $C_1$ | $C_1$ | $C_1$ | $C_1$ | $C_1$ |
| **Lubricant** | $D_1$ | $D_1$ | $D_1$ | $D_1$ | $D_1$ |
| **Lubricant concentration** | $E_0$ | $E_0$ | $E_0$ | $E_0$ | $E_0$ |
| **Stroke length** | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ |

Variable F did not have a significant effect on the responses tested, thus the optimum combination would be irrespective of the level of F in the formulation. The optimum combination of factors tested is predicted as $A_0B_0C_1D_1E_0F_0 \approx F_1$.

Disintegration time seemed to be faster for the soluble formulations than for the insoluble formulations, which caused better disintegration times for the Tablettose® formulations. An area of optimum formulation for both fillers could be predicted from the results. Using the same approach as before, the optimum combination for both the soluble and insoluble formulations could also be predicted. Table 4.7 and 4.8 shows the level of each variable that yielded optimum for the specific response in the soluble (Tablettose®) and insoluble (Emcompress®) formulation.

**Table 4.7:** *The level of each variable that showed optimum values for each response in a soluble formulation, i.e. with Tablettose® as filler.*

| Variable | Response | | | | |
|---|---|---|---|---|---|
| | Disintegration time (sec) | Water uptake 5 min | Water uptake 10 min | Swelling 5 min | Swelling 10 min |
| Disintegrant | $B_0$ | $B_0$ | $B_0$ | $B_0$ | $B_0$ |
| Disintegrant concentration | $C_1$ | $C_1$ | $C_1$ | $C_1$ | $C_1$ |
| Lubricant | $D_1$ | $D_1$ | $D_1$ | $D_1$ | $D_1$ |
| Lubricant concentration | $E_0$ | $E_0$ | $E_0$ | $E_0$ | $E_0$ |
| Stroke length | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ |

**Table 4.8:** *The level of each variable that showed optimum values for each response in an insoluble formulation, i.e. with Emcompress® as filler.*

| Variable | Response | | | | |
|---|---|---|---|---|---|
| | Disintegration time (sec) | Water uptake 5 min | Water uptake 10 min | Swelling 5 min | Swelling 10 min |
| Disintegrant | $B_0$ | $B_0$ | $B_0$ | $B_0$ | $B_0$ |
| Disintegrant concentration | $C_1$ | $C_1$ | $C_1$ | $C_1$ | $C_1$ |
| Lubricant | $D_1$ | $D_1$ | $D_1$ | $D_1$ | $D_1$ |
| Lubricant concentration | $E_1$ | $E_0$ | $E_0$ | $E_0$ | $E_0$ |
| Stroke length | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ | $F_0/F_1$ |

Variable F once again did not have a noticeable effect on any of the responses in the soluble or the insoluble formulations, the optimum combination could be with F on the low or on the high level. The optimum combination for all responses was expected to be the same for the soluble formulation because the overall optimum combination was where variable A was on level 0 (Tablettose®).

The optimum combination for the insoluble formulation was the same as for the soluble formulation, except for variable E, where the optimum disintegration time was observed with variable E on the higher level ($E_1$). Water uptake and swelling, on the other hand were still optimum at level $E_0$.

An area of optimum formulation for both fillers could be predicted from the results. In both soluble and insoluble formulations, tablets formulated with Ac-Di-Sol® as disintegrant showed faster disintegration times than the Explotab® tablets. It was clear from the results that all formulations containing a higher concentration of super disintegrant were more effective in terms of disintegration times, than for the lower concentration. Using a hydrophilic lubricant showed faster disintegration and more swelling and water uptake than the hydrophobic lubricant, resulting in better disintegration times for formulations containing Pruv® as lubricant. The change in concentration of lubricant present in a formulation did affect some responses to a small extent, but disintegration time did not seem to be influenced by an increase in lubricant concentration from 0.5% to 1.0%. The compression force did not influence the disintegration time, or any other response investigated, which showed that the optimum formulation was not dependent upon the compression force exerted on the tablets. The proposed area for an optimum formulation with both Tablettose® and Emcompress® as filler is presented in figure 4.2.

**Figure 4.2:** *The proposed areas of optimum combinations for both Tablettose® and Emcompress® formulations.*

| | | | TABLETTOSE | | | | EMCOMPRESS | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Ac-Di-Sol | | Explotab | | Ac-Di-Sol | | Explotab | |
| | | | 0.5% | 1.0% | 0.5% | 1.0% | 0.5% | 1.0% | 0.5% | 1.0% |
| MgSt | 0.5% | SL1 | | | | | | | | |
| | | SL7 | | | | | | | | |
| | 1.0% | SL1 | | | | | | | | |
| | | SL7 | | | | | | | | |
| Pruv | 0.5% | SL1 | | X | | | | X | | |
| | | SL7 | | X | | | | X | | |
| | 1.0% | SL1 | | | | | | X | | |
| | | SL7 | | | | | | X | | |

## 4.6 CONCLUSION

Although the determination and comparison of disintegration behaviour of the pure disintegrants provides valuable information, their efficiency and the factors affecting their efficiency can only be evaluated optimally in pharmaceutical formulations.

Results of this study showed that the efficiency of disintegrants, irrespective of their mechanism of action, is primarily dependent upon their contact with water, and that any factor that influences this contact, whether process or formulation factor, will affect their efficiency.

A carefully planned statistical design, such as a factorial design could be of great value in studies where factors affecting disintegrant efficiency are investigated.

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# ANNEXURES

## ANNEXURE A: THE DATA OF PURE DISINTEGRANT COMPACTS

### A.1 POTATO STARCH

**Table A.1.1:** *Disintegration times for pure potato starch compacts at various compression forces.*

| Potato Starch | | | | |
|---|---|---|---|---|
| **Average compression force** | **15.8** | **16.7** | **18.0** | **19.1** |
| **Tablet** | **Disintegration time (sec)** | | | |
| **1** | 24.84 | 13.77 | 37.10 | 157.77 |
| **2** | 26.70 | 17.80 | 35.40 | 165.70 |
| **3** | 20.25 | 15.03 | 36.10 | 167.67 |
| **4** | 28.80 | 11.83 | 37.50 | 189.76 |
| **Average** | 25.14 | 14.61 | 36.52 | 170.22 |
| **SD** | 3.641 | 2.511 | 0.978 | 13.709 |
| **RSD** | 14.48% | 17.18% | 2.68% | 8.05% |

**Table A.1.2:** *Properties of pure potato starch compacts at various compression forces.*

| Potato starch | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **15.8** | Weight | 0.1952 | 0.1996 | 0.1984 | 0.1938 | 0.1990 | 0.1972 | 0.0025 | 1.29% |
| | Diameter | 0.4025 | 0.4035 | 0.4045 | 0.3950 | 0.3965 | 0.4004 | 0.0043 | 1.08% |
| | Height | 0.3460 | 0.3520 | 0.3630 | 0.3550 | 0.3630 | 0.3558 | 0.0073 | 2.06% |
| | Volume | 0.1762 | 0.1801 | 0.1867 | 0.1741 | 0.1794 | 0.1793 | 0.0048 | 2.68% |
| | Density | 1.1080 | 1.1082 | 1.0629 | 1.1133 | 1.1095 | 1.1004 | 0.0211 | 1.92% |
| | Porosity | 25.03% | 25.02% | 28.09% | 24.68% | 24.93% | 25.55% | 0.0143 | 5.58% |
| | Hardness | 9.4000 | 5.3000 | 5.7000 | 5.8000 | 5.8000 | 6.4000 | 1.6897 | 26.40% |
| **16.8** | Weight | 0.2001 | 0.2001 | 0.1990 | 0.1965 | 0.2002 | 0.1992 | 0.0016 | 0.79% |
| | Diameter | 0.4030 | 0.4025 | 0.4020 | 0.4030 | 0.4040 | 0.4029 | 0.0007 | 0.18% |
| | Height | 0.3210 | 0.3270 | 0.3240 | 0.3110 | 0.3140 | 0.3194 | 0.0067 | 2.11% |
| | Volume | 0.1638 | 0.1665 | 0.1646 | 0.1587 | 0.1611 | 0.1629 | 0.0030 | 1.87% |
| | Density | 1.2213 | 1.2018 | 1.2093 | 1.2378 | 1.2429 | 1.2226 | 0.0177 | 1.45% |
| | Porosity | 17.37% | 18.69% | 18.18% | 16.25% | 15.90% | 17.28% | 0.0120 | 6.94% |
| | Hardness | 20.8000 | 22.1000 | 16.3000 | 20.4000 | 22.1000 | 20.3400 | 2.3839 | 11.72% |
| **17.8** | Weight | 0.1989 | 0.1975 | 0.1973 | 0.1996 | 0.1968 | 0.1980 | 0.0012 | 0.59% |
| | Diameter | 0.4020 | 0.4020 | 0.4020 | 0.4025 | 0.4025 | 0.4022 | 0.0003 | 0.07% |
| | Height | 0.3020 | 0.2990 | 0.3020 | 0.3080 | 0.3060 | 0.3034 | 0.0036 | 1.18% |
| | Volume | 0.1534 | 0.1519 | 0.1534 | 0.1568 | 0.1558 | 0.1543 | 0.0020 | 1.31% |
| | Density | 1.2967 | 1.3005 | 1.2863 | 1.2728 | 1.2631 | 1.2839 | 0.0158 | 1.23% |
| | Porosity | 12.26% | 12.01% | 12.97% | 13.88% | 14.54% | 13.13% | 0.0107 | 8.15% |
| | Hardness | 27.0000 | 36.8000 | 30.2000 | 22.9000 | 25.7000 | 28.5200 | 5.3204 | 18.66% |
| **18.8** | Weight | 0.1954 | 0.2018 | 0.1995 | 0.1994 | 0.2007 | 0.1994 | 0.0024 | 1.21% |
| | Diameter | 0.4010 | 0.4015 | 0.4020 | 0.4025 | 0.4015 | 0.4017 | 0.0006 | 0.14% |
| | Height | 0.2900 | 0.2920 | 0.2960 | 0.2980 | 0.3030 | 0.2958 | 0.0051 | 1.73% |
| | Volume | 0.1466 | 0.1479 | 0.1503 | 0.1517 | 0.1535 | 0.1500 | 0.0028 | 1.87% |
| | Density | 1.3333 | 1.3641 | 1.3270 | 1.3142 | 1.3074 | 1.3292 | 0.0220 | 1.66% |
| | Porosity | 9.79% | 7.71% | 10.22% | 11.08% | 11.54% | 10.07% | 0.0149 | 14.80% |
| | Hardness | 58.0000 | 105.4000 | 51.1000 | 53.5000 | 63.7000 | 66.3400 | 22.3569 | 33.70% |

**Table A.1.3:** *Swelling and water uptake for pure potato starch compacts at a compression force of 15.8 N.*

| Potato Starch (15.8 N) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.005 | 0.09 | 0.003 | 0.10 | 0.011 | 0.19 | 0.021 | 0.15 | 0.010 | 0.133 | 0.008 | 0.046 | 80.83% | 35.06% |
| 4 | 0.012 | 0.24 | 0.024 | 0.32 | 0.020 | 0.36 | 0.035 | 0.37 | 0.023 | 0.323 | 0.010 | 0.059 | 42.07% | 18.32% |
| 6 | 0.016 | 0.31 | 0.030 | 0.42 | 0.030 | 0.46 | 0.041 | 0.48 | 0.029 | 0.418 | 0.010 | 0.076 | 35.02% | 18.18% |
| 8 | 0.017 | 0.35 | 0.031 | 0.49 | 0.032 | 0.52 | 0.042 | 0.55 | 0.031 | 0.478 | 0.010 | 0.088 | 33.70% | 18.53% |
| 10 | 0.018 | 0.38 | 0.032 | 0.54 | 0.034 | 0.58 | 0.043 | 0.61 | 0.032 | 0.528 | 0.010 | 0.102 | 32.57% | 19.42% |
| 15 | 0.023 | 0.43 | 0.037 | 0.62 | 0.040 | 0.66 | 0.050 | 0.71 | 0.038 | 0.605 | 0.011 | 0.122 | 29.73% | 20.22% |
| 20 | 0.026 | 0.45 | 0.041 | 0.67 | 0.046 | 0.72 | 0.055 | 0.79 | 0.042 | 0.658 | 0.012 | 0.147 | 28.90% | 22.33% |
| 25 | 0.027 | 0.47 | 0.044 | 0.70 | 0.050 | 0.76 | 0.059 | 0.85 | 0.045 | 0.695 | 0.013 | 0.162 | 29.98% | 23.33% |
| 30 | 0.028 | 0.48 | 0.046 | 0.72 | 0.052 | 0.78 | 0.063 | 0.89 | 0.047 | 0.718 | 0.015 | 0.173 | 30.98% | 24.15% |
| 35 | 0.029 | 0.48 | 0.047 | 0.73 | 0.054 | 0.79 | 0.065 | 0.94 | 0.049 | 0.735 | 0.015 | 0.192 | 30.99% | 26.06% |
| 40 | 0.029 | 0.49 | 0.048 | 0.74 | 0.055 | 0.80 | 0.067 | 0.96 | 0.050 | 0.748 | 0.016 | 0.195 | 31.97% | 26.11% |
| 45 | 0.029 | 0.49 | 0.049 | 0.74 | 0.056 | 0.80 | 0.07 | 0.97 | 0.051 | 0.750 | 0.017 | 0.199 | 32.91% | 26.51% |
| 50 | 0.029 | 0.49 | 0.049 | 0.74 | 0.056 | 0.80 | 0.07 | 0.97 | 0.051 | 0.750 | 0.017 | 0.199 | 32.91% | 26.51% |
| 55 | 0.029 | 0.49 | 0.049 | 0.74 | 0.056 | 0.80 | 0.07 | 0.97 | 0.051 | 0.750 | 0.017 | 0.199 | 32.91% | 26.51% |
| 60 | 0.029 | 0.49 | 0.049 | 0.74 | 0.056 | 0.80 | 0.07 | 0.97 | 0.051 | 0.750 | 0.017 | 0.199 | 32.91% | 26.51% |
| 65 | 0.029 | 0.49 | 0.049 | 0.74 | 0.056 | 0.80 | 0.07 | 0.97 | 0.051 | 0.750 | 0.017 | 0.199 | 32.91% | 26.51% |

**Table A.1.4:** *Swelling and water uptake for pure potato starch compacts at a compression force of 16.7 N.*

| Potato Starch (16.7 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.010 | 0.12 | 0.008 | 0.02 | 0.003 | 0.03 | 0.003 | 0.08 | 0.007 | 0.13 | 0.001 | 0.04 | 0.005 | 0.070 | 0.004 | 0.047 | 65.67% | 67.61% |
| 4 | 0.023 | 0.32 | 0.010 | 0.12 | 0.007 | 0.20 | 0.014 | 0.30 | 0.010 | 0.33 | 0.002 | 0.10 | 0.011 | 0.228 | 0.007 | 0.103 | 64.54% | 45.04% |
| 6 | 0.032 | 0.48 | 0.012 | 0.20 | 0.010 | 0.28 | 0.022 | 0.46 | 0.023 | 0.48 | 0.003 | 0.20 | 0.017 | 0.350 | 0.011 | 0.138 | 62.03% | 39.55% |
| 8 | 0.036 | 0.58 | 0.015 | 0.25 | 0.012 | 0.34 | 0.023 | 0.56 | 0.027 | 0.58 | 0.005 | 0.28 | 0.020 | 0.432 | 0.011 | 0.158 | 56.96% | 36.61% |
| 10 | 0.037 | 0.65 | 0.018 | 0.29 | 0.014 | 0.39 | 0.025 | 0.64 | 0.029 | 0.65 | 0.009 | 0.36 | 0.022 | 0.497 | 0.010 | 0.168 | 46.89% | 33.73% |
| 15 | 0.045 | 0.77 | 0.026 | 0.35 | 0.017 | 0.46 | 0.033 | 0.78 | 0.036 | 0.77 | 0.020 | 0.47 | 0.030 | 0.600 | 0.011 | 0.195 | 35.67% | 32.42% |
| 20 | 0.052 | 0.85 | 0.029 | 0.39 | 0.020 | 0.51 | 0.040 | 0.87 | 0.043 | 0.84 | 0.026 | 0.54 | 0.035 | 0.667 | 0.012 | 0.211 | 34.29% | 31.62% |
| 25 | 0.057 | 0.91 | 0.032 | 0.42 | 0.022 | 0.55 | 0.045 | 0.93 | 0.048 | 0.90 | 0.030 | 0.60 | 0.039 | 0.718 | 0.013 | 0.222 | 33.63% | 30.87% |
| 30 | 0.061 | 0.97 | 0.033 | 0.44 | 0.024 | 0.57 | 0.048 | 0.98 | 0.051 | 0.94 | 0.033 | 0.64 | 0.042 | 0.757 | 0.014 | 0.236 | 33.31% | 31.15% |
| 35 | 0.063 | 1.01 | 0.035 | 0.46 | 0.025 | 0.60 | 0.051 | 1.02 | 0.054 | 0.98 | 0.036 | 0.68 | 0.044 | 0.792 | 0.014 | 0.243 | 32.40% | 30.66% |
| 40 | 0.066 | 1.04 | 0.036 | 0.48 | 0.027 | 0.62 | 0.053 | 1.06 | 0.056 | 1.00 | 0.038 | 0.71 | 0.046 | 0.818 | 0.015 | 0.247 | 31.86% | 30.23% |
| 45 | 0.068 | 1.07 | 0.037 | 0.49 | 0.029 | 0.64 | 0.055 | 1.10 | 0.058 | 1.03 | 0.040 | 0.74 | 0.048 | 0.845 | 0.015 | 0.256 | 30.94% | 30.35% |
| 50 | 0.070 | 1.09 | 0.037 | 0.49 | 0.030 | 0.66 | 0.057 | 1.14 | 0.059 | 1.06 | 0.041 | 0.77 | 0.049 | 0.868 | 0.015 | 0.267 | 31.27% | 30.72% |
| 55 | 0.071 | 1.11 | 0.037 | 0.49 | 0.031 | 0.66 | 0.059 | 1.14 | 0.061 | 1.08 | 0.043 | 0.79 | 0.050 | 0.878 | 0.016 | 0.272 | 31.05% | 30.93% |
| 60 | 0.07 | 1.11 | 0.037 | 0.49 | 0.031 | 0.66 | 0.060 | 1.14 | 0.062 | 1.10 | 0.044 | 0.81 | 0.051 | 0.885 | 0.016 | 0.274 | 31.06% | 30.91% |
| 65 | 0.07 | 1.11 | 0.037 | 0.49 | 0.031 | 0.66 | 0.060 | 1.14 | 0.062 | 1.10 | 0.046 | 0.82 | 0.051 | 0.887 | 0.016 | 0.273 | 30.56% | 30.79% |

**Table A.1.5:** *Swelling and water uptake for pure potato starch compacts at a compression force of 18.0 N.*

| Potato Starch (18.0 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.001 | 0.00 | 0.002 | 0.13 | 0.002 | 0.09 | 0.009 | 0.12 | 0.010 | 0.14 | 0.017 | 0.08 | 0.007 | 0.093 | 0.006 | 0.051 | 92.28% | 54.91% |
| 4 | 0.005 | 0.13 | 0.004 | 0.22 | 0.005 | 0.19 | 0.010 | 0.28 | 0.024 | 0.32 | 0.027 | 0.24 | 0.013 | 0.230 | 0.010 | 0.067 | 82.64% | 29.10% |
| 6 | 0.010 | 0.32 | 0.005 | 0.33 | 0.009 | 0.24 | 0.011 | 0.40 | 0.030 | 0.45 | 0.035 | 0.36 | 0.017 | 0.350 | 0.013 | 0.072 | 75.20% | 20.60% |
| 8 | 0.021 | 0.47 | 0.007 | 0.40 | 0.012 | 0.28 | 0.015 | 0.47 | 0.031 | 0.54 | 0.036 | 0.45 | 0.020 | 0.435 | 0.011 | 0.088 | 55.44% | 20.29% |
| 10 | 0.023 | 0.55 | 0.012 | 0.47 | 0.015 | 0.31 | 0.021 | 0.53 | 0.033 | 0.61 | 0.038 | 0.51 | 0.024 | 0.497 | 0.010 | 0.102 | 42.73% | 20.59% |
| 15 | 0.029 | 0.67 | 0.022 | 0.58 | 0.020 | 0.36 | 0.033 | 0.62 | 0.040 | 0.72 | 0.046 | 0.61 | 0.032 | 0.593 | 0.010 | 0.125 | 32.00% | 20.99% |
| 20 | 0.037 | 0.76 | 0.029 | 0.66 | 0.023 | 0.40 | 0.040 | 0.68 | 0.047 | 0.80 | 0.052 | 0.68 | 0.038 | 0.663 | 0.011 | 0.140 | 28.54% | 21.10% |
| 25 | 0.042 | 0.82 | 0.034 | 0.72 | 0.025 | 0.42 | 0.044 | 0.73 | 0.051 | 0.85 | 0.057 | 0.73 | 0.042 | 0.712 | 0.012 | 0.153 | 27.31% | 21.47% |
| 30 | 0.046 | 0.87 | 0.037 | 0.77 | 0.026 | 0.45 | 0.048 | 0.77 | 0.054 | 0.89 | 0.060 | 0.78 | 0.045 | 0.755 | 0.012 | 0.158 | 26.95% | 20.99% |
| 35 | 0.048 | 0.91 | 0.040 | 0.81 | 0.027 | 0.46 | 0.050 | 0.80 | 0.057 | 0.93 | 0.062 | 0.81 | 0.047 | 0.787 | 0.013 | 0.170 | 26.44% | 21.55% |
| 40 | 0.051 | 0.95 | 0.043 | 0.84 | 0.028 | 0.46 | 0.052 | 0.83 | 0.059 | 0.96 | 0.065 | 0.84 | 0.050 | 0.813 | 0.013 | 0.183 | 26.15% | 22.45% |
| 45 | 0.053 | 0.97 | 0.045 | 0.87 | 0.028 | 0.46 | 0.054 | 0.85 | 0.061 | 0.99 | 0.067 | 0.86 | 0.051 | 0.833 | 0.014 | 0.192 | 26.62% | 23.08% |
| 50 | 0.055 | 1.00 | 0.046 | 0.89 | 0.028 | 0.46 | 0.056 | 0.88 | 0.062 | 1.01 | 0.068 | 0.89 | 0.053 | 0.855 | 0.014 | 0.202 | 26.82% | 23.63% |
| 55 | 0.056 | 1.03 | 0.048 | 0.91 | 0.028 | 0.46 | 0.058 | 0.89 | 0.063 | 1.01 | 0.070 | 0.90 | 0.054 | 0.867 | 0.015 | 0.208 | 27.16% | 23.99% |
| 60 | 0.056 | 1.03 | 0.049 | 0.92 | 0.028 | 0.46 | 0.058 | 0.89 | 0.063 | 1.01 | 0.071 | 0.90 | 0.054 | 0.868 | 0.015 | 0.208 | 27.27% | 24.00% |
| 65 | 0.056 | 1.03 | 0.049 | 0.92 | 0.028 | 0.46 | 0.058 | 0.89 | 0.063 | 1.01 | 0.071 | 0.90 | 0.054 | 0.868 | 0.015 | 0.208 | 27.27% | 24.00% |

**Table A.1.6:** *Swelling and water uptake for pure potato starch compacts at a compression force of 19.1 N.*

| Potato Starch (19.1 N) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.003 | 0.00 | 0.000 | 0.01 | 0.002 | 0.00 | 0.010 | 0.03 | 0.004 | 0.010 | 0.004 | 0.014 | 115.98% | 141.42% |
| 4 | 0.005 | 0.00 | 0.000 | 0.01 | 0.008 | 0.00 | 0.010 | 0.03 | 0.006 | 0.010 | 0.004 | 0.014 | 75.64% | 141.42% |
| 6 | 0.006 | 0.00 | 0.002 | 0.01 | 0.008 | 0.00 | 0.010 | 0.03 | 0.007 | 0.010 | 0.003 | 0.014 | 52.55% | 141.42% |
| 8 | 0.007 | 0.00 | 0.005 | 0.01 | 0.010 | 0.00 | 0.011 | 0.03 | 0.008 | 0.010 | 0.003 | 0.014 | 33.38% | 141.42% |
| 10 | 0.009 | 0.01 | 0.008 | 0.01 | 0.012 | 0.00 | 0.013 | 0.03 | 0.011 | 0.013 | 0.002 | 0.013 | 22.67% | 100.66% |
| 15 | 0.010 | 0.05 | 0.010 | 0.01 | 0.017 | 0.02 | 0.014 | 0.03 | 0.013 | 0.028 | 0.003 | 0.017 | 26.69% | 62.10% |
| 20 | 0.011 | 0.08 | 0.010 | 0.02 | 0.018 | 0.05 | 0.015 | 0.03 | 0.014 | 0.045 | 0.004 | 0.026 | 27.38% | 58.79% |
| 25 | 0.013 | 0.11 | 0.011 | 0.05 | 0.020 | 0.07 | 0.016 | 0.04 | 0.015 | 0.068 | 0.004 | 0.031 | 26.11% | 45.86% |
| 30 | 0.015 | 0.13 | 0.012 | 0.06 | 0.021 | 0.10 | 0.018 | 0.05 | 0.017 | 0.085 | 0.004 | 0.037 | 23.47% | 43.49% |
| 35 | 0.017 | 0.16 | 0.012 | 0.06 | 0.022 | 0.11 | 0.019 | 0.08 | 0.018 | 0.103 | 0.004 | 0.043 | 24.02% | 42.43% |
| 40 | 0.018 | 0.18 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.019 | 0.115 | 0.005 | 0.050 | 25.92% | 43.48% |
| 45 | 0.020 | 0.20 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.019 | 0.120 | 0.005 | 0.059 | 25.42% | 49.07% |
| 50 | 0.021 | 0.22 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.019 | 0.125 | 0.005 | 0.068 | 25.58% | 54.45% |
| 55 | 0.02 | 0.23 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.020 | 0.128 | 0.005 | 0.073 | 25.98% | 57.05% |
| 60 | 0.02 | 0.23 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.020 | 0.128 | 0.005 | 0.073 | 25.98% | 57.05% |
| 65 | 0.02 | 0.23 | 0.012 | 0.06 | 0.023 | 0.12 | 0.021 | 0.10 | 0.020 | 0.128 | 0.005 | 0.073 | 25.98% | 57.05% |

## A.2 SODIUM STARCH GLYCOLATE

**Table A.2.1:** *Disintegration times for sodium starch glycolate compacts at various compression forces.*

| Sodium Starch glycolate | | | | |
|---|---|---|---|---|
| **Average compression force** | **17.9** | **18.9** | **19.9** | **21.0** |
| **Tablet** | **Disintegration time (sec)** | | | |
| **1** | 31.27 | 38.80 | 137.38 | 125.64 |
| **2** | 22.10 | 36.70 | 186.00 | 143.50 |
| **3** | 32.08 | 30.60 | 180.49 | 123.34 |
| **4** | 33.39 | 25.40 | 163.17 | 129.28 |
| **Average** | 29.71 | 32.87 | 166.76 | 130.43 |
| **SD** | 5.153 | 6.062 | 21.863 | 9.024 |
| **RSD** | 17.35% | 18.44% | 13.11% | 6.92% |

**Table A.2.2:** *Properties of pure potato starch compacts at various compression forces*

| Sodium starch glycolate | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **17.9** | Weight | 0.1865 | 0.1813 | 0.1871 | 0.1781 | 0.1978 | 0.1862 | 0.0075 | 4.03% |
| | Diameter | 0.4000 | 0.4000 | 0.4000 | 0.4000 | 0.4000 | 0.4000 | 0.0000 | 0.00% |
| | Height | 0.3040 | 0.2990 | 0.2950 | 0.3030 | 0.3080 | 0.3018 | 0.0050 | 1.65% |
| | Volume | 0.1529 | 0.1504 | 0.1483 | 0.1524 | 0.1549 | 0.1518 | 0.0025 | 1.65% |
| | Density | 1.2200 | 1.2058 | 1.2613 | 1.1689 | 1.2771 | 1.2266 | 0.0435 | 3.54% |
| | Porosity | 15.45% | 16.44% | 12.59% | 19.00% | 11.50% | 15.00% | 0.0301 | 20.09% |
| | Hardness | - | - | - | - | - | - | - | - |
| **18.9** | Weight | 0.2068 | 0.2021 | 0.1912 | 0.1977 | 0.2007 | 0.1997 | 0.0058 | 2.89% |
| | Diameter | 0.4010 | 0.4000 | 0.4005 | 0.4020 | 0.4015 | 0.4010 | 0.0008 | 0.20% |
| | Height | 0.3010 | 0.2940 | 0.2800 | 0.2870 | 0.2950 | 0.2914 | 0.0081 | 2.77% |
| | Volume | 0.1521 | 0.1478 | 0.1412 | 0.1458 | 0.1495 | 0.1473 | 0.0041 | 2.81% |
| | Density | 1.3595 | 1.3670 | 1.3546 | 1.3563 | 1.3429 | 1.3560 | 0.0088 | 0.65% |
| | Porosity | 5.79% | 5.27% | 6.13% | 6.01% | 6.94% | 6.03% | 0.0061 | 10.10% |
| | Hardness | 20.0000 | 18.0000 | 13.9000 | 13.9000 | 5.3000 | 14.2200 | 5.6451 | 39.70% |
| **19.9** | Weight | 0.2053 | 0.2086 | 0.2010 | 0.2026 | 0.2043 | 0.2044 | 0.0029 | 1.41% |
| | Diameter | 0.3995 | 0.4000 | 0.4000 | 0.3990 | 0.3995 | 0.3996 | 0.0004 | 0.10% |
| | Height | 0.2840 | 0.2900 | 0.2780 | 0.2850 | 0.2830 | 0.2840 | 0.0043 | 1.51% |
| | Volume | 0.1425 | 0.1458 | 0.1398 | 0.1426 | 0.1420 | 0.1425 | 0.0022 | 1.52% |
| | Density | 1.4412 | 1.4304 | 1.4378 | 1.4208 | 1.4392 | 1.4339 | 0.0084 | 0.58% |
| | Porosity | 0.13% | 0.87% | 0.36% | 1.54% | 0.26% | 0.63% | 0.0058 | 91.87% |
| | Hardness | 29.8000 | 32.7000 | 30.6000 | 29.8000 | 20.0000 | 28.5800 | 4.9409 | 17.29% |
| **20.9** | Weight | 0.2002 | 0.1970 | 0.2075 | 0.2033 | 0.1996 | 0.2015 | 0.0040 | 2.00% |
| | Diameter | 0.4000 | 0.4010 | 0.4010 | 0.4010 | 0.4005 | 0.4007 | 0.0004 | 0.11% |
| | Height | 0.2810 | 0.2760 | 0.2920 | 0.2840 | 0.2810 | 0.2828 | 0.0059 | 2.08% |
| | Volume | 0.1413 | 0.1395 | 0.1476 | 0.1435 | 0.1417 | 0.1427 | 0.0031 | 2.15% |
| | Density | 1.4168 | 1.4124 | 1.4061 | 1.4165 | 1.4090 | 1.4122 | 0.0046 | 0.33% |
| | Porosity | 1.81% | 2.12% | 2.56% | 1.84% | 2.35% | 2.14% | 0.0032 | 15.07% |
| | Hardness | 28.2000 | 26.2000 | 33.5000 | 27.8000 | 36.8000 | 30.5000 | 4.4654 | 14.64% |

**Table A.2.3:** *Swelling and water uptake for sodium starch glycolate compacts at a compression force of 17.9 N.*

| Sodium starch glycolate (17.9 N) | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.036 | 0.42 | 0.017 | 0.46 | 0.043 | 0.51 | 0.022 | 0.56 | 0.030 | 0.49 | 0.012 | 0.061 | 40.91% | 12.46% |
| 4 | 0.063 | 0.71 | 0.053 | 0.94 | 0.071 | 1.02 | 0.059 | 0.97 | 0.062 | 0.91 | 0.008 | 0.137 | 12.28% | 15.09% |
| 6 | 0.084 | 0.85 | 0.074 | 1.19 | 0.094 | 1.28 | 0.082 | 1.25 | 0.084 | 1.14 | 0.008 | 0.199 | 9.85% | 17.38% |
| 8 | 0.104 | 0.94 | 0.092 | 1.38 | 0.112 | 1.53 | 0.102 | 1.47 | 0.103 | 1.33 | 0.008 | 0.267 | 8.03% | 20.09% |
| 10 | 0.119 | 1.00 | 0.106 | 1.53 | 0.131 | 1.78 | 0.118 | 1.67 | 0.119 | 1.50 | 0.010 | 0.345 | 8.62% | 23.11% |
| 15 | 0.149 | 1.13 | 0.134 | 1.84 | 0.163 | 2.28 | 0.149 | 2.04 | 0.149 | 1.82 | 0.012 | 0.495 | 7.96% | 27.19% |
| 20 | 0.166 | 1.20 | 0.149 | 2.02 | 0.190 | 2.74 | 0.171 | 2.35 | 0.169 | 2.08 | 0.017 | 0.655 | 9.98% | 31.52% |
| 25 | 0.175 | 1.26 | 0.158 | 2.11 | 0.204 | 3.04 | 0.183 | 2.65 | 0.180 | 2.27 | 0.019 | 0.771 | 10.61% | 34.04% |
| 30 | 0.191 | 1.31 | 0.173 | 2.15 | 0.211 | 3.04 | 0.195 | 2.82 | 0.193 | 2.33 | 0.016 | 0.778 | 8.11% | 33.40% |
| 35 | 0.208 | 1.34 | 0.187 | 2.19 | 0.221 | 3.04 | 0.209 | 2.82 | 0.206 | 2.35 | 0.014 | 0.762 | 6.85% | 32.47% |
| 40 | 0.224 | 1.36 | 0.199 | 2.23 | 0.232 | 3.04 | 0.220 | 2.82 | 0.219 | 2.36 | 0.014 | 0.751 | 6.44% | 31.78% |
| 45 | 0.239 | 1.42 | 0.211 | 2.29 | 0.242 | 3.04 | 0.231 | 2.82 | 0.231 | 2.39 | 0.014 | 0.721 | 6.05% | 30.12% |
| 50 | 0.253 | 1.49 | 0.222 | 2.32 | 0.251 | 3.04 | 0.241 | 2.82 | 0.242 | 2.42 | 0.014 | 0.688 | 5.86% | 28.45% |
| 55 | 0.267 | 1.53 | 0.233 | 2.33 | 0.260 | 3.04 | 0.251 | 2.82 | 0.253 | 2.43 | 0.015 | 0.669 | 5.82% | 27.55% |
| 60 | 0.280 | 1.60 | 0.243 | 2.34 | 0.268 | 3.04 | 0.260 | 2.82 | 0.263 | 2.45 | 0.016 | 0.638 | 5.91% | 26.02% |
| 65 | 0.293 | 1.63 | 0.253 | 2.34 | 0.276 | 3.04 | 0.269 | 2.82 | 0.273 | 2.46 | 0.017 | 0.624 | 6.08% | 25.40% |
| 70 | 0.305 | 1.66 | 0.263 | 2.34 | 0.284 | 3.04 | 0.277 | 2.82 | 0.282 | 2.47 | 0.018 | 0.611 | 6.20% | 24.79% |

**Table A.2.4:** *Swelling and water uptake for sodium starch glycolate compacts at a compression force of 18.9 N.*

| Sodium starch glycolate (18.9 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.019 | 0.39 | 0.013 | 0.27 | 0.032 | 0.60 | 0.028 | 0.55 | 0.014 | 0.49 | 0.021 | 0.46 | 0.008 | 0.132 | 39.94% | 28.68% |
| 4 | 0.044 | 0.66 | 0.048 | 0.83 | 0.065 | 1.06 | 0.062 | 1.06 | 0.047 | 0.98 | 0.053 | 0.92 | 0.010 | 0.172 | 18.00% | 18.75% |
| 6 | 0.062 | 0.81 | 0.078 | 1.24 | 0.091 | 1.46 | 0.089 | 1.47 | 0.075 | 1.33 | 0.079 | 1.26 | 0.012 | 0.270 | 14.84% | 21.40% |
| 8 | 0.076 | 0.90 | 0.098 | 1.57 | 0.109 | 1.79 | 0.113 | 1.83 | 0.100 | 1.68 | 0.099 | 1.55 | 0.014 | 0.379 | 14.49% | 24.41% |
| 10 | 0.088 | 0.98 | 0.115 | 1.84 | 0.124 | 2.03 | 0.130 | 2.11 | 0.117 | 1.94 | 0.115 | 1.78 | 0.016 | 0.458 | 14.04% | 25.75% |
| 15 | 0.112 | 1.10 | 0.148 | 2.35 | 0.146 | 2.42 | 0.161 | 2.59 | 0.145 | 2.36 | 0.142 | 2.16 | 0.018 | 0.603 | 12.76% | 27.84% |
| 20 | 0.119 | 1.17 | 0.169 | 2.69 | 0.162 | 2.70 | 0.186 | 2.99 | 0.160 | 2.67 | 0.159 | 2.44 | 0.025 | 0.724 | 15.51% | 29.63% |
| 25 | 0.133 | 1.19 | 0.175 | 2.93 | 0.172 | 2.85 | 0.189 | 2.99 | 0.168 | 2.84 | 0.167 | 2.56 | 0.021 | 0.768 | 12.42% | 30.01% |
| 30 | 0.149 | 1.20 | 0.189 | 3.08 | 0.185 | 2.91 | 0.197 | 2.99 | 0.181 | 2.86 | 0.180 | 2.61 | 0.018 | 0.791 | 10.22% | 30.35% |
| 35 | 0.164 | 1.20 | 0.201 | 3.08 | 0.196 | 2.91 | 0.207 | 2.99 | 0.191 | 2.86 | 0.192 | 2.61 | 0.017 | 0.791 | 8.67% | 30.35% |
| 40 | 0.179 | 1.20 | 0.211 | 3.08 | 0.206 | 2.91 | 0.217 | 2.99 | 0.201 | 2.86 | 0.203 | 2.61 | 0.015 | 0.791 | 7.18% | 30.35% |
| 45 | 0.192 | 1.20 | 0.220 | 3.08 | 0.215 | 2.91 | 0.226 | 2.99 | 0.210 | 2.86 | 0.213 | 2.61 | 0.013 | 0.791 | 6.09% | 30.35% |
| 50 | 0.205 | 1.20 | 0.229 | 3.08 | 0.224 | 2.91 | 0.234 | 2.99 | 0.219 | 2.86 | 0.222 | 2.61 | 0.011 | 0.791 | 5.01% | 30.35% |
| 55 | 0.218 | 1.20 | 0.238 | 3.08 | 0.233 | 2.91 | 0.243 | 2.99 | 0.228 | 2.86 | 0.232 | 2.61 | 0.010 | 0.791 | 4.15% | 30.35% |
| 60 | 0.231 | 1.20 | 0.247 | 3.08 | 0.242 | 2.91 | 0.250 | 2.99 | 0.235 | 2.86 | 0.241 | 2.61 | 0.008 | 0.791 | 3.31% | 30.35% |
| 65 | 0.243 | 1.20 | 0.255 | 3.08 | 0.250 | 2.91 | 0.258 | 2.99 | 0.243 | 2.86 | 0.250 | 2.61 | 0.007 | 0.791 | 2.74% | 30.35% |
| 70 | 0.255 | 1.20 | 0.263 | 3.08 | 0.258 | 2.91 | 0.266 | 2.99 | 0.250 | 2.86 | 0.258 | 2.61 | 0.006 | 0.791 | 2.46% | 30.35% |

**Table A.2.5:** *Swelling and water uptake for sodium starch glycolate compacts at a compression force of 19.9 N.*

| Sodium starch glycolate (19.9 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.000 | 0.11 | 0.001 | 0.31 | 0.014 | 0.23 | 0.009 | 0.26 | 0.002 | 0.26 | 0.014 | 0.30 | 0.007 | 0.25 | 0.007 | 0.072 | 97.52% | 29.52% |
| 4 | 0.008 | 0.34 | 0.029 | 0.69 | 0.043 | 0.72 | 0.041 | 0.81 | 0.019 | 0.67 | 0.030 | 0.85 | 0.028 | 0.68 | 0.013 | 0.181 | 46.81% | 26.57% |
| 6 | 0.024 | 0.55 | 0.050 | 0.98 | 0.069 | 1.17 | 0.070 | 1.29 | 0.045 | 1.06 | 0.061 | 1.34 | 0.053 | 1.07 | 0.017 | 0.286 | 32.82% | 26.88% |
| 8 | 0.039 | 0.73 | 0.067 | 1.22 | 0.090 | 1.55 | 0.091 | 1.66 | 0.071 | 1.44 | 0.088 | 1.74 | 0.074 | 1.39 | 0.020 | 0.371 | 27.06% | 26.69% |
| 10 | 0.052 | 0.91 | 0.082 | 1.40 | 0.113 | 1.95 | 0.109 | 1.97 | 0.091 | 1.68 | 0.110 | 2.11 | 0.093 | 1.67 | 0.023 | 0.450 | 25.27% | 26.95% |
| 15 | 0.081 | 1.31 | 0.107 | 1.59 | 0.151 | 2.61 | 0.142 | 2.56 | 0.130 | 2.29 | 0.152 | 2.95 | 0.127 | 2.22 | 0.028 | 0.637 | 22.10% | 28.73% |
| 20 | 0.112 | 1.80 | 0.113 | 1.71 | 0.180 | 3.12 | 0.174 | 3.12 | 0.157 | 2.71 | 0.182 | 3.11 | 0.153 | 2.60 | 0.033 | 0.670 | 21.30% | 25.82% |
| 25 | 0.120 | 1.93 | 0.128 | 1.82 | 0.183 | 3.12 | 0.177 | 3.12 | 0.182 | 3.14 | 0.184 | 3.11 | 0.162 | 2.71 | 0.030 | 0.645 | 18.42% | 23.84% |
| 30 | 0.130 | 1.97 | 0.145 | 1.90 | 0.190 | 3.12 | 0.185 | 3.12 | 0.193 | 3.18 | 0.193 | 3.11 | 0.173 | 2.73 | 0.028 | 0.619 | 16.10% | 22.66% |
| 35 | 0.142 | 2.01 | 0.160 | 1.96 | 0.200 | 3.12 | 0.196 | 3.12 | 0.197 | 3.18 | 0.204 | 3.11 | 0.183 | 2.75 | 0.026 | 0.593 | 14.04% | 21.57% |
| 40 | 0.153 | 2.14 | 0.175 | 2.01 | 0.210 | 3.12 | 0.208 | 3.12 | 0.206 | 3.18 | 0.215 | 3.11 | 0.195 | 2.78 | 0.025 | 0.548 | 12.76% | 19.72% |
| 45 | 0.167 | 2.31 | 0.188 | 2.06 | 0.220 | 3.12 | 0.218 | 3.12 | 0.216 | 3.18 | 0.225 | 3.11 | 0.206 | 2.82 | 0.023 | 0.496 | 11.18% | 17.62% |
| 50 | 0.181 | 2.41 | 0.200 | 2.11 | 0.231 | 3.12 | 0.229 | 3.12 | 0.225 | 3.18 | 0.236 | 3.11 | 0.217 | 2.84 | 0.022 | 0.461 | 9.99% | 16.23% |
| 55 | 0.193 | 2.50 | 0.213 | 2.17 | 0.241 | 3.12 | 0.239 | 3.12 | 0.234 | 3.18 | 0.245 | 3.11 | 0.228 | 2.87 | 0.020 | 0.426 | 8.93% | 14.85% |
| 60 | 0.204 | 2.57 | 0.225 | 2.29 | 0.250 | 3.12 | 0.248 | 3.12 | 0.243 | 3.18 | 0.254 | 3.11 | 0.237 | 2.90 | 0.019 | 0.374 | 8.10% | 12.91% |
| 65 | 0.215 | 2.62 | 0.238 | 2.50 | 0.260 | 3.12 | 0.257 | 3.12 | 0.252 | 3.18 | 0.263 | 3.11 | 0.248 | 2.94 | 0.018 | 0.299 | 7.35% | 10.17% |
| 70 | 0.224 | 2.66 | 0.252 | 2.71 | 0.263 | 3.12 | 0.266 | 3.12 | 0.260 | 3.18 | 0.272 | 3.11 | 0.256 | 2.98 | 0.017 | 0.233 | 6.67% | 7.81% |

**Table A.2.6:** *Swelling and water uptake for sodium starch glycolate compacts at a compression force of 21.0 N.*

| Sodium starch glycolate (21.0 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.004 | 0.22 | 0.001 | 0.25 | 0.002 | 0.22 | 0.006 | 0.23 | 0.003 | 0.28 | 0.015 | 0.27 | 0.005 | 0.25 | 0.005 | 0.026 | 99.01% | 10.57% |
| 4 | 0.034 | 0.71 | 0.003 | 0.80 | 0.036 | 0.68 | 0.031 | 0.63 | 0.032 | 0.75 | 0.046 | 0.81 | 0.030 | 0.73 | 0.014 | 0.070 | 47.58% | 9.61% |
| 6 | 0.059 | 1.16 | 0.004 | 1.23 | 0.061 | 1.12 | 0.055 | 0.98 | 0.056 | 1.19 | 0.072 | 1.27 | 0.051 | 1.16 | 0.024 | 0.102 | 46.70% | 8.79% |
| 8 | 0.081 | 1.56 | 0.030 | 1.60 | 0.083 | 1.48 | 0.074 | 1.34 | 0.077 | 1.56 | 0.095 | 1.68 | 0.073 | 1.54 | 0.022 | 0.116 | 30.57% | 7.56% |
| 10 | 0.102 | 1.95 | 0.060 | 1.93 | 0.102 | 1.83 | 0.094 | 1.66 | 0.097 | 1.92 | 0.115 | 2.08 | 0.095 | 1.90 | 0.019 | 0.140 | 19.57% | 7.41% |
| 15 | 0.140 | 2.64 | 0.110 | 2.71 | 0.139 | 2.44 | 0.133 | 2.37 | 0.136 | 2.60 | 0.156 | 2.85 | 0.136 | 2.60 | 0.015 | 0.176 | 10.98% | 6.76% |
| 20 | 0.169 | 3.16 | 0.153 | 3.16 | 0.169 | 3.02 | 0.166 | 2.98 | 0.170 | 3.15 | 0.172 | 3.04 | 0.167 | 3.09 | 0.007 | 0.081 | 4.14% | 2.62% |
| 25 | 0.172 | 3.16 | 0.175 | 3.16 | 0.182 | 3.15 | 0.172 | 3.16 | 0.173 | 3.15 | 0.177 | 3.04 | 0.175 | 3.14 | 0.004 | 0.048 | 2.21% | 1.52% |
| 30 | 0.179 | 3.16 | 0.178 | 3.16 | 0.185 | 3.15 | 0.179 | 3.16 | 0.180 | 3.15 | 0.186 | 3.04 | 0.181 | 3.14 | 0.003 | 0.048 | 1.89% | 1.52% |
| 35 | 0.190 | 3.16 | 0.185 | 3.16 | 0.194 | 3.15 | 0.189 | 3.16 | 0.190 | 3.15 | 0.195 | 3.04 | 0.191 | 3.14 | 0.004 | 0.048 | 1.90% | 1.52% |
| 40 | 0.201 | 3.16 | 0.195 | 3.16 | 0.203 | 3.15 | 0.200 | 3.16 | 0.199 | 3.15 | 0.205 | 3.04 | 0.201 | 3.14 | 0.003 | 0.048 | 1.72% | 1.52% |
| 45 | 0.212 | 3.16 | 0.204 | 3.16 | 0.213 | 3.15 | 0.210 | 3.16 | 0.209 | 3.15 | 0.214 | 3.04 | 0.210 | 3.14 | 0.004 | 0.048 | 1.72% | 1.52% |
| 50 | 0.221 | 3.16 | 0.213 | 3.16 | 0.223 | 3.15 | 0.220 | 3.16 | 0.219 | 3.15 | 0.223 | 3.04 | 0.220 | 3.14 | 0.004 | 0.048 | 1.69% | 1.52% |
| 55 | 0.231 | 3.16 | 0.222 | 3.16 | 0.232 | 3.15 | 0.229 | 3.16 | 0.228 | 3.15 | 0.231 | 3.04 | 0.229 | 3.14 | 0.004 | 0.048 | 1.60% | 1.52% |
| 60 | 0.240 | 3.16 | 0.231 | 3.16 | 0.241 | 3.15 | 0.239 | 3.16 | 0.237 | 3.15 | 0.240 | 3.04 | 0.238 | 3.14 | 0.004 | 0.048 | 1.55% | 1.52% |
| 65 | 0.249 | 3.16 | 0.240 | 3.16 | 0.250 | 3.15 | 0.248 | 3.16 | 0.245 | 3.15 | 0.248 | 3.04 | 0.247 | 3.14 | 0.004 | 0.048 | 1.49% | 1.52% |
| 70 | 0.257 | 3.16 | 0.248 | 3.16 | 0.252 | 3.15 | 0.256 | 3.16 | 0.253 | 3.15 | 0.255 | 3.04 | 0.254 | 3.14 | 0.003 | 0.048 | 1.29% | 1.52% |

## A.3 EXPLOTAB®

**Table A.3.1:** *Disintegration times Explotab® compacts at various compression forces.*

| Explotab | | | | |
|---|---|---|---|---|
| **Average compression force** | **17.8** | **18.8** | **20.0** | **20.9** |
| **Tablet** | **Disintegration time (sec)** | | | |
| **1** | 51.69 | 56.43 | 92.90 | 135.50 |
| **2** | 43.68 | 62.40 | 81.20 | 136.10 |
| **3** | 49.75 | 52.10 | 85.10 | 129.80 |
| **4** | 57.81 | 60.34 | 90.90 | 141.60 |
| **Average** | 50.73 | 57.82 | 87.53 | 135.75 |
| **SD** | 5.823 | 4.544 | 5.359 | 4.824 |
| **RSD** | 11.48% | 7.86% | 6.12% | 3.55% |

**Table A.3.2:** *Properties of pure Explotab® compacts at various compression forces*

| Explotab | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **17.8** | Weight | 0.1955 | 0.1948 | 0.1985 | 0.2003 | 0.1994 | 0.1977 | 0.0024 | 1.23% |
| | Diameter | 0.4045 | 0.4035 | 0.4045 | 0.4045 | 0.4045 | 0.4043 | 0.0004 | 0.11% |
| | Height | 0.3460 | 0.3380 | 0.3380 | 0.3410 | 0.3490 | 0.3424 | 0.0049 | 1.44% |
| | Volume | 0.1779 | 0.1730 | 0.1738 | 0.1754 | 0.1795 | 0.1759 | 0.0027 | 1.56% |
| | Density | 1.0988 | 1.1263 | 1.1420 | 1.1423 | 1.1111 | 1.1241 | 0.0192 | 1.70% |
| | Porosity | 27.23% | 25.41% | 24.37% | 24.35% | 26.42% | 25.56% | 0.0127 | 4.96% |
| | Hardness | 13.9000 | 20.4000 | 19.2000 | 10.6000 | 18.0000 | 16.4200 | 4.0709 | 24.79% |
| **18.8** | Weight | 0.1972 | 0.1978 | 0.2000 | 0.1959 | 0.2016 | 0.1985 | 0.0023 | 1.15% |
| | Diameter | 0.4020 | 0.4030 | 0.4030 | 0.4035 | 0.4035 | 0.4030 | 0.0006 | 0.15% |
| | Height | 0.3150 | 0.3200 | 0.3280 | 0.3260 | 0.3370 | 0.3252 | 0.0083 | 2.57% |
| | Volume | 0.1600 | 0.1633 | 0.1674 | 0.1668 | 0.1724 | 0.1660 | 0.0047 | 2.82% |
| | Density | 1.2326 | 1.2110 | 1.1946 | 1.1744 | 1.1691 | 1.1963 | 0.0263 | 2.19% |
| | Porosity | 18.37% | 19.80% | 20.89% | 22.23% | 22.58% | 20.77% | 0.0174 | 8.37% |
| | Hardness | 61.3000 | 28.6000 | 34.7000 | 22.1000 | 18.4000 | 33.0200 | 16.9934 | 51.46% |
| **20** | Weight | 0.2039 | 0.2061 | 0.2042 | 0.2028 | 0.1998 | 0.2034 | 0.0023 | 1.14% |
| | Diameter | 0.4035 | 0.4020 | 0.4025 | 0.4025 | 0.4025 | 0.4026 | 0.0005 | 0.14% |
| | Height | 0.3200 | 0.3150 | 0.3160 | 0.3140 | 0.3080 | 0.3146 | 0.0043 | 1.38% |
| | Volume | 0.1637 | 0.1600 | 0.1609 | 0.1599 | 0.1568 | 0.1603 | 0.0025 | 1.55% |
| | Density | 1.2452 | 1.2882 | 1.2691 | 1.2685 | 1.2741 | 1.2690 | 0.0155 | 1.22% |
| | Porosity | 17.53% | 14.69% | 15.95% | 16.00% | 15.63% | 15.96% | 0.0103 | 6.43% |
| | Hardness | 42.9000 | 73.5000 | 72.7000 | 66.6000 | 51.5000 | 61.4400 | 13.6143 | 22.16% |
| **20.9** | Weight | 0.1884 | 0.1955 | 0.1998 | 0.2023 | 0.1923 | 0.1957 | 0.0056 | 2.86% |
| | Diameter | 0.4020 | 0.4010 | 0.4005 | 0.4025 | 0.4020 | 0.4016 | 0.0008 | 0.20% |
| | Height | 0.2790 | 0.2900 | 0.2960 | 0.3040 | 0.2930 | 0.2924 | 0.0091 | 3.12% |
| | Volume | 0.1417 | 0.1466 | 0.1492 | 0.1548 | 0.1488 | 0.1482 | 0.0047 | 3.19% |
| | Density | 1.3295 | 1.3339 | 1.3390 | 1.3070 | 1.2922 | 1.3203 | 0.0199 | 1.51% |
| | Porosity | 11.95% | 11.66% | 11.33% | 13.45% | 14.42% | 12.56% | 0.01319 | 10.50% |
| | Hardness | 98.1000 | 100.5000 | 131.2000 | 65.4000 | 75.2000 | 94.0800 | 25.5650 | 27.17% |

**Table A.3.3:** *Swelling and water uptake for pure Explotab® compacts at a compression force of 17.8 N.*

| Explotab (17.8 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.007 | 0.21 | 0.017 | 0.23 | 0.027 | 0.30 | 0.015 | 0.03 | 0.020 | 0.18 | 0.017 | 0.19 | 0.008 | 0.115 | 47.83% | 60.53% |
| 4 | 0.019 | 0.29 | 0.030 | 0.33 | 0.038 | 0.44 | 0.030 | 0.10 | 0.033 | 0.32 | 0.030 | 0.30 | 0.008 | 0.142 | 26.02% | 47.86% |
| 6 | 0.026 | 0.33 | 0.033 | 0.38 | 0.041 | 0.50 | 0.040 | 0.14 | 0.039 | 0.42 | 0.036 | 0.35 | 0.007 | 0.150 | 19.49% | 42.30% |
| 8 | 0.027 | 0.35 | 0.034 | 0.40 | 0.042 | 0.54 | 0.043 | 0.19 | 0.040 | 0.49 | 0.037 | 0.39 | 0.008 | 0.144 | 20.18% | 36.66% |
| 10 | 0.029 | 0.37 | 0.037 | 0.41 | 0.045 | 0.57 | 0.044 | 0.24 | 0.042 | 0.54 | 0.039 | 0.43 | 0.007 | 0.136 | 18.81% | 31.92% |
| 15 | 0.038 | 0.39 | 0.046 | 0.43 | 0.053 | 0.60 | 0.053 | 0.34 | 0.052 | 0.64 | 0.048 | 0.48 | 0.007 | 0.113 | 14.76% | 23.51% |
| 20 | 0.046 | 0.40 | 0.052 | 0.44 | 0.059 | 0.62 | 0.061 | 0.41 | 0.059 | 0.69 | 0.055 | 0.51 | 0.007 | 0.103 | 12.37% | 20.13% |
| 25 | 0.051 | 0.40 | 0.056 | 0.44 | 0.063 | 0.63 | 0.068 | 0.45 | 0.064 | 0.72 | 0.060 | 0.53 | 0.008 | 0.102 | 12.43% | 19.38% |
| 30 | 0.056 | 0.40 | 0.060 | 0.44 | 0.066 | 0.63 | 0.072 | 0.48 | 0.068 | 0.75 | 0.064 | 0.54 | 0.007 | 0.100 | 10.87% | 18.60% |
| 35 | 0.059 | 0.40 | 0.063 | 0.44 | 0.070 | 0.63 | 0.075 | 0.50 | 0.070 | 0.75 | 0.067 | 0.54 | 0.007 | 0.100 | 10.59% | 18.47% |
| 40 | 0.063 | 0.40 | 0.066 | 0.44 | 0.072 | 0.63 | 0.079 | 0.52 | 0.073 | 0.75 | 0.071 | 0.55 | 0.007 | 0.101 | 10.02% | 18.51% |
| 45 | 0.066 | 0.40 | 0.069 | 0.44 | 0.075 | 0.63 | 0.082 | 0.52 | 0.075 | 0.75 | 0.073 | 0.55 | 0.007 | 0.101 | 9.63% | 18.51% |
| 50 | 0.069 | 0.40 | 0.072 | 0.44 | 0.077 | 0.63 | 0.085 | 0.52 | 0.076 | 0.75 | 0.076 | 0.55 | 0.007 | 0.101 | 9.23% | 18.51% |
| 55 | 0.070 | 0.40 | 0.070 | 0.44 | 0.080 | 0.63 | 0.090 | 0.52 | 0.080 | 0.75 | 0.078 | 0.55 | 0.010 | 0.101 | 12.27% | 18.51% |
| 60 | 0.070 | 0.40 | 0.070 | 0.44 | 0.080 | 0.63 | 0.090 | 0.52 | 0.080 | 0.75 | 0.078 | 0.55 | 0.010 | 0.101 | 12.27% | 18.51% |
| 65 | 0.070 | 0.40 | 0.070 | 0.44 | 0.080 | 0.63 | 0.090 | 0.52 | 0.080 | 0.75 | 0.078 | 0.55 | 0.010 | 0.101 | 12.27% | 18.51% |
| 70 | 0.070 | 0.40 | 0.070 | 0.44 | 0.080 | 0.63 | 0.090 | 0.52 | 0.080 | 0.75 | 0.078 | 0.55 | 0.010 | 0.101 | 12.27% | 18.51% |
| 75 | 0.070 | 0.40 | 0.070 | 0.44 | 0.080 | 0.63 | 0.090 | 0.52 | 0.080 | 0.75 | 0.078 | 0.55 | 0.010 | 0.101 | 12.27% | 18.51% |

**Table A.3.4:** *Swelling and water uptake for pure Explotab® compacts at a compression force of 18.8 N.*

| Explotab (18.8 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.012 | 0.00 | 0.011 | 0.01 | 0.000 | 0.00 | 0.012 | 0.14 | 0.015 | 0.07 | 0.010 | 0.04 | 0.006 | 0.061 | 57.88% | 138.80% |
| 4 | 0.029 | 0.04 | 0.021 | 0.15 | 0.017 | 0.08 | 0.021 | 0.30 | 0.027 | 0.18 | 0.023 | 0.15 | 0.005 | 0.100 | 21.30% | 67.00% |
| 6 | 0.042 | 0.19 | 0.023 | 0.29 | 0.028 | 0.20 | 0.026 | 0.43 | 0.033 | 0.33 | 0.030 | 0.29 | 0.007 | 0.099 | 24.46% | 34.41% |
| 8 | 0.045 | 0.32 | 0.025 | 0.40 | 0.038 | 0.33 | 0.027 | 0.52 | 0.034 | 0.47 | 0.034 | 0.41 | 0.008 | 0.087 | 24.16% | 21.32% |
| 10 | 0.047 | 0.41 | 0.028 | 0.48 | 0.040 | 0.44 | 0.030 | 0.59 | 0.037 | 0.57 | 0.036 | 0.50 | 0.008 | 0.079 | 21.16% | 15.90% |
| 15 | 0.055 | 0.59 | 0.037 | 0.63 | 0.047 | 0.61 | 0.039 | 0.71 | 0.047 | 0.73 | 0.045 | 0.65 | 0.007 | 0.062 | 16.02% | 9.52% |
| 20 | 0.064 | 0.71 | 0.044 | 0.73 | 0.057 | 0.71 | 0.046 | 0.79 | 0.054 | 0.81 | 0.053 | 0.75 | 0.008 | 0.047 | 15.44% | 6.25% |
| 25 | 0.072 | 0.81 | 0.049 | 0.78 | 0.064 | 0.78 | 0.051 | 0.84 | 0.059 | 0.87 | 0.059 | 0.82 | 0.009 | 0.039 | 16.03% | 4.79% |
| 30 | 0.078 | 0.89 | 0.052 | 0.83 | 0.070 | 0.85 | 0.055 | 0.88 | 0.063 | 0.91 | 0.064 | 0.87 | 0.011 | 0.032 | 16.81% | 3.66% |
| 35 | 0.083 | 0.97 | 0.055 | 0.86 | 0.074 | 0.91 | 0.059 | 0.92 | 0.067 | 0.94 | 0.068 | 0.92 | 0.011 | 0.041 | 16.72% | 4.42% |
| 40 | 0.087 | 1.04 | 0.057 | 0.89 | 0.079 | 0.95 | 0.062 | 0.95 | 0.070 | 0.97 | 0.071 | 0.96 | 0.012 | 0.054 | 17.22% | 5.61% |
| 45 | 0.092 | 1.09 | 0.060 | 0.92 | 0.082 | 1.00 | 0.064 | 0.98 | 0.072 | 0.99 | 0.074 | 1.00 | 0.013 | 0.061 | 17.72% | 6.13% |
| 50 | 0.095 | 1.14 | 0.062 | 0.95 | 0.085 | 1.05 | 0.067 | 1.00 | 0.074 | 1.00 | 0.077 | 1.03 | 0.013 | 0.072 | 17.53% | 6.99% |
| 55 | 0.099 | 1.17 | 0.063 | 0.98 | 0.089 | 1.09 | 0.069 | 1.01 | 0.076 | 1.00 | 0.079 | 1.05 | 0.015 | 0.079 | 18.57% | 7.53% |
| 60 | 0.102 | 1.21 | 0.065 | 1.00 | 0.092 | 1.13 | 0.071 | 1.01 | 0.078 | 1.00 | 0.082 | 1.07 | 0.015 | 0.096 | 18.64% | 8.94% |
| 65 | 0.104 | 1.24 | 0.067 | 1.02 | 0.095 | 1.18 | 0.071 | 1.01 | 0.079 | 1.00 | 0.083 | 1.09 | 0.016 | 0.112 | 19.01% | 10.26% |
| 70 | 0.107 | 1.28 | 0.069 | 1.04 | 0.097 | 1.21 | 0.071 | 1.01 | 0.079 | 1.00 | 0.085 | 1.11 | 0.017 | 0.128 | 19.74% | 11.58% |
| 75 | 0.110 | 1.30 | 0.070 | 1.05 | 0.10 | 1.25 | 0.071 | 1.01 | 0.079 | 1.00 | 0.086 | 1.12 | 0.018 | 0.142 | 20.98% | 12.66% |

**Table A.3.5:** *Swelling and water uptake for pure Explotab® compacts at a compression force of 20.0 N.*

| Explotab (20.0 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.021 | 0.27 | 0.028 | 0.37 | 0.021 | 0.41 | 0.021 | 0.55 | 0.029 | 0.44 | 0.011 | 0.30 | 0.022 | 0.390 | 0.006 | 0.101 | 29.60% | 26.00% |
| 4 | 0.043 | 0.62 | 0.042 | 0.57 | 0.037 | 0.68 | 0.048 | 0.78 | 0.046 | 0.73 | 0.034 | 0.53 | 0.042 | 0.652 | 0.005 | 0.096 | 12.76% | 14.70% |
| 6 | 0.054 | 0.78 | 0.049 | 0.66 | 0.046 | 0.86 | 0.058 | 0.90 | 0.054 | 0.84 | 0.048 | 0.69 | 0.052 | 0.788 | 0.005 | 0.096 | 8.83% | 12.23% |
| 8 | 0.059 | 0.86 | 0.050 | 0.71 | 0.052 | 1.00 | 0.064 | 0.99 | 0.055 | 0.90 | 0.053 | 0.78 | 0.056 | 0.873 | 0.005 | 0.115 | 9.31% | 13.15% |
| 10 | 0.060 | 0.91 | 0.051 | 0.74 | 0.053 | 1.12 | 0.065 | 1.05 | 0.057 | 0.93 | 0.054 | 0.85 | 0.057 | 0.933 | 0.005 | 0.137 | 9.11% | 14.64% |
| 15 | 0.065 | 0.97 | 0.057 | 0.77 | 0.063 | 1.32 | 0.071 | 1.12 | 0.063 | 0.96 | 0.061 | 0.95 | 0.063 | 1.015 | 0.005 | 0.186 | 7.32% | 18.34% |
| 20 | 0.071 | 1.00 | 0.061 | 0.78 | 0.074 | 1.49 | 0.076 | 1.15 | 0.067 | 0.97 | 0.070 | 1.03 | 0.070 | 1.070 | 0.005 | 0.238 | 7.65% | 22.25% |
| 25 | 0.076 | 1.01 | 0.065 | 0.78 | 0.082 | 1.60 | 0.080 | 1.16 | 0.069 | 0.97 | 0.076 | 1.09 | 0.075 | 1.102 | 0.007 | 0.276 | 8.71% | 25.06% |
| 30 | 0.079 | 1.02 | 0.068 | 0.78 | 0.090 | 1.71 | 0.082 | 1.17 | 0.071 | 0.97 | 0.081 | 1.13 | 0.079 | 1.130 | 0.008 | 0.316 | 10.15% | 27.93% |
| 35 | 0.082 | 1.02 | 0.071 | 0.78 | 0.096 | 1.77 | 0.083 | 1.17 | 0.072 | 0.97 | 0.085 | 1.17 | 0.082 | 1.147 | 0.009 | 0.338 | 11.32% | 29.48% |
| 40 | 0.084 | 1.02 | 0.073 | 0.78 | 0.100 | 1.84 | 0.085 | 1.17 | 0.072 | 0.97 | 0.088 | 1.22 | 0.084 | 1.167 | 0.010 | 0.365 | 12.39% | 31.28% |
| 45 | 0.086 | 1.02 | 0.074 | 0.78 | 0.104 | 1.89 | 0.086 | 1.17 | 0.072 | 0.97 | 0.091 | 1.25 | 0.086 | 1.180 | 0.012 | 0.384 | 13.71% | 32.58% |
| 50 | 0.088 | 1.02 | 0.074 | 0.78 | 0.107 | 1.92 | 0.086 | 1.17 | 0.072 | 0.97 | 0.094 | 1.30 | 0.087 | 1.193 | 0.013 | 0.398 | 14.97% | 33.32% |
| 55 | 0.088 | 1.02 | 0.074 | 0.78 | 0.109 | 1.94 | 0.086 | 1.17 | 0.072 | 0.97 | 0.097 | 1.30 | 0.088 | 1.197 | 0.014 | 0.405 | 15.95% | 33.84% |
| 60 | 0.088 | 1.02 | 0.074 | 0.78 | 0.110 | 1.94 | 0.086 | 1.17 | 0.072 | 0.97 | 0.100 | 1.30 | 0.088 | 1.197 | 0.015 | 0.405 | 16.66% | 33.84% |
| 65 | 0.088 | 1.02 | 0.074 | 0.78 | 0.110 | 1.94 | 0.086 | 1.17 | 0.072 | 0.97 | 0.103 | 1.30 | 0.089 | 1.197 | 0.015 | 0.405 | 17.15% | 33.84% |
| 70 | 0.088 | 1.02 | 0.074 | 0.78 | 0.110 | 1.94 | 0.09 | 1.17 | 0.072 | 0.97 | 0.103 | 1.30 | 0.089 | 1.197 | 0.015 | 0.405 | 17.15% | 33.84% |
| 75 | 0.088 | 1.02 | 0.074 | 0.78 | 0.110 | 1.94 | 0.09 | 1.17 | 0.072 | 0.97 | 0.103 | 1.30 | 0.089 | 1.197 | 0.015 | 0.405 | 17.15% | 33.84% |

**Table A.3.6:** *Swelling and water uptake for pure Explotab® compacts at a compression force of 20.9 N.*

| Explotab (20.9 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.016 | 0.22 | 0.026 | 0.28 | 0.011 | 0.28 | 0.001 | 0.00 | 0.014 | 0.09 | 0.027 | 0.21 | 0.016 | 0.180 | 0.010 | 0.112 | 61.55% | 62.36% |
| 4 | 0.030 | 0.34 | 0.041 | 0.40 | 0.024 | 0.41 | 0.005 | 0.05 | 0.028 | 0.19 | 0.035 | 0.27 | 0.027 | 0.277 | 0.012 | 0.139 | 45.47% | 50.07% |
| 6 | 0.033 | 0.41 | 0.048 | 0.46 | 0.030 | 0.50 | 0.026 | 0.19 | 0.037 | 0.24 | 0.037 | 0.30 | 0.035 | 0.350 | 0.008 | 0.125 | 21.54% | 35.78% |
| 8 | 0.034 | 0.44 | 0.049 | 0.49 | 0.032 | 0.56 | 0.037 | 0.27 | 0.040 | 0.27 | 0.038 | 0.31 | 0.038 | 0.390 | 0.006 | 0.124 | 15.54% | 31.74% |
| 10 | 0.036 | 0.47 | 0.051 | 0.51 | 0.033 | 0.60 | 0.043 | 0.32 | 0.041 | 0.29 | 0.040 | 0.32 | 0.041 | 0.418 | 0.006 | 0.126 | 15.29% | 30.21% |
| 15 | 0.043 | 0.49 | 0.059 | 0.53 | 0.039 | 0.65 | 0.047 | 0.37 | 0.048 | 0.30 | 0.046 | 0.32 | 0.047 | 0.443 | 0.007 | 0.137 | 14.30% | 30.85% |
| 20 | 0.047 | 0.50 | 0.065 | 0.54 | 0.045 | 0.70 | 0.055 | 0.40 | 0.055 | 0.31 | 0.050 | 0.33 | 0.053 | 0.463 | 0.007 | 0.147 | 13.67% | 31.80% |
| 25 | 0.050 | 0.50 | 0.070 | 0.54 | 0.048 | 0.72 | 0.061 | 0.41 | 0.060 | 0.31 | 0.054 | 0.33 | 0.057 | 0.468 | 0.008 | 0.153 | 14.27% | 32.67% |
| 30 | 0.052 | 0.50 | 0.073 | 0.54 | 0.051 | 0.73 | 0.066 | 0.41 | 0.065 | 0.31 | 0.056 | 0.33 | 0.061 | 0.470 | 0.009 | 0.156 | 14.59% | 33.26% |
| 35 | 0.053 | 0.50 | 0.076 | 0.54 | 0.053 | 0.73 | 0.070 | 0.41 | 0.069 | 0.31 | 0.059 | 0.33 | 0.063 | 0.470 | 0.010 | 0.156 | 15.30% | 33.26% |
| 40 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.074 | 0.41 | 0.072 | 0.31 | 0.061 | 0.33 | 0.066 | 0.470 | 0.010 | 0.156 | 15.41% | 33.26% |
| 45 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.077 | 0.41 | 0.076 | 0.31 | 0.063 | 0.33 | 0.067 | 0.470 | 0.011 | 0.156 | 16.49% | 33.26% |
| 50 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.080 | 0.41 | 0.079 | 0.31 | 0.063 | 0.33 | 0.068 | 0.470 | 0.012 | 0.156 | 17.84% | 33.26% |
| 55 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.083 | 0.41 | 0.082 | 0.31 | 0.063 | 0.33 | 0.069 | 0.470 | 0.013 | 0.156 | 19.29% | 33.26% |
| 60 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.08 | 0.41 | 0.083 | 0.31 | 0.063 | 0.33 | 0.069 | 0.470 | 0.014 | 0.156 | 19.79% | 33.26% |
| 65 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.08 | 0.41 | 0.083 | 0.31 | 0.063 | 0.33 | 0.069 | 0.470 | 0.014 | 0.156 | 19.79% | 33.26% |
| 70 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.08 | 0.41 | 0.083 | 0.31 | 0.063 | 0.33 | 0.069 | 0.470 | 0.014 | 0.156 | 19.79% | 33.26% |
| 75 | 0.054 | 0.50 | 0.077 | 0.54 | 0.055 | 0.73 | 0.08 | 0.41 | 0.083 | 0.31 | 0.063 | 0.33 | 0.069 | 0.470 | 0.014 | 0.156 | 19.79% | 33.26% |

## A.4 AVICEL®

**Table A.4.1:** *Disintegration times of pure Avicel® compacts at various compression forces.*

| Avicel | | | | |
|---|---|---|---|---|
| **Average compression force** | **15.0** | **16.1** | **17.1** | **18.0** |
| **Tablet** | **Disintegration time (sec)** | | | |
| **1** | 14.70 | 129.40 | 900.00 | 900.00 |
| **2** | 17.00 | 130.60 | 900.00 | 900.00 |
| **3** | 13.70 | 155.50 | 900.00 | 900.00 |
| **4** | 9.50 | 183.90 | 900.00 | 900.00 |
| **Average** | 13.73 | 149.85 | 900.00 | 900.00 |
| **SD** | 3.137 | 25.691 | 0.000 | 0.000 |
| **RSD** | 22.86% | 17.14% | 0.00% | 0.00% |

**Table A.4.2:** *Properties of pure Avicel® compacts at various compression forces*

| Avicel | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **15.0** | Weight | 0.2012 | 0.1938 | 0.1973 | 0.1940 | 0.1993 | 0.1971 | 0.0032 | 1.65% |
| | Diameter | 0.4015 | 0.4005 | 0.4010 | 0.4010 | 0.4015 | 0.4011 | 0.0004 | 0.10% |
| | Height | 0.5010 | 0.4920 | 0.5000 | 0.4850 | 0.5110 | 0.4978 | 0.0098 | 1.98% |
| | Volume | 0.2538 | 0.2480 | 0.2527 | 0.2451 | 0.2589 | 0.2517 | 0.0053 | 2.12% |
| | Density | 0.7927 | 0.7814 | 0.7808 | 0.7915 | 0.7698 | 0.7832 | 0.0093 | 1.19% |
| | Porosity | 47.57% | 48.32% | 48.36% | 47.65% | 49.09% | 48.20% | 0.0062 | 1.28% |
| | Hardness | 56.0000 | 50.3000 | 51.1000 | 53.1000 | 47.8000 | 51.6600 | 3.0811 | 5.96% |
| **16.0** | Weight | 0.1982 | 0.1991 | 0.2023 | 0.1988 | 0.1963 | 0.1989 | 0.0022 | 1.09% |
| | Diameter | 0.4005 | 0.4010 | 0.4005 | 0.4010 | 0.4010 | 0.4008 | 0.0003 | 0.07% |
| | Height | 0.3750 | 0.3850 | 0.3910 | 0.3780 | 0.3810 | 0.3820 | 0.0062 | 1.63% |
| | Volume | 0.1890 | 0.1946 | 0.1971 | 0.1910 | 0.1925 | 0.1929 | 0.0031 | 1.62% |
| | Density | 1.0484 | 1.0233 | 1.0263 | 1.0407 | 1.0195 | 1.0316 | 0.0123 | 1.20% |
| | Porosity | 30.66% | 32.32% | 32.12% | 31.17% | 32.57% | 31.77% | 0.0082 | 2.57% |
| | Hardness | 136.5000 | 125.4000 | 129.9000 | 129.1000 | 143.0000 | 132.7800 | 6.9747 | 5.25% |
| **17.0** | Weight | 0.1958 | 0.1946 | 0.1978 | 0.2023 | 0.1997 | 0.1980 | 0.0031 | 1.55% |
| | Diameter | 0.4010 | 0.4005 | 0.4005 | 0.4005 | 0.4005 | 0.4006 | 0.0002 | 0.06% |
| | Height | 0.3370 | 0.3360 | 0.3370 | 0.3380 | 0.3400 | 0.3376 | 0.0015 | 0.45% |
| | Volume | 0.1703 | 0.1694 | 0.1699 | 0.1704 | 0.1714 | 0.1703 | 0.0007 | 0.44% |
| | Density | 1.1497 | 1.1489 | 1.1643 | 1.1873 | 1.1651 | 1.1630 | 0.0156 | 1.34% |
| | Porosity | 23.96% | 24.02% | 23.00% | 21.48% | 22.94% | 23.08% | 0.0103 | 4.47% |
| | Hardness | 186.3 | 209.2 | 233.7 | 241.5 | 200.6 | 214.26 | 22.9885 | 10.73% |
| **18.0** | Weight | 0.2024 | 0.2005 | 0.2015 | 0.2015 | 0.1990 | 0.2010 | 0.0013 | 0.64% |
| | Diameter | 0.4005 | 0.4000 | 0.4005 | 0.4005 | 0.3995 | 0.4002 | 0.0004 | 0.11% |
| | Height | 0.3130 | 0.3190 | 0.3120 | 0.3210 | 0.3120 | 0.3154 | 0.0043 | 1.36% |
| | Volume | 0.1578 | 0.1604 | 0.1573 | 0.1618 | 0.1565 | 0.1588 | 0.0023 | 1.42% |
| | Density | 1.2827 | 1.2499 | 1.2811 | 1.2452 | 1.2716 | 1.2661 | 0.0175 | 1.39% |
| | Porosity | 15.16% | 17.33% | 15.27% | 17.65% | 15.90% | 16.26% | 0.0116 | 7.13% |
| | Hardness | 313.0000 | 276.2000 | 273.4000 | 297.1000 | 304.8000 | 292.9000 | 17.4814 | 5.97% |

**Table A.4.3:** *Swelling and water uptake for pure Avicel® compacts at a compression force of 15.0 N.*

| Avicel (15.0 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.066 | 1.29 | 0.055 | 0.98 | 0.043 | 0.82 | 0.015 | 1.43 | 0.015 | 0.91 | 0.039 | 1.086 | 0.023 | 0.261 | 59.79% | 24.05% |
| 4 | 0.137 | 2.20 | 0.155 | 2.08 | 0.144 | 1.63 | 0.119 | 2.39 | 0.081 | 1.91 | 0.127 | 2.042 | 0.029 | 0.289 | 22.76% | 14.17% |
| 6 | 0.177 | 2.92 | 0.209 | 2.91 | 0.196 | 2.40 | 0.180 | 3.13 | 0.153 | 2.67 | 0.183 | 2.806 | 0.021 | 0.279 | 11.56% | 9.96% |
| 8 | 0.212 | 3.10 | 0.244 | 3.00 | 0.233 | 2.77 | 0.218 | 3.21 | 0.203 | 3.02 | 0.222 | 3.020 | 0.016 | 0.162 | 7.41% | 5.38% |
| 10 | 0.229 | 3.10 | 0.248 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.236 | 3.04 | 0.240 | 3.030 | 0.009 | 0.151 | 3.76% | 4.98% |
| 15 | 0.234 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.008 | 0.151 | 3.11% | 4.98% |
| 20 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 25 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 30 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 35 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 40 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 45 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 50 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 55 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |
| 60 | 0.235 | 3.10 | 0.249 | 3.00 | 0.250 | 2.80 | 0.235 | 3.21 | 0.241 | 3.04 | 0.242 | 3.030 | 0.007 | 0.151 | 3.01% | 4.98% |

**Table A.4.4:** *Swelling and water uptake for pure Avicel® compacts at a compression force of 16.1 N.*

| Avicel (16.1 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.035 | 0.77 | 0.021 | 0.78 | 0.033 | 0.67 | 0.047 | 0.82 | 0.024 | 0.69 | 0.027 | 0.91 | 0.031 | 0.773 | 0.009 | 0.088 | 30.13% | 11.35% |
| 4 | 0.092 | 1.28 | 0.074 | 1.28 | 0.075 | 1.19 | 0.086 | 1.28 | 0.068 | 1.13 | 0.082 | 1.38 | 0.080 | 1.257 | 0.009 | 0.086 | 11.07% | 6.88% |
| 6 | 0.115 | 1.63 | 0.097 | 1.60 | 0.096 | 1.54 | 0.109 | 1.62 | 0.088 | 1.45 | 0.107 | 1.72 | 0.102 | 1.593 | 0.010 | 0.091 | 9.80% | 5.72% |
| 8 | 0.133 | 1.91 | 0.113 | 1.85 | 0.114 | 1.84 | 0.125 | 1.90 | 0.105 | 1.72 | 0.125 | 2.02 | 0.119 | 1.873 | 0.010 | 0.099 | 8.60% | 5.27% |
| 10 | 0.148 | 2.17 | 0.126 | 2.11 | 0.129 | 2.11 | 0.139 | 2.16 | 0.118 | 1.95 | 0.140 | 2.27 | 0.133 | 2.128 | 0.011 | 0.105 | 8.21% | 4.94% |
| 15 | 0.177 | 2.60 | 0.155 | 2.61 | 0.160 | 2.67 | 0.168 | 2.59 | 0.146 | 2.49 | 0.169 | 2.68 | 0.163 | 2.607 | 0.011 | 0.068 | 6.84% | 2.62% |
| 20 | 0.185 | 2.63 | 0.168 | 2.68 | 0.184 | 3.01 | 0.173 | 2.60 | 0.170 | 2.84 | 0.177 | 2.70 | 0.176 | 2.743 | 0.007 | 0.155 | 4.05% | 5.64% |
| 25 | 0.186 | 2.63 | 0.169 | 2.68 | 0.187 | 3.02 | 0.174 | 2.60 | 0.176 | 2.88 | 0.178 | 2.70 | 0.178 | 2.752 | 0.007 | 0.164 | 3.93% | 5.95% |
| 30 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 35 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 40 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 45 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 50 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 55 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |
| 60 | 0.186 | 2.63 | 0.170 | 2.68 | 0.187 | 3.02 | 0.175 | 2.60 | 0.177 | 2.88 | 0.178 | 2.70 | 0.179 | 2.752 | 0.007 | 0.164 | 3.67% | 5.95% |

**Table A.4.5:** *Swelling and water uptake for pure Avicel® compacts at a compression force of 17.1 N.*

| Avicel (17.1 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 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 | 0.00% | 0.00% |
| 2 | 0.007 | 0.520 | 0.020 | 0.400 | 0.017 | 0.340 | 0.025 | 0.530 | 0.023 | 0.710 | 0.018 | 0.500 | 0.007 | 0.142 | 38.35% | 28.46% |
| 4 | 0.038 | 0.760 | 0.050 | 0.670 | 0.048 | 0.390 | 0.053 | 0.780 | 0.058 | 0.990 | 0.049 | 0.718 | 0.007 | 0.218 | 14.99% | 30.31% |
| 6 | 0.056 | 0.930 | 0.062 | 0.850 | 0.059 | 0.410 | 0.066 | 0.960 | 0.072 | 1.200 | 0.063 | 0.870 | 0.006 | 0.288 | 9.91% | 33.14% |
| 8 | 0.067 | 1.070 | 0.071 | 0.980 | 0.063 | 0.460 | 0.076 | 1.130 | 0.082 | 1.390 | 0.072 | 1.006 | 0.007 | 0.341 | 10.39% | 33.92% |
| 10 | 0.075 | 1.190 | 0.077 | 1.090 | 0.064 | 0.500 | 0.083 | 1.270 | 0.091 | 1.550 | 0.078 | 1.120 | 0.010 | 0.387 | 12.82% | 34.51% |
| 15 | 0.091 | 1.440 | 0.084 | 1.300 | 0.073 | 0.620 | 0.099 | 1.580 | 0.110 | 1.890 | 0.091 | 1.366 | 0.014 | 0.471 | 15.45% | 34.47% |
| 20 | 0.095 | 1.650 | 0.091 | 1.470 | 0.083 | 0.740 | 0.103 | 1.830 | 0.115 | 2.150 | 0.097 | 1.568 | 0.012 | 0.527 | 12.52% | 33.58% |
| 25 | 0.107 | 1.880 | 0.100 | 1.610 | 0.090 | 0.830 | 0.115 | 2.050 | 0.128 | 2.340 | 0.108 | 1.742 | 0.014 | 0.575 | 13.40% | 32.99% |
| 30 | 0.118 | 1.930 | 0.107 | 1.730 | 0.096 | 0.920 | 0.127 | 2.170 | 0.139 | 2.370 | 0.117 | 1.824 | 0.017 | 0.560 | 14.29% | 30.71% |
| 35 | 0.129 | 1.950 | 0.114 | 1.840 | 0.100 | 0.980 | 0.135 | 2.190 | 0.143 | 2.370 | 0.124 | 1.866 | 0.017 | 0.537 | 13.85% | 28.76% |
| 40 | 0.134 | 1.950 | 0.119 | 1.920 | 0.104 | 1.040 | 0.138 | 2.190 | 0.144 | 2.370 | 0.128 | 1.894 | 0.016 | 0.512 | 12.67% | 27.02% |
| 45 | 0.135 | 1.950 | 0.125 | 1.950 | 0.108 | 1.090 | 0.139 | 2.190 | 0.145 | 2.370 | 0.130 | 1.910 | 0.014 | 0.491 | 11.11% | 25.72% |
| 50 | 0.135 | 1.950 | 0.129 | 1.950 | 0.111 | 1.150 | 0.139 | 2.190 | 0.145 | 2.370 | 0.132 | 1.922 | 0.013 | 0.466 | 9.87% | 24.27% |
| 55 | 0.135 | 1.950 | 0.131 | 1.950 | 0.114 | 1.200 | 0.139 | 2.190 | 0.145 | 2.370 | 0.133 | 1.932 | 0.012 | 0.446 | 8.82% | 23.07% |
| 60 | 0.135 | 1.950 | 0.132 | 1.950 | 0.117 | 1.240 | 0.139 | 2.190 | 0.145 | 2.370 | 0.134 | 1.940 | 0.010 | 0.429 | 7.84% | 22.13% |

**Table A.4.6:** *Swelling and water uptake for pure Avicel® compacts at a compression force of 18.0 N.*

| Avicel (18.0 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 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 | 0.00% | 0.00% |
| 2 | 0.011 | 0.420 | 0.020 | 0.340 | 0.009 | 0.350 | 0.020 | 0.280 | 0.016 | 0.300 | 0.015 | 0.338 | 0.005 | 0.054 | 33.35% | 15.99% |
| 4 | 0.037 | 0.670 | 0.036 | 0.580 | 0.036 | 0.540 | 0.038 | 0.490 | 0.033 | 0.500 | 0.036 | 0.556 | 0.002 | 0.073 | 5.20% | 13.13% |
| 6 | 0.048 | 0.840 | 0.046 | 0.730 | 0.047 | 0.670 | 0.047 | 0.620 | 0.041 | 0.620 | 0.046 | 0.696 | 0.003 | 0.092 | 6.06% | 13.27% |
| 8 | 0.056 | 0.960 | 0.053 | 0.840 | 0.055 | 0.780 | 0.049 | 0.710 | 0.047 | 0.730 | 0.052 | 0.804 | 0.004 | 0.101 | 7.45% | 12.52% |
| 10 | 0.061 | 1.060 | 0.055 | 0.930 | 0.060 | 0.870 | 0.051 | 0.790 | 0.049 | 0.820 | 0.055 | 0.894 | 0.005 | 0.107 | 9.62% | 11.96% |
| 15 | 0.064 | 1.250 | 0.060 | 1.110 | 0.064 | 1.080 | 0.060 | 0.970 | 0.055 | 1.000 | 0.061 | 1.082 | 0.004 | 0.110 | 6.13% | 10.15% |
| 20 | 0.074 | 1.400 | 0.069 | 1.270 | 0.074 | 1.190 | 0.070 | 1.120 | 0.063 | 1.130 | 0.070 | 1.222 | 0.005 | 0.116 | 6.47% | 9.50% |
| 25 | 0.083 | 1.550 | 0.077 | 1.390 | 0.083 | 1.310 | 0.078 | 1.250 | 0.071 | 1.260 | 0.078 | 1.352 | 0.005 | 0.124 | 6.35% | 9.15% |
| 30 | 0.090 | 1.660 | 0.085 | 1.510 | 0.090 | 1.410 | 0.085 | 1.360 | 0.078 | 1.370 | 0.086 | 1.462 | 0.005 | 0.126 | 5.76% | 8.59% |
| 35 | 0.097 | 1.770 | 0.091 | 1.600 | 0.097 | 1.500 | 0.091 | 1.460 | 0.084 | 1.470 | 0.092 | 1.560 | 0.005 | 0.130 | 5.85% | 8.32% |
| 40 | 0.102 | 1.860 | 0.096 | 1.700 | 0.103 | 1.580 | 0.096 | 1.570 | 0.089 | 1.560 | 0.097 | 1.654 | 0.006 | 0.128 | 5.79% | 7.76% |
| 45 | 0.107 | 1.950 | 0.102 | 1.790 | 0.109 | 1.630 | 0.101 | 1.630 | 0.093 | 1.640 | 0.102 | 1.728 | 0.006 | 0.141 | 6.08% | 8.19% |
| 50 | 0.112 | 2.010 | 0.106 | 1.860 | 0.113 | 1.690 | 0.106 | 1.640 | 0.098 | 1.700 | 0.107 | 1.780 | 0.006 | 0.153 | 5.61% | 8.58% |
| 55 | 0.116 | 2.030 | 0.110 | 1.900 | 0.118 | 1.700 | 0.110 | 1.650 | 0.102 | 1.760 | 0.111 | 1.808 | 0.006 | 0.155 | 5.63% | 8.60% |
| 60 | 0.119 | 2.030 | 0.114 | 1.910 | 0.120 | 1.700 | 0.114 | 1.650 | 0.105 | 1.800 | 0.114 | 1.818 | 0.006 | 0.155 | 5.19% | 8.52% |

## A.5 AC-DI-SOL®

**Table A.5.1:** *Disintegration times of pure Ac-Di-Sol® compacts at various compression forces*

| Ac-Di-Sol | | | | |
|---|---|---|---|---|
| **Average compression force** | **15.0** | **16.1** | **16.9** | **18.0** |
| **Tablet** | **Disintegration time (sec)** | | | |
| **1** | 428.17 | 506.20 | 343.00 | 356.90 |
| **2** | 365.90 | 530.30 | 302.50 | 354.60 |
| **3** | 521.41 | 455.20 | 329.70 | 358.70 |
| **4** | 406.80 | 495.50 | 330.30 | 314.20 |
| **Average** | 430.57 | 496.80 | 326.38 | 346.10 |
| **SD** | 65.840 | 31.320 | 17.057 | 21.333 |
| **RSD** | 15.29% | 6.30% | 5.23% | 6.16% |

**Table A.5.2:** *Properties of pure Ac-Di-Sol® compacts at various compression forces*

| Ac-Di-Sol | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression Force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **15.0** | Weight | 0.1972 | 0.1950 | 0.1963 | 0.1982 | 0.1951 | 0.1964 | 0.0014 | 0.70% |
| | Diameter | 0.4015 | 0.4025 | 0.4020 | 0.4025 | 0.4020 | 0.4021 | 0.0004 | 0.10% |
| | Height | 0.4690 | 0.4670 | 0.4590 | 0.4660 | 0.4610 | 0.4644 | 0.0042 | 0.91% |
| | Volume | 0.2376 | 0.2378 | 0.2331 | 0.2373 | 0.2341 | 0.2360 | 0.0022 | 0.93% |
| | Density | 0.8299 | 0.8201 | 0.8420 | 0.8353 | 0.8333 | 0.8321 | 0.0081 | 0.97% |
| | Porosity | 46.21% | 46.85% | 45.43% | 45.86% | 46.00% | 46.07% | 0.0052 | 1.13% |
| | Hardness | 18.0000 | 20.4000 | 23.3000 | 21.2000 | 21.7000 | 20.9200 | 1.9460 | 9.30% |
| **16.1** | Weight | 0.1971 | 0.1973 | 0.1954 | 0.1967 | 0.2007 | 0.1974 | 0.0020 | 1.00% |
| | Diameter | 0.4005 | 0.4010 | 0.4015 | 0.4015 | 0.4015 | 0.4012 | 0.0004 | 0.11% |
| | Height | 0.3530 | 0.3580 | 0.3800 | 0.3760 | 0.3830 | 0.3700 | 0.0136 | 3.67% |
| | Volume | 0.1780 | 0.1809 | 0.1925 | 0.1905 | 0.1940 | 0.1872 | 0.0073 | 3.88% |
| | Density | 1.1076 | 1.0905 | 1.0150 | 1.0326 | 1.0343 | 1.0560 | 0.0405 | 3.83% |
| | Porosity | 28.22% | 29.33% | 34.22% | 33.08% | 32.97% | 31.56% | 0.0262 | 8.31% |
| | Hardness | 113.2000 | 97.2000 | 72.3000 | 74.8000 | 72.3000 | 85.9600 | 18.4803 | 21.50% |
| **16.9** | Weight | 0.1981 | 0.1965 | 0.1944 | 0.1979 | 0.1870 | 0.1948 | 0.0046 | 2.36% |
| | Diameter | 0.3995 | 0.3995 | 0.4005 | 0.3995 | 0.3990 | 0.3996 | 0.0005 | 0.14% |
| | Height | 0.3140 | 0.3200 | 0.3210 | 0.3270 | 0.3080 | 0.3180 | 0.0072 | 2.28% |
| | Volume | 0.1575 | 0.1605 | 0.1618 | 0.1640 | 0.1541 | 0.1596 | 0.0039 | 2.42% |
| | Density | 1.2578 | 1.2242 | 1.2013 | 1.2065 | 1.2134 | 1.2207 | 0.0224 | 1.84% |
| | Porosity | 18.49% | 20.66% | 22.14% | 21.81% | 21.36% | 20.89% | 0.0145 | 6.96% |
| | Hardness | 204.7000 | 175.3000 | 167.9000 | 173.7000 | 154.9000 | 175.3000 | 18.2882 | 10.43% |
| **18.0** | Weight | 0.1980 | 0.1985 | 0.1959 | 0.1972 | 0.1957 | 0.1971 | 0.0012 | 0.63% |
| | Diameter | 0.3990 | 0.3995 | 0.3985 | 0.3990 | 0.3990 | 0.3990 | 0.0004 | 0.09% |
| | Height | 0.2970 | 0.2980 | 0.2950 | 0.2960 | 0.2970 | 0.2966 | 0.0011 | 0.38% |
| | Volume | 0.1486 | 0.1495 | 0.1472 | 0.1481 | 0.1486 | 0.1484 | 0.0008 | 0.55% |
| | Density | 1.3324 | 1.3280 | 1.3305 | 1.3315 | 1.3169 | 1.3279 | 0.0063 | 0.48% |
| | Porosity | 13.65% | 13.94% | 13.77% | 13.71% | 14.65% | 13.94% | 0.0041 | 2.95% |
| | Hardness | 243.5000 | 246.4000 | 273.8000 | 258.7000 | 252.9000 | 255.0600 | 12.0180 | 4.71% |

**Table A.5.3:** *Swelling and water uptake for pure AC-Di-Sol® compacts at a compression force of 15.0 N.*

| Ac-Di-Sol (15.0 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.016 | 0.21 | 0.007 | 0.18 | 0.024 | 0.44 | 0.014 | 0.43 | 0.010 | 0.29 | 0.014 | 0.31 | 0.006 | 0.121 | 45.75% | 39.04% |
| 4 | 0.032 | 0.34 | 0.020 | 0.43 | 0.037 | 0.52 | 0.034 | 0.55 | 0.025 | 0.46 | 0.030 | 0.46 | 0.007 | 0.082 | 23.48% | 17.86% |
| 6 | 0.035 | 0.44 | 0.022 | 0.45 | 0.039 | 0.59 | 0.038 | 0.62 | 0.027 | 0.50 | 0.032 | 0.52 | 0.007 | 0.082 | 22.97% | 15.68% |
| 8 | 0.036 | 0.51 | 0.023 | 0.46 | 0.040 | 0.65 | 0.038 | 0.67 | 0.028 | 0.53 | 0.033 | 0.56 | 0.007 | 0.092 | 21.85% | 16.23% |
| 10 | 0.039 | 0.57 | 0.025 | 0.50 | 0.042 | 0.69 | 0.040 | 0.71 | 0.030 | 0.57 | 0.035 | 0.61 | 0.007 | 0.089 | 20.82% | 14.64% |
| 15 | 0.047 | 0.69 | 0.032 | 0.59 | 0.048 | 0.77 | 0.045 | 0.81 | 0.036 | 0.66 | 0.042 | 0.70 | 0.007 | 0.088 | 17.22% | 12.45% |
| 20 | 0.054 | 0.78 | 0.038 | 0.66 | 0.053 | 0.82 | 0.051 | 0.88 | 0.040 | 0.72 | 0.047 | 0.77 | 0.008 | 0.086 | 16.09% | 11.08% |
| 25 | 0.059 | 0.86 | 0.042 | 0.72 | 0.056 | 0.86 | 0.055 | 0.95 | 0.044 | 0.77 | 0.051 | 0.83 | 0.008 | 0.089 | 14.96% | 10.73% |
| 30 | 0.064 | 0.92 | 0.045 | 0.77 | 0.058 | 0.92 | 0.059 | 1.02 | 0.047 | 0.82 | 0.055 | 0.89 | 0.008 | 0.097 | 15.03% | 10.95% |
| 35 | 0.068 | 0.99 | 0.048 | 0.81 | 0.061 | 0.95 | 0.063 | 1.08 | 0.050 | 0.86 | 0.058 | 0.94 | 0.009 | 0.107 | 14.88% | 11.37% |
| 40 | 0.071 | 1.05 | 0.051 | 0.86 | 0.063 | 0.99 | 0.066 | 1.14 | 0.052 | 0.90 | 0.061 | 0.99 | 0.009 | 0.113 | 14.51% | 11.44% |
| 45 | 0.075 | 1.10 | 0.053 | 0.90 | 0.066 | 1.03 | 0.069 | 1.20 | 0.055 | 0.94 | 0.064 | 1.03 | 0.009 | 0.121 | 14.73% | 11.72% |
| 50 | 0.078 | 1.16 | 0.056 | 0.93 | 0.068 | 1.07 | 0.073 | 1.25 | 0.057 | 0.98 | 0.066 | 1.08 | 0.010 | 0.130 | 14.62% | 12.08% |
| 55 | 0.081 | 1.21 | 0.058 | 0.97 | 0.070 | 1.11 | 0.076 | 1.31 | 0.059 | 1.01 | 0.069 | 1.12 | 0.010 | 0.140 | 14.80% | 12.52% |
| 60 | 0.084 | 1.27 | 0.060 | 1.00 | 0.072 | 1.15 | 0.079 | 1.35 | 0.061 | 1.05 | 0.071 | 1.16 | 0.011 | 0.147 | 14.98% | 12.59% |
| 65 | 0.087 | 1.32 | 0.062 | 1.04 | 0.074 | 1.18 | 0.081 | 1.39 | 0.063 | 1.09 | 0.073 | 1.20 | 0.011 | 0.149 | 14.94% | 12.36% |
| 70 | 0.090 | 1.39 | 0.064 | 1.07 | 0.076 | 1.22 | 0.084 | 1.44 | 0.065 | 1.11 | 0.076 | 1.25 | 0.011 | 0.165 | 15.11% | 13.22% |
| 75 | 0.094 | 1.45 | 0.066 | 1.10 | 0.077 | 1.24 | 0.086 | 1.48 | 0.065 | 1.11 | 0.078 | 1.28 | 0.013 | 0.181 | 16.21% | 14.22% |
| 80 | 0.098 | 1.50 | 0.066 | 1.12 | 0.077 | 1.24 | 0.086 | 1.48 | 0.065 | 1.11 | 0.078 | 1.29 | 0.014 | 0.190 | 17.78% | 14.71% |
| 85 | 0.101 | 1.50 | 0.066 | 1.12 | 0.077 | 1.24 | 0.086 | 1.48 | 0.065 | 1.11 | 0.079 | 1.29 | 0.015 | 0.190 | 19.01% | 14.71% |
| 90 | 0.103 | 1.50 | 0.066 | 1.12 | 0.077 | 1.24 | 0.086 | 1.48 | 0.065 | 1.11 | 0.079 | 1.29 | 0.016 | 0.190 | 19.85% | 14.71% |

**Table A.5.4:** *Swelling and water uptake for pure AC-Di-Sol® compacts at a compression force of 16.1 N.*

| Ac-Di-Sol (16.1 N) | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.012 | 0.03 | 0.010 | 0.01 | 0.003 | 0.00 | 0.004 | 0.00 | 0.015 | 0.01 | 0.009 | 0.01 | 0.005 | 0.012 | 58.72% | 122.47% |
| 4 | 0.013 | 0.03 | 0.018 | 0.02 | 0.008 | 0.00 | 0.012 | 0.02 | 0.020 | 0.06 | 0.014 | 0.03 | 0.005 | 0.022 | 33.92% | 84.27% |
| 6 | 0.013 | 0.06 | 0.022 | 0.06 | 0.011 | 0.04 | 0.012 | 0.07 | 0.020 | 0.11 | 0.016 | 0.07 | 0.005 | 0.026 | 32.24% | 39.35% |
| 8 | 0.013 | 0.10 | 0.022 | 0.08 | 0.014 | 0.07 | 0.013 | 0.12 | 0.020 | 0.14 | 0.016 | 0.10 | 0.004 | 0.029 | 26.08% | 28.07% |
| 10 | 0.014 | 0.13 | 0.022 | 0.10 | 0.015 | 0.09 | 0.014 | 0.15 | 0.021 | 0.17 | 0.017 | 0.13 | 0.004 | 0.033 | 23.04% | 26.15% |
| 15 | 0.019 | 0.17 | 0.025 | 0.12 | 0.019 | 0.12 | 0.019 | 0.21 | 0.025 | 0.21 | 0.021 | 0.17 | 0.003 | 0.045 | 15.36% | 27.14% |
| 20 | 0.023 | 0.21 | 0.027 | 0.14 | 0.022 | 0.14 | 0.024 | 0.25 | 0.028 | 0.24 | 0.025 | 0.20 | 0.003 | 0.055 | 10.44% | 27.97% |
| 25 | 0.026 | 0.23 | 0.029 | 0.15 | 0.024 | 0.15 | 0.027 | 0.27 | 0.031 | 0.26 | 0.027 | 0.21 | 0.003 | 0.058 | 9.86% | 27.59% |
| 30 | 0.028 | 0.25 | 0.031 | 0.15 | 0.025 | 0.15 | 0.029 | 0.30 | 0.033 | 0.27 | 0.029 | 0.22 | 0.003 | 0.070 | 10.39% | 31.19% |
| 35 | 0.030 | 0.27 | 0.032 | 0.17 | 0.027 | 0.16 | 0.031 | 0.31 | 0.034 | 0.29 | 0.031 | 0.24 | 0.003 | 0.069 | 8.40% | 29.08% |
| 40 | 0.031 | 0.28 | 0.033 | 0.17 | 0.028 | 0.17 | 0.032 | 0.33 | 0.036 | 0.30 | 0.032 | 0.25 | 0.003 | 0.075 | 9.11% | 30.07% |
| 45 | 0.033 | 0.29 | 0.033 | 0.17 | 0.029 | 0.17 | 0.034 | 0.34 | 0.037 | 0.31 | 0.033 | 0.26 | 0.003 | 0.080 | 8.63% | 31.44% |
| 50 | 0.033 | 0.29 | 0.033 | 0.17 | 0.030 | 0.17 | 0.034 | 0.34 | 0.038 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.57% | 31.89% |
| 55 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 60 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 65 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 70 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 75 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 80 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 85 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |
| 90 | 0.033 | 0.29 | 0.033 | 0.17 | 0.032 | 0.17 | 0.034 | 0.34 | 0.039 | 0.32 | 0.034 | 0.26 | 0.003 | 0.082 | 8.11% | 31.89% |

**Table A.5.5:** *Swelling and water uptake for pure AC-Di-Sol® compacts at a compression force of 16.9 N.*

| Ac-Di-Sol (16.9 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.000 | 0.00 | 0.003 | 0.00 | 0.008 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.002 | 0.00 | 0.003 | 0.000 | 158.77% | 0.00% |
| 4 | 0.003 | 0.01 | 0.004 | 0.05 | 0.018 | 0.03 | 0.003 | 0.03 | 0.001 | 0.01 | 0.001 | 0.00 | 0.005 | 0.02 | 0.007 | 0.019 | 132.64% | 81.22% |
| 6 | 0.005 | 0.04 | 0.005 | 0.09 | 0.023 | 0.07 | 0.007 | 0.07 | 0.005 | 0.05 | 0.004 | 0.03 | 0.009 | 0.06 | 0.008 | 0.023 | 91.05% | 36.78% |
| 8 | 0.007 | 0.07 | 0.006 | 0.13 | 0.023 | 0.10 | 0.009 | 0.10 | 0.009 | 0.08 | 0.007 | 0.05 | 0.011 | 0.09 | 0.007 | 0.029 | 64.28% | 32.06% |
| 10 | 0.008 | 0.10 | 0.008 | 0.16 | 0.024 | 0.12 | 0.011 | 0.12 | 0.011 | 0.10 | 0.009 | 0.07 | 0.013 | 0.11 | 0.007 | 0.033 | 51.62% | 28.83% |
| 15 | 0.011 | 0.13 | 0.014 | 0.22 | 0.026 | 0.15 | 0.017 | 0.16 | 0.015 | 0.13 | 0.012 | 0.10 | 0.017 | 0.15 | 0.005 | 0.044 | 32.44% | 29.20% |
| 20 | 0.013 | 0.15 | 0.020 | 0.24 | 0.029 | 0.16 | 0.020 | 0.18 | 0.018 | 0.15 | 0.015 | 0.12 | 0.020 | 0.17 | 0.005 | 0.045 | 25.61% | 26.31% |
| 25 | 0.015 | 0.17 | 0.025 | 0.26 | 0.031 | 0.17 | 0.023 | 0.20 | 0.020 | 0.17 | 0.017 | 0.12 | 0.023 | 0.18 | 0.005 | 0.051 | 22.89% | 27.87% |
| 30 | 0.017 | 0.18 | 0.028 | 0.28 | 0.033 | 0.17 | 0.024 | 0.20 | 0.022 | 0.17 | 0.018 | 0.13 | 0.025 | 0.19 | 0.006 | 0.056 | 22.98% | 29.54% |
| 35 | 0.018 | 0.19 | 0.030 | 0.29 | 0.034 | 0.18 | 0.026 | 0.21 | 0.023 | 0.18 | 0.020 | 0.14 | 0.027 | 0.20 | 0.006 | 0.056 | 20.86% | 28.06% |
| 40 | 0.020 | 0.19 | 0.032 | 0.30 | 0.036 | 0.18 | 0.027 | 0.22 | 0.025 | 0.19 | 0.021 | 0.14 | 0.028 | 0.21 | 0.006 | 0.060 | 20.89% | 29.05% |
| 45 | 0.021 | 0.20 | 0.033 | 0.31 | 0.037 | 0.19 | 0.029 | 0.22 | 0.026 | 0.19 | 0.022 | 0.14 | 0.029 | 0.21 | 0.006 | 0.063 | 19.92% | 29.93% |
| 50 | 0.022 | 0.20 | 0.034 | 0.31 | 0.037 | 0.19 | 0.030 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.030 | 0.21 | 0.006 | 0.063 | 18.35% | 29.93% |
| 55 | 0.022 | 0.20 | 0.035 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 60 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 65 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 70 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 75 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 80 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 85 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |
| 90 | 0.022 | 0.20 | 0.04 | 0.31 | 0.037 | 0.19 | 0.031 | 0.22 | 0.027 | 0.19 | 0.023 | 0.14 | 0.031 | 0.21 | 0.006 | 0.063 | 18.72% | 29.93% |

**Table A.5.6:** *Swelling and water uptake for pure AC-Di-Sol® compacts at a compression force of 18.0 N.*

| Ac-Di-Sol (18.0 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.003 | 0.00 | 0.002 | 0.00 | 0.001 | 0.00 | 0.001 | 0.00 | 0.001 | 0.00 | 0.001 | 0.00 | 0.001 | 0.00 | 0.000 | 0.000 | 37.27% | 0.00% |
| 4 | 0.004 | 0.02 | 0.004 | 0.00 | 0.002 | 0.02 | 0.002 | 0.00 | 0.003 | 0.00 | 0.002 | 0.00 | 0.003 | 0.00 | 0.001 | 0.009 | 34.40% | 223.61% |
| 6 | 0.004 | 0.06 | 0.007 | 0.03 | 0.002 | 0.05 | 0.004 | 0.04 | 0.006 | 0.03 | 0.004 | 0.02 | 0.005 | 0.03 | 0.002 | 0.011 | 42.38% | 33.53% |
| 8 | 0.004 | 0.09 | 0.010 | 0.07 | 0.004 | 0.09 | 0.006 | 0.09 | 0.009 | 0.08 | 0.006 | 0.06 | 0.007 | 0.08 | 0.002 | 0.013 | 34.99% | 16.72% |
| 10 | 0.006 | 0.12 | 0.012 | 0.11 | 0.006 | 0.12 | 0.008 | 0.12 | 0.011 | 0.12 | 0.007 | 0.10 | 0.009 | 0.11 | 0.003 | 0.009 | 29.41% | 7.85% |
| 15 | 0.011 | 0.17 | 0.018 | 0.18 | 0.011 | 0.18 | 0.014 | 0.20 | 0.016 | 0.18 | 0.012 | 0.19 | 0.014 | 0.19 | 0.003 | 0.009 | 20.17% | 4.81% |
| 20 | 0.015 | 0.20 | 0.023 | 0.23 | 0.015 | 0.21 | 0.019 | 0.25 | 0.021 | 0.22 | 0.018 | 0.25 | 0.019 | 0.23 | 0.003 | 0.018 | 15.80% | 7.71% |
| 25 | 0.017 | 0.22 | 0.027 | 0.27 | 0.018 | 0.24 | 0.023 | 0.29 | 0.024 | 0.24 | 0.022 | 0.29 | 0.023 | 0.27 | 0.003 | 0.025 | 14.35% | 9.44% |
| 30 | 0.019 | 0.23 | 0.029 | 0.29 | 0.021 | 0.26 | 0.025 | 0.31 | 0.027 | 0.26 | 0.025 | 0.32 | 0.025 | 0.29 | 0.003 | 0.028 | 11.68% | 9.64% |
| 35 | 0.021 | 0.24 | 0.031 | 0.30 | 0.022 | 0.28 | 0.027 | 0.33 | 0.029 | 0.28 | 0.027 | 0.35 | 0.027 | 0.31 | 0.003 | 0.031 | 12.30% | 10.11% |
| 40 | 0.022 | 0.25 | 0.033 | 0.32 | 0.024 | 0.29 | 0.029 | 0.35 | 0.030 | 0.29 | 0.029 | 0.37 | 0.029 | 0.32 | 0.003 | 0.036 | 11.17% | 11.04% |
| 45 | 0.023 | 0.25 | 0.035 | 0.32 | 0.025 | 0.30 | 0.030 | 0.35 | 0.032 | 0.30 | 0.031 | 0.38 | 0.031 | 0.33 | 0.004 | 0.035 | 11.92% | 10.50% |
| 50 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 55 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 60 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 65 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 70 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 75 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 80 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 85 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |
| 90 | 0.024 | 0.25 | 0.035 | 0.32 | 0.026 | 0.30 | 0.031 | 0.35 | 0.032 | 0.30 | 0.032 | 0.39 | 0.031 | 0.33 | 0.003 | 0.038 | 10.48% | 11.55% |

## A.6 KOLLIDON® CL

**Table A.6.1:** *Disintegration times of pure Kollidon® CL compacts at various compression forces*

| Kollidon | | | |
|---|---|---|---|
| **Average compression force** | **17.0** | **17.9** | **18.9** |
| **Tablet** | **Disintegration time (sec)** | | |
| **1** | 19.21 | 22.99 | 27.13 |
| **2** | 20.3 | 23.3 | 27.9 |
| **3** | 21.2 | 23.7 | 28.84 |
| **4** | 21.9 | 24.5 | 29.47 |
| **Average** | 20.65 | 23.62 | 28.35 |
| **SD** | 1.163 | 0.653 | 1.025 |
| **RSD** | 5.63% | 2.77% | 3.62% |

**Table A.6.2:** *Properties of pure Kollidon® CL compacts at various compression forces*

| Kollidon | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Average compression force** | **Tablet** | **1** | **2** | **3** | **4** | **5** | **Average** | **SD** | **RSD** |
| **16.0** | Weight | 0.2068 | 0.2015 | 0.2019 | 0.2068 | 0.1997 | 0.2033 | 0.0033 | 1.61% |
| | Diameter | 0.4045 | 0.4045 | 0.4035 | 0.4040 | 0.4030 | 0.4039 | 0.0007 | 0.16% |
| | Height | 0.5220 | 0.4980 | 0.5030 | 0.5090 | 0.4870 | 0.5038 | 0.0130 | 2.58% |
| | Volume | 0.2684 | 0.2561 | 0.2574 | 0.2611 | 0.2486 | 0.2583 | 0.0073 | 2.81% |
| | Density | 0.7704 | 0.7868 | 0.7844 | 0.7920 | 0.8034 | 0.7874 | 0.0120 | 1.52% |
| | Porosity | 36.85% | 35.51% | 35.70% | 35.08% | 34.15% | 35.46% | 0.0098 | 2.77% |
| | Hardness | 73.1000 | 79.3000 | 78.9000 | 83.8000 | 87.0000 | 80.4200 | 5.2884 | 6.58% |
| **17.0** | Weight | 0.2064 | 0.1994 | 0.2025 | 0.2026 | 0.2021 | 0.2026 | 0.0025 | 1.23% |
| | Diameter | 0.4020 | 0.4010 | 0.4015 | 0.4010 | 0.4010 | 0.4013 | 0.0004 | 0.11% |
| | Height | 0.4200 | 0.4090 | 0.4110 | 0.4150 | 0.4110 | 0.4132 | 0.0044 | 1.06% |
| | Volume | 0.2133 | 0.2067 | 0.2082 | 0.2097 | 0.2077 | 0.2091 | 0.0026 | 1.23% |
| | Density | 0.9676 | 0.9647 | 0.9725 | 0.9660 | 0.9730 | 0.9688 | 0.0038 | 0.39% |
| | Porosity | 20.69% | 20.93% | 20.29% | 20.82% | 20.25% | 20.59% | 0.0031 | 1.51% |
| | Hardness | 218.6000 | 211.3000 | 211.3000 | 202.3000 | 203.9000 | 209.4800 | 6.5667 | 3.13% |
| **18.0** | Weight | 0.2017 | 0.2046 | 0.1998 | 0.2013 | 0.1998 | 0.2014 | 0.0020 | 0.98% |
| | Diameter | 0.3990 | 0.3990 | 0.3980 | 0.4015 | 0.3990 | 0.3993 | 0.0013 | 0.33% |
| | Height | 0.3910 | 0.4010 | 0.3890 | 0.4020 | 0.3920 | 0.3950 | 0.0060 | 1.53% |
| | Volume | 0.1956 | 0.2006 | 0.1937 | 0.2037 | 0.1961 | 0.1979 | 0.0041 | 2.07% |
| | Density | 1.0310 | 1.0197 | 1.0317 | 0.9884 | 1.0187 | 1.0179 | 0.0176 | 1.73% |
| | Porosity | 15.49% | 16.41% | 15.43% | 18.99% | 16.50% | 16.57% | 0.0144 | 8.70% |
| | Hardness | 304.8000 | 294.2000 | 310.5000 | 223.9000 | 298.7000 | 286.4200 | 35.4885 | 12.39% |
| **19.0** | Weight | 0.2009 | 0.2055 | 0.2028 | 0.2018 | 0.2034 | 0.2029 | 0.0017 | 0.86% |
| | Diameter | 0.3985 | 0.3980 | 0.3985 | 0.3985 | 0.3980 | 0.3983 | 0.0003 | 0.07% |
| | Height | 0.3920 | 0.4010 | 0.3920 | 0.3900 | 0.3930 | 0.3936 | 0.0043 | 1.09% |
| | Volume | 0.1956 | 0.1996 | 0.1956 | 0.1946 | 0.1957 | 0.1962 | 0.0019 | 0.99% |
| | Density | 1.0269 | 1.0294 | 1.0366 | 1.0368 | 1.0396 | 1.0338 | 0.0054 | 0.52% |
| | Porosity | 15.83% | 15.62% | 15.03% | 15.02% | 14.79% | 15.26% | 0.0044 | 2.91% |
| | Hardness | 277.0000 | 307.7000 | 310.1000 | 304.8000 | 308.5000 | 301.6200 | 13.8967 | 4.61% |

**Table A.6.3:** *Swelling and water uptake for pure Kollidon® CL compacts at a compression force of 17.0 N.*

| Kollidon (17.0 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.043 | 0.85 | 0.013 | 0.77 | 0.050 | 0.96 | 0.018 | 1.19 | 0.020 | 1.60 | 0.031 | 1.08 | 0.029 | 1.08 | 0.015 | 0.299 | 50.83% | 27.77% |
| 4 | 0.097 | 1.60 | 0.060 | 1.35 | 0.105 | 1.52 | 0.103 | 1.74 | 0.114 | 1.60 | 0.094 | 1.59 | 0.096 | 1.57 | 0.019 | 0.128 | 19.61% | 8.17% |
| 6 | 0.129 | 1.90 | 0.094 | 1.60 | 0.128 | 1.52 | 0.128 | 1.74 | 0.130 | 1.60 | 0.121 | 1.59 | 0.122 | 1.66 | 0.014 | 0.138 | 11.44% | 8.34% |
| 8 | 0.138 | 1.90 | 0.115 | 1.60 | 0.142 | 1.52 | 0.143 | 1.74 | 0.144 | 1.60 | 0.130 | 1.59 | 0.135 | 1.66 | 0.011 | 0.138 | 8.28% | 8.34% |
| 10 | 0.139 | 1.90 | 0.122 | 1.60 | 0.155 | 1.52 | 0.153 | 1.74 | 0.157 | 1.60 | 0.143 | 1.59 | 0.145 | 1.66 | 0.013 | 0.138 | 9.14% | 8.34% |
| 15 | 0.144 | 1.90 | 0.151 | 1.60 | 0.186 | 1.52 | 0.183 | 1.74 | 0.187 | 1.60 | 0.177 | 1.59 | 0.171 | 1.66 | 0.019 | 0.138 | 11.04% | 8.34% |
| 20 | 0.154 | 1.90 | 0.179 | 1.60 | 0.212 | 1.52 | 0.207 | 1.74 | 0.213 | 1.60 | 0.207 | 1.59 | 0.195 | 1.66 | 0.024 | 0.138 | 12.20% | 8.34% |
| 25 | 0.162 | 1.90 | 0.205 | 1.60 | 0.236 | 1.52 | 0.220 | 1.74 | 0.237 | 1.60 | 0.235 | 1.59 | 0.216 | 1.66 | 0.029 | 0.138 | 13.52% | 8.34% |
| 30 | 0.171 | 1.90 | 0.230 | 1.60 | 0.258 | 1.52 | 0.231 | 1.74 | 0.259 | 1.60 | 0.261 | 1.59 | 0.235 | 1.66 | 0.034 | 0.138 | 14.64% | 8.34% |
| 35 | 0.180 | 1.90 | 0.253 | 1.60 | 0.276 | 1.52 | 0.250 | 1.74 | 0.269 | 1.60 | 0.284 | 1.59 | 0.252 | 1.66 | 0.038 | 0.138 | 14.93% | 8.34% |
| 40 | 0.190 | 1.90 | 0.269 | 1.60 | 0.283 | 1.52 | 0.268 | 1.74 | 0.283 | 1.60 | 0.305 | 1.59 | 0.266 | 1.66 | 0.040 | 0.138 | 14.91% | 8.34% |
| 45 | 0.199 | 1.90 | 0.281 | 1.60 | 0.300 | 1.52 | 0.285 | 1.74 | 0.302 | 1.60 | 0.311 | 1.59 | 0.280 | 1.66 | 0.041 | 0.138 | 14.68% | 8.34% |
| 50 | 0.207 | 1.90 | 0.297 | 1.60 | 0.317 | 1.52 | 0.301 | 1.74 | 0.320 | 1.60 | 0.324 | 1.59 | 0.294 | 1.66 | 0.044 | 0.138 | 14.99% | 8.34% |
| 55 | 0.215 | 1.90 | 0.316 | 1.60 | 0.333 | 1.52 | 0.316 | 1.74 | 0.333 | 1.60 | 0.335 | 1.59 | 0.308 | 1.66 | 0.046 | 0.138 | 15.06% | 8.34% |
| 60 | 0.224 | 1.90 | 0.332 | 1.60 | 0.344 | 1.52 | 0.331 | 1.74 | 0.340 | 1.60 | 0.341 | 1.59 | 0.319 | 1.66 | 0.047 | 0.138 | 14.64% | 8.34% |
| 65 | 0.232 | 1.90 | 0.342 | 1.60 | 0.351 | 1.52 | 0.343 | 1.74 | 0.344 | 1.60 | 0.345 | 1.59 | 0.326 | 1.66 | 0.046 | 0.138 | 14.18% | 8.34% |
| 70 | 0.241 | 1.90 | 0.348 | 1.60 | 0.356 | 1.52 | 0.350 | 1.74 | 0.347 | 1.60 | 0.347 | 1.59 | 0.332 | 1.66 | 0.044 | 0.138 | 13.41% | 8.34% |
| 75 | 0.248 | 1.90 | 0.349 | 1.60 | 0.357 | 1.52 | 0.352 | 1.74 | 0.348 | 1.60 | 0.347 | 1.59 | 0.334 | 1.66 | 0.042 | 0.138 | 12.61% | 8.34% |
| 80 | 0.248 | 1.90 | 0.349 | 1.60 | 0.357 | 1.52 | 0.352 | 1.74 | 0.348 | 1.60 | 0.347 | 1.59 | 0.334 | 1.66 | 0.042 | 0.138 | 12.61% | 8.34% |

**Table A.6.4:** *Swelling and water uptake for pure Kollidon® CL compacts at a compression force of 17.9 N*

| Kollidon (17.9 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.017 | 1.00 | 0.022 | 0.32 | 0.001 | 1.04 | 0.022 | 0.44 | 0.019 | 0.84 | 0.017 | 0.70 | 0.016 | 0.72 | 0.008 | 0.295 | 48.00% | 40.73% |
| 4 | 0.097 | 1.86 | 0.064 | 0.97 | 0.065 | 1.91 | 0.052 | 0.77 | 0.081 | 1.68 | 0.080 | 1.40 | 0.073 | 1.43 | 0.016 | 0.475 | 21.82% | 33.15% |
| 6 | 0.140 | 2.19 | 0.091 | 1.40 | 0.125 | 1.91 | 0.060 | 0.83 | 0.124 | 2.10 | 0.111 | 2.10 | 0.109 | 1.76 | 0.029 | 0.535 | 26.62% | 30.50% |
| 8 | 0.155 | 2.19 | 0.111 | 1.71 | 0.139 | 1.91 | 0.070 | 0.84 | 0.137 | 2.10 | 0.136 | 2.27 | 0.125 | 1.84 | 0.030 | 0.529 | 24.28% | 28.78% |
| 10 | 0.156 | 2.19 | 0.122 | 1.85 | 0.141 | 1.91 | 0.079 | 0.86 | 0.137 | 2.10 | 0.145 | 2.27 | 0.130 | 1.86 | 0.027 | 0.517 | 21.03% | 27.75% |
| 15 | 0.160 | 2.19 | 0.125 | 1.87 | 0.149 | 1.91 | 0.101 | 0.90 | 0.141 | 2.10 | 0.147 | 2.27 | 0.137 | 1.87 | 0.021 | 0.502 | 15.39% | 26.77% |
| 20 | 0.169 | 2.19 | 0.134 | 1.87 | 0.165 | 1.91 | 0.118 | 0.99 | 0.153 | 2.10 | 0.154 | 2.27 | 0.149 | 1.89 | 0.019 | 0.467 | 13.04% | 24.72% |
| 25 | 0.188 | 2.19 | 0.147 | 1.87 | 0.202 | 1.91 | 0.131 | 1.20 | 0.166 | 2.10 | 0.164 | 2.27 | 0.166 | 1.92 | 0.026 | 0.387 | 15.61% | 20.12% |
| 30 | 0.209 | 2.19 | 0.164 | 1.87 | 0.207 | 1.91 | 0.146 | 1.74 | 0.181 | 2.10 | 0.173 | 2.27 | 0.180 | 2.01 | 0.025 | 0.205 | 13.68% | 10.19% |
| 35 | 0.226 | 2.19 | 0.182 | 1.87 | 0.220 | 1.91 | 0.187 | 2.10 | 0.195 | 2.10 | 0.185 | 2.27 | 0.199 | 2.07 | 0.019 | 0.156 | 9.57% | 7.53% |
| 40 | 0.242 | 2.19 | 0.199 | 1.87 | 0.235 | 1.91 | 0.205 | 2.10 | 0.209 | 2.10 | 0.198 | 2.27 | 0.215 | 2.07 | 0.019 | 0.156 | 8.86% | 7.53% |
| 45 | 0.258 | 2.19 | 0.215 | 1.87 | 0.249 | 1.91 | 0.211 | 2.10 | 0.222 | 2.10 | 0.209 | 2.27 | 0.227 | 2.07 | 0.021 | 0.156 | 9.21% | 7.53% |
| 50 | 0.273 | 2.19 | 0.231 | 1.87 | 0.262 | 1.91 | 0.225 | 2.10 | 0.234 | 2.10 | 0.220 | 2.27 | 0.241 | 2.07 | 0.021 | 0.156 | 8.93% | 7.53% |
| 55 | 0.288 | 2.19 | 0.247 | 1.87 | 0.275 | 1.91 | 0.241 | 2.10 | 0.247 | 2.10 | 0.230 | 2.27 | 0.255 | 2.07 | 0.022 | 0.156 | 8.67% | 7.53% |
| 60 | 0.302 | 2.19 | 0.261 | 1.87 | 0.288 | 1.91 | 0.254 | 2.10 | 0.259 | 2.10 | 0.239 | 2.27 | 0.267 | 2.07 | 0.023 | 0.156 | 8.73% | 7.53% |
| 65 | 0.316 | 2.19 | 0.274 | 1.87 | 0.300 | 1.91 | 0.267 | 2.10 | 0.270 | 2.10 | 0.246 | 2.27 | 0.279 | 2.07 | 0.025 | 0.156 | 9.00% | 7.53% |
| 70 | 0.327 | 2.19 | 0.287 | 1.87 | 0.309 | 1.91 | 0.279 | 2.10 | 0.280 | 2.10 | 0.252 | 2.27 | 0.289 | 2.07 | 0.026 | 0.156 | 9.02% | 7.53% |
| 75 | 0.336 | 2.19 | 0.298 | 1.87 | 0.310 | 1.91 | 0.288 | 2.10 | 0.287 | 2.10 | 0.252 | 2.27 | 0.295 | 2.07 | 0.028 | 0.156 | 9.43% | 7.53% |
| 80 | 0.343 | 2.19 | 0.309 | 1.87 | 0.310 | 1.91 | 0.294 | 2.10 | 0.290 | 2.10 | 0.252 | 2.27 | 0.300 | 2.07 | 0.030 | 0.156 | 9.98% | 7.53% |

**Table A.6.5:** *Swelling and water uptake for pure Kollidon® CL compacts at a compression force of 18.9 N*

| Kollidon (18.9 N) | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1 | | 2 | | 3 | | 4 | | 5 | | 6 | | Average | | SD | | RSD | |
| Sec | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW | WU | SW |
| 0 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.00 | 0.000 | 0.000 | 0.00% | 0.00% |
| 2 | 0.013 | 0.28 | 0.004 | 0.27 | 0.003 | 0.16 | 0.027 | 0.38 | 0.033 | 0.32 | 0.012 | 0.21 | 0.015 | 0.27 | 0.012 | 0.078 | 79.63% | 28.88% |
| 4 | 0.041 | 0.66 | 0.034 | 0.66 | 0.025 | 0.67 | 0.054 | 0.77 | 0.055 | 0.68 | 0.036 | 0.55 | 0.041 | 0.67 | 0.012 | 0.070 | 28.87% | 10.54% |
| 6 | 0.062 | 0.98 | 0.055 | 0.97 | 0.057 | 1.03 | 0.074 | 1.10 | 0.074 | 1.00 | 0.058 | 0.91 | 0.063 | 1.00 | 0.009 | 0.064 | 13.53% | 6.38% |
| 8 | 0.077 | 1.24 | 0.072 | 1.27 | 0.080 | 1.33 | 0.093 | 1.42 | 0.089 | 1.27 | 0.080 | 1.31 | 0.082 | 1.31 | 0.008 | 0.064 | 9.51% | 4.90% |
| 10 | 0.092 | 1.47 | 0.091 | 1.61 | 0.098 | 1.58 | 0.110 | 1.68 | 0.104 | 1.52 | 0.100 | 1.61 | 0.099 | 1.58 | 0.007 | 0.074 | 7.28% | 4.70% |
| 15 | 0.121 | 1.94 | 0.129 | 2.2 | 0.133 | 2.11 | 0.146 | 2.29 | 0.136 | 2.07 | 0.135 | 2.23 | 0.133 | 2.14 | 0.008 | 0.126 | 6.20% | 5.91% |
| 20 | 0.137 | 2.23 | 0.158 | 2.63 | 0.162 | 2.57 | 0.176 | 2.72 | 0.164 | 2.54 | 0.151 | 2.45 | 0.158 | 2.52 | 0.013 | 0.170 | 8.33% | 6.72% |
| 25 | 0.142 | 2.4 | 0.167 | 2.63 | 0.176 | 2.60 | 0.177 | 2.72 | 0.190 | 2.97 | 0.153 | 2.45 | 0.168 | 2.63 | 0.017 | 0.205 | 10.44% | 7.80% |
| 30 | 0.151 | 2.43 | 0.168 | 2.63 | 0.177 | 2.60 | 0.179 | 2.72 | 0.192 | 3.04 | 0.157 | 2.45 | 0.171 | 2.65 | 0.015 | 0.223 | 8.87% | 8.42% |
| 35 | 0.157 | 2.43 | 0.173 | 2.63 | 0.178 | 2.60 | 0.184 | 2.72 | 0.194 | 3.04 | 0.164 | 2.45 | 0.175 | 2.65 | 0.013 | 0.223 | 7.67% | 8.42% |
| 40 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.191 | 2.72 | 0.196 | 3.04 | 0.171 | 2.45 | 0.180 | 2.65 | 0.013 | 0.223 | 6.98% | 8.42% |
| 45 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.178 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.66% | 8.42% |
| 50 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 55 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 60 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 65 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 70 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 75 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |
| 80 | 0.162 | 2.43 | 0.180 | 2.63 | 0.178 | 2.60 | 0.192 | 2.72 | 0.196 | 3.04 | 0.179 | 2.45 | 0.181 | 2.65 | 0.012 | 0.223 | 6.63% | 8.42% |

# ANNEXURE B: THE DATA OF THE SOLUBLE AND INSOLUBLE FORMULATIONS

## B.1 FORMULATION 1

**Table B.1.1:** *Properties of tablets of formulation 1.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 297.4 | 3.97 | 8.03 | 67.8 | 31 |
| 2 | 297.2 | 3.95 | 8.02 | 67.8 | 45 |
| 3 | 297.7 | 3.95 | 8.02 | 63.7 | 48 |
| 4 | 297.5 | 4.00 | 8.03 | 77.2 | 51 |
| 5 | 297.0 | 4.05 | 8.02 | 63.3 | 52 |
| 6 | 297.1 | 4.00 | 8.03 | 71.5 | 54 |
| 7 | 297.3 | 4.01 | 8.01 | 68.6 | |
| 8 | 298.7 | 3.96 | 8.02 | 69.1 | |
| 9 | 297.8 | 4.05 | 8.02 | 65.0 | |
| 10 | 295.1 | 3.97 | 8.02 | 69.1 | |
| 11 | 297.7 | | | | |
| 12 | 298.4 | | | | |
| 13 | 297.6 | | | | |
| 14 | 297.1 | | | | |
| 15 | 296.9 | | | | |
| 16 | 298.1 | | | | |
| 17 | 297.3 | | | | |
| 18 | 296.9 | | | | |
| 19 | 298.0 | | | | |
| 20 | 296.4 | | | | |
| Average | 297.4 | 4.0 | 8.0 | 68.3 | 46.8 |
| Standard deviation | 0.76 | 0.04 | 0.01 | 4.06 | 8.38 |
| %RSD | 0.26% | 0.94% | 0.08% | 5.94% | 17.89% |

**Table B.1.2:** *The water uptake and swelling of tablets from formulation 1.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.111 | 0.122 | 1.590 | 1.590 |
| 2 | 0.114 | 0.125 | 1.800 | 1.800 |
| 3 | 0.107 | 0.118 | 1.700 | 1.710 |
| 4 | 0.115 | 0.125 | 1.890 | 1.890 |
| 5 | 0.091 | 0.100 | 1.290 | 1.290 |
| Average | 0.108 | 0.118 | 1.654 | 1.656 |
| SD | 0.00979 | 0.01046 | 0.23223 | 0.23277 |

## B.2 FORMULATION 2

**Table B.2.1:** *Properties of tablets of formulation 2.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 295.6 | 3.93 | 8.03 | 63.3 | 31 |
| 2 | 295.5 | 3.92 | 8.03 | 57.6 | 40 |
| 3 | 295.4 | 4.04 | 8.02 | 64.2 | 42 |
| 4 | 296.0 | 4.04 | 8.02 | 63.3 | 43 |
| 5 | 293.0 | 3.93 | 8.02 | 61.3 | 44 |
| 6 | 295.4 | 4.00 | 8.03 | 59.7 | 46 |
| 7 | 295.2 | 4.06 | 8.03 | 60.5 | |
| 8 | 295.1 | 3.95 | 8.02 | 57.6 | |
| 9 | 295.5 | 4.00 | 8.02 | 56.8 | |
| 10 | 294.6 | 4.03 | 8.04 | 59.2 | |
| 11 | 295.7 | | | | |
| 12 | 295.2 | | | | |
| 13 | 296.4 | | | | |
| 14 | 296.1 | | | | |
| 15 | 295.0 | | | | |
| 16 | 295.9 | | | | |
| 17 | 296.0 | | | | |
| 18 | 296.2 | | | | |
| 19 | 295.9 | | | | |
| 20 | 296.0 | | | | |
| Average | 295.5 | 4.0 | 8.0 | 60.4 | 41.0 |
| Standard deviation | 0.741 | 0.053 | 0.007 | 2.638 | 5.292 |
| %RSD | 0.25% | 1.33% | 0.09% | 4.37% | 12.91% |

**Table B.2.2:** *The water uptake and swelling of tablets from formulation 2.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.144 | 0.159 | 1.940 | 1.940 |
| 2 | 0.135 | 0.146 | 1.990 | 1.990 |
| 3 | 0.128 | 0.139 | 2.000 | 2.000 |
| 4 | 0.137 | 0.149 | 1.940 | 1.940 |
| 5 | 0.118 | 0.129 | 1.880 | 1.880 |
| Average | 0.132 | 0.144 | 1.950 | 1.950 |
| SD | 0.00986 | 0.01122 | 0.04796 | 0.04796 |

## B.3 FORMULATION 3

**Table B.3.1:** *Properties of tablets from formulation 3.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 293.2 | 4.02 | 8.06 | 50.7 | 130 |
| 2 | 297.1 | 4.06 | 8.05 | 57.6 | 142 |
| 3 | 297.1 | 4.01 | 8.03 | 53.5 | 148 |
| 4 | 295.0 | 4.04 | 8.03 | 53.1 | 150 |
| 5 | 296.6 | 3.93 | 8.02 | 52.3 | 151 |
| 6 | 296.0 | 4.01 | 8.04 | 57.6 | 154 |
| 7 | 296.5 | 3.85 | 8.05 | 47.4 | |
| 8 | 296.1 | 4.02 | 8.02 | 44.1 | |
| 9 | 294.5 | 3.77 | 8.02 | 51.1 | |
| 10 | 297.0 | 4.00 | 8.05 | 52.3 | |
| 11 | 296.7 | | | | |
| 12 | 296.5 | | | | |
| 13 | 296.5 | | | | |
| 14 | 297.1 | | | | |
| 15 | 296.3 | | | | |
| 16 | 296.0 | | | | |
| 17 | 297.3 | | | | |
| 18 | 295.4 | | | | |
| 19 | 296.5 | | | | |
| 20 | 294.8 | | | | |
| Average | 296.1 | 4.0 | 8.0 | 52.0 | 145.8 |
| Standard deviation | 1.049 | 0.093 | 0.015 | 4.115 | 8.727 |
| %RSD | 0.35% | 2.35% | 0.19% | 7.92% | 5.98% |

**Table B.3.2:** *The water uptake and swelling of tablets from formulation 3.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.000 | 0.000 | 0.580 | 0.700 |
| 2 | 0.000 | 0.000 | 0.730 | 0.810 |
| 3 | 0.000 | 0.000 | 0.490 | 0.610 |
| 4 | 0.000 | 0.000 | 0.480 | 0.610 |
| 5 | 0.000 | 0.000 | 0.510 | 0.630 |
| Average | 0.000 | 0.000 | 0.558 | 0.672 |
| SD | 0 | 0 | 0.10378 | 0.08556 |

## B.4 FORMULATION 4

**Table B.4.1:** *Properties of tablets from formulation 4.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 289.4 | 3.97 | 8.03 | 50.3 | 111 |
| 2 | 290.9 | 3.95 | 8.02 | 53.9 | 115 |
| 3 | 289.7 | 3.92 | 8.02 | 54.3 | 117 |
| 4 | 289.3 | 3.94 | 8.01 | 55.6 | 117 |
| 5 | 290.4 | 3.94 | 8.03 | 53.1 | 118 |
| 6 | 289.4 | 3.95 | 8.02 | 51.5 | 119 |
| 7 | 289.8 | 3.92 | 8.02 | 51.9 | |
| 8 | 289.0 | 3.95 | 8.05 | 52.7 | |
| 9 | 291.3 | 3.94 | 8.03 | 50.7 | |
| 10 | 289.6 | 3.94 | 8.03 | 50.7 | |
| 11 | 289.0 | | | | |
| 12 | 289.0 | | | | |
| 13 | 289.2 | | | | |
| 14 | 290.6 | | | | |
| 15 | 290.9 | | | | |
| 16 | 289.3 | | | | |
| 17 | 289.8 | | | | |
| 18 | 290.2 | | | | |
| 19 | 290.8 | | | | |
| 20 | 289.7 | | | | |
| Average | 289.9 | 3.9 | 8.0 | 52.5 | 116.2 |
| Standard deviation | 0.722 | 0.015 | 0.011 | 1.760 | 2.858 |
| %RSD | 0.25% | 0.37% | 0.13% | 3.35% | 2.46% |

**Table B.4.2:** *The water uptake and swelling of tablets from formulation 4.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.000 | 0.000 | 1.310 | 1.570 |
| 2 | 0.000 | 0.000 | 1.190 | 1.520 |
| 3 | 0.000 | 0.000 | 1.290 | 1.500 |
| 4 | 0.000 | 0.000 | 1.270 | 1.450 |
| 5 | 0.000 | 0.000 | 1.120 | 1.350 |
| Average | 0.000 | 0.000 | 1.236 | 1.478 |
| SD | 0 | 0 | 0.07925 | 0.08349 |

## B.5 FORMULATION 5

**Table B.5.1:** *Properties of tablets from formulation 5.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 300.9 | 4.03 | 8.03 | 93.2 | 24 |
| 2 | 303.2 | 3.92 | 8.05 | 87.4 | 31 |
| 3 | 302.3 | 4.07 | 8.02 | 89.9 | 38 |
| 4 | 302.0 | 4.08 | 8.03 | 84.6 | 42 |
| 5 | 303.0 | 3.91 | 8.02 | 94.0 | 43 |
| 6 | 300.5 | 3.89 | 8.02 | 82.1 | 45 |
| 7 | 301.3 | 3.90 | 8.02 | 86.2 | |
| 8 | 302.7 | 4.05 | 8.05 | 85.0 | |
| 9 | 302.5 | 4.11 | 8.02 | 83.8 | |
| 10 | 302.9 | 3.96 | 8.02 | 89.1 | |
| 11 | 300.3 | | | | |
| 12 | 300.9 | | | | |
| 13 | 300.9 | | | | |
| 14 | 301.6 | | | | |
| 15 | 300.2 | | | | |
| 16 | 301.9 | | | | |
| 17 | 300.7 | | | | |
| 18 | 303.0 | | | | |
| 19 | 302.2 | | | | |
| 20 | 302.4 | | | | |
| Average | 301.8 | 4.0 | 8.0 | 87.5 | 37.2 |
| Standard deviation | 0.989 | 0.085 | 0.012 | 3.976 | 8.134 |
| %RSD | 0.33% | 2.12% | 0.15% | 4.54% | 21.89% |

**Table B.5.2:** *The water uptake and swelling of tablets from formulation 5.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.109 | 0.120 | 1.500 | 1.530 |
| 2 | 0.101 | 0.113 | 1.280 | 1.310 |
| 3 | 0.093 | 0.106 | 1.460 | 1.510 |
| 4 | 0.095 | 0.109 | 1.550 | 1.600 |
| 5 | 0.099 | 0.112 | 1.350 | 1.390 |
| Average | 0.099 | 0.112 | 1.428 | 1.468 |
| SD | 0.00623 | 0.00524 | 0.11077 | 0.11628 |

## B.6 FORMULATION 6

**Table B.6.1:** *Properties of tablets from formulation 6.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 304.1 | 4.07 | 8.03 | 108.7 | 48 |
| 2 | 288.0 | 3.91 | 8.04 | 104.2 | 54 |
| 3 | 296.0 | 4.05 | 8.04 | 109.5 | 70 |
| 4 | 297.4 | 3.90 | 8.03 | 105.0 | 72 |
| 5 | 296.3 | 4.00 | 8.05 | 99.3 | 73 |
| 6 | 286.9 | 4.07 | 8.02 | 93.6 | 75 |
| 7 | 293.7 | 3.98 | 8.02 | 90.3 | |
| 8 | 300.5 | 4.07 | 8.05 | 100.1 | |
| 9 | 281.2 | 4.06 | 8.02 | 103.0 | |
| 10 | 289.7 | 3.95 | 8.03 | 109.9 | |
| 11 | 294.4 | | | | |
| 12 | 293.4 | | | | |
| 13 | 284.8 | | | | |
| 14 | 300.9 | | | | |
| 15 | 299.6 | | | | |
| 16 | 291.1 | | | | |
| 17 | 292.6 | | | | |
| 18 | 299.5 | | | | |
| 19 | 281.0 | | | | |
| 20 | 293.6 | | | | |
| Average | 293.2 | 4.0 | 8.0 | 102.4 | 65.3 |
| Standard deviation | 6.473 | 0.068 | 0.012 | 6.629 | 11.378 |
| %RSD | 2.21% | 1.69% | 0.14% | 6.48% | 17.42% |

**Table B.6.2:** *The water uptake and swelling of tablets from formulation 6.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.060 | 0.075 | 0.770 | 0.820 |
| 2 | 0.075 | 0.089 | 0.930 | 0.980 |
| 3 | 0.073 | 0.088 | 0.850 | 0.900 |
| 4 | 0.071 | 0.088 | 0.850 | 0.910 |
| 5 | 0.066 | 0.081 | 0.920 | 0.980 |
| Average | 0.069 | 0.084 | 0.864 | 0.918 |
| SD | 0.00604 | 0.00606 | 0.06465 | 0.06648 |

## B.7 FORMULATION 7

**Table B.7.1:** *Properties of tablets from formulation 7.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 303.5 | 4.10 | 8.03 | 66.6 | 31 |
| 2 | 303.8 | 4.08 | 8.03 | 61.7 | 32 |
| 3 | 303.2 | 4.09 | 8.02 | 69.1 | 33 |
| 4 | 302.3 | 4.08 | 8.02 | 62.1 | 33 |
| 5 | 305.3 | 4.11 | 8.03 | 63.7 | 34 |
| 6 | 302.7 | 4.10 | 8.02 | 67.0 | 34 |
| 7 | 304.0 | 4.11 | 8.02 | 62.5 | |
| 8 | 302.6 | 4.09 | 8.02 | 65.0 | |
| 9 | 301.9 | 4.07 | 8.03 | 61.3 | |
| 10 | 304.3 | 4.10 | 8.03 | 66.6 | |
| 11 | 303.9 | | | | |
| 12 | 303.3 | | | | |
| 13 | 303.0 | | | | |
| 14 | 303.4 | | | | |
| 15 | 302.3 | | | | |
| 16 | 303.3 | | | | |
| 17 | 302.6 | | | | |
| 18 | 304.3 | | | | |
| 19 | 303.3 | | | | |
| 20 | 303.2 | | | | |
| Average | 303.3 | 4.09 | 8.03 | 64.56 | 32.83 |
| Standard deviation | 0.813 | 0.01 | 0.01 | 2.69 | 1.17 |
| %RSD | 0.27% | 0.33% | 0.07% | 4.16% | 3.56% |

**Table B.7.2:** *The water uptake and swelling of tablets from formulation 7.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.121 | 0.135 | 1.810 | 1.810 |
| 2 | 0.129 | 0.141 | 1.840 | 1.840 |
| 3 | 0.135 | 0.149 | 1.850 | 1.850 |
| 4 | 0.128 | 0.143 | 1.790 | 1.790 |
| 5 | 0.134 | 0.149 | 1.830 | 1.830 |
| Average | 0.129 | 0.143 | 1.824 | 1.824 |
| SD | 0.00559 | 0.0059 | 0.02408 | 0.02408 |

## B.8 FORMULATION 8

**Table B.8.1:** *Properties of tablets from formulation 8.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 301.2 | 4.10 | 8.03 | 78.0 | 40 |
| 2 | 302.0 | 4.11 | 8.03 | 78.0 | 41 |
| 3 | 302.3 | 4.06 | 8.01 | 71.1 | 41 |
| 4 | 302.0 | 4.10 | 8.03 | 82.5 | 42 |
| 5 | 302.6 | 4.09 | 8.02 | 74.0 | 43 |
| 6 | 301.6 | 4.11 | 8.02 | 74.8 | 45 |
| 7 | 301.8 | 4.06 | 8.03 | 78.5 | |
| 8 | 301.7 | 4.11 | 8.03 | 79.3 | |
| 9 | 302.1 | 4.07 | 8.02 | 76.0 | |
| 10 | 302.6 | 4.08 | 8.03 | 75.6 | |
| 11 | 303.1 | | | | |
| 12 | 300.9 | | | | |
| 13 | 301.2 | | | | |
| 14 | 301.6 | | | | |
| 15 | 303.3 | | | | |
| 16 | 301.9 | | | | |
| 17 | 300.7 | | | | |
| 18 | 303.0 | | | | |
| 19 | 303.6 | | | | |
| 20 | 301.5 | | | | |
| Average | 302.0 | 4.1 | 8.0 | 76.8 | 42.0 |
| Standard deviation | 0.800 | 0.020 | 0.007 | 3.178 | 1.789 |
| %RSD | 0.26% | 0.50% | 0.09% | 4.14% | 4.26% |

**Table B.8.2:** *The water uptake and swelling of tablets from formulation 8.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.107 | 0.122 | 1.570 | 1.590 |
| 2 | 0.112 | 0.128 | 1.820 | 1.820 |
| 3 | 0.108 | 0.125 | 1.440 | 1.450 |
| 4 | 0.119 | 0.133 | 1.760 | 1.770 |
| 5 | 0.119 | 0.133 | 1.650 | 1.660 |
| Average | 0.113 | 0.128 | 1.648 | 1.658 |
| SD | 0.00579 | 0.00487 | 0.15123 | 0.14721 |

## B.9 FORMULATION 9

**Table B.9.1:** *Properties of tablets from formulation 9.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 366.8 | 3.55 | 8.01 | 162.6 | 900 |
| 2 | 366.7 | 3.51 | 8.01 | 159.8 | 900 |
| 3 | 365.4 | 3.50 | 8.00 | 164.3 | 900 |
| 4 | 366.5 | 3.56 | 8.02 | 155.7 | 900 |
| 5 | 366.3 | 3.53 | 8.02 | 176.5 | 900 |
| 6 | 365.4 | 3.54 | 8.03 | 174.1 | 900 |
| 7 | 366.6 | 3.51 | 8.01 | 162.2 | |
| 8 | 366.3 | 3.52 | 8.01 | 174.9 | |
| 9 | 366.0 | 3.52 | 8.02 | 157.7 | |
| 10 | 366.0 | 3.51 | 8.01 | 143.8 | |
| 11 | 366.0 | | | | |
| 12 | 366.2 | | | | |
| 13 | 367.0 | | | | |
| 14 | 367.5 | | | | |
| 15 | 366.6 | | | | |
| 16 | 366.3 | | | | |
| 17 | 366.9 | | | | |
| 18 | 365.8 | | | | |
| 19 | 367.3 | | | | |
| 20 | 365.6 | | | | |
| Average | 366.4 | 3.53 | 8.01 | 163.16 | 900 |
| Standard deviation | 0.584 | 0.020 | 0.008 | 10.053 | 0 |
| %RSD | 0.16% | 0.56% | 0.11% | 6.16% | 0 |

**Table B.9.2:** *The water uptake and swelling of tablets from formulation 9.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.100 | 0.108 | 1.130 | 1.130 |
| 2 | 0.095 | 0.101 | 1.290 | 1.290 |
| 3 | 0.083 | 0.092 | 1.100 | 1.100 |
| 4 | 0.096 | 0.105 | 1.210 | 1.210 |
| 5 | 0.077 | 0.085 | 1.100 | 1.110 |
| Average | 0.090 | 0.098 | 1.166 | 1.168 |
| SD | 0.00973 | 0.00952 | 0.08264 | 0.08075 |

## B.10 FORMULATION 10

**Table B.10.1:** *Properties of tablets from formulation 10.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 378.1 | 3.59 | 8.03 | 180.2 | 900 |
| 2 | 376.9 | 3.60 | 8.02 | 172.4 | 900 |
| 3 | 376.4 | 3.54 | 8.01 | 170.0 | 900 |
| 4 | 377.1 | 3.60 | 8.02 | 188.8 | 900 |
| 5 | 379.7 | 3.58 | 8.04 | 176.1 | 900 |
| 6 | 379.1 | 3.61 | 8.04 | 170.4 | 900 |
| 7 | 378.7 | 3.57 | 8.02 | 179.4 | |
| 8 | 379.3 | 3.58 | 8.02 | 182.2 | |
| 9 | 377.1 | 3.60 | 8.01 | 176.5 | |
| 10 | 378.5 | 3.60 | 8.01 | 168.3 | |
| 11 | 378.0 | | | | |
| 12 | 378.3 | | | | |
| 13 | 377.2 | | | | |
| 14 | 378.6 | | | | |
| 15 | 378.1 | | | | |
| 16 | 377.8 | | | | |
| 17 | 376.5 | | | | |
| 18 | 376.2 | | | | |
| 19 | 378.3 | | | | |
| 20 | 378.0 | | | | |
| Average | 377.9 | 3.59 | 8.02 | 176.43 | 900 |
| Standard deviation | 0.985 | 0.021 | 0.011 | 6.407 | 0 |
| %RSD | 0.26% | 0.57% | 0.14% | 3.63% | 0 |

**Table B.10.2:** *The water uptake and swelling of tablets from formulation 10.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.000 | 0.000 | 0.010 | 0.080 |
| 2 | 0.000 | 0.000 | 0.010 | 0.040 |
| 3 | 0.000 | 0.000 | 0.000 | 0.000 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 |
| 5 | 0.000 | 0.000 | 0.000 | 0.000 |
| Average | 0.000 | 0.000 | 0.004 | 0.024 |
| SD | 0 | 0 | 0.00548 | 0.03578 |

## B.11 FORMULATION 11

**Table B.11.1:** *Properties of tablets from formulation 11.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 364.7 | 3.49 | 8.02 | 171.6 | 46 |
| 2 | 368.1 | 3.54 | 8.02 | 151.2 | 47 |
| 3 | 359.4 | 3.46 | 8.01 | 176.5 | 47 |
| 4 | 364.6 | 3.45 | 8.02 | 162.2 | 49 |
| 5 | 361.0 | 3.49 | 8.02 | 144.2 | 50 |
| 6 | 364.8 | 3.53 | 8.02 | 174.9 | 52 |
| 7 | 360.1 | 3.51 | 8.01 | 145.9 | |
| 8 | 364.7 | 3.51 | 8.02 | 151.2 | |
| 9 | 361.1 | 3.54 | 8.03 | 161.8 | |
| 10 | 361.0 | 3.50 | 8.01 | 182.6 | |
| 11 | 365.4 | | | | |
| 12 | 361.8 | | | | |
| 13 | 360.0 | | | | |
| 14 | 358.9 | | | | |
| 15 | 367.3 | | | | |
| 16 | 359.2 | | | | |
| 17 | 366.1 | | | | |
| 18 | 361.4 | | | | |
| 19 | 361.0 | | | | |
| 20 | 361.1 | | | | |
| Average | 362.6 | 3.50 | 8.02 | 162.21 | 48.5 |
| Standard deviation | 2.836 | 0.031 | 0.006 | 13.752 | 2.258 |
| %RSD | 0.78% | 0.88% | 0.08% | 8.48% | 4.66% |

**Table B.11.2:** *The water uptake and swelling of tablets from formulation 11.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.155 | 0.164 | 2.270 | 2.290 |
| 2 | 0.136 | 0.140 | 2.140 | 2.140 |
| 3 | 0.114 | 0.118 | 1.820 | 1.820 |
| 4 | 0.140 | 0.145 | 2.300 | 2.300 |
| 5 | 0.123 | 0.127 | 2.060 | 2.060 |
| Average | 0.134 | 0.139 | 2.118 | 2.122 |
| SD | 0.01582 | 0.01766 | 0.19292 | 0.19703 |

## B.12 FORMULATION 12

**Table B.12.1:** *Properties of tablets from formulation 12.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 373.6 | 3.41 | 8.02 | 134.8 | 900 |
| 2 | 366.1 | 3.51 | 8.02 | 141.8 | 900 |
| 3 | 369.4 | 3.55 | 8.03 | 129.9 | 900 |
| 4 | 371.2 | 3.53 | 8.02 | 125.4 | 900 |
| 5 | 369.7 | 3.51 | 8.03 | 135.3 | 900 |
| 6 | 355.5 | 3.50 | 8.02 | 126.3 | 900 |
| 7 | 369.1 | 3.51 | 8.02 | 138.9 | |
| 8 | 372.8 | 3.54 | 8.03 | 124.6 | |
| 9 | 368.7 | 3.41 | 8.02 | 133.2 | |
| 10 | 368.3 | 3.55 | 8.02 | 129.5 | |
| 11 | 373.5 | | | | |
| 12 | 355.7 | | | | |
| 13 | 355.9 | | | | |
| 14 | 370.4 | | | | |
| 15 | 366.6 | | | | |
| 16 | 369.5 | | | | |
| 17 | 359.6 | | | | |
| 18 | 371.1 | | | | |
| 19 | 368.2 | | | | |
| 20 | 356.0 | | | | |
| Average | 366.5 | 3.50 | 8.02 | 131.97 | 900 |
| Standard deviation | 6.287 | 0.052 | 0.005 | 5.824 | 0 |
| %RSD | 1.72% | 1.47% | 0.06% | 4.41% | 0 |

**Table B.12.2:** *The water uptake and swelling of tablets from formulation 12.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.000 | 0.000 | 0.000 | 0.000 |
| 2 | 0.000 | 0.000 | 0.000 | 0.020 |
| 3 | 0.000 | 0.000 | 0.000 | 0.000 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 |
| 5 | 0.000 | 0.000 | 0.000 | 0.000 |
| Average | 0.000 | 0.000 | 0.000 | 0.004 |
| SD | 0 | 0 | 0 | 0.00894 |

## B.13 FORMULATION 13

**Table B.13.1:** *Properties of tablets from formulation 13.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 367.7 | 3.55 | 8.02 | 158.9 | 165 |
| 2 | 369.3 | 3.53 | 8.01 | 168.3 | 175 |
| 3 | 368.1 | 3.57 | 8.01 | 166.7 | 199 |
| 4 | 369.3 | 3.53 | 8.01 | 156.5 | 234 |
| 5 | 369.6 | 3.55 | 8.01 | 189.2 | 260 |
| 6 | 368.9 | 3.51 | 8.01 | 171.2 | 247 |
| 7 | 368.6 | 3.52 | 8.01 | 166.3 | |
| 8 | 368.6 | 3.54 | 8.01 | 176.9 | |
| 9 | 367.7 | 3.53 | 8.01 | 169.6 | |
| 10 | 369.7 | 3.55 | 8.01 | 176.1 | |
| 11 | 369.4 | | | | |
| 12 | 367.3 | | | | |
| 13 | 369.7 | | | | |
| 14 | 367.6 | | | | |
| 15 | 369.3 | | | | |
| 16 | 368.6 | | | | |
| 17 | 369.4 | | | | |
| 18 | 369.5 | | | | |
| 19 | 367.7 | | | | |
| 20 | 368.3 | | | | |
| Average | 368.7 | 3.54 | 8.01 | 169.97 | 213.33 |
| Standard deviation | 0.803 | 0.018 | 0.003 | 9.357 | 39.368 |
| %RSD | 0.22% | 0.49% | 0.04% | 5.51% | 18.45% |

**Table B.13.2:** *The water uptake and swelling of tablets from formulation 13.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.024 | 0.030 | 0.860 | 0.880 |
| 2 | 0.024 | 0.034 | 0.700 | 0.720 |
| 3 | 0.031 | 0.042 | 1.040 | 1.050 |
| 4 | 0.020 | 0.027 | 0.690 | 0.710 |
| 5 | 0.021 | 0.028 | 0.640 | 0.640 |
| Average | 0.024 | 0.032 | 0.786 | 0.800 |
| SD | 0.0043 | 0.0061 | 0.16426 | 0.16508 |

## B.14 FORMULATION 14

**Table B.14.1:** *Properties of tablets from formulation 14.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 370.4 | 3.53 | 8.03 | 190 | 62 |
| 2 | 368.9 | 3.53 | 8.00 | 202.7 | 65 |
| 3 | 369.5 | 3.52 | 8.01 | 194.9 | 67 |
| 4 | 369.6 | 3.50 | 8.04 | 182.2 | 69 |
| 5 | 370.0 | 3.52 | 8.02 | 172.4 | 73 |
| 6 | 369.1 | 3.54 | 8.00 | 178.2 | 74 |
| 7 | 369.6 | 3.50 | 8.01 | 202.3 | |
| 8 | 369.8 | 3.49 | 8.01 | 184.3 | |
| 9 | 368.5 | 3.48 | 8.02 | 177.7 | |
| 10 | 369.1 | 3.50 | 8.01 | 179.8 | |
| 11 | 369.2 | | | | |
| 12 | 368.3 | | | | |
| 13 | 367.2 | | | | |
| 14 | 370.1 | | | | |
| 15 | 370.6 | | | | |
| 16 | 369.6 | | | | |
| 17 | 369.9 | | | | |
| 18 | 368.7 | | | | |
| 19 | 369.4 | | | | |
| 20 | 371.6 | | | | |
| Average | 369.5 | 3.51 | 8.02 | 186.45 | 68.33 |
| Standard deviation | 0.930 | 0.020 | 0.013 | 10.584 | 4.633 |
| %RSD | 0.25% | 0.56% | 0.16% | 5.68% | 6.78% |

**Table B.14.2:** *The water uptake and swelling of tablets from formulation 14.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.137 | 0.147 | 2.440 | 2.440 |
| 2 | 0.132 | 0.141 | 2.380 | 2.380 |
| 3 | 0.136 | 0.144 | 2.350 | 2.350 |
| 4 | 0.136 | 0.145 | 2.400 | 2.400 |
| 5 | 0.133 | 0.142 | 2.400 | 2.400 |
| Average | 0.135 | 0.144 | 2.394 | 2.394 |
| SD | 0.00217 | 0.00239 | 0.03286 | 0.03286 |

## B.15 FORMULATION 15

**Table B.15.1:** *Properties of tablets from formulation 15.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 365.7 | 3.54 | 8.02 | 151.6 | 900 |
| 2 | 367.0 | 3.54 | 8.02 | 147.9 | 900 |
| 3 | 368.7 | 3.50 | 8.03 | 150.4 | 900 |
| 4 | 368.8 | 3.52 | 8.02 | 138.5 | 900 |
| 5 | 368.1 | 3.53 | 8.02 | 134.8 | 900 |
| 6 | 367.2 | 3.55 | 8.02 | 140.2 | 900 |
| 7 | 367.1 | 3.55 | 8.01 | 138.1 | |
| 8 | 363.8 | 3.57 | 8.02 | 164.3 | |
| 9 | 363.1 | 3.51 | 8.02 | 141.4 | |
| 10 | 368.6 | 3.53 | 8.02 | 150.4 | |
| 11 | 366.7 | | | | |
| 12 | 365.0 | | | | |
| 13 | 364.0 | | | | |
| 14 | 367.3 | | | | |
| 15 | 366.0 | | | | |
| 16 | 368.2 | | | | |
| 17 | 365.2 | | | | |
| 18 | 368.6 | | | | |
| 19 | 367.1 | | | | |
| 20 | 368.3 | | | | |
| Average | 366.7 | 3.53 | 8.02 | 145.76 | 900 |
| Standard deviation | 1.758 | 0.021 | 0.005 | 8.863 | 0 |
| %RSD | 0.48% | 0.58% | 0.06% | 6.08% | 0 |

**Table B.15.2:** *The water uptake and swelling of tablets from formulation 15.*

| | Water uptake (ml) | | Swelling (mm) | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.000 | 0.000 | 0.000 | 0.000 |
| 2 | 0.000 | 0.000 | 0.040 | 0.160 |
| 3 | 0.000 | 0.000 | 0.050 | 0.180 |
| 4 | 0.000 | 0.000 | 0.000 | 0.000 |
| 5 | 0.000 | 0.000 | 0.050 | 0.050 |
| Average | 0.000 | 0.000 | 0.028 | 0.078 |
| SD | 0 | 0 | 0.02588 | 0.08672 |

## B.16 FORMULATION 16

**Table B.16.1:** *Properties of tablets from formulation 16.*

| Tablet | Weight (mg) | Thickness (mm) | Diameter (mm) | Hardness (N) | Disintegration time (sec) |
|---|---|---|---|---|---|
| 1 | 368.6 | 3.52 | 8.04 | 103.8 | 163 |
| 2 | 373.2 | 3.53 | 8.03 | 117.3 | 170 |
| 3 | 372.4 | 3.52 | 8.02 | 121.8 | 180 |
| 4 | 369.4 | 3.51 | 8.03 | 108.7 | 186 |
| 5 | 372.5 | 3.54 | 8.04 | 114.0 | 253 |
| 6 | 374.1 | 3.55 | 8.03 | 117.3 | 255 |
| 7 | 368.1 | 3.55 | 8.03 | 106.2 | |
| 8 | 372.1 | 3.52 | 8.03 | 110.7 | |
| 9 | 370.8 | 3.53 | 8.04 | 120.9 | |
| 10 | 372.8 | 3.49 | 8.03 | 115.6 | |
| 11 | 372.9 | | | | |
| 12 | 369.2 | | | | |
| 13 | 371.7 | | | | |
| 14 | 371.5 | | | | |
| 15 | 371.2 | | | | |
| 16 | 368.7 | | | | |
| 17 | 372.4 | | | | |
| 18 | 368.6 | | | | |
| 19 | 372.3 | | | | |
| 20 | 371.1 | | | | |
| Average | 371.2 | 3.53 | 8.03 | 113.63 | 201.17 |
| Standard deviation | 1.800 | 0.018 | 0.006 | 6.104 | 41.691 |
| %RSD | 0.48% | 0.52% | 0.08% | 5.37% | 20.72% |

**Table B.16.2:** *The water uptake and swelling of tablets from formulation 16.*

| | Water uptake (ml) | | Swelling | |
|---|---|---|---|---|
| Tablet | 5 min | 10 min | 5 min | 10 min |
| 1 | 0.032 | 0.086 | 0.430 | 1.240 |
| 2 | 0.039 | 0.052 | 0.460 | 0.580 |
| 3 | 0.056 | 0.113 | 0.730 | 1.600 |
| 4 | 0.038 | 0.090 | 0.450 | 0.930 |
| 5 | 0.032 | 0.096 | 0.340 | 1.160 |
| Average | 0.039 | 0.087 | 0.482 | 1.102 |
| SD | 0.00984 | 0.02231 | 0.14653 | 0.37831 |