Metabolic markers to distinguish between moniliformin and 3-bromopyruvate induced pyruvate dehydrogenase and rotenone-induced respiratory chain complex I deficiencies in HeLa cells

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Firstly I want to express my deepest gratitude to my heavenly Father, who blessed me with incredible gifts and this awesome opportunity.

Blessing and glory and wisdom, thanksgiving and honor and power and might, be to our God forever and ever. Amen. (Revelation 7:12)

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Abstract

Deficiencies of the pyruvate dehydrogenase complex enzyme and of the mitochondrial respiratory chain enzymes in humans both result in similar metabolic profiles in blood and urine. It is therefore almost impossible to distinguish between the two conditions based on the metabolic profile alone. Definitive diagnosis can only be made by assessing enzyme function in muscle biopsies. The aim of this study was to attempt to identify a method that is easy, non-invasive and definitive to distinguish between deficiencies in the two enzyme complexes.

HeLa cells were treated with moniliformin and 3-bromopyruvate (inhibitors of pyruvate dehydrogenase) and rotenone (inhibitor of complex I) to induce pyruvate dehydrogenase complex and mitochondrial respiratory chain deficiencies respectively. After inhibition for 24 hours, the media were transferred to a clean tube and centrifuged. The cells were scraped off, sonified and centrifuged. Organic acid analyses were done on the media and cell extracts using gas chromatography-mass spectrometry. Identification of the organic acids in the chromatogram was done by using AMDIS software and a library compiled by Prof L.J. Mienie at the metabolic laboratory of the North-West University, Potchefstroom.

I tested several hypotheses in order to achieve the aim of this study. The measured organic acid levels varied markedly which made it difficult to interpret. Organic acid comparisons of cell extracts were not significantly different, and were therefore not discussed.

Not enough data was obtained to calculate the ratio limits of 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid. This approach was therefore rejected. The calculation of the ratio limit of phenylpyruvic acid, phenyllactic acid and phenylacetic acid could also not be done because these molecules could not be detected in the medium. This approach was also rejected. No discernable pattern was observed in the principle component analysis (PCA). Our results therefore make it doubtful that PCA can be used as a tool to diagnose and distinguish between deficiencies in the pyruvate dehydrogenase complex enzymes and mitochondrial respiratory chain enzymes.

With inhibition of pyruvate dehydrogenase, the ratios of citric acid to succinic acid and citric acid to fumaric acid were significantly decreased and fumaric acid to malic was significantly increased. Respiratory chain inhibition with rotenone had no marked effect on these three ratios. It is therefore likely that calculation of these ratios may distinguish between pyruvate dehydrogenase defect and a respiratory chain defect. This will have to be verified in patients with proven enzyme defects.

Opsomming

Defekte in die pirovaat dehydrogenase kompleks ensieme en die mitochondriale respiratoriese ketting ensieme veroorsaak eenderse metaboliese profiele in die bloed en uriene. Dit is gevolglik byna onmoontlik om tussen die twee defekte te onderskei op grond van metaboliese profiele alleenlik. Definitiewe diagnose kan slegs gemaak word deur die ensiemfunksie te meet in spierbiopsies. Die doel van hierdie studie is om 'n metode te probeer ontwikkel wat maklik, nie-indringbaar en definitief is om tussen defekte in die twee ensieme te onderskei.

HeLa selle is met moniliformin en 3-hydroksiepirovaat (inhibeerders van pirovaat dehydrogenase) en rotenone (inhibeerder van kompleks I) behandel om onderskeidelik die pirovaat dehydrogenase kompleks en die mitochondriale respiratoriese ketting defekte te induseer. Na 24 uur, is die medium oorgedra na 'n skoon buis en gesentrifugeer. Die selle is afgeskraap, gesoniseer en gesentrifugeer. Organiese suurkonsentrasie bepalings in beide medium en selekstraksies is met gaschromatografie-massaspektrometrie gedoen. AMDIS sagteware en 'n organiese suur biblioteek, saamgestel deur Prof L.J. Mienie van die metabolisme laboratorium van die Noord Wes Universiteit, Potchefstroom, is gebruik om die organiese sure in die chromatogramme te identifiseer.

Ten einde die doel van die studie te bereik, het ek verskeie hipoteses getoets. Die organiese suur metings het geweldig gevarieer, wat dit moeilik gemaak het om te interpreteer. Statistiese vergelyking van die organiese sure in die sel ekstrakte was nie betekenisvol verskillend, en is daarom nie bespreek nie.

Te min data is verkry om die verhouding van 4-hydroksiefenielpirovaat, 4-hydroksiefeniellaktaat en 4-hydroksiefenielasynsuur te bereken. Hierdie benadering word dus verwerp. Die berekening van fenielpirovaat, feniellaktaat en fenielasynsuur kon nie gedoen word nie omdat die molekules nie opgespoor word in die medium nie. Hierdie benadering word dus ook verwerp. Daar is nie 'n onderskeibare patroon in die principle component analysis (PCA) nie. Ons resultate maak dit onwaarskynlik dat die PCA gebruik kan word as 'n metode waarmee gediagnoseer kan word en onderskei kan word tussen defekte in die pirovaat dehydrogenase ensiem en mitochondriale respiratoriese ketting ensieme.

Inhibisie van die pirovaat dehydrogenase ensiem het veroorsaak dat die verhoudings van sitroensuur tot suksiensuur en sitroensuur tot fumaarsuur betekenisvol verlaag en fumaarsuur tot malaat betekenisvol verhoog. Inhibisie van die respiratoriese ketting met rotenone het geen betekenisvolle effek op hierdie drie verhoudings gehad nie. Dit is dus hoogs waarskynlik dat die

berekening van hierdie verhoudings moontlik kan onderskei tussen pirovaat dehydrogenase en respiratoriese ketting defekte. Dit moet geverifieer word in pasiente met bewese ensiemdefekte.

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List of abbreviations:

#	:	Number
%	:	Percent
˚C	:	Degrees centigrade
® or ™	:	Trademark
µ	:	Micro: 10^{-6}
μ_c	:	Designated control group
μ_i	:	Experimental groups
µl	:	Microlitre
µM	:	Micromole
α	:	Alpha
β	:	Beta
ADP	:	Adenosine dephosphate
AMDIS	:	Automated mass spectral deconvolution and identification system
ANOVA	:	Analysis of variance
ATP	:	Adenosine triphosphate
AZT	:	Azidothymidine
B	:	3-bromopyruvate
BCA		bicinchoninic acid
BSTFA	:	N,O-bis-(trimetylsilyl)trifluoroacetamide)
C	:	Control
Ca^{2+}	:	Calcium
CO_2	:	Carbon dioxide
CoA	:	Coenzyme A
DLAT gene	:	Gene encodes dihydrolipoamide acetyltransferase
DMEM	:	Dulbecco's modified eagles medium
DMSO	:	Dimethylsulfoxide
DNA	:	Deoxyribonucleic acid
Dpi	:	Dots per inch
e^-	:	Electron
e.g.	:	For example
E_1	:	Pyruvate dehydrogenase component of pyruvate
E_2	:	Dihydrolipoyl transacetylase component of pyruvate dehydrogenase complex enzyme
$E_{2\text{-}B}$	:	Subunit binding domain

E_{2I}	:	Inner domains
E_3	:	Dihydrolipoyl dehydrogenase component of pyruvate dehydrogenase complex enzyme
et al.	:	And others
eV	:	Electron volt
FAD^+	:	Flavin adenine dinucleotide
FBS	:	Fetal bovine serum
Fe/S	:	Iron sulphur
FMN	:	Flavomonucleotide
g	:	Gravitational force
g	:	Gram
GC-MS	:	Gas chromatography-mass spectrometry
GDH	:	Glutamate dehydrogenase
GOT or AST		Glutamate oxaloacetate transaminase
GPT or ALT	:	Glutamate pyruvate transaminase
H	:	High concentration
H^+	:	Hydrogen ion
H_2O	:	Water
HCl	:	Hydrochloric acid
i.e.	:	That is
I	:	Complex I, NADH:ubiquinone oxidoreductase
II	:	Complex II, succinate-ubiquinone oxidoreductase
III	:	Complex III, ubiquinol-ferricytochrome c oxidoreductase
IV	:	Complex IV, cytochrome c oxidoreductase
kDa	:	Kilodaltons
L	:	Low concentration
L_1 & L_2	:	Lipoyl domains
LHON	:	Leber hereditary optic neuropathy
LS	:	Leigh syndrome
M	:	Moniliformin
MELAS	:	Mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes
mg	:	Milligram
mg/L	:	Milligram per Litre
Mg^{2+}	:	Magnesium
mL	:	Millilitre
mM	:	Milimolar
MERRF	:	Myoclonic epilepsy with ragged-red fibers
mtDNA	:	Mitochondrial DNA

MTND1	:	Mitochondrial-encoded components of complex I
n	:	Nano: 10^{-9}.'
Na_2SO_4	:	Sodium sulphate
NAD^+	:	Nicotinamide adenine dinucleotide (oxidized)
NADH	:	Nicotinamide adenine dinucleotide (reduced)
NaOH	:	Sodium hydroxide
NBT	:	Nitrotetrazolium blue chloride
NBTH	:	Nitrotetrazolium blue chloride (reduced)
NDUFV1	:	Nuclear-encoded genes
NH_2	:	Amine
nM	:	Nanomolar
Nps	:	Nucleotide pairs
Nr	:	Number
NWU	:	North-west university
O_2	:	Molecular oxygen
OXPHOS	:	Oxidative phosphorylation
P/S	:	Penisillien-streptomysin
PBS	:	Phosphate buffered saline
PCA	:	Principal component analysis
PDH-a	:	Non-phosphorylated form of PDH
PDHA1 gene	:	E_1 α-subunit gene
PDH-b	:	Phosphorylated form of PDH
PDHB gene	:	E_1 β-subunit gene
PDHc	:	Pyruvate dehydrogenase complex enzyme
PDK	:	E_1 kinase
PDP	:	E_1 phosphatase
pH	:	The cologarithm of the activity of dissolved hydrogen ions
PSST	:	Hydrophilic components of Complex I
QH_2	:	Ubiquinol
R	:	Rotenone
RC	:	Mitochondrial respiratory chain
ROS	:	Reactive oxygen species
Rpm	:	Revolutions per minute
SAS®	:	Statistical analysis system
Spp	:	Species
TCA	:	Tricarboxylic acid
TMCS	:	Trimethylchlorosilane
TPP	:	Lipoic acid and thiamine pyrophosphate
TYKY	:	Hydrophilic components of Complex I

v/v	:	Volume per volume
V	:	Complex V, ATP synthase

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(Shortened names)

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CHAPTER 1

Introduction

Defects in both the pyruvate dehydrogenase complex enzyme (PDHc) and the mitochondrial respiratory chain enzyme (RC) cause increased levels of lactic acid in the plasma of humans (Robinson, 2006). Moreover, deficiencies in the PDHc and the RC enzymes both result in similar changes in the metabolic profiles in blood and urine. It is therefore almost impossible to distinguish between the two conditions based only on the metabolic profile. Lactic academia is also a very common indicator of enzyme deficiencies which further complicates the diagnosis of PDHc or RC. It is present in forty four diseases (Appendix A, Metagene online: Knowledge base for inborn errors of metabolism (ANON, 2007)). According to Appendix A, the following deficiencies only have lactic academia as a characteristic biochemical diagnostic metabolite: Respiratory Chain Deficiencies (which also is the cause of syndromes listed and indicated with the superscript $^{\text{mitochondrial oxidative defects (MOD)}}$) Mitochondrial DNA Depletion Syndrome^{MOD}, Myoclonic Epilepsy and Ragged Red Fiber Disease (MERRF)^{MOD}, Benign Infantile Mitochondrial Myopathy and Cardiomyopathy (BIMC)^{MOD}, Lethal Infantile Mitochondrial Disease (LIMD)^{MOD}, Leigh's syndrome^{MOD}, Benign Infantile Mitochondrial Myopathy (BIMM)^{MOD}, Chronic Progressive External Ophthalmoplegia and Kearns-Sayre Syndrome^{MOD}, Mitochondrial-Encephalopathy-Lactic Acidosis-Stroke (MELAS)^{MOD}, Congenital Lactic Acidosis, Pyruvate dehydrogenase deficiency (E_1 and E_2), Pyruvate Dehydrogenase E_3-Binding Protein Deficiency and Thiamine Deficieny [DD]) (ANON, 2007).

Definitive diagnosis of PDHc or RC enzyme deficiencies can only be made by assessing enzyme function. A muscle biopsy is required to do this because normal enzyme activity in leukocytes and fibroblasts may be measured due to mitochondrial DNA heteroplasmy (Frye & Benke, 2007). This can lead to a false positive result. The ethical issues surrounding acquisition of muscle biopsies from babies also preclude testing muscle RC enzyme activity. To acquire muscle biopsies is an invasive surgical procedure done under anaesthesia which, in itself poses a potential risk to newborn babies.

Ideally, the difference between PDHc and RC enzymes must be identified by a method that is not only easier and less invasive but also definitive. The following four hypotheseses were tested.

1. Ratio limits of the intermediates of the tricarboxylic acid (TCA) cycle:

A possible hypothesis is to develop a specific ratio limit of the intermediates of the tricarboxylic acid (TCA) cycle.

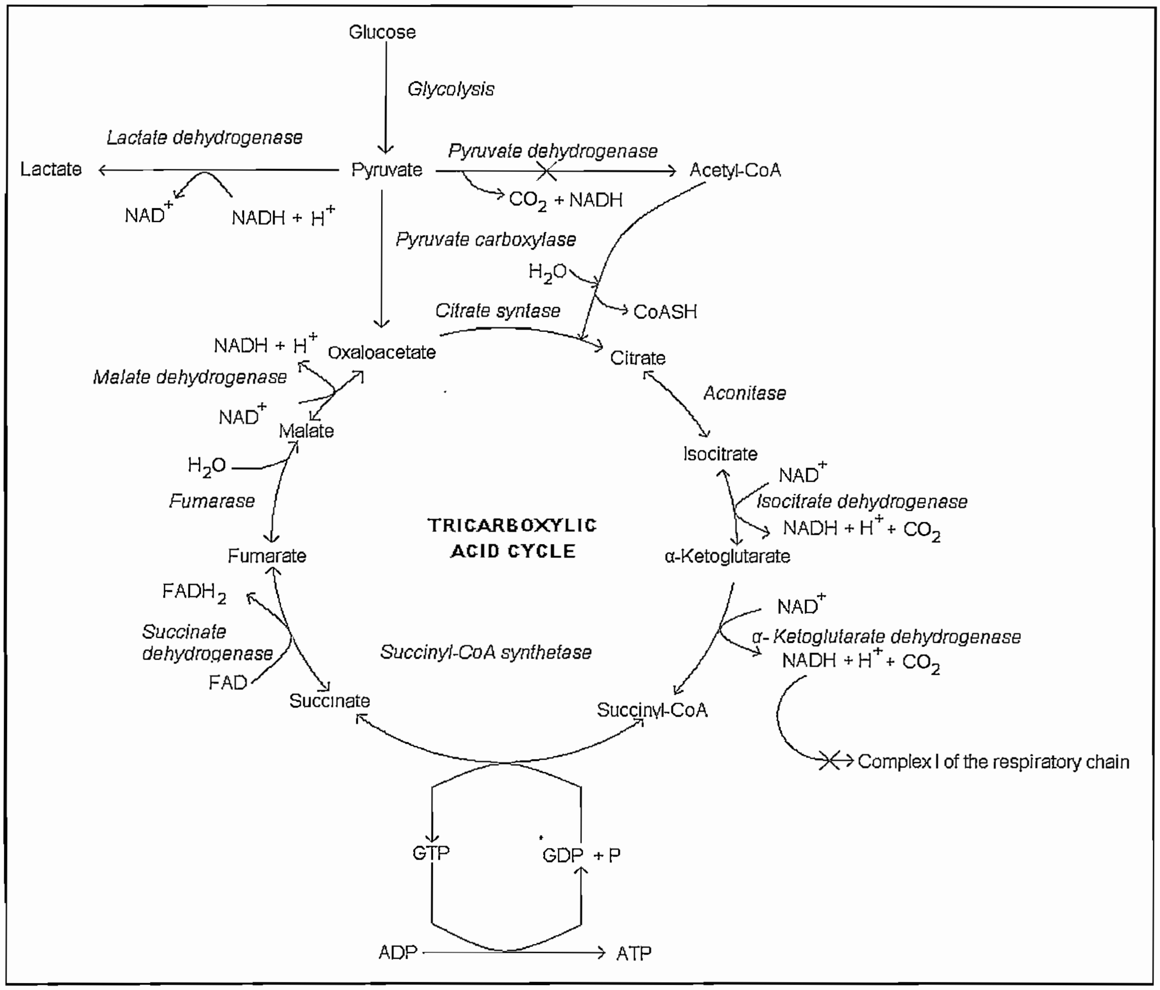

Figure 1.1: An illustration of the link between glycolysis, the TCA cycle and the respiratory chain (Adapted from Garrett & Grisham, 2005:610).

Figure 1.1 illustrates the link between glycolysis, the TCA cycle and the respiratory chain. A deficiency in PDHc blocks the conversion of pyruvate into acetyl CoA. It can therefore be expected that the intermediates formed in the TCA cycle may be lower than normal. A vital factor that controls the TCA cycle activity is the intramitochondrial ratio of NAD^+ to NADH. With inhibition of electron transport, a decrease in the NAD^+/NADH ratio is seen (Mathews, *et al.*, 1990:487). This limits the activities of certain enzymes, such as pyruvate dehydrogenase, citrate synthase, isocitrate dehydrogenase, and α–ketoglutarate dehydrogenase. NADH therefore turns the TCA cycle off (Garret & Grisham, 2005:631).

These enzymes can therefore not metabolize the products that formed in the previous step. One could expect that, if inhibition of pyruvate dehydrogenase by NADH should increase, the ratio of pyruvate to acetyl-CoA should be high. Also, if citrate synthase is inhibited, the ratio of acetyl-coA and oxaloacetate to citrate should increase. Similarly with inhibition of isocitrate dehydrogenase, the ratio of isocitrate to α–ketoglutarate should be high. If α–ketoglutarate dehydrogenase is inhibited, the ratio α–ketoglutarate to succinyl-CoA should increase.

2. Ratio limit of 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid:

Another possible hypothesis is to develop a specific ratio limit for 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid. 4-hydroxyphenylpyruvic acid is converted to 4-hydroxyphenylacetic acid or 4-hydroxyphenyllactic acid (figure 1.2). Pyruvate dehydrogenase catalyzes the reaction where 4-hydroxyphenylacetic acid is formed (Schomburg, 2007).

Therefore, less 4-hydroxyphenylacetic acid must form if the pyruvate dehydrogenase enzyme complex is defective when compared to defective mitochondrial respiratory chain enzymes. Theoretically different ratios of these metabolites could result due to deficiencies of PDHc or RC. If it can be proved that the ratio of 4-hydroxyphenylacetic acid to 4-hydroxyphenyllactic acid is indicative of PDHc or RC defects in HeLa cells, this approach to differentiate will have a large impact on the health and wellness of patients with these disorders. This is so because treatment strategies can be adjusted, at least in part, to compensate for the deficiencies.

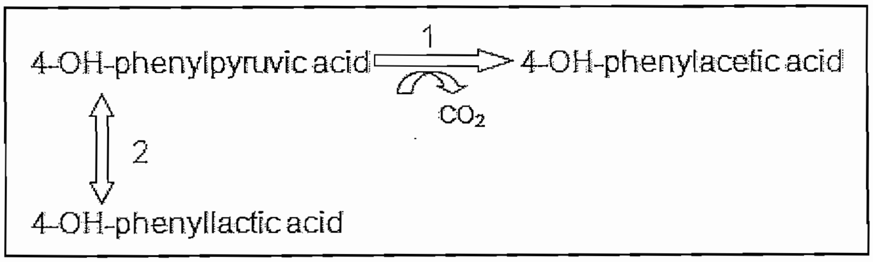

Figure 1.2: Metabolism of 4-OH-phenylpyruvic acid: 1 = Pyruvate dehydrogenase; 2 = Lactate dehydrogenase (Adapted from Mitchell, *et al.*, 2001:1778).

3. Ratio limit of phenylpyruvic acid, phenyllactic acid and phenylacetic acid:

Phenylpyruvic acid is converted to phenylacetic acid or phenyllactic acid (Mathews, *et al.*, 1990: 723). By using a similar approach as hypothesis 1, but with phenylpyruvic acid as the metabolite, it might be possibly to distinguish between PDHc or RC defects.

4. Principle Component analysis (PCA):

In this case, the data will be analysed without having a fixed hypothesis. This, together with statistical analysis and filtering of interesting variables, may provide a workable hypothesis. In this case, the aim is to use the biomarkers that emerged from principle component analysis as important to possibly distinguish between pyruvate dehydrogenase complex deficiency and a deficiency in the mitochondrial respiratory chain.

This study will investigate the four hypotheseses in HeLa cells, a human epithelial carcinoma cell line. HeLa cells were chosen because they metabolize glucose terminally via the TCA cycle (Barban & Schulze, 1956). Although cultured HeLa cells also use glutamine as a source of energy, fairly constant intracellular levels of the TCA cycle intermediates are maintained irrespective if the growth medium was enriched with glucose, galactose or fructose (Reitzer, et al., 1978). In addition, HeLa cells contain all the enzymes involved in the TCA cycle in equal concentrations to that in normal tissues (Dajani, et al, 1961; Barban & Schulze, 1956). There are, however, evidence that tumour cells have reduced TCA cycle activity (Dajani, et al, 1961). This must be kept in mind when results are interpreted.

The use of a cell line provides a clean approach to investigate the effects of inhibition of PDHc and RC on TCA cycle. It assesses the effect of less pyruvate entering the TCA cycle through inhibition of PDHc and of inhibition of the respiratory chain on the intermediates of the TCA cycle in a system where the metabolic activity of other cells in an experimental animal will not affect the results. Once differences in the metabolites of the TCA cycle in HeLa cells are found, similar inhibitions can be done in normal experimental animals. This can verify that the differences in HeLa cells are also present in more complex conditions where different cell types are present and the metabolic activity of these cells are under the influence of hormones, cytokines and alterations in plasma levels of various nutrients. If similar differences are found in the experimental animals, patients with proven defects in PDHc and RC can be investigated in order to prove that the findings in HeLa cells and experimental animals can be used to differentiate between defects in PDHc and RC.

In view of this approach, the cell line that is used and the difference in metabolism when compared to that of humans and experimental animals become irrelevant. It is true that the inhibition of the enzyme complexes does not represent the defect in humans. However, chemical inhibition can be used to mimic defective enzyme complexes. Thus, this study is a "prove of concept" study that can hopefully be more informative than using a more complicated experimental animal and is also much cheaper. It also underwrites the current view that research should preferably be conducted on cell lines rather than experimental animals or humans (as proposed by the South African Medical Research Council).

CHAPTER 2

Literature review

Literature Survey Of Pyruvate Dehydrogenase Enzyme Complex, Pyruvate Dehydrogenase Complex Deficiency, Respiratory Chain Complex I and Respiratory Chain Complex I Deficiency

2.1 Pyruvate dehydrogenase enzyme complex

2.1.1 Pyruvate dehydrogenase enzyme complex (PDHc): an overview

During glycolysis, pyruvate is produced and is an important source of acetyl-CoA for entry into the TCA cycle. The oxidative decarboxylation of pyruvate to acetyl-CoA by PDHc provides the link between glycolysis and the TCA cycle (Garrett & Grisham, 2005:612).

The overall reaction of PDHc is summarised in figure 2.1.

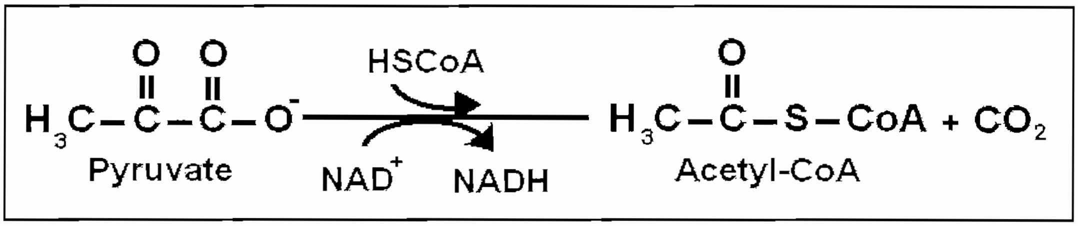

Figure 2.1: The action of PDHc (Adapted from Garrett & Grisham, 2005:612).

PDHc is a multi-enzyme complex containing three primary enzymes; pyruvate dehydrogenase (E_1), dihydrolipoyl transacetylase (E_2) and dihydrolipoyl dehydrogenase (E_3) (Patel & Roche, 1990; Palmer, 2001:83), two regulatory enzymes (kinase and phosphatase), and an additional protein X, which is an E_3-binding protein (Patel & Roche, 1990). The molecular mass of the complex is $8x10^6$ Da and contains 30 copies of the E_1 enzyme, 60 copies of the E_2 enzyme, 12 copies of the E_3 enzyme, and 12 copies of E_3BP. The E_3-binding protein is necessary for proper interaction of the E_2 and E_3 components (Lib *et al.*, 2002). The E_1-alpha subunit contains the E_1 active site and plays a key role in the function of the PDHc (Brown *et al.*, 1994).

The complex is held together by non-covalent forces and may dissociate easily. The sub-units of the E_1 protein can be separated from those of the E_2 and E_3 proteins at alkaline pH. At a neutral pH and high urea concentration, E_2 and E_3 can be separated from each other. The multienzyme complex will spontaneously reform if all the sub-units are mixed together at neutral pH, in the absence of urea. If E_2 is not present, the E_1 and E_3 subunits can not re-associate (Palmer, 2001:83).

The complex also requires 5 different coenzymes: Coenzyme A (CoA), nicotinamide adenine dinucleotide (NAD^+), flavin adenine dinucleotide (FAD), lipoic acid and thiamine pyrophosphate (TPP). FAD, lipoic acid and TPP are tightly bound to enzymes of the complex (King, 2007). TPP is associated with E_1, while the side chain of lipoamide (lipoic acid with an amide linkage) is covalently bound to a lysyl residue of E_2 and E_3 contains a prosthetic group, FAD (Palmer, 2001:83). CoA and NAD^+ are carriers of the products of the PDHc reaction (King, 2007).

E_1-component:

The E_1-component is a tetramer containing two 41kDa α-subunits and two 36kDa β-subunits. This component catalyzes the rate-limiting step in the overall PDHc reaction. E_1 have tryptophan and lysine residues positioned near the two TPP-binding sites that may take part in TPP binding.

When E_1 reacts with TPP, the circular dichroism spectrum is changed because of the formation of a charge transfer complex between the thiazolium ring of TPP and a tryptophan indole group of the protein. Numerous TPP binding enzymes show a common structural pattern, containing conserved amino acids located at constant 30-residue segment intervals (Patel & Roche, 1990).

A specific phosphatase dephosphorylates and activates the α-subunit of E_1, while a specific kinase phosphorylates and inactivates it (Patel & Roche, 1990). There are three phosphoserine residues (sites 1, 2, and 3) on the E_1. Sites 1 and 2 are located on a tetradecapeptide and site 3 is located on an unrelated nonapeptide (Patel & Roche, 1990).

E_2-component:

The E_2-component consists of four domains connected by three hinge regions (figure 2.2). This 59.5 kDa multidomain allows assembly into a large inner framework with flexibility connected to outer domains. This flexibility allows them to anchor the other components of the PDHc while transmitting intermediates between well-separated active sites.

The outer structure contains two lipoyl domains (L_1 and L_2) of approximately 100 amino acids. Each domain contains a lipoyl prosthetic group attached to a specific lysine. The E_1 kinase and E_1 phosphatase associate with specific regions in the outer domain structure of the E_2. The assembled E_2 component can bind at least 15 kinase molecules. The subunit binding domain ($E_{2\text{-}B}$)

of the mammalian complex binds the E_1 component and the inner domains (E_{2I}) binds to protein X and catalyze the transacetylation reaction (Patel & Roche, 1990).

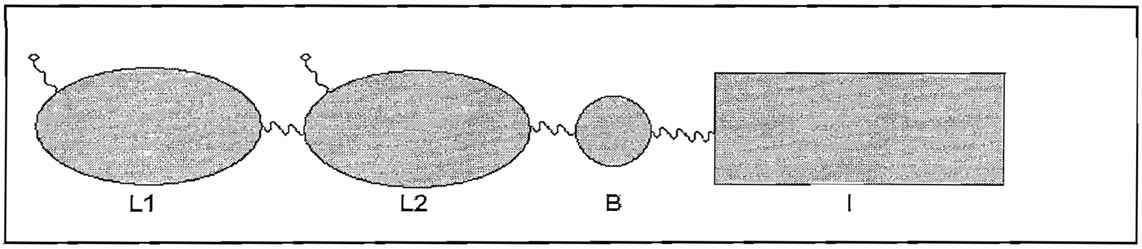

Figure 2.2: Structure of the E_2 component. The lipoyl domains are designated by L, the subunit binding domains by B, and the inner domain by I. The four domains are connected with hinge regions (Adapted from Patel & Roche, 1990).

<u>E_3-component:</u>

E_3 is a homodimer containing two 50,216 Da polypeptides. The dimers respectively bind noncovalently with a molecule of FAD. E_3 has four structural domains: The FAD-binding domain, the NADPH-binding domain, the central domain and the interface domain. The FAD-binding domain contains a redox active thiol center (the disulfide active site) (Patel & Roche, 1990). E_3 belongs to the pyridine nucleotide-disulfide oxidoreductases family of flavoproteins and follows a bi-bi ping-pong mechanism. A catalytic intermediate (EH_2) is formed when dihydrolipoamide donate two electrons to the enzyme. These electrons are shared between the FAD and the reactive disulfide. EH_2 donates the electrons to NAD^+ through a charge transfer complex between a thiolate anion and FAD (Patel & Roche, 1990).

<u>Protein X:</u>

Protein X has an inner and outer domain structure. It contains a NH_2 lipoyl domain, related to, but different from the two lipoyl domains of the E_2-subunit. Protein X mainly serves as a high-affinity binding site for the E_3-component (Reed & Hackert, 1990). An indication of another role is that protein X must be incorporated during the assembly of the core (Patel & Roche, 1990).

2.1.2 Pyruvate dehydrogenase enzyme complex (PDHc): the reaction

The reaction is complex and consists of four steps to convert pyruvate to acetyl CoA (figure 2.3).

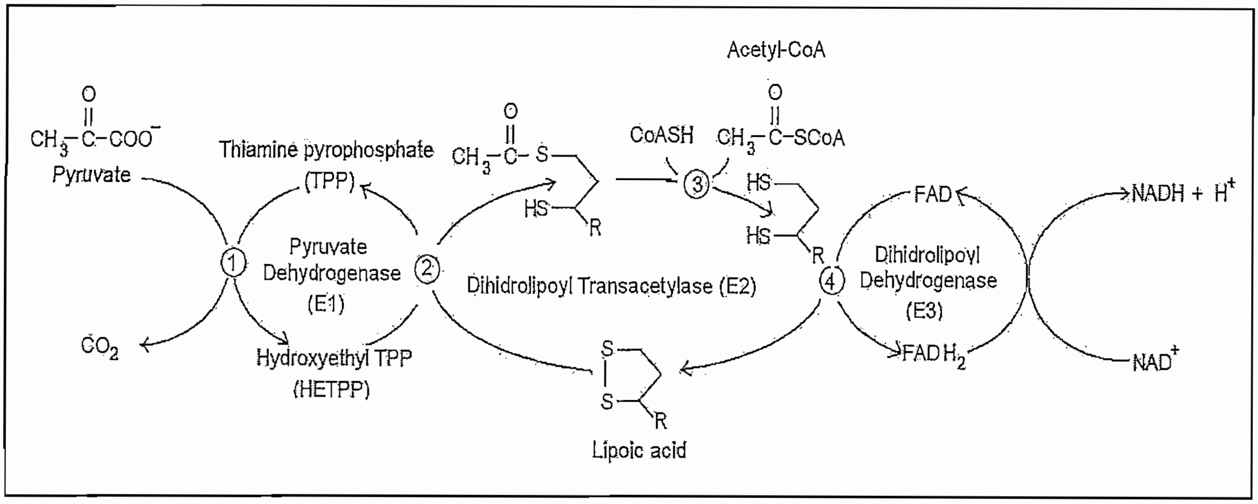

Figure 2.3: The mechanism of PDHc to convert pyruvate to Acetyl-CoA (Adapted from Garret & Grisham, 2005:614-615).

Step 1:

The attack of TPP on pyruvate leads to decarboxylation of pyruvate. This reaction is catalyzed by the E_1 component of the complex. The carbon atom between the nitogen and sulfur atoms in the thiazole ring is very acidic. It ionizes to form a carbanion that adds to the carbonyl group of pyruvate. The positively charged ring of TPP acts to stabilize the negative charge that develops on the carbon that is under attack (Styer, 1995:802). This stabilization takes place by resonance interaction. A double bond forms at the nitrogen atom. When this resonance-stabilized intermediate is protonated, it forms hydroxyethyl-TPP (Garret & Grisham, 2005:614-615).

Step 2:

The hydroxyethyl group on TPP is oxidized to an acetyl group and is then transferred to lipoamide. The disulfide group of lipoamide is the oxidant, and is converted into the sulfhydryl form. This reaction forms acetyllipoamide and is also catalyzed by E_1 (Lehninger, 1975:450-451).

Step 3:

The acetyl group is transferred from acetyllipoamide to CoA by a nucleophilic attack by coenzyme A on the carbonyl-carbon (Styer, 1995:802; Garret & Grisham, 2005: 614-615). In this step the energy-rich thioester bond is preserved because the acetyl group is transferred to CoA. This reaction is catalyzed by the E_2 component of the complex (Styer, 1995:802).

Step 4:

The oxidized form of lipoamide is regenerated by E_3 when two electrons are transferred to an FAD prosthetic group. The FAD bound to the E_3 protein has the ability to transfer the electrons to NAD^+ (Styer, 1995:802). Thereby NAD^+ is reduced to NADH (Garrett & Grisham, 2005:614-615).

2.1.3 Regulation of pyruvate dehydrogenase enzyme complex (PDHc)

Two regulatory enzymes (specific E_1-kinase and E_1-phosphatase) regulate the PDHc activity. These enzymes phosphorylate and dephosphorylate the three serine residues in the E_1 α-subunit to inactivate or activate the complex respectively (Lib *et al.*, 2002). Phosphorylation is catalyzed by E_1-kinase and dephosphorylation by E_1-phosphatase. NADH and acetyl-CoA accumulate when the cell energy charge is high. High levels of NADH, acetyl-CoA and ATP therefore up-regulate E_1-kinase activity. An increased level of pyruvate, ADP, NAD^+, H^+, Ca^{2+} and CoA inhibits E_1-kinase. Pyruvate is a powerful negative effector on E_1-kinase; when pyruvate levels increase the non-phosphorylated form of PDH (PDH-a) will be dominant, even at high levels of NADH and acetyl-CoA. Pyruvate thereby retain PDH in the active form (PDH-a) (King, 2007).

The regulation of E_1-phosphatase is not completely understood, but Mg^{2+} and Ca^{2+} play a role. Activation is tissue specific. In adipose tissue, insulin increases PDHc activity and in cardiac muscle, catecholamines increase PDHc activity. NADH and acetyl-CoA (products of PDHc) acts as negative allosteric effectors by reducing the affinity of the enzyme for pyruvate on the non-phosphorylated (PDH-a) form (King, 2007; figure 2.4).

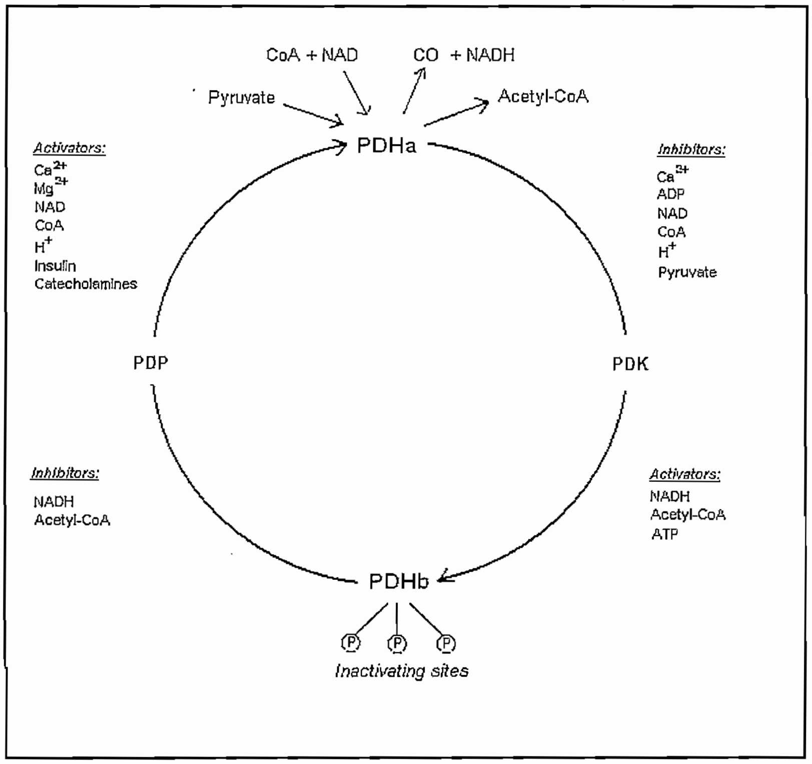

Figure 2.4: The regulation of PDHc activity. PDHa = non-phosphorylated form; PDHb = phosphorylated form; PDK = E_1-kinase; PDP = E_1-phosphatase (Adapted from King, 2007)

2.1.4 Pyruvate dehydrogenase complex (PDHc) deficiency

Description:

PDHc deficiency is one of the most common genetic disorders associated with abnormal mitochondrial metabolism. Mitochondria are the organelles inside cells that are responsible for energy production and respiration (Johnson, 2002). A disturbance in mitochondrial function affects the overall function of an organism (Clay, *et al.,* 2001). An important process in the mitochondria is the TCA cycle. It is a major biochemical pathway that generates energy from carbohydrates and produces most of the ATP needed for cells to function properly (Frye & Benke, 2007).

After glucose is catabolised to pyruvate during glycolysis, pyruvate can enter one of two pathways:

- If the energy charge in cells is sufficient, pyruvate is directed towards gluconeogenesis, which occurs mainly in the liver and, to a lesser extent, in the cortex of kidneys.
- If the energy charge is low, pyruvate is converted into acetyl CoA, which enters the tricarboxylic acid (TCA) cycle. The NADH that is produced during this reaction is a source

of electrons for the respiratory chain. The conversion of pyruvate is not part of the tricarboxylic acid cycle. It is however essential to enable carbohydrates to enter the tricarboxylic acid cycle (Lehninger, 1975, 450-451).

Individuals with PDHc deficiency have errors in one or more of the three enzymes within the PDHc. The most common are errors in E_1 (Frye & Benke, 2007).

Genetic profile:

The most common form of pyruvate dehydrogenase enzyme complex (PDHc) deficiency is caused by mutations in the X-linked E_1 alpha gene. Modifications in recessive genes cause the other deficiencies (Frye & Benke, 2007).

Genes responsible for PDHc deficiency:

- The E_1 α-subunit gene (PDHA1 gene) has been mapped to Xp22.2-p22.1 (Borglum, *et al.*, 1997). There are more than 90 mutations of the E_1 alpha enzyme subunit (Frye & Benke, 2007). Since the gene is on the X-chromosome, PDHA is a sex-linked disease (Johnson, 2002). The E_1 β-subunit gene (PDHB gene) has been mapped to 3p13-q23 (Olson, *et al.*, 1990).
- A mutation in the DLAT gene (mapped to 11q23.1) causes a deficiency of the E_2 enzyme. (Head, *et al.*, 2005). A shortage of lipoic acid may cause an E_2 enzyme deficiency because lipoic acid is a cofactor for the E_2 enzyme (Frye & Benke, 2007).
- The E_3 enzyme has been mapped to 7q31-32 and is inherited autosomal recessive. This enzyme also plays a part in the branched-chain ketoacid dehydrogenase and alpha-ketoglutarate dehydrogenase (Frye & Benke, 2007).
- The X protein gene has been mapped to 11p13 and is inherited autosomal recessive (Aral, *et al.*, 1997).

Signs and symptoms:

Malfunction in PDHc deprives the body of energy (Frye & Benke, 2007). Tissues that require large amounts of oxygen and are dependent on carbohydrates for energy supply, such as the brain and the central nervous system, are most sensitive to PDHc deficiency (Johnson, 2002). Figure 2.5 illustrates the dependence of the brain on glucose for energy supply. The brain uses almost half of the ingested glucose. Patients with PDHc deficiency therefore present with neurological impairment (Brown *et al.*, 1994:875).

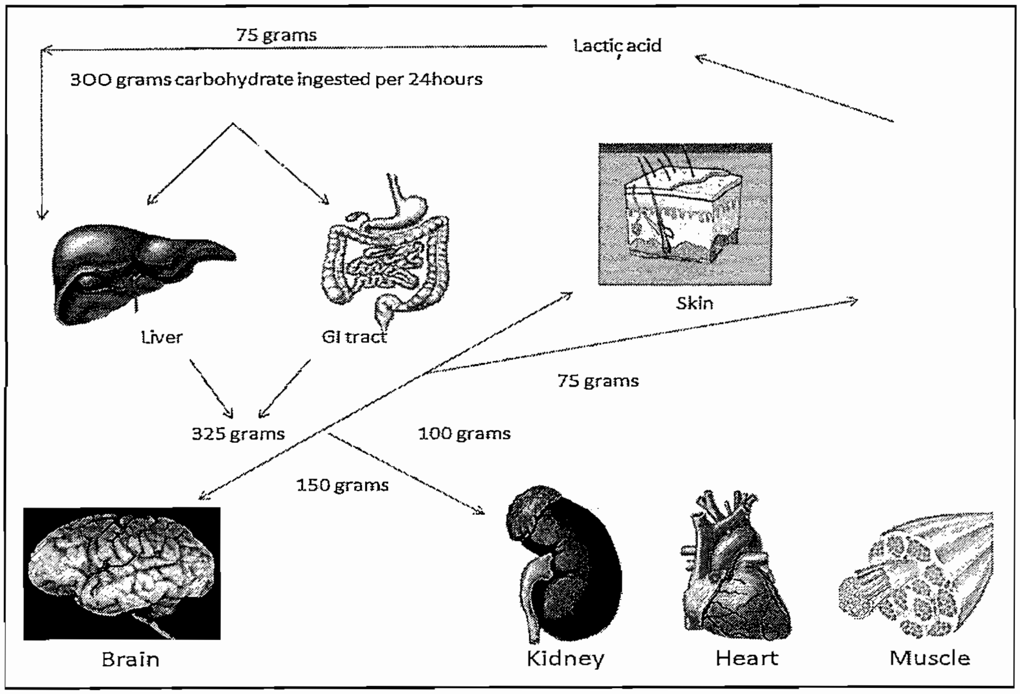

Figure 2.5: A schematic representation of the daily fluctuation of glucose and lactic acid in an average 70kg man that consumes 300 grams of carbohydrate per 24 hours. Following processing by the gastrointestinal tract and liver, 250 g of the carbohydrate is released as glucose. Another 75 g is generated by the Cori cycle to give a total liver output of 325 g of glucose. Of this, 150 g is utilized by the brain and 100 g by peripheral tissue, including the heart, skeletal muscle and kidney. Various tissues but mainly skin and blood, catabolise glucose to lactic acid to produce approximately 75 g lactic acid per day. This is returned to the liver and used to produce glucose via gluconeogenesis. The brain and skeletal muscle produce small amounts of lactic acid. An equivalent amount is re-used oxidatively by the heart and the kidney cortex (Adapted from Robinson, 2006).

A consequence of PDHc deficiency is accumulation of lactate in cells. Increased levels results in nonspecific, but common symptoms such as lethargy, poor feeding and tachypnea (Frye & Benke, 2007).

The progressive neurological, nonspecific symptoms in children with PDHc deficiency usually manifest themselves in:

- Retarded developmental and growth delay
- Mental retardation
- Poor acquisition or loss of motor milestones
- Alternating ataxia
- Poor muscle tone
- Abnormal eye movements and poor response to visual stimuli
- Seizures (usually start in infancy)
- Periodic dystonia (associated with an E_2-subunit deficiency)
- Progressive dystonia (associated with an E_1-α-subunit deficiency) (Frye & Benke, 2007)

Respiratory symptoms (apnea, dyspnea, Cheyne-Stokes respiration and respiratory depression) are nonspecific signs of metabolic and neurologic disease or severe lactic acidosis (Frye & Benke, 2007).

Choreoathetosis and progressive encephalopathy are present in children. Also found are dysmorphology, i.e., narrow forehead, frontal bossing, wide nasal bridge, upturned nose, flared nostrils and long philtrum. An X-component deficiency has been associated with trigonocephaly, supranasal lipoma, hypertelorism, thin upper lip, bilateral epicanthus, upward slant of the eyes, high palate and pectus excavatum (Frye & Benke, 2007).

Congenital brain malformations are found in individuals with severe deficiencies of PDHc and microcephaly may result. Abnormal development of the cerebrum, cerebellum, and brainstem are the parts of the brain generally affected by PDHc deficiency. The brain ventricles are on average much bigger than normal and the corpus callosum is usually under-developed or absent (Johnson, 2002).

Leukodystrophy and cerebellar ataxia (periods wherein the neurons within the cerebellum act with incoordination) is observed in many individuals affected with PDHc deficiency. Cerebellar ataxia attacks usually reoccur every three to six months throughout life. The severity decreases after puberty (Johnson, 2002).

Diagnosis:

Brain malformations are visible using ultrasound before birth or with MRI after birth. This may result from many factors and not only PDHc deficiency (Johnson, 2002). Definitive diagnosis is established by showing abnormal activity of one or more of the pyruvate dehydrogenase complex enzymes (Johnson, 2002 & Frye & Benke, 2007). Blood and fibroblasts are the easiest to obtain for enzyme analysis. Unfortunately, mosaicism can result in normal enzymatic activity in these cells, thus requiring a tissue biopsy if the diagnosis is strongly suspected (Frye & Benke, 2007).

Treatment and management:

Treatment of PDHc deficiency depends on the symptoms (Johnson, 2002). A diet high in fat, including beer as an alternative source of the chemical acetyl-CoA is recommended (Johnson, 2002). To prevent lactate build-up, carbohydrate intake should be restricted to 3-4 mg/kg/min. The caloric intake should therefore consist of 65-80% fat, 10% protein, and carbohydrates to make up the balance (Frye & Benke, 2007). Dietary supplements of thiamine, liproic acid and L-carnitine can be of use in some cases to optimize PDHc function (Johnson, 2002 & Frye & Benke, 2007). Dichloro-acetate reduces the inhibitory phosphorylation of PDHc and oral citrate may be used to treat acidosis (Frye & Benke, 2007).

The untoward symptoms may be relieved by

- Intervention programs for developmental delays and mental retardation
- Anti-convulsants to control seizures, and muscle relaxants to control spasticity or surgery to release the permanent muscle, tendon, and ligament tightening (contracture) at the joints (Frye & Benke, 2007).

Prognosis:

The prognosis for PDHc deficiency affected individuals varies widely. Individuals with mild deficiencies in the E_1-enzyme of the PDHc have a better prognosis than those with deficiencies in the E_2- and E_3- PDHc enzymes (Johnson, 2002 & Frye & Benke, 2007). The most seriously affected individuals will die at early age, unless gene or enzyme replacement therapy becomes available. For the less severely affected, several treatments may improve quality of life. Individuals with only mild defects can live normal life spans, their quality of life is only limited by the degree of mental impairment and muscle spasticity (Johnson, 2002). Dichloroacetate may be more effective in patients with particular mutations of the E_1 subunit, demonstrating a biochemical correction of PDHc deficiency. It is however doubtful that biochemical treatment can successfully reverse structural central nervous system abnormalities (Frye & Benke, 2007).

2.2 An overview of oxidative phosphorylation and a detailed discussion of respiratory chain complex I

Since errors in complex I is the most frequent affected complex of the oxidative phosphorylation (OXPHOS) system (Smeitink, et al., 1998 & Ugalde, 2004b) a detailed discussion of respiratory chain complex I is given. Only a short summary of oxidative phosphorylation will be given.

2.2.1 The oxidative phosphorylation system: an overview

Mitochondria are subcellular organelles that produce energy for cellular processes (Bindoff, 1999) and are the major sites of ATP production via the electron-transport chain and oxidative phosphorylation (OXPHOS) (Leonard *et al.*, 2000). OXPHOS is fixed in the inner mitochondrial membrane and consists of five multi-subunit enzyme complexes and two mobile electron carriers (ubiquinone and cytochrome *c*) (Smeitink, *et al.*, 1998; figure 2.6).

The five large protein complexes are NADH-ubiquinol oxidoreductase (EC 1.6.5.3) (Complex I), succinate-ubiquinone oxidoreductase (Complex II; EC 1.3.5.1), ubiquinol-ferricytochrome c oxidoreductase (Complex III; EC 1.1.10.2.2), cytochrome c oxidoreductase (Complex IV; EC 1.9.3.1) and the ATP synthase (Complex V; EC 3.6.3.14) (Fernandez-Vizarra, *et al.*, 2008).

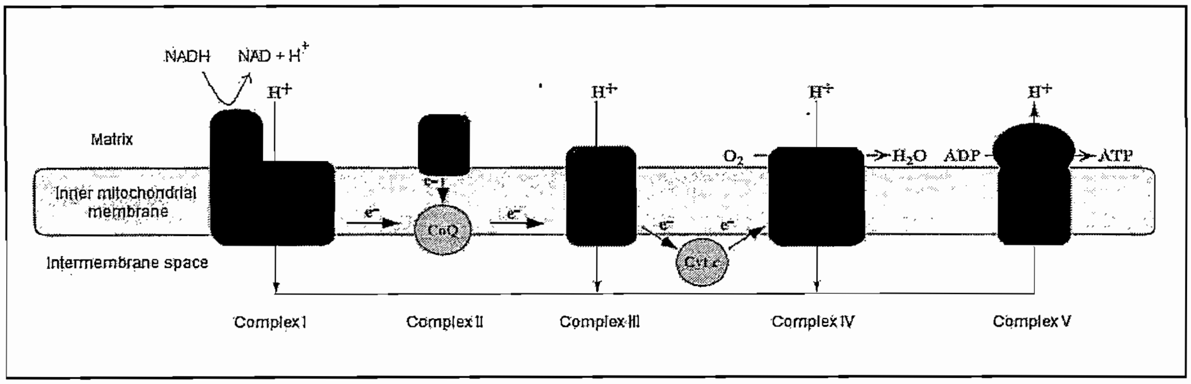

Figure 2.6: Schematic representation of the OXPHOS system complexes. The electron (e^-) and proton (H^+) flows are indicated by arrows. CoQ= ubiquinone, Cyt c = cytochrome c (Adapted from Hinttala, 2006).

Reduced co-factors (i.e. reduced nicotinamide adenine dinucleotide (NADH) and reduced flavoproteins, flavin adenine dinucleotide ($FADH_2$) are generated by the TCA cycle and fatty acid oxidation pathways (Bindoff, 1999). These cofactors are re-oxidized at different locations within the respiratory chain and electrons are donated into the particular complexes (Bindoff, 1999).

When reducing electrons pass along the complexes of the chain, an electrochemical gradient (proton motive force) results across the inner membrane (Smeitink, 2004 & Leonard *et al.*, 2000). This provides the energy to pump hydrogen ions across the inner membrane at complexes I, III, and IV (Leonard *et al.*, 2000.). At the end of the chain, complex IV transfers electrons to molecular oxygen, while ATPase (complex V) allows hydrogen ions back into the matrix. This effectively discharges the electrochemical gradient and the energy that it generates is the driving force that produces the energy carrier ATP from ADP (Janssen *et al.*, 2006; Leonard *et al.*, 2000. & Bindoff, 1999).

2.2.2 Complex I structure

Errors in complex I is the most frequent cause of mitochondrial disease (Smeitink, *et al.,* 1998 & Ugalde, 2004b). Complex I is a multiheteromeric enzyme complex, the largest respiratory chain complex with a molecular mass of approximately 980 kDa (Fernandez-Vizarra, *et al.*, 2008). It consists of 46 polypeptide subunits, a non-covalently bound flavomonucleotide (FMN) group and eight iron sulphur (Fe/S) clusters. Seven of the 46 subunits, the ND-subunits, are encoded for by mitochondrial DNA (mtDNA) and are therefore synthesized only in the mitochondrion. The remaining 39 are encoded by nuclear genes and transported into the organelles (Ugalde, 2004a).

Complex I has a L-shaped structure, formed by two arms perpendicular to each other (Friedrich, *et al.*, 1998; figure 2.7B). One arm, the hydrophobic arm, is embedded in the mitochondrial inner membrane and the hydrophilic peripheral arm protrudes into the mitochondrial matrix (Sazanov, 2007). The hydrophilic components are 75, 51, 49, 30 and 24 kDa, TYKY and PSST subunits (Hinttala, 2006). The hydrophilic arm contains the catalytic core of the enzyme, the NADH-binding site, the primary electron acceptor flavin mononucleotide (FMN) and eight or nine iron-sulfur (Fe-S) clusters (Sazanov, 2007). The hydrophobic components, ND1–ND6 and ND4L are the seven subunits encoded for by the mitochondrial genome (Lenaz, *et al.*, 2006).

The iron-sulfur clusters on the hydrophilic peripheral arm are arranged in a chain of seven clusters linking two catalytic sites of the enzyme. The N3 cluster is positioned in the 51 kDa (NDUFV1) metalloprotein. The NADH-binding site and the primary electron FMN are also situated at this position. The N1b, N4, N5 and N7 clusters are positioned in the 75 kDa subunit (NDUFS1). The

N6b and N6b clusters are positioned in the TYKY subunit (NDUFS8) in the connecting domain. The N2 cluster is positioned in the PSST subunit (NDUFS7) (Janssen *et al.*, 2006; figure 2.7A).

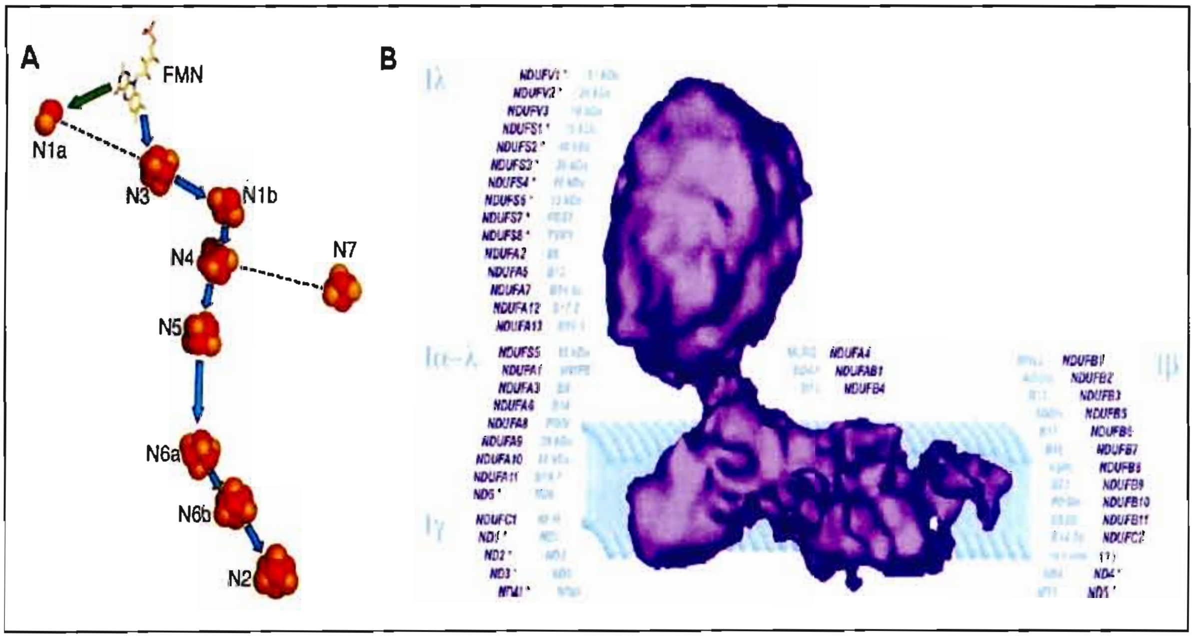

Figure 2.7: Arrangement of redox centres (A) and subunit composition (B) of mammalian complex I. The bovine subunit nomenclature is shown next to the boot-structure and the human subunit nomenclature is shown next to that. Subunits depicted with a $*$ are the subunits in which mutations have been analyzed (used with permission from Sazanov, 2007. & Janssen *et al.*, 2006).

2.2.3 Complex I reaction

The main functions of Complex I are to conserve the NAD^+/NADH ratio in the mitochondrial matrix, to provide ubiquinol to complex III and to contribute to the proton motive force, as the driving force to produce ATP (Hinttala, 2006). This enzyme catalyzes the first step of the mitochondrial respiratory chain and is therefore the primary entry point of electrons into the respiratory chain (Lenaz, *et al.*, 2006 & Fernandez-Vizarra, *et al.*, 2008). When NADH binds to complex I, two electrons are transferred from NADH to ubiquinone (CoQ). The electrons are then transferred to a noncovalently bound flavin mononucleotide (FMN). Electrons are finally converted through redox centres to ubiquinone (Q), which is reduced to ubiquinol (QH_2). The redox centres consist of eight iron-sulfur clusters: two binuclear clusters (N1a and N1b) and six tetranuclear clusters (N2, N3-N6a, N6b) (Janssen *et al.*, 2006).

These redox reactions are coupled to the translocation of four protons (H^+) across the mitochondrial inner membrane into the intramembrane space to generate the electrochemical potential to produce ATP (Ugalde 2004b). The reaction is as follows:

$NADH + H^+ + Q + 4H^+_{matrix} \rightarrow NAD^+ + QH_2 + 4H^+_{intermembrane\ space}$ (Janssen *et al.*, 2006).

Electron transfer from FMN to ubiquinone most likely utilizes the following pathway because it is the shortest route:

FMN→ N3→ N1b→ N4→ N5→ N6a→ N6b→ N2→ Q

The N2 cluster interacts with semiquinone bound to complex I, suggesting that this is the final step in the iron-sulphur chain. The Ni-binding site is also conserved in complex I and lies adjacent to the N2 cluster (Hinttala, 2006).

The N1a cluster can accept electrons from FMN but cannot pass them directly on to the main redox chain, perhaps because of the relatively long distance between N1a and N3. It was suggested that cluster N1a has antioxidant activity through preventing excessive reactive oxygen species (ROS) generation (Janssen *et al.*, 2006).

Two main models are postulated for proton pumping by complex I:

1. The Q-cycle mechanism is a direct, redox-driven model. It postulates that quinone-binding sites and proton translocation components in the membrane are in close contact with the redox centres in the peripheral arm. This permits direct interaction.
2. The indirect postulate is a conformation driven model. It postulates that the redox centres of the peripheral arm are linked to the distal proton translocating components (positioned at the end of the membrane arm) through long-range conformational changes.

It is also possible that these mechanisms can work in combination. This implies that complex I contain two energy-coupling sites (Janssen *et al.*, 2006).

2.2.4 Complex I deficiency

Description:

Complex I deficiencies are the most common OXPHOS deficiency. It can be caused by mutations in both nuclear-encoded and mitochondrial-encoded genes where several mutations have been found. However, many complex I deficiencies have not yet been characterised (Smeitink, *et al.*, 1998; Ugalde *et al.,* 2004a).

Genetic profile:

Mutations in nuclear-encoded genes are the major cause of complex I deficiency (Triepels *et al.*, 2001). Complex I deficiency with autosomal recessive inheritance results from mutation in nuclear-encoded genes, and includes NDUFV1 (Gene map locus 11q13), NDUFV2 (Gene map locus 18p11.31-p11.2), NDUFS1 (Gene map locus 2q33-q34), NDUFS2 (Gene map locus 1q23), NDUFS3 (Gene map locus 11p11.11), NDUFS4 (Gene map locus 5q11.1), NDUFS6 (Gene map locus 5pter-p15.33), NDUFS7 (Gene map locus 19p13), NDUFS8 (Gene map locus 11q13) and NDUFA2 (Gene map locus 5q31.2) (Anderson, *et al.*, 1981).

Complex I deficiency with mitochondrial inheritance has been associated with mutations in 6 mitochondrial-encoded components of complex I: MTND1 (encoded by the guanine-rich heavy (H) strand of the mtDNA between nucleotide pairs (nps) 3307 and 4262), MTND2 (encoded by the guanine-rich heavy (H) strand of the mtDNA between nucleotide pairs (nps) 4470 and 5511), MTND3 (encoded by the guanine-rich heavy (H) strand of the mtDNA between nucleotide pairs (nps) 10059 and 10404), MTND4 (encoded by the guanine-rich heavy (H) strand of the mtDNA between nucleotide pairs (nps) 10760 and 12137), MTND5 (encoded by the guanine-rich heavy strand of the mtDNA between nucleotide pairs (nps) 12337 and 14148) and MTND6 (encoded by the guanine-rich heavy strand of the mtDNA between 14149 and 14673 nps) (Anderson, *et al.*, 1981).

Signs and symptoms:

Mitochondrial diseases are multisystem disorders presenting with neuromuscular and cardiac symptoms (Oglesbee, *et al.*, 2006.). Malfunction in complex I deprives the body of energy. Organs and tissues, such as the brain, heart, skeletal muscle, liver, kidney and endocrine tissue, that depend primarily on the ATP-generating capacity of their mitochondria to meet their energy demands are most sensitive to complex I deficiency (Koopman *et al.,* 2005: C 1440; Smeitink, *et* *al*., 1998). Symptoms of the mitochondrial respiratory chain complex I deficiency are summarized in table 2.1.

Table 2.1: Symptoms of mitochondrial respiratory chain complex I deficiency (Adapted from Koopman *et al* 2005: C 1440; Smeitink, *et al*., 1998.; Bhattacharya, *et al*., 2003)

Organ involved	Symptom	Organ involved	Symptom
General systemic	Vomiting & diarrhea	Heart	Cardiomyopathy
	Lethargy		Conduction disorders
	Drowsiness	Kidney	Tubulopathy
	Malaise/ sleep disorder		Tubulointerstitial nephritis
	Failure to thrive		Fanconi syndrome
	Growth retardation		Renal failure
Central nervous system	Stroke like episodes	Muscle	Exercise intolerance
	Mental and motor retardation		Muscle pain
	Ataxia		Hypotonia & hypertonia
	Neurological deterioration		Myoclonus
	Headache & migraine		Rhabdomyolysis
	Hemiparetic cerebral palsy	Liver	Liver failure
	Encephalopathy		Hepatomegaly
	Cortical or cerebral atrophy		Cholestasis
Eye & ear	Cataract/corneal opacities	Pancreas	Pancreatic insufficiency
	Ptosis		Pancreatitis
	Progressive external ophtalmoplegia		
	Retinitis pigmentosa		
	Sensorineural hearing loss		

Diagnosis:

Since the clinical spectrum of complex I deficiency is wide, and diverse patterns of inheritance are present, diagnosis of mitochondrial disorders is complicated (Oglesbee, *et al*., 2006). When a mitochondrial defect is suspected, enzymatic or immunochemical measurement methods are used to diagnose it. Cultured skin fibroblasts can be used even though not all deficiencies that occur in muscle cells are present (Smeitink, *et al*., 1998). In view of this, a skeletal muscle biopsy is the cornerstone of diagnostic evaluation (Smeitink, *et al*., 1998; Oglesbee, *et al*., 2006). Most patients have a considerable residual enzymatic activity. As a result, we know of no patients that have been described in which the complex I activity could not be measured. On the other hand, very low complex I activity may not be compatible with life. Different phenotypes are recognized. Leigh syndrome (LS) is the most frequent. Other specific mitochondrial disorders that have been associated with complex I deficiency include Leber hereditary optic neuropathy (LHON), myoclonic epilepsy with ragged-red fibres (MERRF) and mitochondrial myopathy, encephalopathy, lactic acidosis and stroke-like episodes (MELAS) (Smeitink, *et al*., 1998).

Treatment and management:

There is currently no specific treatment for respiratory chain disease. Treatment with bicarbonate and/or dialysis may correct severe lactic acidosis (Leonard *et al.*, 2000). Dichloroacetate may also be used to lower blood lactate levels. Side effects such as painful peripheral neuropathy may occur (Bhattacharya, 2003). Seizures can be managed with anticonvulsants. Avoid phenobarbitone, since it inhibits oxidative phosphorylation. Sodium valproate inhibits numerous pathways of intermediary metabolism and can be used under controlled conditions in patients with OXPHOS deficiencies, because there is no sufficient substitute to treat serious epilepsy (Leonard *et al.*, 2000; Bindoff, 1999). It is important to avoid known mitochondrial toxins. Antibiotics such as tetracycline (which disrupts intramitochondrial protein synthesis) and ciprofloxacin (which depletes mtDNA) should not be used because it is risky. Aminoglycoside antibiotics affects individuals with a mutation in the 12s rRNA and they should use it. Antiviral agents such as azidothymidine (AZT) also deplete mtDNA (Bindoff, 1999).

There are subjective reports that supplements, such as ubiquinone, ascorbic acid, riboflavin, thiamin, vitamin E, and succinate improve symptoms (Leonard *et al.*, 2000). A balanced diet is important. Fasting increases fatty acid oxidation and consequently the activity of the respiratory chain. This can add an extra burden on the respiratory chain (Bindoff, 1999).

Several hypotheses of treatment to stabilize or even cure complex I disorders are entertained. These include a) substrate by-passing of complex I, b) gene therapy with alternative dehydrogenases, c) radical scavenging, d) correction of abnormal mitochondrial calcium signalling, e) anti-apoptotic treatment, and f) controlling negative environmental factors. In order to evaluate the effects of these treatments, development of complex I deficient animal models is critical, and therefore a major area of investigation (Smeitink, *et al*., 2004).

2.3 Problem statement, hypotheses, aims and strategy

Problem statement:

Deficiencies in both the pyruvate dehydrogenase complex enzyme (PDHc) and the mitochondrial respiratory chain enzyme (RC) cause increased levels of lactic acid in the plasma of humans (Robinson, 2006). Moreover, deficiencies in both enzyme complexes in humans result in similar changes in the metabolic profiles in blood and urine. It is therefore almost impossible to distinguish between the two conditions based only on the metabolic profile. Therefore, definitive diagnosis can only be made by assessing enzyme function. A muscle biopsy is required to do this because normal RC enzyme activity in leukocytes and fibroblasts may be measured as a result of mitochondrial DNA mosaicism (Frye & Benke, 2007). This can lead to a false positive diagnosis. The ethical issues surrounding acquisition of muscle biopsies from babies also preclude testing muscle RC enzyme activity. It is a highly invasive surgical procedure to acquire muscle biopsies under anaesthesia. Anaesthesia in itself poses a potential risk to newborn babies.

Aim:

The aim was to identify a method that is not only easier and less invasive but also definitive to distinguish between deficiencies in the pyruvate dehydrogenase enzyme complex enzymes and mitochondrial respiratory chain enzymes.

Strategy and experimental design:

First, the above deficiencies had to be induced in a model. This was done by inhibiting HeLa cells with pyruvate dehydrogenase and respiratory complex I inhibitors respectively. After the HeLa cells were incubated for 24 hours, the medium and cells were used to analyse organic acid metabolism. Three inhibitors were used: Moniliformin and 3-bromopyruvate to chemically induce pyruvate dehydrogenase deficiency and rotenone to chemically induce complex I deficiency.

Inhibitors:

Moniliformin is a highly toxic fungal metabolite produced by several species of Fusarium, most of which are commonly found on basic harvest, such as maize (Burmeister, 1979). It is normally isolated as the potassium derivative, but is mostly isolated as the sodium salt of semi-squaric acid (1-hydroxycyclobutl-ene-3,4-dione). The molecular formula is C_4HO_3Na (figure 2.8) and the molecular mass is 120.04 (Burmeister, 1979).

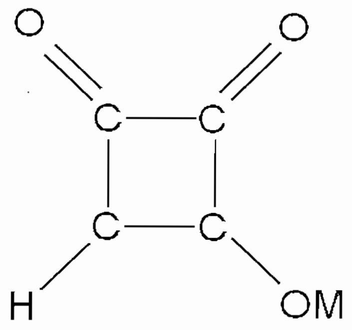

Figure 2.8: Structure of moniliformin

Moniliformin acts as a suicide enzyme inactivator. It requires chemical activation by the target enzyme. After activation, a chemical reaction takes place between the inhibitor and the enzyme, causing irreversible inhibition of the enzyme. Micromolar concentrations of moniliformin inhibit mitochondrial pyruvate and α- ketoglutaric acid oxidation selectively (Gathercole, *et al.*, 1986).

There is a structural similarity between moniliformin and pyruvate. This and the dependence of moniliformin on thiamin pyrophosphate for inhibition, makes complex formation between thiamin pyrophosphate and moniliformin on the active site of the enzyme possible. This reaction is analogous to complex formation between thiamin pyrophosphate and pyruvate (Gathercole, *et al.*, 1986).

Moniliformin acts as a suicide inhibitor on pyruvate dehydrogenase because it complies with the experimental criteria which identify suicide enzyme inhibitors, i.e.:
1) loss of enzyme activity is time-dependent, which provides good, but not definitive, evidence that covalent modification has taken place and the loss of enzyme activity at constant moniliformin concentration follows first-order kinetics for at least 15 minutes with the K_i value of 0.24mM; (2) the rate of inactivation is independent to the moniliformin concentration at high concentrations and follows saturation kinetics; (3) the rate of inactivation decreases as the substrate concentration increases at a given inhibitor concentration; and (4) enzyme inactivation is irreversible because the inhibitor binds covalently to the enzyme (Gathercole, *et al.*, 1986; Abeles & Maycock, 1976).

Moniliformin inhibits pyruvate dehydrogenase (E_1), but not dihydrolipoyl transacetylase (E_2) and dihydrolipoyl dehydrogenase (E_3) (Gathercole, *et al.*, 1986).

Two concentrations of moniliformin (110.2 µM and 220.4 µM) were used. The concentrations were chosen on the basis of results published by Gathercole, *et al.* (1986). They found an inhibition of approximately 85% in pyruvate dehydrogenase activity within 20 minutes in the presence of 2mM TPP (thiamin pyrophosphate) and 220.4 µM moniliformin (Gathercole, *et al.*, 1986).

3-Bromopyruvate is a synthetic brominated derivative of pyruvic acid. It is a colourless to white solid. The molecular formula is $C_3H_3BrO_3$ and its molecular mass is 166.92 (NCBI, 2008). The structure is given in figure 2.9.

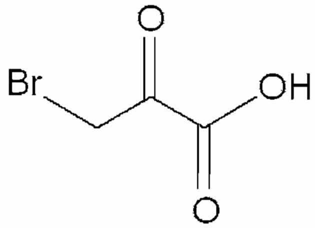

Figure 2.9: Structure of 3-bromopyruvate

Bromopyruvate is an effective inhibitor of the isolated E_1 component, and the intact PDHc complex. It has some remarkable differences in its mode of action on the two forms of the enzyme. Bromopyruvate initially acts as a competitive inhibitor of the isolated E_1 component with the K_i of 90 ± 15µM. Prolonged incubation of the enzyme with bromopyruvate causes an irreversible inhibition which requires thiamine pyrophosphate. The inclusion of pyruvate, its substrate, protects against inhibition of the isolated E_1 component (Lowe & Perham, 1984).

Bromopyruvate inhibits the intact pyruvate dehydrogenase complex irreversibly. The loss of the overall complex activity is dependent on TPP and the rate of inhibition is greatly increased in the presence of pyruvate (Lowe & Perham, 1984; Maldonado, 1972). This confirms that, under these conditions, bromopyruvate does not react at the pyruvate binding sites. It rather suggests that bromopyruvate reacts with the S-acetyldihydrolipoic acid residues that are generated on the E_2 enzyme component in the presence of the substrate (Lowe & Perham, 1984).

Two concentrations of bromopyruvate (3.75mM and 5.2mM) were used. They were chosen on the basis of results obtained in *Escherichia coli* (Apfel, *et al,* 1983). They found an inhibition of approximately 90% of pyruvate dehydrogenase activity within 2 minutes in the presence of 0.2mM TPP and 3.75mM 3-bromopyruvate (Apfel, *et al,* 1983).

Rotenone is a strong inhibitor of mitochondrial electron transport. It is isolated from the roots of several plants, particularly from Derris *spp* grown in Malaya, the East Indies and South America, and Lonchocarpus grown in Central and South America. These plants are toxic to fish and are used to poison arrowheads (Gosselin, 1984:896). Rotenone is colourless crystals and are unstable when exposed to air or light. The molecular formula is $C_{23}H_{22}O_6$ and molecular weight is 394.42 (Hayes, 1982). The structure is given in figure 2.10.

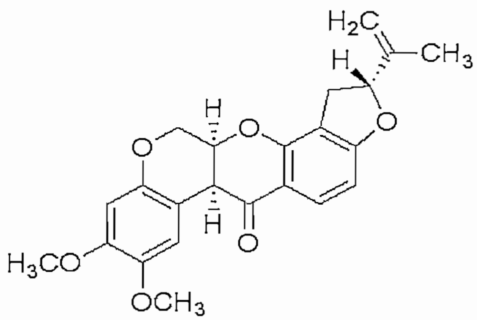

Figure 2.10: Structure of rotenone, a complex I inhibitor (Adapted from Gupta, R.C., 2007:499).

Rotenone is a common Class II inhibitor of NADH–UQ reductase. It inhibits complex I of the respiratory chain in a non-competitive manner by inhibiting the electron-transfer from the iron sulphur cluster to ubiquinone (Friedrich, *et al.,* 1994). This prevents the energy conversion of NADH to ATP because it inhibits the oxidation of the reduced NADH to NAD^+. In doing this, it blocks the oxidation of glutamate, α-ketogluturate and pyruvate by NAD^+ (Gupta, R.C., 2007:500).

Two concentrations of rotenone (10nM and 1000nM) were used. They were chosen on the basis of results from previous studies done locally on HeLa cells (Reinecke, *et al.*, 2006.). They showed that rotenone inhibits complex I activity in a dose-dependent manner and that it can be used as an in vitro model of complex I (NADH:ubiquinone oxidoreductase) deficiency in which various levels of deficiency can be mimicked by using different concentrations. According to the results, a low concentration of 10 nM rotenone can reduce complex I activity to less than 50 % and a concentration of 1000nM reduce complex I activity to 85% after only 24 hours incubation (Reinecke, *et al.*, 2006.).

In short, the study was done as follows: After the HeLa cells were incubated with two concentrations each of the three inhibitors, the growth medium and cell lysates were analysed to determine the effect of inhibition on organic acid metabolites, focusing on the intermediates of the

TCA cycle. Ratios of citric acid to succinic acid and citric acid to fumaric acid decreased significantly and the ratio of fumaric acid to malic acid increased significantly with inhibition of pyruvate dehydrogenase. None of these ratios were significantly affected when complex I of the respiratory chain was inhibited.

After the HeLa cells are inhibited, the medium and cells will be used in organic acid analysis.

CHAPTER 3

Materials and methods

3.1 Introduction

This chapter discusses the methods that were used to test the hypotheses put forward in chapter 1. Pyruvate dehydrogenase was inhibited with moniliformin and 3-bromopyruvate and the respiratory complex I with rotenone in HeLa cells. Two concentrations of each inhibitor were chosen in accordance to previous studies (Gathercole, *et al.*, 1986; Apfel, *et al,* 1983; Reinecke, *et al.*, 2006.). After inhibitors were added, the HeLa cells were incubated for 24 hours. The time was chosen in accordance to previous studies done on HeLa cells (Reinecke, *et al.*, 2006.) in order to make the results comparable and to limit the role of media composition changes on cellular function (Reinecke, *et al.*, 2006.). After incubation, the medium and cell lysates were analysed to determine the organic acid metabolites. Organic acids were quantified by means of gas chromatography.

3.2 Cell culture and inhibitor treatment

3.2.1 Cell culture

HeLa cells is an immortal cell line derived from cervical cancer cells from Henrietta Lacks, who died in 1951 (Sharrer, 2006).

Standard culturing procedures:

HeLa cells (NRBM[1] , ATCC No. 0001) were grown and maintained at 37°C and 5% CO_2 in a humidified HERA cell incubator (Kendro Laboratory products[2]). They were cultured in Dulbecco's modified Eagle's medium (DMEM, with 4 mM L-glutamine, 4500 mg/L glucose and sodium pyruvate, HyClone®[3]) containing 10% v/v FBS (fetal bovine serum, GIBCO®[4] E.U approved origin) and 1% v/v penicillin-streptomycin antibiotic solution (with penicillin 10000 units/ml and streptomycin10000 µg/ml GIBCO®). Cells were cultured in 25 cm^2 and 75 cm^2 flasks containing 5 or 10 ml medium respectively. Medium was removed 2 to 3 times per week after the cells reached 90% confluence. After media were removed, the cells were washed twice with 1 x PBS (without

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[1] The National Repository for Biological materials of the National Cancer Association of South Africa is in association with Highveld Biological, JHB, South Africa.

[2] Kendro Laboratory Products, GmbH, Hanau, Germany.

[3] HyClone® is a registered trademark of Thermo Scientific, Utah, U.S.A.

[4] GIBCO® is a registered trademark of Invitrogen Corporation., Grand Island, New York, U.S.A.

calcium or magnesium, Biowhittaker™[5]) and trypsinised with 1 x trypsin (GIBCO®) for inhibition or culturing purposes. All procedures were done aseptically.

3.2.2 Inhibitor treatment

3-Bromopyruvate, moniliformin, rotenone and thiamine pyrophospahate were purchased from Sigma Aldrich[6]. Ethanol was purchased from Merck[7]. For the sake of completeness, the preparation and concentrations of the stock solutions are given in Appendix B. The cells were treated with the pyruvate dehydrogenase and complex I inhibitors as follows (each set of inhibitions was repeated a total of seven times):

Flask one: Moniliformin with a final concentration of 110.2 μM: 50 μl TPP, 25 μl moniliformin stock solution and 2425 μl medium were filtered through Acrodisc syringe filters. Following this, 500 μl FCS, 50μl P/S and 1950 μl medium were added and the total mixture was added to the flask containing the cultured HeLa cells.

Flask two: Moniliformin with a final concentration of 220.4 μM: 50 μl TPP, 50 μl moniliformin stock solution and 2400 μl medium were filtered through Acrodisc syringe filters. Following this, 500 μl FCS, 50μl P/S and 1950 μl medium were added and the total mixture was added to the flask containing the cultured HeLa cells.

Flask three: 3-bromopyruvate with a final concentration of 3.75 mM: 50 μl TPP, 50 μl 3-bromopyruvate stock solution (375 mM) and 4900 μl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask four: 3-bromopyruvate with a final concentration of 5.2 mM: 50 μl TPP, 50 μl 3-bromopyruvate stock solution (520 mM) and 4900μl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask five: Moniliformin and rotenone with a final concentration of 110.2 μM and 10 nM respectively: 50 μl TPP, 25 μl moniliformin stock solution and 2375 μl medium were filtered through Acrodisc syringe filters. Following this, 50 μl rotenone stock (1 μM), 500 μl FCS, 50 μl P/S and

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[5] **Biowhittaker™ is a trademark of Cambrex Bio Science Inc., Walkersville, Maryland, U.S.A.**
[6] **Sigma Chemical Co., St. Louis, MO., USA.**
[7] **Merck, Darmstadt, Germany**

1950 µl medium were added and the total mixture was added to the flask containing the cultured HeLa cells.

Flask six: Moniliformin and rotenone with a final concentration of 220.4 µM and 1000 nM respectively: 50 µl TPP, 50 µl moniliformin stock solution and 2350 µl medium were filtered through Acrodisc syringe filters. Following this, 50 µl rotenone stock (100 µM), 500 µl FCS, 50 µl P/S and 1950 µl medium were added and the total mixture was added to the flask containing the cultured HeLa cells.

Flask seven: 3-bromopyruvate and rotenone with a final concentration of 3.75 mM and 10 nM respectively: 50 µl TPP, 50 µl 3-bromopyruvate stock solution (375 mM), 50 µl rotenone stock (1 µM) and 4850 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask eight: 3-bromopyruvate and rotenone with a final concentration of 5.2 mM and 1000 nM respectively: 50 µl TPP, 50 µl 3-bromopyruvate stock solution (520 mM), 50 µl rotenone stock (100 µM), and 4850 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask nine: Rotenone with a final concentration of 10 nM: 50 µl rotenone stock (1 µM) and 4950 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask ten: Rotenone with a final concentration of 1000 nM: 50 µl rotenone stock (100 µM) and 4950 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask eleven: Control: 50 µl TPP and 4950 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

Flask twelve: Control for rotenone (ethanol added): 50 µl ethanol and 4950 µl medium (containing 10% FCS and 1% P/S) were added to the flask containing the cultured HeLa cells.

All the flasks were then incubated for 24 hours at 37°C and 5% CO_2 in a humidified incubator.

3.3 Tissue preparation

Following incubation with the inhibitors, the media were transferred to a clean tube, marked 1 to 12 in accordance with the samples. The tubes were centrifuged at 1500x*g* for 10 minutes, where after the supernatant was transferred to a new tube. This tube was stored at -80°C until the extractions and assays were done.

After the medium was transferred, the cells were washed twice with 5 ml PBS and the PBS was aspirated. The cells were removed by adding 300 µl PBS to each sample flask (nrs.1-12) and scraped off. These cells were placed in eppendorf tubes and stored at -80°C until sonication.
Sonication: The cells were thawed on ice, positioned in the chamber of the sonicator and lysed for 5 seconds. The cell debris was centrifuged in a pre-cooled centrifuge and rotor at 4°C for 15 minutes at 13000x*g*. The supernatant was transferred to a clean tube and stored at -80°C until the extractions and assays were done.

3.4 Organic acid analysis:

Hundred µl of the internal standard, 3-phenylbutyric acid, (Sigma Aldrich[6]) was added to 1ml of the supernatant (from either the medium or the cells) in kimax tubes. When the supernatant from the cells was used, it was made up from 280 µl to 1 ml with Milli-Q®[8] water. Ten drops 5 N sodiumhydroxide (Merck[7]) and 300 µl hydroxylamine (0.05 g hydroxylamine hydrochloride in 2 ml water, Sigma Aldrich[6]) was then added and heated at 70°C for 30 minutes. Following this, it was cooled to room temperature and 17 drops of 5 N hydrochloric acid (Merck[7]) was added (Tuchman *et al.,* 1984). Hydroxylamine was added to stabilize the keto-acids.

Organic acids were analysed using the method of Erasmus (1987), where more than one solvent is used to isolate organic acids more effectively. Six ml ethyl acetate (Merck[7]) was added to hydroxylamine mixture and placed on the roto-torgue for 30 minutes. It was then centrifuged at 2800x*g* for 3 minutes and the organic phase aspirated into a clean tube. Three ml diethylether (Merck[7]) was added to the aqueous phase, placed on the roto-torgue for 10 minutes and subsequently centrifuged at 2800x*g* for 3 minutes. The diethylether organic phase was transferred to the previous aspirated ethyl acetate phase. Na_2SO_4 (Sigma Aldrich[6]) was added, the mixture

[8] **Milli-Q water is a registered trademark of Millipore Corporation. Billerica, MA, U.S.A.**

was vortexed and again centrifuged at 2800x*g* for 3 minutes. The organic phase was transferred to a kimax tube and dried under nitrogen at 40°C.

Derivatisation of the samples were done by adding 40 µl BSTFA (Sigma Aldrich[6]), 8 µl TMCS (Sigma Aldrich[6]) and 8µl pyridine (Merck[7]) to all the samples as per the SOP's of the Laboratory for Inherited Metabolic Defects. It was incubated at 70°C for 45 minutes. One µl of the derivatised solution was injected onto a Hewlett Packard 6890 gas chromatograph (GC) ported to a 5973 mass spectrometer (MS). The GC was equipped with a VF1-MS GC column (30m × 0.32mm × 0.25mm I.D.). The injector temperature was set at 280°C. Helium at a flow rate of 2.0 mL/min was used as the carrier gas. Initial oven temperature was 60°C, which increased at a rate of 4 °C/min to 120°C and then to a final concentration of 285°C at a rate of 6°C/min. The oven temperature was maintained at 285 °C. Ionisation was done by electron impact with a potential of 70eV and MS analysis was done in scan mode.

Identification of the organic acids in the chromatogram was done by using the automated mass spectral deconvolution and identification system (AMDIS software). The library that was used was compiled by Prof L.J. Mienie of the Laboratory for Inherited Metabolic Defects and it contains the common organic acids (NWU Potchefstroom campus).

3.5 PCA:

The BioGoggles program was used to discover biomarkers by filtering interesting variables using Principal Component Analysis (PCA). During the organic acid analysis, complex data sets arise and with PCA it is possible to extract relevant information from these data sets and so reduce the components in the data set (Katajamaa, *et al.*, 2007; Ringnér, 2008). PCA is a simple method that reduces the data complexity by calculating new variables, called principal components, which represent the original variables and so record the largest variation in the dataset (Ringnér, 2008). It identifies variables that are important in the data set, by expressing the differences between samples, and visualizes and interprets them by using a series of simple plots (Berman, 2009).

3.6 Statistical analysis:

A nonparametric test was used to test for differences because the assumptions of the ANOVA were not met (Berenson, *et al.*, 2001:403). The SAS® system was used to test for differences between the medians of several experimental groups (μ_i) and a designated control group (μ_c) simultaneously. First, the Kruskal-Wallis rank procedure was used to test for differences in the medians. The Kruskal-Wallis procedure is more powerful than the one way ANOVA *F* test under conditions where the assumptions of the *F* test are not met, as is the case of this data set (Berenson, *et al.*, 2001:429). We then used the post hoc analysis of Dunn for simultaneous nonparametric inference analysis in the one-way layout for all groups to test for significant differences (Dunn, 1964).

The method of Dunn offers the following advantages: (1) the symmetry assumption, which is often difficult to assess in drug discovery settings with small sample sizes, may be relaxed or even ignored; (2) equal sample sizes are not required, and (3) relatively small total sample sizes may be analyzed.

It is important to note that only metabolites where the test gave significant differences are given in results and discussion. A 5% level of significance was selected. In the case of the post hoc analysis of Dunn, the level of significance is adjusted by the formula:

Level of significance (α) = level of significance/the number of comparisons to the control (1)

With the pyruvate dehydrogenase inhibitors, 4 groups were compared to the control group. The level of significance (α) was therefore 0.0125. In the case of the complex I inhibitors, 6 groups were compared to the control group. The level of significance (α) was therefore 0.008.

CHAPTER 4

Enzyme analysis: Methods and Results

HeLa cells were inhibited with pyruvate dehydrogenase and respiratory complex I inhibitors respectively. Three inhibitors were used: Moniliformin and 3-bromopyruvate to induce experimental pyruvate dehydrogenase deficiency and rotenone to induce experimental complex I deficiency.

Moniliformin acts as a suicide enzyme inactivator of isolated bovine heart pyruvate dehydrogenase (Gathercole, *et al.*, 1986). In this study we used two concentrations (110.2 µM and 220.4 µM). The loss of pyruvate dehydrogenase activity is approximately 85% inhibition within 20 minutes when 220.4 µM moniliformin was used (Gathercole, *et al.*, 1986).

Bromopyruvate inhibits the intact pyruvate dehydrogenase complex irreversibly (Lowe & Perham, 1984; Maldonado, 1972). We used two concentrations of 3-bromopyruvate (3.75mM and 5.2mM). The loss of pyruvate dehydrogenase activity is about 90% within 2 when 3.75mM 3-bromopyruvate was used (Apfel, *et al,* 1983).

Rotenone results in increased loss of complex I activity in HeLa cells (Reinecke, *et al,* 2006). Accordingly rotenone concentrations of 10 nM and 1000nM reduced complex I activity to less than 50 % and 20% respectively after only 24 hours of incubation (Reinecke, *et al.*, 2004.). The results obtained by Reinecke, *et al.* (2006) on HeLa cells correlates with results obtained by Koopman (2004) on fibroblast cultures. In view of these findings, we did not measure the inhibition of RC complex I with rotenone.

4.1 Pyruvate dehydrogenase enzyme activity dipstick assay:

4.1.1 Introduction

To quantify the pyruvate dehydrogenase (PDH) enzyme activity, the PDH enzyme activity dipstick assay was used (Figure 4.1C, MitoSciences®[9]). This kit is used to quickly determine activity in human, bovine, mouse, or rat samples. Capture antibodies, striped onto nitrocellulose membrane, proficiently capture the large PDH enzyme complex in its intact and functionally active state while a wicking pad draws the sample through the antibody bands.

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[9] **MitoSciences®, Eugene, Oregon, U.S.A.**

The NADH produced by PDHc reduces nitrotetrazolium blue chloride (NBT) to NBTH. NBT is a chromogen which, in the presence of diaphorase and after a fixed time period, is reduced to NBTH, to form an insoluble intensely colored precipitate at the capture line. (Figure 4.1A & 4.1B) The colour intensity of the band is proportional to PDHc activity. If the colour intensity is high, it indicates that PDHc activity is high. Conversely, if its low, the PDHc activity is low. If no bands form, there is no PDHc activity. The signal intensity of the formed NBTH (the color band on the dipstick) is measured by scanning the dipstick and quantification by densitometry (see 4.1.2.3).

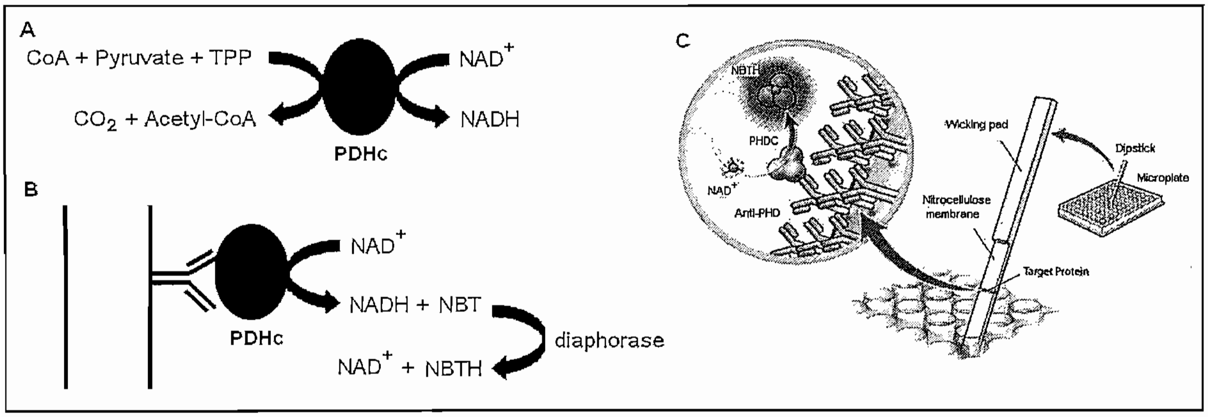

Figure 4.1 PDHc enzyme activity dipstick assay reaction. (A) The PDHc reaction generates $NADH^+$ (B) Immunocaptured PDHc produce NADH and reduces NBT, which forms a colored precipitate at the PDHc immunocapture zone. (C) The dipstick assay uses the lateral flow concept, whereby capture antibodies are striped onto nitrocellulose membrane and a wicking pad draws the sample through the antibody bands.

The dipstick enzyme assay is a very simple, rapid and sensitive assay and it requires minimal sample preparation because it does not require isolation of mitochondria. Crude preparations can be used which makes the method suitable for a wide range of sample types. This assay only captures PDHc which makes it specific. Because lactate dehydrogenase uses the same substrates (pyruvate and NAD^+) as pyruvate dehydrogenase, spectrophotometric methods cannot be used for crude samples. Two other methods to measure PDHc activity have been described, the radioisotope method and the spectrophotometric method. The radioisotope method is sensitive but dangerous and safety requirements needs to be addressed when using radioisotopes. The spectrophotometric methods measures NADH formed and as mentioned , lactate dehydrogenase will affect the measurement of NADH. The spectrophotometric methods is therefore only suitable for isolated mitochondria.

4.1.2 Measurement of PDHc using the PDH enzyme activity dipstick assay

The pyruvate dehydrogenase enzyme activity dipstick assay kit contains dipsticks, a 96-well microplate and reagents. The reagents include Buffer #1 (Sample buffer), Buffer #2 (Blocking buffer), Detergent, Reagent mixture #1 (Enzyme substrate mix), Reagent mixture #2 (Diaphorase) and Reagent mixture #3 (NBT).

4.1.2.1 Determining the working range:

There were only a limited amount of the positive control samples and a standard curve could therefore not be constructed as recommended (Kit insert). We did use a working range as a guideline (table 4.1). Protein content optimization was done by preparing three different protein concentrations (0, 1 & 2 µg/µL) from the control sample and using a total volume of 50 µL of each in the assay. Two µg/µL of each sample was used because 2 µg/µL formed an intensely colored precipitate at the capture line on the dipstick.

Table 4.1 Suggested working range for different sample types

Sample type	Working range/ sample volume
Tissue mitochondria	1-10 µg/ 25 µL
Muscle tissue extract	10-100 µg/ 25 µL
Liver tissue extract	25-150 µg/ 25 µL
Fibroblast extract	40-250 µg/ 50 µL
Hepatocellular carcinoma extract	20-160 µg/ 50 µL

4.1.2.2 Sample preparation:

Following incubation of the HeLa cells with the inhibitors, the medium was removed and the cells washed twice with 5ml PBS. The PBS was aspirated and discarded. The cells were removed from the flask by adding 300 µl PBS to each sample flask and then scraping it off. These samples were transferred to eppendorf tubes and centrifuged at 10000 x *g* for 10 minutes. Excess PBS was removed and the cell pellet was stored at −80 °C until the dipstick assay could be done. For analysis, the cells were thawed on ice and re-suspended in 25 µL PBS. The protein concentrations were determined by bicinchoninic acid (BCA) analysis (Smith *et al*, 1985) and the samples prepared for the dipstick analysis. The sample preparation step is critical in the assay. Because I used cultured cell extracts, sample preparation method 3 of the dipstick assay protocol was used. The cells were diluted with the appropriate volumes of PBS (instead of Buffer # 1 as the protocol indicates) to a protein content of 2 µg/µL. A volume of 1/10 of the supplied detergent was added.

The preparation of each sample is summarized in table 4.2. Samples were kept on ice for 10 minutes and then centrifuged for 10 minutes at 3000 rpm. The extracted supernatant was transferred to a new tube. After sample preparation, the dipstick assay was done.

Table 4.2 The preparation of each sample for a total protein content of 2 µg/µL. M=Monilifromin, 3-B=3-Bromopyruvate, conc= concentration and vol=volume

	Sample conc. (µg/µl)	Sample vol. (µl)	PBS (µl)	Detergent (µl)	Total vol. (µl)
Blank	0	0	60	0	60
Control	14.2	8.5	45.5	6	60
M (110.2µM)	11.9	10.1	43.9	6	60
M (220.4µM)	11.65	10.3	43.7	6	60
3-B (3.75mM)	10.2	11.8	42.2	6	60
3-B (5.2mM)	12.8	9.4	46.6	6	60

4.1.2.3 Dipstick procedure:

Fifty µL of the diluted samples were added to 50 µL of Buffer #2 in the wells of the microplate and mixed. The dipstick, with its nitrocellulose end down, was then inserted to the sample mix in the microplate well. The sample wicked up from the thin nitrocellulose end to the thick wicking pad of the dipstick. This step requires more or less 45 minutes. After wicking was complete, the sample mix was washed by adding 40 µL of Buffer #1 and again wicked for 20 minutes. The activity buffer was prepared by combining Buffer #1, Reagent mixtures #1, #2, and #3 as per table 4.3.

Table 4.3: The preparation of activity buffer

Number of dipsticks	**Buffer #1 (mL)**	**Reagent mix #1 (µL)**	**Reagent mix #2 (µL)**	**Reagent mix #3 (µL)**
10	3.3	166	133	7
20	6.6	333	266	14
30	10	500	400	20

Next, 300 µL of activity buffer was added to an empty microplate well for each dipstick. The wicking pads were removed from the dipsticks and placed in the activity buffer. The signal appeared 5-7mm from the bottom of the dipstick in approximately 20 minutes (Figure 4.2). The dipsticks were left to develop for 60minutes. After the signal developed, the dipsticks were washed for 5 minutes with 300 µL deionized water in an empty well of the microplate. The dipstick was dried and the signal intensity was measured by scanning it with a Scanjet 3800 Scanner (Hewlett Packard[10]) at grey scale picture setting and 600 dots per inch (dpi) resolution.

After scanning the dipstick, the image was saved as a bitmap file and imported into the imaging software GeneTools®[11] for quantification using densitometry. The Genetools® software was set to 'manual band quantification'. Band quantification was done by positioning a rectangle over the area where the band is visible. To ensure similar rectangles for quantification of the dipsticks, the 'spots' option was selected. To subtract the background from the raw value, the option 'background' correction was selected and set to 'manual mode'. A second rectangle was selected just below the first one (Figures 4.2A - 4.2C). After this, an arbitrary value (called "volume") that represents the density or intensity for each band (minus the background) is given by the software.

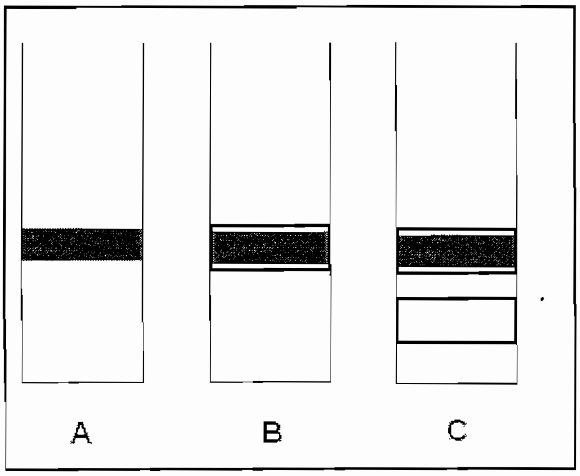

Figure 4.2 Quantification of bands on the pyruvate dehydrogenase enzyme activity dipstick assay. (A) a dipstick with a color band, (B) the rectangle positioned over the area where the band is visible and (C) a second rectangle was selected just below the first one to correct for background.

[10] **Hewlett Packard, Palo Alto, California, U.S.A.**
[11] **GeneTools®, Syngene, Cambridge, U.K.**

4.2 Results

The pyruvate dehydrogenase enzyme activity dipstick assay is reproducible, since a batch-to-batch variation of approximately 10% was observed (Personal communication with Anni Thomas).

Figure 4.3 shows the dipstick scans of the blank, control and inhibited samples. The clarity of the scanned dipsticks were excellent. On the dipsticks of the blank and 3-bromopyruvate samples, no bands were observed, indicating low or no PDHc activity. The intensely colored precipitate at the capture line (the band) of the dipsticks of the control and moniliformin samples indicate high PDHc activity. Figure 4.4 summarises the data of the quantified dipsticks as a graphic representation of the specific activities (Volume/µg/1 hr) of the inhibitor and control samples.

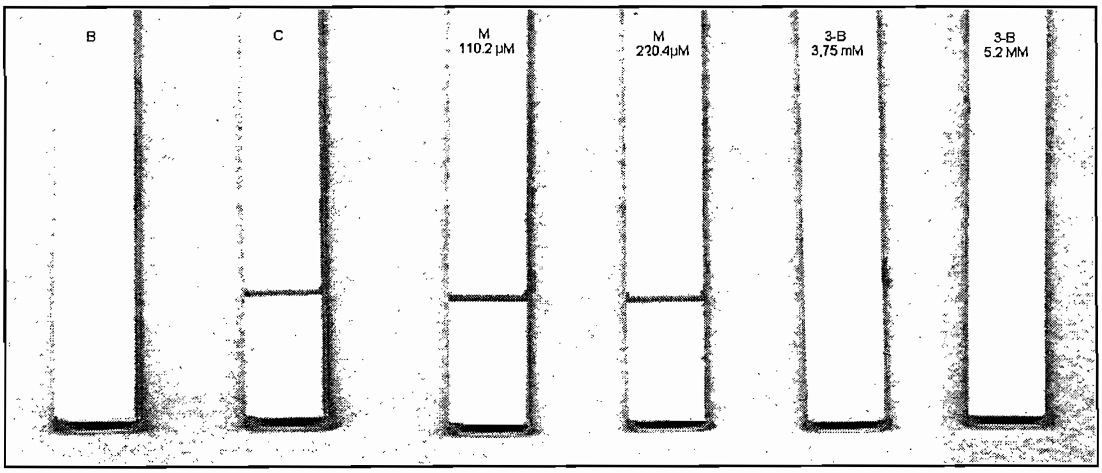

Figure 4.3 Dipstick scan of the inhibitor and control samples. (B=Blank, C=Control, M=Monilifromin, 3B= 3-Bromopyruvate)

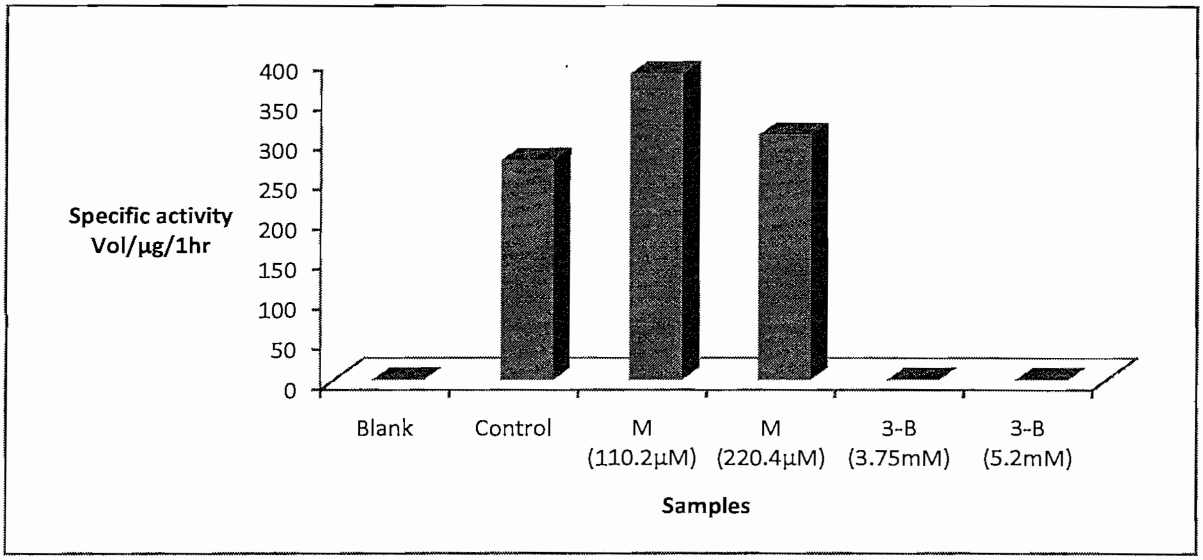

Figure 4.4 Graphic representation of the specific activities (Volume/µg/1 hr) of the inhibitor and control samples. M=Monilifromin, 3-B=3-Bromopyruvate

The two concentrations of moniliformin (110.2 µM and 220.4 µM) were chosen on the basis of published results (Gathercole, *et al,* 1986). PDHc activity was inhibited by approximately 85% within 20 minutes in the presence of 2mM TPP (thiamin pyrophosphate) and 220.4 µM moniliformin (Gathercole, *et al*., 1986). My results clearly showed that moniliformin did not inhibit PDHc in HeLa cells (figure 4.4) and therefore did not induce an experimental pyruvate dehydrogenase deficiency in the HeLa cells. There are two possible reasons. First, the experimental approach differed in the two studies and second, species difference may explain the results. Gathercole, *et al*. (1986) isolated PDHc from bovine heart muscle cells and inhibited it with moniliformin. In this study, cultured HeLa cells, where PDHc were not isolated, were used and inhibited with moniliformin. It is possible that moniliformin did not cross the HeLa cell membrane and could therefore not inhibit PDHc in intact HeLa cells.

The two concentrations of bromopyruvate (3.75mM and 5.2mM) were chosen on the basis of results obtained in *Escherichia coli* (Apfel, *et al,* 1983). Inhibition of approximately 90% of pyruvate dehydrogenase activity was achieved within 2 minutes in the presence of 0.2mM TPP and 3.75mM 3-bromopyruvate (Apfel, *et al,* 1983). In this study 3-bromopyruvate inhibited PDHc completely (figure 4.4) and therefore induced an experimental pyruvate dehydrogenase deficiency in the HeLa cells. The results of inhibition of PDHc activity is therefore important to keep in mind when the results on changes in metabolite profile in HeLa cells are interpreted.

CHAPTER 5

Results and Discussion

Complex I is the most frequently affected complex of the oxidative phosphorylation (OXPHOS) system (Smeitink, et al., 1998 & Ugalde, 2004b). Therefore, only complex I was inhibited with rotenone. Errors in the other complexes of OXPHOS will most likely also inhibit ATP synthesis and will have similar clinical manifestations as errors in complex I. It is therefore reasonable to assume that effects of inhibition of the other complexes will have similar outcomes than inhibition of complex I.

The measurements varied markedly (Appendix C) which makes it difficult to interpret. This may be due to the inhibitors influencing the growth of the cells on a negative level and consequently their metabolism. This was most likely due to the fact that ATP synthesis was inhibited by 3-bromopyruvate and rotenone. The HeLa cells without treatment (controls) and those treated with moniliformin grew exponentially because they have reached their stationary phase of growth of confluence. This indicates a high metabolic activity. This also correlates with the results obtained in 5.2, where moniliformin did not inhibit PDHc of the HeLa cells. The cells treated with the 3-bromopyruvate remained stagnant and did not grow as well. Rotenone inhibitors killed many cells after 24H inhibition (figures 5.1 to 5.5). This may be because of ROS-mediated cell death as a result of the rotenone inhibition (Reinecke, *et al.*, 2006.). Freezing and thawing the cells could also, at least in part, caused the variability. Not all seven studies were done on the same day.

The results obtained from the cell extracts were inconclusive and are therefore not given and discussed. Only the results that were obtained in the medium in which the cells were grown will therefore be discussed. It is important to note that the measurements in the media were much higher than in the cell extracts, probable because the TCA cycle intermediates were excreted into the medium (Appendix C). This has to be investigated.

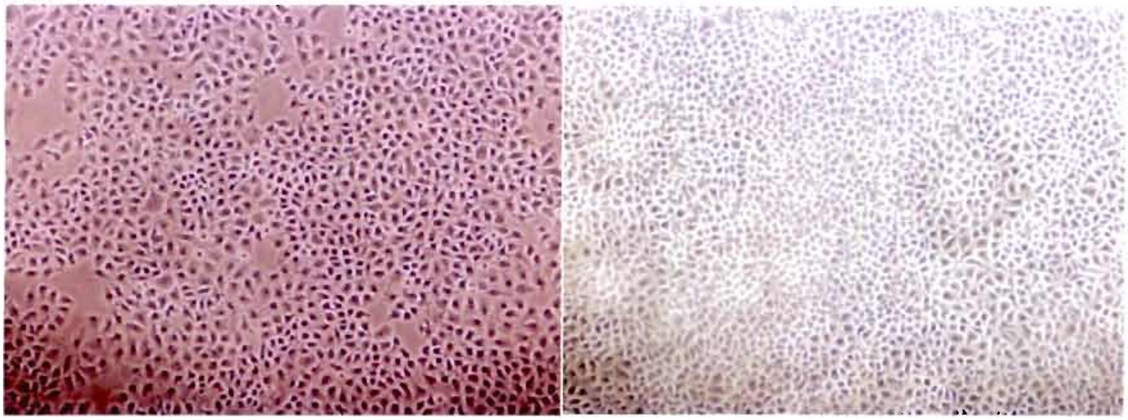

Figure 5.1: HeLa cells where only medium was added (control for PDHc) at t=0 (left panel) and t=24H (right panel)

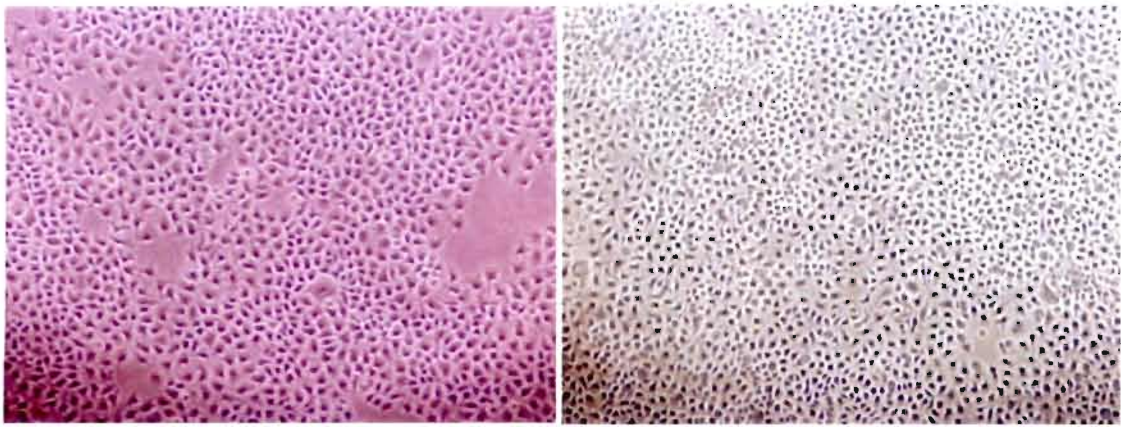

Figure 5.2: HeLa cells where medium and ethanol were added (control for complex I) at t=0 (left panel) and t=24H (right panel)

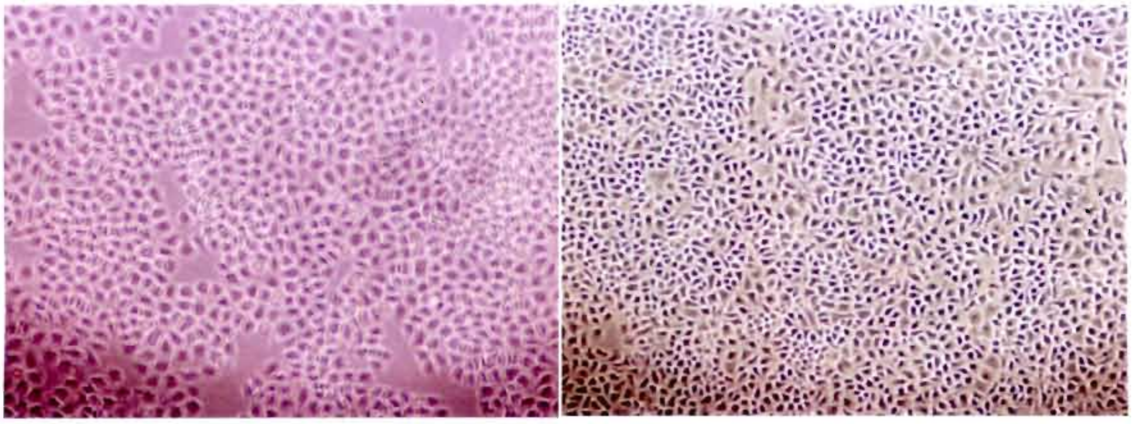

Figure 5.3: HeLa cells treated with moniliformin (220.4µM) at t=0 (left panel) and t=24H (right panel)

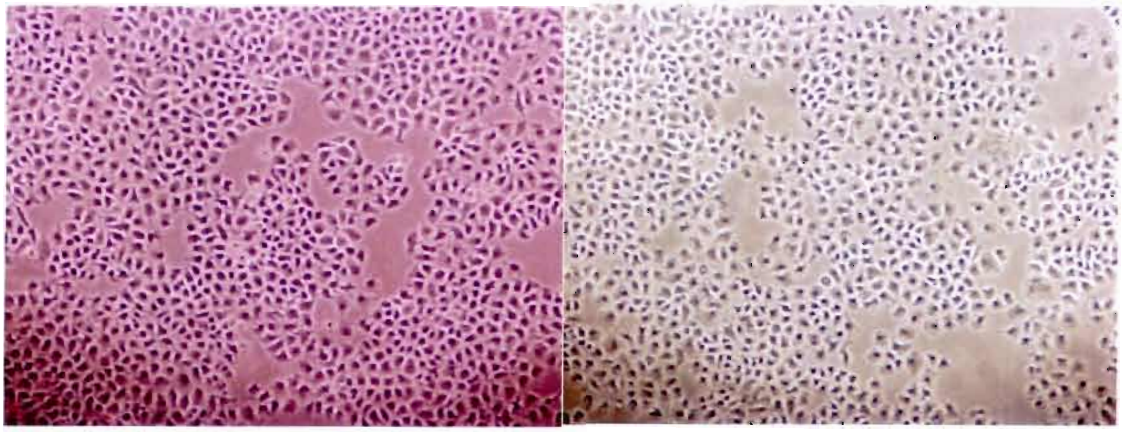

Figure 5.4: HeLa cells treated with bromopyruvate (5.2mM) at t=0 (left panel) and t=24H (right panel)

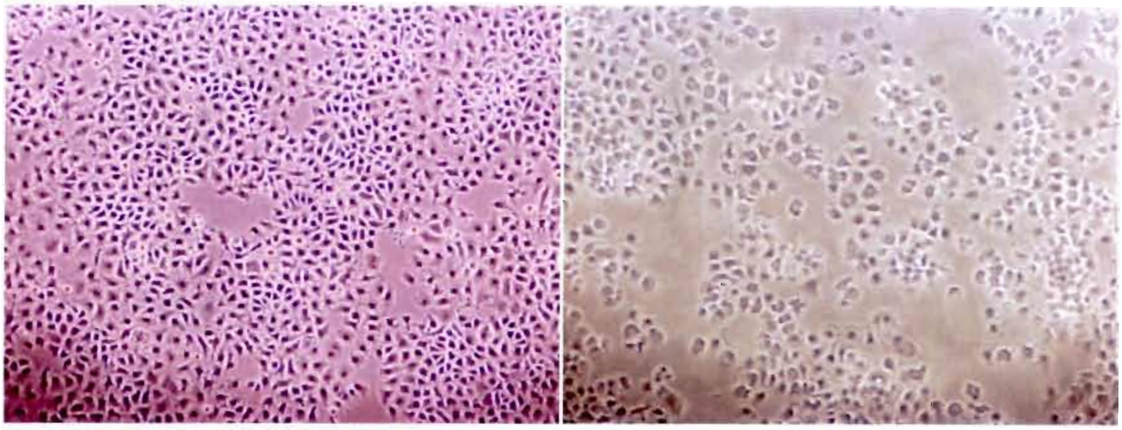

Figure 5.5: HeLa cells treated with rotenone (1000nM) at t=0 (left panel) and t=24H (right panel)

5.1. Ratio limit of the intermediates of the tricarboxylic acid (TCA) cycle

Several calculated ratios were non-informative (results not given because they were not significantly different), probably as a result of the amphibolic nature of the TCA cycle. All of the reactions, except where oxaloacetate is converted to citrate and α-ketoglutarate to succinate, can switch between forward and reverse reactions. This can cause large fluctuations in the TCA cycle intermediates.

When compared to the control, the ratio of citric acid to succinic acid significantly decreased with pyruvate dehydrogenase inhibition with 3-bromopyruvate. With the complex I inhibitor, only the combinations of 3-bromopyruvate (3.75 mM) and rotenone (10 nM) and 3-bromopyruvate (5.2 mM) and rotenone (1000 nM) were significantly decreased when compared to the control. The differences were most likely caused by the effect of 3-bromopyruvate and not because of rotenone inhibition because rotenone alone had no effect on the ratio (table 5.1 and figure 5.6).

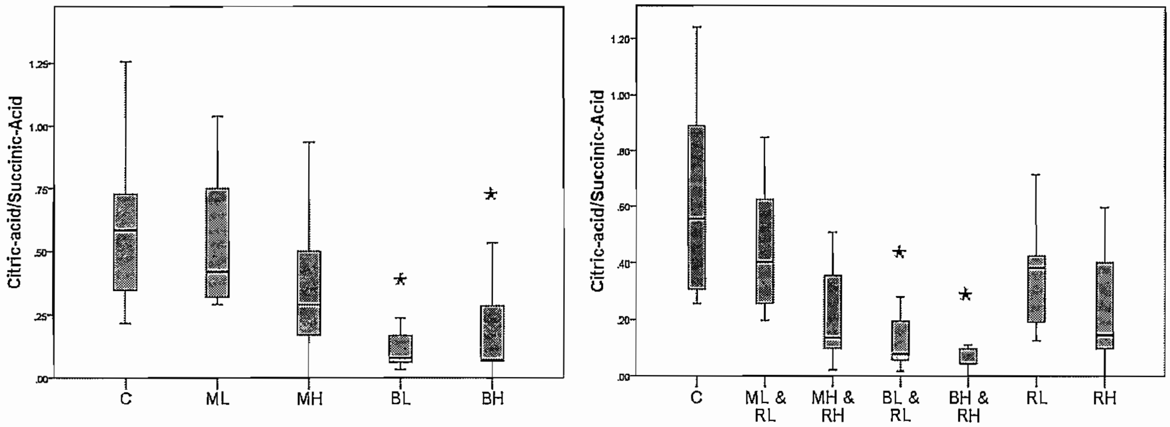

Figure 5.6: The ratio of citric acid to succinic acid in the medium. The plot present the median ± the 95% confidence interval as a block and the minimum and maximum values as bars. Asterisks (*) indicate groups that were statistically significantly different from the control (Left panel=pyruvate dehydrogenase inhibitors, Right panel=respiratory chain inhibitor, C=control, M=moniliformin, B=3-bromopyruvate, R=rotenone, L=low concentration, H=high concentration)

When compared to the control, the ratio of citric acid to fumaric acid significantly decreased with inhibition of pyruvate dehydrogenase with the high concentration of 3-bromopyruvate. With the complex I inhibitors, only the combinations of moniliformin (220.4 µM) and rotenone (1000 nM), 3-bromopyruvate (3.75 mM) and rotenone (10 nM) and 3-bromopyruvate (5.2 mM) and rotenone (1000 nM) significantly decreased (table 5.1 and figure 5.7). Similar to the results in figure 5.6, the rotenone does not seem to have an effect since rotenone alone had no measurable effect on the ratio.

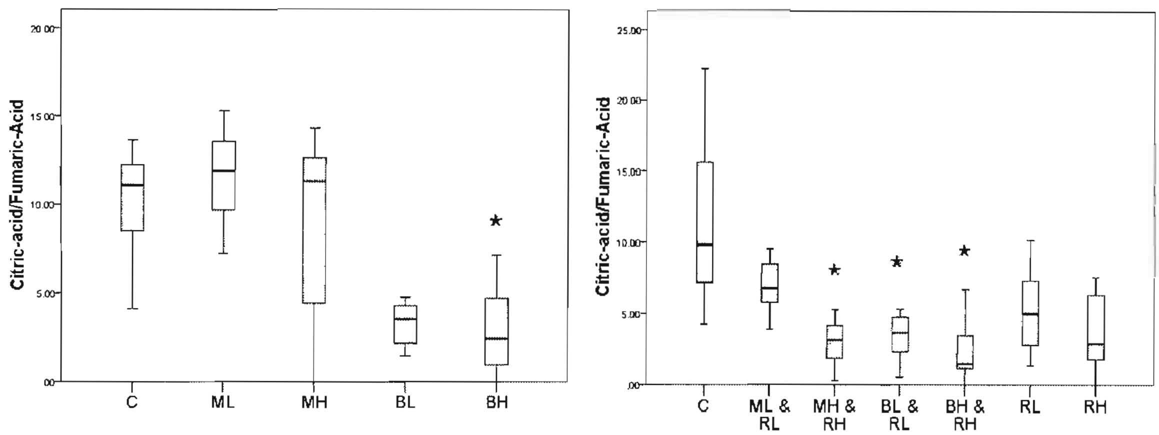

Figure 5.7: The ratio of citric acid to fumaric acid in the medium. The plot present the median ± 95% confidence interval as a block and the minimum and maximum values as bars. Asterisks (*) indicate statisticly significant differences between the control group and the inhibitor groups (Left panel=pyruvate dehydrogenase inhibitors, Right panel=respiratory chain inhibitor, C=control, M=moniliformin, B=3-bromopyruvate, R=rotenone, L=low concentration, H=high concentration)

When compared to the control, the fumaric acid to malic acid ratio significantly increased when pyruvate dehydrogenase was inhibited by high concentrations of moniliformin and low concentrations of 3-bromopyruvate. Inhibition of the respiratory chain by rotenone or both respiratory chain and pyruvate dehydrogenase inhibitors had no effect on the ratio (table 5.1 and figure 5.8).

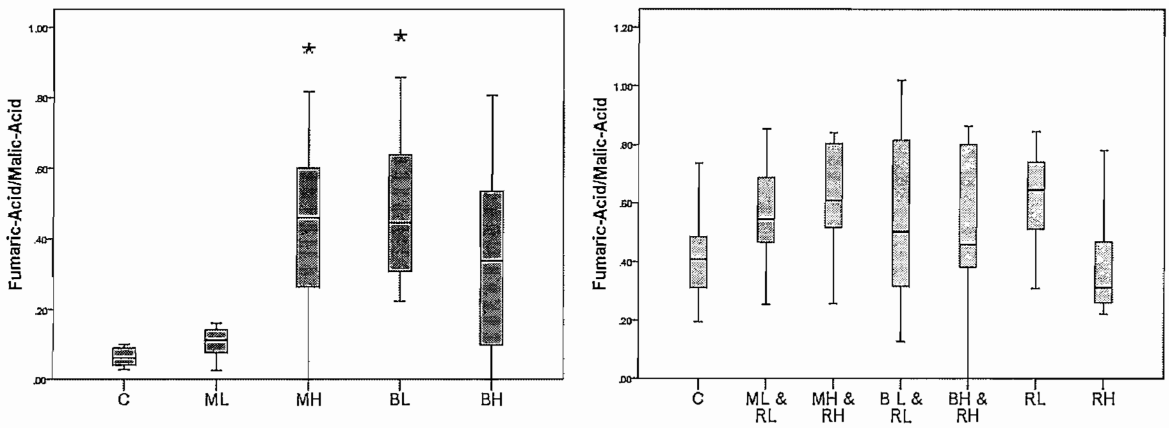

Figure 5.8: The ratio of Fumaric acid to Malic acid in the medium. The plot present the median ± 95% confidence interval as a block and the minimum and maximum values as bars. Asterisks (*) indicate statistically significant differences between the control group and the inhibitor groups (Left panel=pyruvate dehydrogenase inhibitors, Right panel=respiratory chain inhibitor, C=control, M=moniliformin, B=3-bromopyruvate, R=rotenone, L=low concentration, H=high concentration)

Table 5.1 The intermediates of the TCA cycle that differed significantly when compared to the control groups (B = 3-bromopyruvate, M = moniliformin and R = rotenone)

Table 5.1.1 HeLa cells treated with pyruvate dehydrogenase inhibitors

		p-value
Citric Acid	$B_{3.75\ mM}$ Decreased	0.00722
	$B_{5.2\ mM}$ Decreased	0.00505
Fumaric Acid	$B_{3.75\ mM}$ Decreased	0.01141
Citric acid/Succinic acid	$B_{3.75\ mM}$ Decreased	0.00570
	$B_{5.2\ mM}$ Decreased	0.01099
Cirtric acid/Fumaric acid	$B_{5.2\ mM}$ Decreased	0.00668
Fumaric acid/Malic acid	$M_{220.4\ \mu M}$ Increased	0.00910
	$B_{3.75\ mM}$ Increased	0.00146

Table 5.1.2 HeLa cells treated with complex I inhibitors

		p-value
Citric Acid	$B_{3.75\ mM}$ + $R_{10\ nM}$ Decreased	0.00632
	$B_{5.2\ mM}$ + $R_{1000\ nM}$ Decreased	0.00052
Aconic Acid	$M_{110.2\ \mu M}$ +$R_{10\ nM}$ Decreased	0.00748
	$M_{220.4\ \mu M}$+$R_{1000\ nM}$ Decreased	0.00157
	$B_{3.75\ mM}$ + $R_{10\ nM}$ Decreased	0.00707
	$B_{5.2\ mM}$ + $R_{1000\ nM}$ Decreased	0.00076
Malic Acid	$B_{5.2\ mM}$ + $R_{1000\ nM}$ Decreased	0.00138
Citric acid/Succinic acid	$B_{3.75\ mM}$ + $R_{10\ nM}$ Decreased	0.00168
	$B_{5.2\ mM}$ + $R_{1000\ nM}$ Decreased	0.00030
Citric acid/Fumaric acid	$M_{220.4\ \mu M}$ + $R_{1000\ nM}$ Decreased	0.00138
	$B_{3.75\ mM}$ + $R_{10\ nM}$ Decreased	0.00397
	$B_{5.2\ mM}$ + $R_{1000\ nM}$ Decreased	0.00039

There are indications that HeLa cells may not have been the ideal cells to test the hypotheses set forward in this study, although this is still a matter of controversy. TCA cycle activity in tumors are reduced when compared to normal cells, probably because of less enzyme or reduced enzyme activity (Dajani, *et al,* 1961). This is due to an increase in the concentration of reactive oxygen species (ROS), which inhibits aconitase that is responsible to convert citate to isocitrate (Gardner, *et al*., 1995). Because of the rapid metabolism in HeLa cells, it was previously postulated that glucose is the major source of energy. In theory, the energy should be derived from glycolysis, where glucose is converted to pyruvate which undergoes aerobic oxidation in the TCA cycle. However there are several observations that contradict the postulate that glucose is the major energy source. First, cultured HeLa cells use very little radioactive glucose carbon in the TCA cycle. Second, mammalian cells can grow normally in much lower concentrations of glucose, which also results in a reduced lactic acid production. This signifies a reduced glycolytic rate (Reitzer, *et al*., 1978). However recent evidence indicated that OXPHOS and glycolysis participate equally in ATP production in HeLa cells (Piechota *et* al, 2006).

Extracts from HeLa cells contain all the enzymes that are involved in the TCA cycle (Barban & Schulze, 1956). This therefore rules out that the TCA cycle enzymes are not present and can therefore not be the reason for the TCA cycle intermediates not to prove the hypothesis that a specific TCA ratio limit can be used as a method to distinguish between deficiencies in the pyruvate dehydrogenase complex, enzymes and mitochondrial respiratory chain enzymes. In addition, Reinecke, *et al.* (2006) incubated HeLa cells with rotenone and showed a dose-dependent decrease in complex I activity and concluded that HeLa cells can be used as an in vitro model to study complex I (NADH:ubiquinone oxidoreductase) deficiency.

In addition to glycolysis, glutaminolysis is a source of energy in tumor cells (Moreadith, *et al.*, 1984, Reitzer, *et al.*, 1978) where glutamine is converted to glutamate and subsequently to α-ketoglutaric acid (figure 5.9). The conversion proceeds through three different reactions, catalyzed by glutamate dehydrogenase (GDH), glutamate pyruvate transaminase (GPT or ALT) and glutamate oxaloacetate transaminase (GOT or AST). Due to low GDH and GPT activities in tumor cells, the conversion of glutamate to α-ketoglutarate mainly takes place via GOT (Moreadith, *et al.*, 1984). It is important to note that apart from glucose, glutamine is the most abundant organic compound in culture media, i.e. 4mM L-glutamine in DMEM.

The fact that citric acid, which precedes α-ketoglutaric acid, where glutamine enters the TCA cycle, significantly decreased is of particular importance. It clearly indicates that the HeLa cells used the TCA cycle to generate energy since PDHc inhibition decreased the citrate levels. The fact that citric acid and fumaric acid decreased significantly following inhibition of the pyruvate dehydrogenase enzyme complex, and the finding that several calculated ratios also changed significantly as result of the inhibition also indicates that the approach gave indications of what happened to the TCA cycle if acetyl-CoA formation is inhibited.

It is also possible to use galactose to drive the OXPHOS system. However, in the context of this study, it was not advisable since PDHc is excluded by this approach. Efforts to grow HeLa cells on galactose medium without supplementing glutamine were unsuccessful. Cells were usually dead after 2 weeks or survived for as long as 10 weeks, but failed to proliferate (Robinson, et al. 1966). Galactose medium with supplemented glutamine showed that glutamine provided 98% of the ATP used for growth (Reitzer, et al., 1978). Therefore, if galactose medium were used, glutamine would have entered the TCA cycle through α-ketoglutaric acid. The pyruvate dehydrogenase step, which is of significant importance in this study, would have been excluded (figure 5.9).

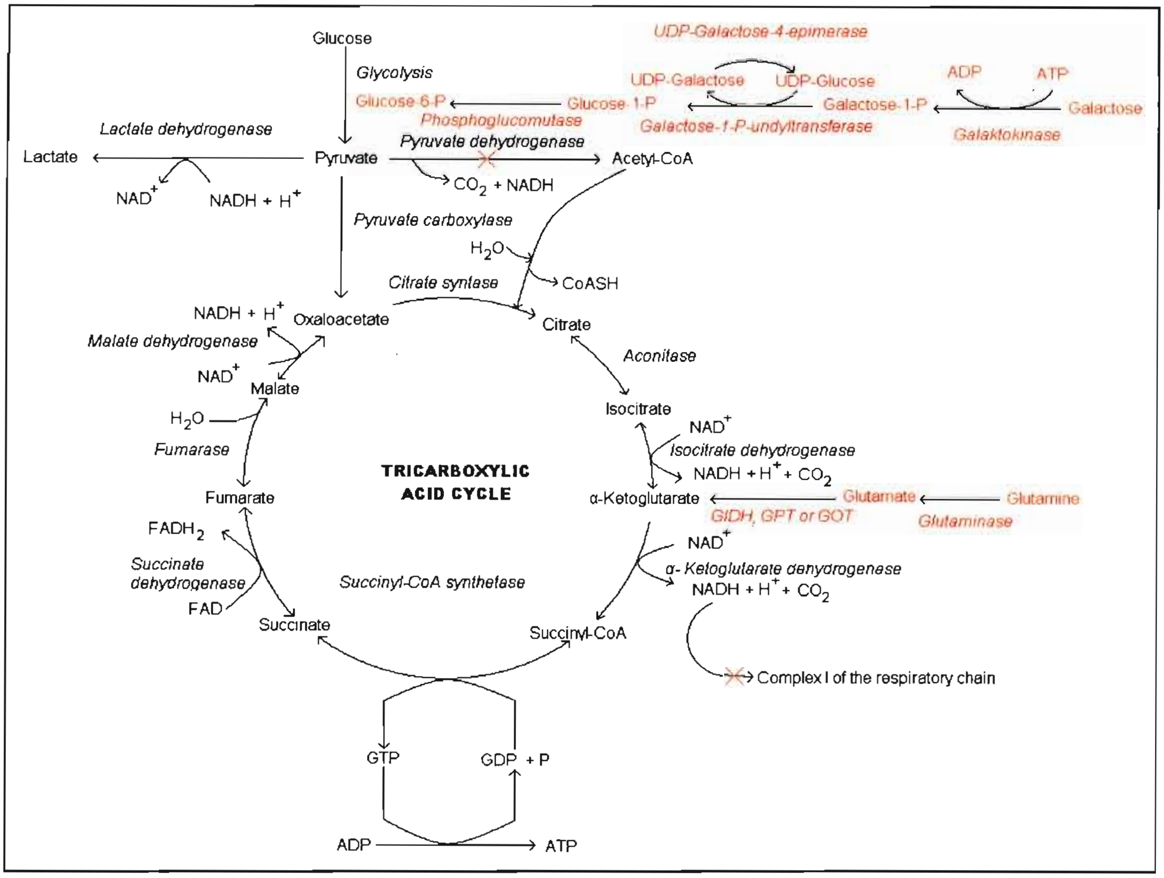

Figure 5.9: The entry of galactose into the glycolysis pathway and the amino acid, glutamine, as an important energy source into the TCA cycle.

5.2. Ratio limit of 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid

4-Hydroxyphenylpyruvic acid is converted to 4-hydroxyphenylacetic acid and 4-hydroxyphenyllactic acid. Figure 1.2 illustrates how pyruvate dehydrogenase enzyme complex catalyzes the reaction where 4-hydroxyphenylacetic acid is formed (Schomburg, 2007). The hypothesis was that less 4-hydroxyphenylacetic acid will form if the pyruvate dehydrogenase enzyme complex is defective as opposed to defective mitochondrial respiratory chain enzymes. Unfortunately, very little of the intermediates were present in the supernatant, suggesting that this hypothesis is not valid. 4-Hydroxyphenylpyruvic acid was detected in only one cell sample. It could therefore not be used to calculate ratio limits. The other ratios (figure 5.10) could also not distinguish between PDHc and or RC inhibition.

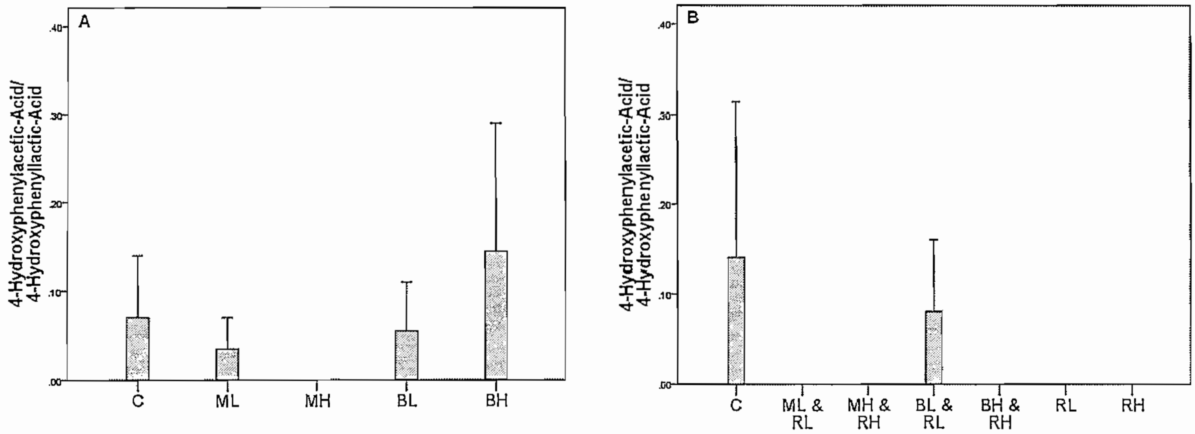

Figure 5.10: The ratio limits of 4-hydroxyphenylacetic-acid to 4-hydroxyphenyllactic-acid in medium treated with pyruvate dehydrogenase inhibitors (A) and complex I inhibitors (B) respectively. C=control, M=moniliformin, B=3-bromopyruvate, R=rotenone, L=low concentration, H=high concentration

5.3. Ratio limit of phenylpyruvic acid, phenyllactic acid and phenylacetic acid

Of the 168 medium and cell samples, phenylpyruvic acid, phenyllactic acid and phenylacetic acid were detected in only eight. Ratios could therefore not be calculated. The reason might be that the phenylacetic acid (normally 91 per cent) is detoxified to phenylacetylglutamine (Chalmers & Lawson, 1982:427). Another possible reason may be that the substrate for the production of phenylpyruvic-acid, phenylalanine was low in the cells and medium. It is, however, clear that these ratio limits are not indicative of PDHc or RC defects. The hypothesis is therefore not valid.

5.4. Principle component analysis:

Principle component analysis (PCA) was done using Biogoggles software. PCA is a powerful tool to identify biomarkers (Katajamaa, *et al.*, 2007). The technologies that were used produce complex data sets. Principle component analysis makes it possible to extract relevant information from these complex data sets with minimal additional effort and so reduce that components in the data set (Katajamaa, *et al.*, 2007; Ringnér, 2008). PCA is a simple method that reduces the data complexity by calculating new variables, called principal components, which represent the original variables and so record the largest variation in the dataset (Ringnér, 2008). It identifies variables that are important in the data set by expressing the differences between samples, and visualizes and interprets them by using a series of simple plots (Berman, 2009).

In this study 3D PCA plots were used. PCA plots components with similar patterns close to each other. If the PCA approach worked, two clusters of data sets would be expected, one for the group that was inhibited and one for the control. The PCA approach was not successful because the group plots did not separate (figures 5.11 to 5.13). The results do, however, not preclude that PCA can be used. In order to get a more definitive answer, more studies will have to be done.

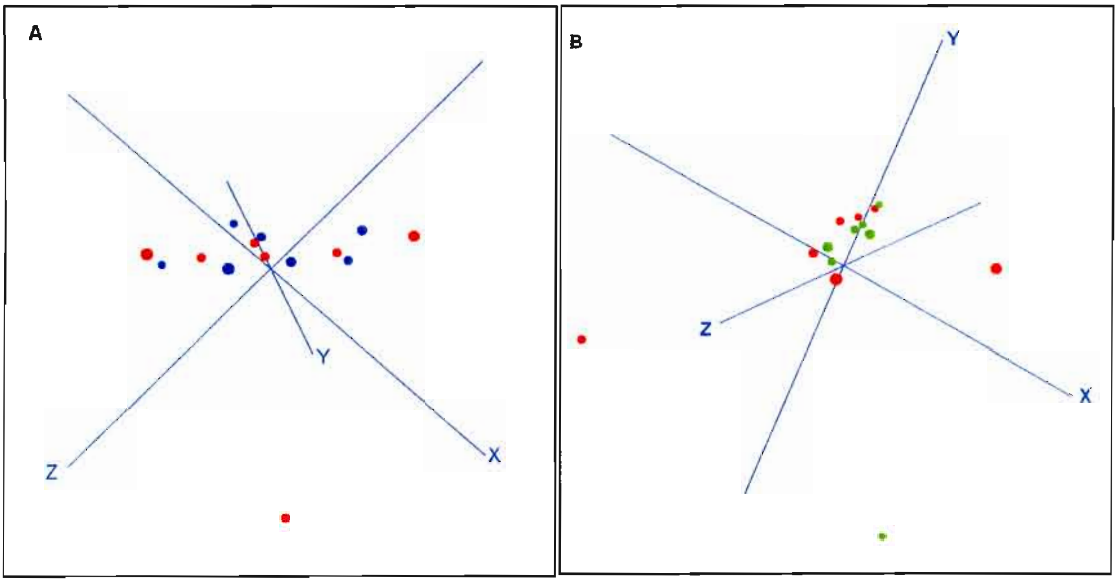

Figure 5.11: 3D PCA plots illustrating the separation of the (A) control (red) and moniliformin (110.2 µM) (blue) and (B) control (red) and moniliformin (220.4 µM) (green) groups.

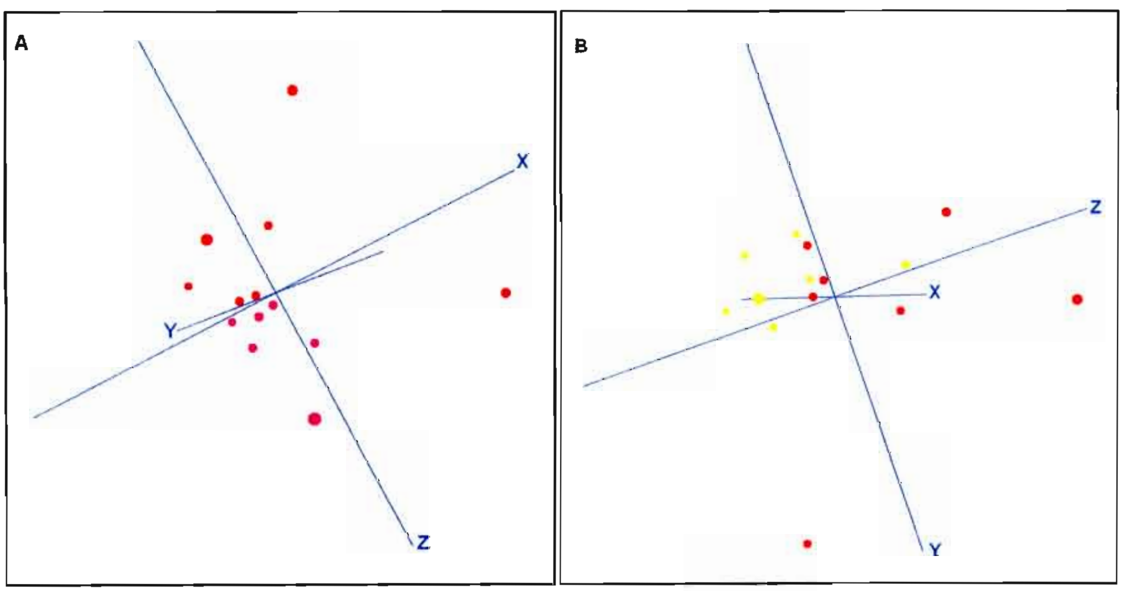

Figure 5.12: 3D PCA plots illustrating the separation of the (A) control (red) and 3-bromopyruvate (3.75 mM) (pink) and (B) control (red) and 3-bromopyruvate (5.2 mM) (yellow) groups.

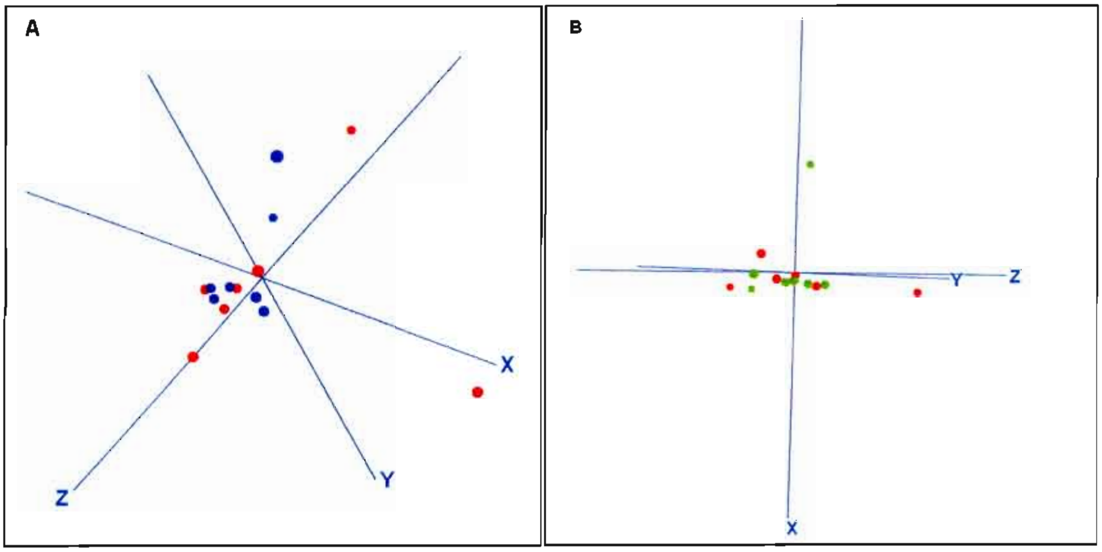

Figure 5.13: 3D PCA plot illustrating the separation of the (A) control (red) and rotenone (10 nM) (blue) and (B) control (red) and rotenone (1000 nM) (green) group.

CHAPTER 6

Conclusion

HeLa cells were used to assess the effect of inhibition of the pyruvate dehydrogenase complex (PDHc) enzyme and complex I of the mitochondrial respiratory chain (RC) on intermediates of the tricarboxylic acid (TCA) cycle. The aim was to identify a diagnostic method that is easy, non-invasive and definitive to distinguish between deficiencies in PDHc and RC. The HeLa cell line was used to provide a clean approach where the inhibitory effect was assessed in only one cell type. One must bear in mind that the metabolic profile in experimental animals is the sum total of metabolism of many cell types where each is under control of hormones, cytokines and nutritional intake.

Four hypotheses were tested. First, the effect of inhibition on intermediates of the TCA cycle was assessed. The concentration of the intermediates and the ratios between intermediates were analysed to test for difference between controls, PDHc inhibition and RC complex I inhibition. Second, the ratios between 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid were tested for significant differences. Third, ratios between phenylpyruvic acid, phenyllactic acid and phenylacetic acid were tested. Fourth, principal component analysis was used to investigate if different patterns of organic acid distribution emerged for the control cells, the PDHc inhibited cells and the RC cells.

No significant differences were measured between ratios for 4-hydroxyphenylpyruvic acid, 4-hydroxyphenyllactic acid and 4-hydroxyphenylacetic acid (figure 5.10). The ratios for phenylpyruvic acid, phenyllactic acid and phenylacetic acid were also not significant different. None of the two approaches was therefore able to distinguish between inhibition of PDHc and RC. The main reason was because the concentration of the intermediates were probable too low to measure with the methods that were used. Since no difference and very little of the compounds were present in the single cell line, the possibility of distinguishing between PDHc and RC deficiencies in experimental animals and patients is remote.

Principal component analysis (PCA) could also not distinguish between differences in the organic acid profiles of control, PDHc inhibited and RC inhibited cells (figures 5.11 to 5.13). Since only seven studies were done, the results does not preclude that PCA will not work. This needs to be investigated in patients with proven PDHc or RC deficiencies.

The intermediates of the TCA cycle were informative. PDHc inhibition, but not inhibition of complex I of the RC affected the intermediates of the TCA cycle (Table 5.1). Both citric acid and fumaric acid levels were significantly decreased when PDHc was inhibited with 3-bromopyruvate. This was to be expected since the formation of acetyl-CoA was inhibited resulting in less acetyl-CoA to enter the TCA cycle (figure 5.10). Of particular importance is the decrease in citric acid. Citric acid precedes α-ketoglutaric acid, the site in the TCA cycle where glutamine can enter the TCA cycle for purposes of energy generation. This indicates that the TCA cycle was operative and that PDHc inhibition decreased acetyl-CoA available for entry into the TCA cycle.

Calculating the ratios of citric acid to succinic acid, citric acid to fumaric acid and fumaric acid to malic acid differed significantly from the control when PDHc was inhibited (figures 5.6 to 5.8). Inhibition of RC had no significant effect on these ratios. Calculating these ratios therefore have the potential to diagnose PDHc deficiencies and to distinguish it from RC deficiencies and should be tested in experimental animals and patients with PDHc or RC deficiencies.

Recommendations:

Since the test groups were relatively small (n=7) it is recommended that this study be repeated so that more studies are available for statistical analysis. This study on PDHc and complex I should be done in knockdown mice to assure that the enzyme of interest is inactive. This is especially in view of the fact that the inhibitors that were used were non-specific and could have affected the outcomes of the study to a certain extent. I also recommend that the citric acid:succinic acid, citric acid:fumaric acid and fumaric acid:malic acid ratios be calculated in patients with proven defects in pyruvate dehydrogenase complex enzymes and with mitochondrial respiratory chain enzymes to verify the feasibility of using these ratios as diagnostic tools.

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Appendix A

Table A: Lactic acidemia is present in the urine and blood of patients with one of the forty four diseases listed below. In this table I included the deficient enzyme in each case, as well as other biochemical diagnostic metabolites that can be measured (other than lactic acidemia) (Metagene online: Knowledge base for inborn errors of metabolism (2007)).

	Deficiency	Enzyme	Biochemical diagnostic metabolites in the blood and/or urine)
1	Long-chain-3-hydroxyacyl-CoA Dehydrogenase Deficiency (LCHAD)	Long-chain-3-hydroxyacyl-CoA dehydrogenase	Glucose ↑ Carnitine ↓ Uric acid ↑ Lactate ↑ 3-Hydroxyadipic acid ↑ 3-Hydroxysuberic acid ↑ 3-Hydroxybutyric acid ↓ Myoglobin ↑ Long chain acyl carnitines ↑ Ammonia n/ ↑ 3-Hydroxysebacic acid ↑ Dicarboxylic acids ↑ 3-Hydroxypalmitoylcarnitine (C16-OH) ↑ 3-Hydroxystearoylcarnitine (C18-OH) ↑ Oleoylcarnitine (C18:1) ↑ 3-Hydroxyoleoylcarnitine (C18:1-OH) ↑
2	Fumaric Aciduria	Fumarase	Fumaric acid ↑ Citrate↑ 2-Oxoglutaric acid ↑ Ammonia ↑
3	3-hydroxy-3-methylglutaryl-CoA Lyase Deficiency	3-hydroxy-3-methylglutaryl CoA lyase,	Methylglutarylcarnitine↑ 3-Hydroxy-3-methylglutaric

		Hydroxymethylglutaryl-CoA lyase	acid ↑ 3-Methylglutaconic acid ↑ 3-Methylglutaric acid ↑ 3-Hydroxyisovaleric acid ↑ 3-Methylcrotonylglycine ↑ Ammonia ↑ Glucose ↑ Adipic acid ↑ Carnitine↓ 3-Methylglutaconic acid ↑ Acylcarnitin ↑
4	Carnitine-acylcarnitine Translocase Deficiency	Carnitine-acylcarnitine translocase, Mitochondrial-membrane carrier protein	Carnitine, total ↓ Dicarboxylic acids ↑ Adipic acid ↑ Acylcarnitin ↑ Ammonia ↑ Glucose ↓ Sebacic acid ↑ Suberic acid ↑
5	Respiratory Chain Deficiencies	Respiratory Chain Enzymes	Pyruvate, blood ↑ Glucose ↓ Myoglobin ↑ Ketone bodies ↑
6	Short Chain Acyl-CoA Dehydrogenase Deficiency (SCAD)	Butyryl-CoA dehydrogenase (Short-chain-acyl-CoA dehydrogenase)	Acylcarnitine/carnitine ratio ↑ Ethylmalonic acid ↑ Glucose ↑ Methylsuccinic acid↑ Butyrylglycine ↑ Hexanoylglycine↑ Acyl-CoA DH: Butyryl CoA + anti-MCAD Ab [+] Adipic acid ↑ Lactate, fed state ↑ Ammonia ↑ Butyrylcarnitine (C4) ↑

7	3-methylglutaconic Aciduria (type ii), x-linked	Mutations in the taffazin gene (TAZ), alteration in cardiolipin remodeling, normal hydratase	3-Methylglutaconic acid ↑ 3-Methylglutaric acid ↑ Succinate ↑ 2-Ethylhydracrilic acid ↑ Pyruvate↑ Cholesterol ↓ Carnitine↓
8	Myoclonic Epilepsy and Ragged Red Fiber Disease (MERRF)		Only Lactate ↑
9	Benign Infantile Mitochondrial Myopathy and Cardiomyopathy (BIMC)	OXPHOS defect	Only Lactate ↑
10	Lethal Infantile Mitochondrial Disease (LIMD)	Tissue specific depletions of mtDNA (some cases)	Only Lactate ↑
11	Pyruvate Dehydrogenase Deficiency (E3)	Dihydrolipoamide dehydrogenase	Pyruvate ↑ Leucine ↑ Isoleucine ↑ Valine ↑ 2-Hydroxybutyrate ↑ 2-Hydroxyisovaleric acid ↑ 2-Oxoglutaric acid ↑ 2-Oxo-n-caproic acid ↑ Ammonia ↑ Glucose n/↓
12	Benign Infantile Mitochondrial Myopathy (BIMM)	Complex IV, cytochrome c oxidase (skeletal muscle)	Only Lactate ↑
13	Liver disease, liver failure, unspecific		N-Acetyltryptophane ↑ N-Acetyltyrosine ↑ Ammonia ↑ Kynurenine + 3-Hydroxykynurenine ↓/ ↑ Coagulation factors abnormal
14	Biotinidase Deficiency	Biotinidase	3-Methylcrotonylglycine ↑ 3-Hydroxypropionic acid ↑

			Methylcitric acid ↑ 3-Hydroxybutyrate ↑ 3-Hydroxyisovaleric acid ↑ 3-Hydroxyisovaleric acid ↑ 3-Hydroxypropionic acid ↑ Citrate ↑ 2-Hydroxybutyrate ↑ Ammonia ↑ Ketone bodies ↑ Acylcarnitin ↑ 3-Hydroxyisovalerylcarnitine (C5-OH) ↑
15	Phosphoenolpyruvate Carboxykinase Deficiency 2 (PEPCK2)	Phosphoenolpyruvate carboxykinase, mitochondrial	Glucose ↓ Pyruvate ↑ Cholesterol ↓ Triglycerides ↑
16	Congenital Lactic Acidosis	Unknown	Pyruvate ↑
17	Pyruvate Carboxylase Deficiency	Pyruvate carboxylase	2-Oxoglutaric acid ↑ Succinate ↑ Fumaric acid ↑ Proline n/↑ Ketone bodies ↑ Alanine ↑ Glucose n/↓
18	Pyruvate Dehydrogenase Deficiency (E1)	Pyruvate dehydrogenase complex	Pyruvate ↑
19	Leigh`s syndrome, Subacute Necrotizing Encephalopathy, SNE	Nuclear and mitochondrial DNA defects	Alanine ↑
20	Fructose-1,6-diphosphatase Deficiency	Fructose-1,6-diphosphatase	Glucose, fasting state 24 h ↑ Uric acid ↑ Alanine ↑ Ketone bodies ↑ Glycerol ↑
21	Fructose Intolerance, hereditary	Fructose 1,6-biphosphate	Glucose, after exposure to

		aldolase B	fructose ↓ Phosphorus, after exposure to fructose ↓ Magnesium, after exposure to fructose ↑ Lactate, after exposure to fructose ↑ Fructose, after exposure to fructose ↑ Reducing substances (Clinitest) [+] Coagulation factors abnormal
22	Glycogenosis, type IA. Von Gierke Disease	Glucose-6-phosphatase, liver, kidney	Uric acid ↑ Cholesterol ↑ Tryglycerides ↑ Glucose, fasting state 24 h ↑ Ketone bodies ↑ Protein, total ↑ Bleeding time ↑
23	Glycogenosis, Type IB	Microsomal Glucose 6-Phosphate (G6P) Translocase	Equivalent to nr 23
24	Glycogenosis, Type IC	Microsomal Phosphate Transport Proteins, T2ß, Pyrophosphate/Phosphate Transporter	Equivalent to nr 23
25	Glycogenosis, Type VI: Hers disease	Phosphorylase	Equivalent to nr 23
26	Chronic Progressive External Ophthalmoplegia and Kearns-Sayre Syndrome	Defect of Oxidative Phosphorylation (OXPHOS)	Glucose ↑
27	Ethylmalonic Encephalopathy	Cytochrome C Oxidase Deficiency in Sceletal Muscle	Butyrylglycine Isovalerylglycine ↑ 2-Methylbutyrylglycine ↑ Isobutyrylglycine ↑

			Ethylmalonic acid ↓ Lactate, fed state ↑ Methylsuccinic acid ↑ Carnitine, free ↓
28	Mitochondrial-Encephalopathy-Lactic Acidosis-Stroke (MELAS)	Mitochondrial Enzyme Defect	Only Lactate ↑
29	3-Hydroxyisobutyric Aciduria	3-Hydroxyisobutyrate Dehydrogenase	3-Hydroxyisobutyric acid ↑ 3-Hydroxypropionic acid ↑ 2-Ethylhydracrilic acid ↑ 3-Hydroxyisovaleric acid ↑ Carnitine, free ↓ Ketone bodies ↑ 3-Hydroxyisovalerylcarnitine (C5-OH) ↑
30	Pearson Syndrome	OXPHOS Defect	3-Methylglutaconic acid ↑ 3-Hydroxy-3-methylglutaric acid ↑ Lactate/Pyruvate ratio ↑ Hemoglobine ↓ Citrulline n/↓
31	Valproate Therapy: Anticonvulasant Hypersensitivity Syndrome Valproate Associated Hepatotoxicity		Glycine ↑ 3-Hydroxypropionic acid ↑ 2-n-propyl-4-pentenoic acid Ammonia Carnitine, total ↓
32	2-Ketoglutarate Dehydrogenase Complex Deficiency	2-Ketoglutarate Dehydrogenase Complex, E1, E2	Citrate n/↑ 2-Oxoglutaric acid ↑ Fumaric acid ↑ Succinate n/↑ Malic acid n/↑ Glucose ↓
33	Asphyxia		Malondialdehyde ↑ Glucose ↓ Myoglobin ↑ Hypoxanthine ↑

			Carnitine, total ↓ 3-Hydroxybutyric acid ↑ 4-Hydroxyphenyllactic acid ↑ 2-Hydroxybutyrate ↑ 2-Oxoisocaproic acid ↑ 2-Hydroxyisovaleric acid ↑ 2-Oxo-3-methylvaleric acid ↑ Uric acid ↑ Uric acid/creatinine ratio ↑ Lactate/Creatinine ratio ↑
34	Pyruvate Dehydrogenase Deficiency (E2)	Dihydrolipoyl Transacetylase	Ammonia ↑
35	Mitochondrial DNA Depletion Syndrome	Decreased Activity of Respiratory Chain Enzymes in Affected Tissues	Dicarboxylic acids ↑
36	Sepsis, Neonatal		Trombocytes CRP ↑
37	2-Methyl-3-Hydroxybutyryl-CoA Dehydrogenase Deficiency	3-Hydroxy-2-Methylbutyryl-CoA Dehydrogenase	2-Methyl-3-hydroxybutyric acid ↑ 2-Ethylhydracrylic acid ↑ Tiglylglycine ↑
38	Feeding: Thiamine Deficieny		Only Lactate ↑
39	3-Methylglutaconic Aciduria, Novel Subtype	Mitochondroial Disorder is Hypothesized	3-Methylglutaconic acid ↑ 3-Methylglutaric acid ↑
40	Mitochondrial Encephalomyopaththy with Elevanted Methylmalonic Acid, SULCA2		Methylmalonic acid ↑ Methylmalonic acid ↑ Succinylcarnitine ↑ 3-Hydroxyisovaleric acid ↑
41	LCAD	3-Hydroxyacyl-CoA DH, Enoyl-CoA hydratase, 3-Ketoacyl-CoA thiolase	Uric acid ↑ Acylcarnitine ↑ Long chain acyl carnitines ↑ Long chain dicarboxylic acids ↑ Long chain acyl-CoA ↑

			Myoglobin ↑ Sebacic acid ↑ Suberic acid ↑
42	3-Methylglutaconic Aciduria, type I	3-methylglutaconyl-CoA hydratase	3-Hydroxyisovaleric acid ↑ 3-Methylglutaconic acid ↑ 3-Methylglutaric acid ↑
43	Pyridoxamine 5-prime-phosphate oxidase deficiency	pyridoxamine 5-prime-phosphate oxidase	Glycine ↑ Treonine ↑
44	Acyl CoA dehydrogenase 9 deficiency	defects in ACAD9 at the protein and mRNA level	Ammonia ↑ Dicarboxylic acids ↑

* n/↓= normal or decreased; ↓ = decreased; ↑ = increased

Appendix B

The stock solutions were prepared as follows:

- Moniliformin:

1mg moniliformin was dissolved in 0.363 ml water for a 22 mM stock solution.

- 3-Bromopyruvate:

313mg 3-bromopyruvate was dissolved in 5 ml water for a 375 mM stock solution. Thereafter it was filtered through Acrodisc syringe filters. 434 mg 3-bromopyruvate was dissolved in 5 ml water for a 520 mM stock solution. Thereafter it was filtered through Acrodisc syringe filters.

- Thiamine pyrophosphate (TPP):

461 mg TPP was dissolved in 5 ml water for a 200 mM stock solution. Thereafter it was filtered through Acrodisc syringe filters.

- Rotenone:

0.133 ml of the 750 μM stock solution was diluted with 0.867 ml water for a 100 μM stock solution. 0.010 ml of the 100 μM stock solution was diluted with 0.990 ml water for a 1 μM stock solution. Thereafter it was filtered through Acrodisc syringe filters.

- Hydroxylamine:

0.05 g Hydroxylamine hydrochloride in 2 ml water.

- 5 N NaOH:

20 g NAOH pellets was dissolved in 100 ml water for a 5 N NaOH stock solution.

- 5 N HCl:

214.59 ml of 36% HCl in 285.41 ml water for a 5 N HCl stock solution.

Appendix C

Organic acids in the medium

Organic acid	Control (PDHc)							Control (Complex I)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	3.23	0.00	0.24	0.00	0.26	0.42	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Octanoic-Acid	0.00	0.00	0.00	0.00	0.31	0.00	0.00	0.00	0.09	0.00	0.00	0.15	0.00	0.05
NoAcid	0.20	0.32	0.94	0.00	0.55	0.00	0.25	0.41	0.10	0.41	0.00	0.39	0.03	0.27
DecAcid	0.17	0.63	0.69	0.00	0.10	0.00	0.00	0.12	0.15	0.00	0.22	0.18	0.00	0.08
EicAcid	0.14	0.28	0.45	0.00	0.00	0.23	0.17	0.22	0.21	0.13	0.13	0.00	0.11	0.28
Dodecanoic-Acid	0.00	1.33	15.41	0.23	1.17	0.00	1.43	0.38	0.55	1.43	0.36	0.75	2.49	1.66
Tridecanoic-Acid	1.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanoic-Acid	0.00	5.04	11.89	1.08	1.01	4.10	1.18	1.95	3.23	3.82	1.19	0.74	2.80	1.37
Palmitic-Acid	20.93	66.22	132.01	21.65	13.06	76.57	30.56	31.38	49.81	70.53	46.15	11.19	45.43	29.22
Heptadecanoic-Acid	0.41	1.20	1.67	0.40	0.12	1.46	0.60	0.81	1.37	1.89	0.61	0.11	1.05	0.68
Octadecanoic-Acid	16.19	54.22	48.01	20.36	7.66	71.18	34.35	20.68	39.56	45.95	40.35	6.72	41.19	40.55
6-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.49	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Isovaleric-Acid	0.00	0.29	0.72	0.00	0.00	0.48	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Docosanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05
3-Methylpimelic-Acid	0.00	0.00	0.90	0.00	0.00	0.00	0.09	0.03	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	0.00	0.00	39.82	0.00	0.00	0.00	0.00	0.00	0.00	0.32	0.24	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	7.80	23.66	0.00	0.76	0.08	0.00	11.78	0.00	0.00	0.00	0.10	0.00	0.00	0.00
3-Methyladipic-Acid	0.00	0.00	2.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.05	0.28	0.23	0.00	0.00	0.18	0.00	7.99	34.37	51.09	0.00	1.21	0.00	0.00
2-Hydroxysebacic-Acid	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.13	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	54.97	0.00	0.00	39.62	0.00	10.82	18.40	26.97	8.01	0.23	0.00	12.48
2-Hydroxyheptanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00
3-Methyladipic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.07	0.00	0.00	0.00
2-Hydroxysebacic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.32	0.00	5.75	0.00	0.00	0.15	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.82	0.00
Palmitelaidic-Acid	0.09	0.98	1.06	0.00	0.08	0.94	0.26	0.12	0.34	0.68	0.04	0.16	0.74	0.39
Oleic-Acid	7.40	27.91	4.48	5.32	3.06	6.48	1.84	1.86	0.00	5.16	1.96	3.17	3.67	0.00
2-Undecenoic-Acid	0.05	0.28	0.23	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
11-Octadecenoic-Acid	7.80	23.66	54.97	0.76	0.08	39.62	11.78	10.82	18.40	26.97	8.01	0.23	20.82	12.48
Arachidonic-Acid	0.50	1.14	0.28	0.00	0.00	3.85	0.52	0.59	1.31	1.36	0.41	0.00	1.72	0.65
9,12-Octadecadienoic-Acid	1.73	5.70	5.10	0.50	0.53	8.26	1.62	2.63	6.15	7.19	1.15	0.45	4.54	3.42
Suberic-Acid	0.04	0.00	1.27	0.00	0.00	0.00	0.00	0.14	0.27	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	1.06	0.00	0.00	0.00	0.59	0.00	0.00	2.68	0.00	0.00	0.00
Azelaic-Acid	0.00	0.00	8.64	0.00	0.00	1.94	2.80	1.74	0.00	3.00	0.63	0.00	0.00	0.87

Tetradecanedioic-Acid	0.00	0.13	130.90	0.00	0.04	0.00	0.00	1.67	0.11	1.30	0.00	0.06	0.00	0.00
Malonic-Acid	3.09	7.71	0.40	2.51	0.04	0.00	0.00	2.71	4.09	2.13	3.20	0.23	0.00	38.04
Citric-acid	33.54	83.21	58.75	19.95	8.37	71.83	12.12	44.88	57.68	110.42	9.85	10.03	51.21	13.60
Aconitic-Acid	0.49	1.77	0.73	0.22	0.36	2.60	0.27	1.86	1.08	2.85	1.45	0.20	2.06	0.77
Succinic-Acid	51.45	66.19	72.91	34.12	38.66	160.18	49.18	53.44	61.15	89.07	38.27	34.00	92.07	42.65
Fumaric-Acid	3.03	7.66	4.31	1.61	2.04	5.95	1.98	2.87	5.87	4.96	2.30	1.57	3.28	1.73
Malic-Acid	7.11	14.14	15.53	5.81	7.30	15.92	3.99	3.90	10.77	25.59	5.64	3.66	12.17	4.91
Lactic-Acid	361.16	311.71	179.42	1237.19	377.52	612.15	525.46	344.78	582.57	231.59	92.89	117.83	523.33	817.26
Lactyllactate	4.47	0.19	0.00	149.19	0.00	0.93	0.31	2.09	18.99	0.08	182.14	0.05	3.61	7.40
Pyruvic-Acid	0.40	0.42	0.45	4.72	0.07	0.92	0.44	0.29	0.78	0.73	0.30	0.10	0.93	0.13
3-Ketobutyric-Acid	4.71	0.00	0.50	0.00	0.00	4.01	4.36	0.00	7.00	4.01	0.04	1.07	1.78	5.13
3-Ketobutyric-AcidtriTMS	0.00	0.00	0.00	0.00	1.38	0.00	0.00	7.62	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.34	0.00	0.00	0.87	0.00	0.53
Oxalic-Acid	3.60	6.64	24.52	3.84	3.18	43.39	15.30	2.10	7.97	18.80	1.46	0.50	4.08	1.58
N-Lactylisoleucine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00
3-Methylglutaconic-Acid	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.41	0.00	0.00	0.00	0.11
3-Hydroxyisobutyric-Acid	3.54	1.84	0.68	3.67	7.22	0.00	4.68	2.32	3.65	1.60	1.38	5.62	3.44	3.52
3-Hydroxyisovaleric-Acid	0.00	0.42	0.00	0.00	0.14	1.18	0.00	0.00	0.59	0.00	4.11	0.36	0.00	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.19	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.27	0.00	0.00	0.30	0.00	0.17
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.07	0.00	0.05	0.00	0.33	0.00	0.11	0.00	0.00	0.00
2-Keto-3-Methylvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.70	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.00	0.00	0.61	3.29	0.29	0.12	0.10	0.00	0.27	0.41	3.25	0.00	0.00
4-Hydroxyphenyllactic-Acid	0.84	1.77	1.75	0.18	0.25	1.55	0.43	0.83	1.52	3.30	0.27	0.39	1.26	0.63
N-Acetyltyrosine	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	1.53	0.00	0.00	0.00	5.10	0.05	0.00	1.96
3-Hydroxypropionic-Acid	1.93	0.48	2.85	1.69	12.84	4.91	5.37	0.76	3.19	2.16	4.92	10.93	3.09	5.51
Methylmalonic-Acid	0.34	0.00	0.00	0.00	0.00	0.00	0.00	37.95	0.00	3.11	0.15	0.00	0.00	0.27
Methylmalonic-Acid-Tritms	0.63	0.61	1.27	0.00	0.00	0.00	0.00	0.05	0.21	1.35	0.18	0.16	0.06	0.00
N-Propionylglycine	0.00	23.18	21.03	0.00	24.89	43.85	17.07	0.00	18.41	32.50	8.74	42.19	37.82	17.58
Glutaric-Acid	0.00	0.51	1.08	0.00	0.30	0.00	0.42	0.33	0.55	0.00	0.76	0.38	0.97	0.26
2,3,4-Trimethyl-3-Hydroxyglutaric-Acid	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketobutyric-Acid	3.21	1.20	1.37	0.00	2.21	0.91	4.23	0.43	3.90	4.58	0.35	2.84	2.70	4.70
2-Hydroxybutyric-Acid	0.00	0.00	0.00	3.63	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Phenylacetylglycine	2.90	6.74	0.92	0.66	0.00	0.00	0.00	2.32	2.27	1.79	0.00	0.00	0.00	0.00
Cyclohexanecarboxylic-Acid	0.00	1.13	0.00	0.00	2.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.13	0.58	0.26	0.00	0.34	1.27	0.00	0.00	0.37	0.59	0.17	0.27	0.00	0.00
4-Hydroxyphenylacetic-Acid	0.00	0.39	0.24	0.00	0.00	0.00	0.00	0.26	0.43	0.00	0.00	0.00	0.00	0.00
Phenylacetic-Acid	0.00	0.36	0.00	0.96	0.00	0.00	1.87	0.51	3.24	3.40	1.01	0.32	1.75	1.66
N-Acetyltyrosine	0.00	0.00	0.23	0.00	0.00	0.00	0.02	0.07	0.00	0.00	0.00	0.00	0.00	0.00

N-Acetylaspartic-Acid	0.00	0.37	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.62	0.00	0.00	0.00
4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	597.19
N-Acetyltyrosine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.73	0.00	0.00	0.00	0.00
N-Acetylaspartic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.30	0.23	0.00	0.00	0.00	0.00	0.04
Pyroglutamic-Acid	114.54	196.33	134.72	120.05	93.74	427.05	161.46	105.77	21.70	153.37	87.51	150.22	302.06	163.86
Uracil	1.96	3.24	0.00	0.00	0.00	4.08	0.96	2.03	2.38	0.00	0.00	0.41	2.91	0.75
Pyrimidinedione	0.86	0.15	0.00	0.00	0.41	0.00	0.00	0.00	0.66	0.00	1.20	0.20	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.27	0.36	0.00	0.00	0.00	0.51	0.00	0.16	0.31	0.00	0.00	0.00	0.00	0.00
2-Hydroxyhippuric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxy-3-Methylglutaric-Acid	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.06	0.30	0.00	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	253.70	18.65	0.00	0.00	0.00	0.00	0.00	143.30	68.50
Benzoic-Acid	0.19	0.47	1.31	0.26	0.89	0.90	0.55	0.30	1.54	1.50	1.55	0.00	0.00	0.76
Hippuric-Acid	3.45	3.98	1.08	1.41	0.00	3.67	0.00	5.95	3.16	3.44	1.93	0.00	2.52	1.32
1-(4-hydroxyphenyl)ethanone	0.00	0.00	8.79	26.83	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.05	0.00	0.13	0.00	0.00	0.00	0.00	0.03	0.08	0.00
2,4,5--Trihydroxybenzeneacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00
2,3-Dihydroxypropanoic-Acid	0.00	1.49	0.00	0.00	0.80	2.96	0.97	0.00	2.15	0.00	0.19	0.72	2.31	0.72
2,4-Dihydroxybenzoic-Acid	0.25	0.18	2.70	0.08	0.00	0.00	3.38	0.07	0.11	0.23	0.00	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	1.59
2,6-Dihydroxybenzoic-Acid	11.68	22.08	180.39	0.17	0.00	0.00	0.00	18.49	54.62	252.79	2.01	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	0.58	0.16	0.00	0.00	0.00	0.00	0.00	0.47	64.82	52.11	0.00	70.52	0.00	0.11
3,6-Dimethylsuberic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.53	0.00	0.41	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.00	0.00	0.54	0.00	4.15	8.42	1.59	0.00	0.00	0.20	0.00	4.10	5.73	0.98
3-Hydorxybenzoic-Acid	0.09	1.22	0.25	0.00	0.05	0.00	0.00	0.12	1.15	0.26	0.09	0.00	0.22	0.08
3-Hydroxyphenylpropionic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.07	1.19	0.66	0.00	0.17	1.10	0.38	0.92	0.00	1.49	0.76	0.14	0.59	0.34
4-Hydroxymandelic-Acid	2.65	0.76	3.34	1.92	0.00	0.00	0.00	0.14	1.84	2.38	0.83	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.00	0.10	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Ketovaleric-Acid	0.00	0.00	0.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.19	0.00	0.00	0.00	0.00	0.00	0.01	0.18	0.00	0.00	0.03	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.00	1.81	0.00	1.85	0.03	0.25	0.03	0.10	0.24	0.00	0.24	0.00	0.08	0.00
Dimethylmalonic-Acid	0.00	0.00	0.66	0.00	0.00	0.00	0.00	0.00	0.00	1.76	0.00	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.02	0.00	0.34	0.00	0.00	0.00	0.00	0.07	0.00	0.29	0.00	0.00	0.19	0.00
Citraconic-Acid	1.36	1.76	0.00	0.38	0.00	0.57	0.00	1.78	0.33	0.09	0.33	0.00	0.00	0.25
Citramalic-Acid	0.25	0.20	0.00	0.00	0.00	0.00	0.00	0.85	0.17	0.27	0.00	0.00	0.00	0.00
Threitol	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Levulinic-Acid	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Maleic-Acid	1.08	0.92	0.87	0.13	0.00	0.13	0.06	0.03	0.27	0.24	6.94	0.66	0.00	0.00
Parabanic-Acid	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pantothenic-Acid	0.00	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Methylmaleic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00
Pantoyllactone	1.13	0.00	0.00	3.12	2.55	0.00	0.00	0.00	4.81	0.00	2.08	2.95	0.00	0.86
Dimethylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pentadecanoic-Acid	0.24	0.70	1.86	0.00	0.13	0.84	0.34	0.51	0.66	1.24	0.70	0.16	0.56	0.33
Urea	6.57	0.77	0.00	0.00	0.00	0.00	0.00	0.00	0.69	0.00	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	2.61	0.43	353.76	640.45	0.00	2.65	0.00	1.16	265.16	469.59	4.45	2.79	2.29	3.24
4-Methylmandelic-Acid	0.00	0.49	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybenzoic-Acid	1.34	0.00	0.00	0.11	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.06
2-Ketopyrrolidine-1-Carboxylic-Acid	1.07	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.61	84.30	51.98	0.00	0.00	0.00
2-Methyl-2-Hydroxybutyric-Acid	0.13	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00
2,3,3-Trihydroxy-2-Propenoic-Acid	0.00	0.47	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.90	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00
2,6,10,14-Tetramethylhexadecanoic-Ac	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.41	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.09	0.00
Citrazinic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,3-Benzenedicarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.41	0.00	0.00	0.00	0.14
N-Acethyl-4-Phenol	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyacetophenone	9.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	9.51	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00
3-Hydroxymandelic-Acid	2.38	1.12	0.00	0.00	0.00	0.00	0.00	2.02	0.32	0.00	0.45	0.00	0.00	0.00
2,2-Dimethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.77	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.23	0.00	0.00	0.57	0.04	0.00	0.00	0.00	0.00	0.41	1.51	0.52	0.00	0.00
2-Hydroxyphenylpropionic-Acid	0.00	3.50	2.88	0.00	0.00	0.00	0.00	0.00	1.63	0.00	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	6.73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenylheptanoic-Acid	0.00	0.00	0.00	0.00	0.04	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenyldecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	1.95	0.48	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.18	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Acrylylglycine	0.00	17.85	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Ethylmethylmalonic-Acid	0.00	20.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.27	0.00	0.00	0.00	0.00
1,2-Butanediol	0.00	0.00	0.00	3.08	0.00	0.00	0.00	0.00	2.23	0.87	3.35	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.49	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00
Cyclopentanecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00

2,3-Dihydroxybutane	0.00	2.00	0.86	0.98	3.81	1.83	1.98	0.12	4.06	1.21	0.93	2.85	2.47	3.46
1,2-Dihydroxypropane	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00
1,4-Dihydroxy-2-Butene	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.11	0.00	0.00	0.00
1,4-Dihydroxybutane	0.00	0.45	0.00	0.00	0.33	0.00	0.00	0.00	0.27	0.00	0.00	0.83	0.16	0.00
4-Phenol	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,13-Dihydroxytridecane	1.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.15	0.00	0.00	0.00	0.00	0.00
1,3-Dihydroxy-2-Ketopropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.37	0.00	0.00
1,3-Dihydroxy-2-Methylpropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00
1,2-Dihydroxy-2-Propane	0.00	0.00	0.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxyethane	0.40	0.66	0.89	0.22	0.44	0.25	0.09	0.47	0.00	14.00	0.31	0.60	0.00	0.00
1,2-Dihydroxycyclohexene	77.70	0.69	0.14	0.00	1.14	0.00	0.00	0.32	162.24	6.27	0.00	2.83	0.77	0.00
1,3-Dihydroxypentane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.79	0.00	0.00
2-Methyl-1,3-Dihydroxybutane	0.00	0.00	0.00	0.62	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactopyranose-Alpha-D	1.33	0.59	3.55	0.58	0.00	0.00	0.00	0.90	0.77	5.10	0.00	0.00	0.00	0.00
Galactopyranose-Beta-D	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.53	0.00	0.00	0.00	0.00	0.00
Glucopyranose	1.21	1.27	0.00	0.00	0.00	1.04	0.00	0.66	0.39	0.00	0.00	0.00	1.40	0.00
Mannitol	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mannose	0.00	0.00	2.19	0.00	0.00	0.00	0.00	0.00	0.00	0.76	0.00	0.00	0.00	0.00
Erythronic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.31	0.00
Glucutol	0.00	0.00	0.00	0.37	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.00	0.96	0.00	0.17	0.00	0.00	0.11	0.89	0.29	4.74	0.00	0.04	0.00	0.07
Arabinitol	0.00	0.00	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.00
Arabinose	0.00	0.00	4.86	0.00	0.00	0.00	0.00	0.00	0.00	3.33	0.00	0.00	0.00	0.00
Rhamnose	0.00	0.00	0.00	0.32	0.00	0.00	0.00	0.85	0.47	0.00	0.00	0.12	0.00	0.09
Ribose	0.00	2.66	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.88	0.00	0.00	0.00	0.00
Galactose	1.25	0.55	0.36	0.13	0.00	0.77	0.18	1.05	0.00	0.00	0.00	0.00	1.02	0.00
Arabinonic-Acid	0.00	0.00	1.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Monoisobutyrylglycerol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7.11	0.00	0.00	0.00	0.00	0.00

Organic acid	Moniliformin (110.2 µM)							Moniliformin (220.4 µM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	2.34	0.00	1.09	0.00	0.68	2.27	0.65	3.82	0.71	2.23	0.00	0.48	1.70	0.00
Octanoic-Acid	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.16	0.23	0.00	0.00
NoAcid	0.42	0.00	0.27	0.00	0.20	0.00	0.13	0.00	0.00	0.36	0.00	0.39	0.09	0.12
DecAcid	0.00	0.15	0.00	0.04	0.10	0.00	0.00	0.00	0.05	0.26	0.06	0.21	0.00	0.20
EicAcid	0.44	0.00	0.24	0.00	0.00	0.34	0.04	0.16	0.12	0.54	0.00	0.00	0.04	0.04
Dodecanoic-Acid	0.60	0.37	0.56	0.14	0.68	0.00	1.00	0.70	0.18	0.67	0.64	0.84	3.57	1.21
Tetradecanoic-Acid	2.06	0.43	1.96	1.10	0.78	3.76	1.60	1.77	2.32	3.83	1.06	0.80	3.30	1.62
Palmitic-Acid	45.30	48.68	47.81	21.42	14.09	83.67	27.74	36.99	47.78	70.42	9.24	11.45	59.55	26.61
Heptadecanoic-Acid	1.03	1.18	0.43	0.26	0.24	2.14	0.51	0.86	1.14	1.87	0.00	0.17	0.86	0.59
Octadecanoic-Acid	31.98	40.16	27.48	17.88	9.40	70.94	25.80	32.74	38.33	39.10	4.68	7.92	49.89	23.28
Isovaleric-Acid	2.02	0.00	0.00	0.00	0.00	0.00	0.00	2.53	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.16	0.44	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.76	0.00	0.00	6.45	2.80	162.88	0.00	0.00	0.00	0.00
2-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.73	0.45	0.00	0.19	0.00	0.00	0.00	0.00	0.14	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	22.43	19.81	7.15	0.00	0.00	14.03	0.00	21.21	24.74	0.39	0.27	29.44	12.76
2-Hydroxyundecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.87	0.20	0.00	0.00	0.00
3-Methyladipic-Acid	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.25	0.20	0.00	0.01	0.00	0.18	0.04	0.21	0.00	0.07	0.00	0.00	0.03	0.00
2-Hydroxysebacic-Acid	0.76	0.00	2.33	0.00	0.00	0.00	0.00	1.61	0.00	1.74	0.00	0.00	0.23	0.00
2-Hydroxytetradecanoic-Acid	16.36	0.00	0.00	0.00	0.00	44.76	0.00	3.38	0.00	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	0.39	0.20	0.21	0.18	0.14	1.42	0.27	0.24	0.37	0.56	0.00	0.09	0.55	0.31
Oleic-Acid	16.83	3.67	24.08	0.92	4.81	8.42	2.63	19.16	3.38	3.32	1.19	4.11	4.16	2.10
2-Undecenoic-Acid	0.25	0.20	0.00	0.01	0.00	0.18	0.04	0.21	0.00	0.07	0.00	0.00	0.03	0.00
11-Octadecenoic-Acid	16.36	22.43	19.81	7.15	0.00	44.76	14.03	3.38	21.21	24.74	0.39	0.27	29.44	12.76
Arachidonic-Acid	0.94	2.36	0.95	0.68	0.24	4.07	0.77	2.28	2.23	0.90	0.00	0.29	1.33	0.73
Linolenic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.32	0.00	0.00	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	0.16	3.49	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	3.54	6.26	5.06	2.72	0.86	9.98	2.15	4.96	5.89	5.61	0.00	0.79	6.16	2.01
Pimelic-Acid	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketohexanoic-Acid	0.00	0.00	0.00	0.53	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.40	0.00	0.00	0.00	0.00	2.51	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	3.34	0.00	0.00	0.00	0.00	0.00	0.00	9.53	0.00	0.00	0.00
Azelaic-Acid	3.48	0.00	0.00	0.00	0.00	4.46	0.95	0.00	0.00	3.08	0.00	0.00	0.00	0.71
Tetradecanedioic-Acid	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.05	5.75	0.16	0.00	0.00	0.00	0.00

Malonic-Acid	0.38	3.59	4.46	2.30	0.22	694.80	0.00	3.08	0.90	2.35	3.27	3.10	0.22	0.00
Citric-acid	28.78	65.40	57.26	15.97	11.55	52.37	16.79	30.04	64.00	37.05	0.00	8.89	36.54	5.33
Aconitic-Acid	0.31	1.03	1.08	1.81	0.00	0.00	1.42	0.62	1.74	0.00	0.00	0.00	0.74	0.28
2-Ketoglutaric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.04	0.00	0.00
Succinic-Acid	50.20	70.63	55.22	38.34	39.57	149.46	58.12	73.02	68.38	62.60	32.39	36.16	125.72	56.73
Fumaric-Acid	2.42	4.81	3.74	1.80	1.59	3.88	1.60	2.50	4.82	3.28	1.15	1.50	2.55	1.81
Malic-Acid	2.28	11.59	9.18	2.60	2.33	13.92	3.96	4.29	10.46	4.01	0.00	2.43	12.16	5.69
Lactic-Acid	407.50	337.65	276.02	52.45	605.35	592.06	889.18	510.68	205.03	484.61	575.93	498.78	301.63	400.81
Lactyllactate	0.67	0.06	0.00	203.89	0.00	1.05	8.22	4.20	0.00	6.92	4.79	0.00	0.21	0.15
Pyruvic-Acid	0.55	3.99	0.49	0.50	9.17	0.38	4.19	1.99	0.97	1.74	10.49	10.00	0.59	0.15
GLYCOLIC-DITMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	1.48	0.63	0.25	0.14	5.26	3.54	7.82	0.49	2.25	15.43	0.15	0.86	2.94	1.68
3-Ketobutyric-AcidtriTMS	0.00	0.00	0.00	0.00	2.20	0.00	0.00	0.00	0.00	0.00	0.00	1.81	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	0.00	2.90	0.00	4.19	5.33	0.00	0.00	1.62	1.63	0.00	0.00	1.00
Oxalic-Acid	4.85	14.27	28.10	4.51	0.09	18.39	3.37	4.66	13.38	2.17	0.09	24.82	20.20	13.78
2-Ketoisocaproic-Acid	0.00	0.00	0.00	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	1.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methylglutaconic-Acid	0.00	0.00	0.00	0.00	0.05	0.08	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyisobutyric-Acid	1.23	1.03	0.79	3.53	8.70	3.12	4.49	2.66	1.11	2.32	0.00	5.93	0.68	2.03
3-Hydroxyisovaleric-Acid	1.16	0.00	0.00	4.07	0.65	1.91	0.00	0.00	0.00	0.00	2.84	0.80	0.00	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.29	0.00	0.00	0.00	0.69	0.00	0.31	0.00	0.00	0.33	0.00	0.30	0.00	0.35
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.52	0.00	0.00	0.14	0.12	0.00	0.00	0.31	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	1.47	0.00	0.00	4.15	0.00	0.00	0.85	0.18	0.00	0.45	4.09	0.10	0.00
4-Hydroxyphenyllactic-Acid	0.83	3.96	2.18	0.47	0.43	1.65	1.71	1.09	3.69	2.71	0.00	0.49	1.28	0.70
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	1.87	2.83	0.00	2.50	1.75	0.00	0.00	0.00	3.08	0.00	1.59
3-Hydroxypropionic-Acid	0.83	0.47	1.52	3.62	4.05	6.42	7.58	2.13	0.66	5.04	2.67	8.13	2.42	2.99
Methylmalonic-Acid	39.89	0.00	0.00	28.36	6.32	0.00	0.00	0.00	0.00	0.00	8.47	0.00	0.70	0.00
Methylmalonic-Acid-Tritms	0.00	0.88	0.63	0.00	0.09	0.88	0.38	0.63	0.31	0.33	0.00	0.14	0.71	0.17
N-Propionylglycine	0.00	41.03	19.94	17.43	45.37	69.45	24.64	0.00	37.01	16.39	11.07	43.63	76.38	23.94
Glutaric-Acid	0.39	0.67	0.39	0.88	0.47	1.92	0.85	1.24	0.39	0.65	0.00	0.61	1.43	0.84
Glutaconic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00
2-Ketobutyric-Acid	3.17	0.32	6.02	0.24	2.19	2.63	6.87	0.82	1.19	6.50	0.60	2.31	2.13	3.98
2-Methyl-3-Ketobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.47	0.00	0.00	0.00	0.00	0.00	0.00
N-Phenylacetylglycine	3.88	0.00	0.00	0.00	0.00	2.67	0.00	5.11	0.00	0.00	0.00	0.00	1.15	0.82
Cyclohexanecarboxylic-Acid	0.00	0.00	0.00	0.00	2.46	0.00	0.00	2.00	0.00	0.00	0.00	3.78	0.00	0.00
2-Hydroxyglutaryllactone	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.55	0.00	0.00	0.00	0.00	0.00	0.00
2-Methylglutaconic-Acid-triTMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.44	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.00	0.50	0.65	0.00	0.32	1.39	0.26	0.11	0.50	0.24	0.00	0.37	0.87	0.00
4-Hydroxyphenylacetic-Acid	0.22	0.28	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Phenylacetic-Acid	0.00	0.00	0.00	0.00	1.43	1.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.81
4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.00	0.00	0.00
N-Acetyltyrosine	0.23	0.00	0.50	0.00	0.00	0.29	0.06	0.56	0.00	0.00	0.00	0.00	0.28	0.06
Pyroglutamic-Acid	201.74	20.57	168.30	151.41	143.28	433.69	182.64	207.09	196.80	155.22	0.00	140.49	369.98	176.74
Uracil	1.29	3.94	0.48	0.00	1.88	7.36	1.00	1.66	3.40	0.58	0.00	0.00	3.22	0.67
Pyrimidinedione	0.79	0.00	0.84	0.00	1.35	1.03	0.21	1.50	1.15	0.00	0.10	1.01	0.95	0.39
5-Methylpyrimidine-2,4-Diol	0.00	0.34	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00	2.33	0.00	0.00	0.00
2-Hydroxyhippuric-Acid	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxy-3-Methylglutaric-Acid	0.00	0.15	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	267.11	68.69	0.00	0.00	0.00	0.00	0.00	173.96	55.68
Benzoic-Acid	0.00	0.28	0.14	0.92	1.55	0.00	0.95	0.42	0.18	0.37	0.95	0.85	0.77	0.73
Hippuric-Acid	4.63	2.26	1.16	2.33	0.00	6.10	1.84	6.86	2.27	0.73	0.00	0.00	0.00	1.59
1-(4-hydroxyphenyl)ethanone	0.00	0.00	10.01	0.01	0.00	0.00	0.00	0.00	0.28	0.00	8.21	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.03	0.07	0.05	0.00	0.00	0.00	0.00	0.03	0.00	0.08
2,3-Dihydroxypropanoic-Acid	0.63	1.98	1.85	0.14	0.31	3.25	1.12	1.00	1.77	0.95	0.18	0.57	3.26	1.02
2,4-Dihydroxybenzoic-Acid	0.06	0.30	0.16	0.05	0.00	0.03	0.00	0.26	0.44	0.10	0.00	0.02	0.18	0.00
2,5-Furandicarboxylic-Acid	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.98	0.00	0.00	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	0.67	22.06	47.90	0.10	0.00	0.00	0.00	0.50	35.86	55.84	0.18	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	0.11	148.89	0.00	0.00	0.00	0.37	0.34	0.27	142.25	0.00	0.69	0.00	0.33	0.30
2-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.15	1.60	0.00	1.56	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.00	0.00	0.33	0.00	1.37	7.83	0.47	0.00	0.00	0.07	0.00	2.67	10.05	0.67
3-Hydorxybenzoic-Acid	0.07	0.48	0.38	0.76	0.09	0.40	0.11	0.10	0.18	0.40	0.15	0.09	0.30	0.00
4-Hydroxbenzoic-Acid	0.75	0.64	0.60	0.00	0.22	1.05	0.43	0.66	0.93	0.61	0.39	0.23	0.94	0.93
4-Hydroxycinnamic-Acid	0.00	0.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxymandelic-Acid	0.07	0.00	0.97	0.15	0.00	0.00	0.00	0.20	0.92	0.24	1.22	0.00	0.00	0.00
5-Hydroxyhydantoin	0.15	0.00	0.00	0.04	0.02	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.04
4-Hydroxyphenylacrylic-Acid	1.66	0.00	0.00	0.00	0.02	0.20	0.04	0.00	0.00	0.00	0.00	0.00	0.13	0.05
Dimethylmalonic-Acid	0.13	0.00	0.00	0.35	0.00	0.00	0.00	0.00	0.00	0.76	0.00	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.08	74.68	0.19	1.33	0.00	0.38	0.00	1.73	100.58	0.16	0.00	0.00	0.00	31.42
Citraconic-Acid	2.35	0.91	0.00	0.42	0.00	0.00	0.00	1.95	0.00	0.13	0.26	0.00	0.00	0.00
Citramalic-Acid	0.50	0.13	0.00	0.00	0.00	0.00	0.00	0.71	0.00	0.16	0.00	0.00	0.00	0.00
Threitol	0.07	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.10	0.10	0.00	0.00	0.00	0.00
Maleic-Acid	0.20	0.31	0.25	2.03	0.70	1.19	0.00	1.48	0.23	0.18	0.76	0.09	0.39	0.70
Pantothenic-Acid	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pantoyllactone	0.32	0.00	0.00	2.74	2.51	0.00	2.82	1.28	0.00	2.68	2.80	3.09	0.00	0.00
Pentadecanoic-Acid	0.27	0.00	0.84	0.00	0.23	0.86	0.40	0.10	0.10	1.16	0.15	0.00	0.65	0.36
Pyrrole-2-Carboxylic-Acid	0.00	0.00	2.46	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Urea	2.33	2.33	0.00	0.00	0.00	0.00	1.43	8.72	2.06	0.00	0.00	0.00	0.00	0.00

3,3-Dihydroxy-7,11-Dimethyldodecanoi	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.13	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	561.08	1.05	1.06	473.00	0.00	1.53	0.00	447.35	1.64	4.35	1.41	370.76	2.72	0.00
2,4,6-Trihydroxy-1,3,5-Triazine	0.00	0.00	0.36	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylmandelic-Acid	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00
2,3-Dihydroxybenzoic-Acid	0.36	0.00	0.10	0.17	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.17	159.19	0.00	0.00	0.00	0.13	0.00	87.92	17.37	0.00	0.00	0.00	0.10	0.00
1,2,3-Trihydroxypropane	0.00	0.00	0.00	0.00	0.22	0.00	0.00	2.78	0.00	0.00	0.75	0.25	0.00	0.00
2,6,10,14-Tetramethylhexadecanoic-Ac	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methyl-2-Propylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.08	0.05	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.89	0.00	0.00	0.06	0.00	0.00
1,3-Benzenedicarboxylic-Acid	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxy-2-Methylbutyric-Acid	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.01
3-Hydroxymandelic-Acid	0.00	0.16	1.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dimethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.94	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methoxymandelic-Acid	0.00	0.00	0.00	3.64	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-Ketovaleric-Acid	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.62	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.00	0.00	1.32	0.00	0.00	0.00	0.00	0.00	0.88	1.09	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	0.00	5.71	0.00	0.00	0.00	0.00	0.00	0.00	5.27	0.00	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	5.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxycinnamic-Acid	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methyl-4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.71	0.00	0.00	0.00	0.00	0.00
4-Hydroxy-3-Penten-2-One	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenyldecanoic-Acid	0.00	0.00	0.00	0.00	0.01	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	2.80	0.00	0.00	0.00	0.00	0.00	0.00	2.12	0.00
Ethylmethylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	34.79	0.00	0.00	0.00	0.00	0.00
Glyoxylic-Acid	3.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Butanediol	0.74	0.00	0.00	0.23	0.00	0.00	0.00	1.13	0.00	0.87	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00	0.00	0.00
Tiglic-Acid	0.00	0.00	2.54	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.73	2.16	0.59	1.52	1.19	3.40	1.80	0.00	2.14	0.25	0.43	0.02	3.90	0.00
1,2-Dihydroxypropane	0.00	0.00	0.00	0.00	0.00	0.00	6.80	0.53	0.00	0.00	0.00	2.12	0.00	0.00
2,4-Dihydroxy-4-Methyl-2-Pentene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.33	0.00	0.00	0.00	0.00	0.00	0.00
1,4-Dihydroxy-2-Butene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.63	0.00
1,4-Dihydroxybutane	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.20	1.22	0.00	0.20	0.00	0.00
1,13-Dihydroxytridecane	0.00	0.00	0.00	0.21	0.00	0.00	0.00	0.00	1.52	0.00	0.13	0.00	0.00	0.00
1,3-Dihydroxy-3-Methylbutane	0.00	0.00	0.00	1.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxy-3-Methylbutane	0.00	0.00	0.00	0.88	0.00	0.00	0.00	3.97	0.00	0.00	0.00	0.00	0.00	0.00

1,2-Dihydroxy-4-Methylpentane	0.00	0.00	0.00	0.00	0.06	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	1.07
1,2-Dihydroxyethane	0.13	0.76	0.05	0.00	0.30	0.35	0.00	0.00	0.56	0.81	0.08	0.17	0.00	0.00
1,2-Dihydroxycyclohexene	17.69	2.27	1.82	17.69	1.70	0.83	0.00	0.34	45.23	45.77	0.00	1.10	1.15	0.00
1,6-Dihydroxyhexaan	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.90	0.00	0.00	0.00
1,3-Dihydroxy-2-Ethylpropane	2.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.92	0.00	0.00	0.13
1,5-Dihydroxypentane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.55	0.00	0.00	0.00
Galactopyranose-Alpha-D	1.22	1.93	2.21	0.00	0.00	0.00	0.00	2.01	0.54	2.07	0.00	0.00	1.22	0.00
Glucopyranose	0.72	0.00	0.66	0.04	0.00	1.35	0.00	1.82	0.46	0.96	0.08	0.00	1.36	0.00
Mannonic1,4-Lactone	0.00	0.14	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mannitol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
Mannose	0.00	0.10	0.28	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fructofuranose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00
Glucutol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01
Fucose	1.10	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.00	1.17	0.16	0.00	0.00	0.00
Arabinose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.64	0.00	0.00	0.00	0.00
Rhamnose	0.00	0.00	0.00	0.01	0.00	0.81	0.34	1.58	0.61	0.00	0.00	0.00	0.89	0.00
Ribose	0.00	0.00	2.27	0.00	0.00	0.00	0.00	0.00	0.00	1.12	0.00	0.00	0.00	0.00
Galactose	1.09	3.57	0.00	0.00	0.00	2.19	0.41	1.41	0.15	0.00	0.00	0.00	2.61	0.00
2-Monoisobutyrylglycerol	4.34	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sorbopyranose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00

Organic acid	3-bromopyruvate (3.75 mM)							3-bromopyruvate (5.2 mM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	1.05	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.68	0.62	0.00
Octanoic-Acid	0.12	0.00	0.00	0.00	0.08	0.05	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00
Hexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.51	0.00	0.00	0.00
NoAcid	0.49	0.00	0.18	0.00	0.50	0.18	0.10	7.02	0.19	0.14	0.00	0.27	0.07	0.00
DecAcid	0.00	0.00	0.05	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
EicAcid	0.16	0.11	0.03	0.00	0.00	0.19	0.06	1.20	0.29	0.00	0.00	0.55	0.22	0.00
Dodecanoic-Acid	0.42	0.53	0.62	0.06	0.70	1.55	1.18	11.19	0.61	0.63	0.00	1.77	2.21	0.00
Tetradecanoic-Acid	1.59	2.14	0.72	0.54	1.60	2.84	2.88	50.40	0.84	0.89	0.55	1.28	4.21	0.00
Palmitic-Acid	32.19	77.91	63.44	38.01	23.94	56.67	43.01	963.58	77.98	65.55	36.17	76.66	64.18	33.02
Heptadecanoic-Acid	0.75	1.81	1.50	0.51	0.65	1.24	0.85	18.60	0.79	0.82	0.56	1.93	1.53	0.00
Octadecanoic-Acid	20.43	53.70	38.98	30.43	16.45	43.69	34.90	633.49	55.09	40.42	28.23	48.51	50.38	31.66
2-Ethylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.37	0.00	0.00	0.00
2-Heptenoic-Acid	0.00	0.00	1.36	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6-Octadecenoic-Acid	0.00	0.00	0.74	13.41	0.00	0.00	0.00	0.00	0.00	1.30	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.08	0.00	1.23	0.00	0.00	0.00	0.17	0.00	0.00
5-Hydroxyvaleric-Acid	0.00	1.71	26.73	10.35	9.26	0.00	0.00	0.00	4.26	0.00	5.84	0.00	0.00	0.00
2-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	311.94	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	15.84	0.00	0.00	19.50	0.00	0.00	24.18	431.70	40.67	26.08	18.00	36.18	0.00	16.92
2-Hydroxyundecanoic-Acid	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyhexacosanoic-Acid	0.00	0.00	0.00	0.00	0.04	0.02	0.00	0.00	0.00	0.00	0.00	0.01	0.04	0.00
3-Hydroxylauric-Acid	0.57	0.19	0.00	0.15	0.00	0.15	0.09	0.00	0.00	0.00	0.15	0.08	0.14	0.00
2-Hydroxysebacic-Acid	0.00	0.00	3.26	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.24	0.00	0.31	0.00
2-Hydroxytetradecanoic-Acid	0.00	20.44	29.66	0.00	0.00	30.81	0.00	0.00	0.00	0.00	0.00	0.00	35.99	0.00
Palmitelaidic-Acid	0.61	2.13	0.98	0.60	0.21	1.95	0.99	8.48	1.58	0.58	0.45	1.58	2.16	0.00
N-Valerylglycine	11.57	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oleic-Acid	16.91	0.00	30.87	19.55	7.01	0	1.29	460.53	2.44	4.04	19.10	0.00	6.82	3.37
2-Undecenoic-Acid	0.57	0.19	0.00	0.15	0.00	0.15	0.09	0.00	0.00	0.00	0.15	0.08	0.14	0.00
11-Octadecenoic-Acid	15.84	40.44	29.66	19.50	0.00	30.81	24.18	431.70	40.67	26.08	18.00	36.18	35.99	16.92
Arachidonic-Acid	1.98	5.59	2.87	2.65	0.73	4.21	2.55	44.98	5.20	2.53	2.55	5.22	4.01	0.00
Linolenic-Acid	0.00	0.00	0.00	0.00	0.00	1.80	0.00	0.00	0.96	0.00	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	20.03	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	5.80	14.87	8.15	6.03	1.27	7.00	5.36	136.23	14.05	6.69	5.66	7.77	7.33	0.00
Pimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00
2-Hexenedioic-Acid	1.31	0.00	0.00	0.88	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

2-Hexenoic-Acid	1.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	0.53	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00
Azelaic-Acid	0.67	0.00	0.00	0.00	0.00	0.85	0.84	4.65	0.00	0.00	0.00	0.00	0	0.00
Tetradecanedioic-Acid	0.00	0.06	0.18	0.08	0.00	0.00	0.00	1.69	0.00	0.00	0.00	0.00	0.00	0.00
Malonic-Acid	0.62	1.23	0.35	0.33	1.38	0.47	1.50	13.98	0.26	0.28	1.59	1.26	0.00	0.00
Citric-acid	3.10	23.28	14.31	3.22	0.82	5.17	1.96	1.43	18.67	13.97	2.09	5.21	4.89	0.00
Aconitic-Acid	0.00	0.31	0.53	0.25	0.00	0.00	0.00	0.00	0.19	0.10	0.18	1.20	0.00	0.00
Succinic-Acid	42.80	61.86	60.09	32.77	24.88	65.10	39.04	2.68	64.84	49.04	32.16	78.18	68.98	38.05
Fumaric-Acid	0.82	2.84	3.01	1.16	0.56	1.47	1.24	0.00	3.04	1.95	1.09	2.13	1.49	0.00
Malic-Acid	1.10	3.32	6.75	4.10	1.68	6.58	2.33	0.00	7.21	5.79	1.68	2.64	7.51	0.00
Lactic-Acid	127.44	142.45	220.54	560.07	342.01	421.74	122.05	137.34	106.52	168.67	511.61	81.35	349.80	166.49
Lactyllactate	0.00	0.00	0.00	0.07	0.00	0.09	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.00
Pyruvic-Acid	11.14	7.58	0.35	0.31	0.21	1.46	3.76	323.28	0.11	0.62	18.55	10.31	0.48	0.00
GLYCOLIC-DITMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.24	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	6.39	0.99	18.79	0.84	2.87	7.12	3.67	265.38	0.40	4.95	3.91	0.00	1.73	0.00
3-Ketobutyric-AcidtriTMS	0.00	0.00	0.00	0.00	0.84	0.00	0.00	0.00	0.00	0.00	0.00	2.70	0.00	0.00
3-Hydroxybutyric-Acid	4.56	0.00	0.85	2.85	0.00	4.78	1.31	0.00	0.00	0.25	2.60	0.00	4.22	0.00
N-Acrylglycine	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00
Oxalic-Acid	10.93	28.04	2.20	45.90	39.42	16.92	67.14	9.13	26.38	13.37	51.80	41.26	42.97	94.36
N-Isovalerylglycine	1.72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methylglutaconic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00
3-Hydroxyisobutyric-Acid	1.26	0.00	0.00	0.89	0	2.85	0.82	0.00	1.13	0.00	46.61	0	2.79	0.00
3-Hydroxyisovaleric-Acid	0.00	0.00	0.00	4.69	2.89	0.00	0.00	0.00	0.00	0.00	0.00	0	1.99	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.00	0.00	0.00	0.00	0.42	0.00	0.00	0.00	0.00	0.00	0.00	0.67	0.31	0.00
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.09	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Keto-3-Methylvaleric-Acid	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	5.68	1.33	0.00	3.07	0.00	0.00	52.93	0.00	0.00	0.00	1.36	2.10	0.00
4-Hydroxyphenyllactic-Acid	0.58	2.47	0.87	0.39	0.15	1.27	0.13	0.00	0.76	0.72	0.26	0.63	0.62	0.00
2-Methyl-3-Ketovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	3.24	0.00	0.00	0.00	0.00	0.00	0.00	2.53	0.00
3-Hydroxypropionic-Acid	9.66	8.01	18.42	74.32	42.73	77.09	10.30	13.2	13.51	13.40	78.70	26.03	86.17	19.22
Methylmalonic-Acid	0.00	1.83	0.00	0.43	0	0.00	0.00	0.00	0.00	0.00	0.00	0	60.89	0.00
Methylmalonic-Acid-Tritms	0.74	0.30	0.53	0.40	0.03	0.47	0.00	0.00	0.49	1.57	0.00	1.32	0.00	0.00
N-Propionylglycine	0.00	1.21	0.00	0.00	0.89	2.33	0.55	0.00	0.00	0.00	0.00	0.88	1.22	0.00
Glutaric-Acid	0.00	0.43	0.57	1.03	0.09	0.60	0.83	0.00	0.73	0.45	1.05	1.59	0.60	0.00
Glutaconic-Acid	0.00	0.00	0.00	27.94	0.00	0.00	0.00	0.87	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketobutyric-Acid	0.66	1.16	1.97	2.09	3.45	0.76	0.28	33.08	1.82	0.39	1.19	5.82	6.81	0.00
2-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	3.48	0.00	0.00	0.00	0.00	0.00	2.14	0.00	0.00	0.00

2-Methyl-3-Ketobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00
N-Phenylacetylglycine	1.30	0.64	0.66	0.95	0.00	0.50		0.00	3.02	0.74	0.60	0.00	0.00	0.06
Cyclohexanecarboxylic-Acid	0.00	0.00	2.46	0.00	6.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.09	0.75	0.18	0.00	0.00	0.66	0.00	0.00	0.41	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacetic-Acid	0.24	0.26	0.00	0.00	0.00	0.00	0.00	0.00	2.35	0.00	0.00	0.00	0.18	0.00
Phenylacetic-Acid	0	1.22	0.88	0.00	0.00	3.64	0.00	0.00	1.31	0.00	0.00	0.00	2.63	0.00
Phenylpyruvic-Acid	12.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	22.13	2.28	0.00
N-Acetyltyrosine	0.21	0.00	0.39	0.00	0.00	0.00	0.66	0.00	0.00	0.38	0.00	0.02	0.14	0.00
Pyroglutamic-Acid	110.23	317.30	242.85	153.05	162.38	296.97	206.47	0.00	252.33	189.48	151.70	446.40	129.36	199.76
Uracil	0.97	1.02	0.22	0.00	0.00	0.33	0.41	3.98	0.69	0.00	0.00	0.71	0.00	0.00
Pyrimidinedione	30.87	28.82	30.33	30.37	0.00	30.24	26.85	0.00	24.25	32.33	38.32	29.27	33.56	0.00
2-Hydroxyhippuric-Acid	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00
3-Hydroxy-3-Methylglutaric-Acid	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.08	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	67.98	61.42	0.00	0.00	0.00	0.00	45.95	118.59	57.26
Benzoic-Acid	0	0.54	0.00	0.81	0.00	1.13	0.65	0.00	0	0.23	0.87	0.57	0.86	0.00
Hippuric-Acid	2.71	2.68	0.76	2.67	0.00	1.73	1.30	0.00	4.07	1.4	2.24	0.00	1.96	0.00
1-(4-hydroxyphenyl)ethanone	19.72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	28.09	0	0	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0	0.00	0.00	0.00	0.09	0.00	0.15	0.00	0	0	0	0.00	0.00	0.00
2,3-Dihydroxypropanoic-Acid	31.32	48.71	36.75	29.93	12.50	29.53	15.55	0.00	26.1	42.93	33.13	28.36	46.45	13.34
2,4-Dihydroxybenzoic-Acid	0	0	0.44	0.09	0.00	0.00	0.00	0.21	0.71	0.29	0	0.00	0.16	0.00
2,5-Furandicarboxylic-Acid	0	0	0	0.09	0.00	0.00	0.02	0.00	1.76	2.92	0.82	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	0.07	16.19	57.56	0	0.00	0.00	0.00	25.10	37.03	58.3	0.16	0.00	0.00	0.00
2-Hydroxy-5-Methoxybenzoic-Acid	0.1	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	0.64	0	0	0	0.00	0.57	0.31	0.00	0	0	0.17	0.74	0.42	0.00
2-Hydroxyisobutyric-Acid	0	0	1.47	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0
3-Hydorxybenzoic-Acid	0.08	0.6	1.55	0.02	0.00	0.00	0.10	0.00	0.41	0.25	0.07	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.1	0.76	0.58	0.43	0.46	0.63	0.41	0.00	0.85	0.53	0	0.00	0.61	0.00
4-Hydroxymandelic-Acid	1.73	1.85	2.77	0.73	0.00	0.00	0.00	45.35	2.79	2.73	0.98	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0	0	0	0	0.00	0.00	0.00	0.00	0	0.12	0	0.00	0.00	0.00
5-Hydroxyhydantoin	0.01	0	0	0.06	0.00	0.05	0.00	0.93	0	0	0	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.11	0	0.84	0	0.00	0.00	0.00	0.00	2.27	2.4	0	0.00	0.00	0.00
Dimethylmalonic-Acid	0.1	0	0.74	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.04	0	0	3.42	0.00	0.00	0.00	0.00	0	0.1	0	0.00	0.16	0.00
Citraconic-Acid	8.26	4.14	0	4.15	0.00	0.00	0.00	0.00	18.98	0	0.36	0.00	0.00	0.00
Citramalic-Acid	0.32	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Threitol	0	0	0	0	0.00	0.00	0.00	2.66	0	0	0	0.00	0.00	0.00
Maleic-Acid	1.15	0.1	0.07	1.29	0.15	0.13	0.32	12.70	1.14	0.19	0.18	1.47	0.00	0.00
Parabanic-Acid	0	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.15	0.00	0.00

Pantothenic-Acid	0.00	0	0	0	0.00	0.00	0.00	0.00	0.19	0	0	0.00	0.00	0.00
2-Isopropyl-3-Ketobutyric-Acid	0.00	0.28	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Mandelic-acid	0	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.32	0.00	0.00
Methylmaleic-Acid	0.61	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Pantoyllactone	0.55	0.6	0.9	2.51	3.62	5.25	0.49	0.00	0	0.56	3.55	3.31	3.41	0.00
Pentadecanoic-Acid	0.55	1.33	1.12	0.38	0.51	0.85	0.54	13.79	1.21	1	0.36	1.62	1.12	0.00
Pyrrole-2-Carboxylic-Acid	1.28	0	2.36	0	0.00	0.00	0.00	0.00	0	1.6	0	0.00	0.00	0.00
Urea	9.29	0	0	0	0.00	0.00	0.62	0.00	0	0	25.1	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	1.85	574.76	366.65	469.67	491.80	3.03	1.06	0	0.81	0	537.11	1.10	2.98	156.26
2,3-Dihydroxybenzoic-Acid	0.81	0.05	0.03	0.00	0.00	0.00	0.00	9.65	0	0.47	0.1	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.19	3.65	0.00	84.22	0.00	0.00	0.00	0.00
2,4-Dihydroxy-2-(Hydroxymethyl)butyric-A	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.74	0.00	0.00	0.00	0.00	0.00
2-Methyl,2,3-Dihydroxypropanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.38	0.00	0.00	0.71	0.00	0.00
2,3,3-Trihydroxy-2-Propenoic-Acid	0.58	4.43	0.41	4.92	0.28	0.27	1.24	0.00	3.77	0.00	2.77	0.55	0.57	0.00
2,3-Dihydroxyacrylic-Acid	0.05	0.12	1.99	0.04	0.10	1.51	0.00	0	0.00	3.67	0.07	0.26	2.47	0.00
1,2,3-Trihydroxypropane	2.84	0.00	0.00	0.00	1.22	0.00	0.00	218.31	0.00	0.00	1.22	0	0.00	0.00
2,6,10,14-Tetramethylhexadecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00
2-Methyl-2-Propylmalonic-Acid	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0	0.00	0.00	0.00	0.00	1.48	0.00	3.27	0.00	0.00	0.00	1.87	1.37	0.00
Citrazinic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.09	0.00	0.00
2-Hydroxy-2-Methylbutyric-Acid	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.55	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.22	0.30	0.36	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.72	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.33	0.00	1.05	0.00	0.00	0.00	0.35	9.09	0.00	0.38	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00
2-Hydroxyphenylpropionic-Acid	0	0.00	0.00	2.63	0.00	1.65	0.00	32.29	4.42	0.00	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	5.44	5.97	3.10	0.00	0.00	0.00	0.00	166.48	0.00	0.00	2.57	0.00	0.00	0.00
3,4-Dihydroxyphenylheptanoic-Acid	0.00	0	0.00	0.00	0.00	0.00	0.42	0.00	0.00	0.00	0.00	0.00	22.07	0.00
3,4-Dihydroxy-3,7,11-Trimethyldodecanoic	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0	0	0.00	0.00	0.00	0.00	0.00	38.08	0.00	0.00	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	1.40	0.00	0.00	0.00	0.00	0.00	0.00	1.64	0.00
Hydroxymalonic-Acid	0.00	0.00	0.00	0.00	13.37	0.00	0.67	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00
2-Methyl-1,2-Dihydroxubutane	0	0	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylhexanoic-Acid	0	0	0.00	0.00	0.00	0.00	0.00	7.56	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Butanediol	0	0	0.00	0.08	0.00	0.00	0.00	0	0.00	0.00	0.02	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.51	0	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.57	0.00	0.00
2,3-Dihydroxybutane	0.33	1.61	0.47	0.27	1.28	6.28	1.09	12.69	2.72	92.78	0.26	0	6.87	128.05
Succinic-Anhydride	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	32.37	0.00	0.00	0.00

1,4-Dihydroxy-2-Butene	0.00	0	0.00	0.00	0.00	9.04	0.00	0.00	0.00	0.00	0.00	0.00	5.43	0.00
1,4-Dihydroxybutane	0.75	1.63	0.00	2.62	0.38	0.00	1.70	0.00	0.33	0.00	3003.00	0.81	0.12	0.00
1,13-Dihydroxytridecane	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.13	0.00	1.28	0.00	0.00	0.00
1,3-Dihydroxy-2-Ketopropane	0	0	0.08	0.00	0.00	0.07	0.21	0.00	0.00	0.11	0.00	0.10	0.06	0.00
1,3-Dihydroxy-2-Methylpropane	0.00	0.00	1.12	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sarcosine	0.27	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,3-Dihydroxy-3-Methylbutane	0.00	0.00	0.00	0.92	0.00	0.00	0.00	0.00	0.00	0.00	1.32	0.00	0.00	0.00
1,2-Dihydroxy-2-Propane	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.57	0.00
1,2-Dihydroxy-3-Methylbutane	0.7	0	0.00	2.49	0.00	0.00	0.00	464.00	0.00	0.00	2.41	0.00	0.00	0.00
1,2-Dihydroxyethane	3.1	0.35	6.27	0.00	0.48	0.24	0.00	19.69	24.21	0.12	1.77	0.22	0.62	0.00
1,2-Dihydroxycyclohexene	0.36	204.78	4.83	0.40	0.85	0.39	0.19	22.04	0.73	3.84	1.39	2.98	0.56	0.00
2,4-Dihydroxybutane	0	0	0.00	0.00	0.00	0.00	0.00	13.32	0.00	0.00	0.00	0.00	0.00	0.00
Galactopyranose-Alpha-D	1.73	0.82	0.00	0.00	0.00	0.84	0.00	26.15	0.87	3.29	0.00	0.00	1.18	0.00
Glucopyranose	0.00	0	0.00	0.06	0.00	0.62	0.12	0.00	0.00	0.00	0.07	1.10	0.00	0.00
Galactitol	0.00	0	0.00	0.00	0.00	0.00	0.00	24.98	0.00	0.00	0.00	0.00	0.00	0.00
Glucono-1,5-Lactone	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.79	0.00	1.57	0.00	0.00
Galactaric-Acid	0.00	0	0.00	0.00	0.00	0.00	0.00	12.96	0.00	0.00	0.00	0.00	0.00	0.00
Mannonic1,4-Lactone	0.28	0	0.00	0.00	0.03	0.00	0.00	1.59	0.00	0.00	0.00	0.00	0.00	0.00
Mannitol	0.00	0	0.00	0.00	0.00	0.00	0.00	152.93	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.00	0.66	0.00	0.00	0.00	0.00	0.19	0.00	0.74	0.00	0.00	0.00	0.96	0.00
Arabinose	0.00	0	2.32	0.00	0.00	0.45	0.00	0.00	0.32	2.99	0.00	0.00	0.55	0.00
Rhamnose	0.00	0.69	0.00	0.11	0.00	0.00	0.00	10.05	0.58	0.00	0.00	0.00	0.00	0.00
Ribose	0.00	0	1.54	0.00	0.00	0.00	0.00	0.81	0.00	2.49	0.00	0.00	0.00	0.00
Galactose	1.26	0.76	0.00	0.00	0.00	0.54	0.00	32.56	0.88	0.00	0.00	0.37	0.98	0.00
2-Monoisobutyrylglycerol	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.73	0.00	0.00
Monostearylglycerol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00

Organic acid	Moniliformin (110.2 µM) and Rotenone (10 nM)							Moniliformin (220.4 µM) and Rotenone (1000 nM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	2.24	1.15	0.67	0.09	0.06	1.70	0.36	2.28	0.00	0.00	0.00	0.32	0.00	0.29
Octanoic-Acid	0.00	0.00	0.21	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00
Hexanoic-Acid	0.00	0.00	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NoAcid	0.00	0.04	0.24	0.06	0.24	0.06	0.15	0.00	0.00	0.32	0.00	0.25	0.00	0.11
DecAcid	0.00	0.00	0.37	0.25	0.09	0.00	0.00	0.13	0.00	0.15	0.24	0.19	0.00	0.00
EicAcid	0.11	0.00	0.19	0.20	0.00	0.00	0.02	0.21	0.00	0.09	0.00	0.00	0.29	0.22
Dodecanoic-Acid	0.43	0.44	0.40	1.30	0.60	1.83	0.66	0.00	0.42	0.48	0.32	0.57	4.14	1.24
Tridecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanoic-Acid	1.97	3.53	2.53	2.92	0.62	1.05	0.98	1.59	3.98	3.16	0.25	0.97	5.54	1.81
Palmitic-Acid	44.55	55.29	46.66	58.42	11.60	41.68	22.49	32.93	70.50	62.33	19.19	13.81	110.71	34.06
Heptadecanoic-Acid	0.94	1.23	0.93	1.37	0.14	0.57	0.42	0.82	1.85	1.47	0.33	0.21	2.29	0.75
Octadecanoic-Acid	30.28	39.49	25.17	50.43	8.43	33.79	19.75	23.59	51.59	34.22	16.97	10.25	91.64	35.41
2-Octenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,4-Hexadienedioic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methylbutyric-Acid	0.00	0.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00
2-Ethylhexanoic-Acid	0.00	0.00	0.39	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.36	0.00	0.00
Isovaleric-Acid	2.43	0.35	0.65	0.00	0.00	0.00	0.00	2.38	0.74	0.00	0.00	0.00	0.37	0.00
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.74	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00	0.00	0.14	0.21
3-Hydroxycapric-Acid	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.70	0.10
5-Hydroxyvaleric-Acid	0.00	12.05	30.42	1.19	0.00	1.54	0.00	6.64	0.28	38.42	0.00	0.00	0.00	0.00
2-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	1.18	0.00	0.00	0.00	0.00	0.00	0.00	0.62	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	18.67	2.73	3.37	0.00	10.74	0.00	7.94	27.12	2.81	5.62	60.80	17.61
2-Hydroxyundecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00
3-Methyladipic-Acid	0.13	0.16	0.00	0.11	0.00	0.03	0.00	0.03	0.00	0.00	0.00	0.00	0.21	0.00
3-Hydroxylauric-Acid	0.19	0.11	0.40	0.00	0.06	0.00	0.00	0.41	0.23	0.27	0.00	0.00	0.30	0.00
2-Hydroxysebacic-Acid	0.00	0.00	0.95	0.00	0.00	0.00	0.00	0.58	0.00	3.49	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.41	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	20.46	24.49	0.00	0.00	0.00	20.38	0.00	14.86	0.00	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	0.52	0.94	0.14	0.00	0.16	0.45	0.31	0.40	1.38	0.74	0.00	0.04	2.00	0.40
Oleic-Acid	22.21	5.04	1.67	2.09	4.17	2.91	2.09	15.67	34.53	26.40	4.34	5.03	10.68	3.59
2-Undecenoic-Acid	0.19	0.11	0.40	0.00	0.06	0.00	0.00	0.41	0.23	0.27	0.00	0.00	0.30	0.00
11-Octadecenoic-Acid	20.46	24.49	18.67	2.73	3.37	20.38	10.74	14.86	7.94	27.12	2.81	5.62	60.80	17.61
Arachidonic-Acid	1.72	2.44	0.34	0.11	0.16	1.64	0.44	0.82	4.89	1.35	0.24	0.13	6.45	1.44
9-Octadecenoic-Acid	0.00	0.00	0.00	0.62	0.00	0.00	1.59	0.00	0.00	0.00	0.00	0.00	0.00	0.00

9,12-Octadecadienoic-Acid	6.27	6.90	3.64	2.39	0.77	4.19	0.00	4.63	13.43	7.92	0.82	0.91	14.71	3.25
Pimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00
2-Ketohexanoic-Acid	0.00	0.00	0.00	0.93	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00
Suberic-Acid	0.17	0.00	0.00	0.00	0.00	3.61	0.00	0.27	0.50	0.60	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	1.85	0.00	0.00	0.00	0.00	0.00	0.00	1.10	0.00	0.00	4.49
Azelaic-Acid	2.29	0.00	1.69	0.00	0.00	3.20	0.65	0.91	1.87	2.63	0.00	0.00	5.88	0.80
Tetradecanedioic-Acid	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.08	0.28	0.01	0.00	0.00	0.00
Malonic-Acid	2.64	1.47	3.05	1.00	0.55	0.00	2.60	1.18	0.81	1.05	1.07	8.44	0.79	1.97
Citric-acid	29.68	78.29	45.08	8.23	13.41	20.36	9.67	14.53	28.27	28.49	0.58	5.07	24.23	2.79
Aconitic-Acid	0.19	2.04	0.00	0.60	0.00	0.00	0.15	0.00	0.45	0.00	0.19	0.00	0.00	0.40
2-Ketoglutaric-Acid	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00
Succinic-Acid	73.30	65.10	53.21	36.13	33.38	71.10	48.88	53.46	55.50	65.18	30.05	37.64	183.36	47.54
Fumaric-Acid	3.84	8.50	4.72	2.10	2.15	3.00	1.81	3.56	5.38	6.71	1.95	1.97	7.59	2.40
Malic-Acid	7.74	9.97	6.04	3.87	3.62	11.84	4.12	7.84	6.68	8.34	2.33	3.42	29.51	3.94
Lactic-Acid	132.59	368.16	636.39	158.89	330.14	235.98	995.11	376.57	373.60	162.84	284.96	377.08	508.39	725.04
Lactyllactate	3.99	0.62	48.23	202.56	0.04	0.00	7.69	0.42	0.20	1.43	215.30	0.07	0.88	4.32
Pyruvic-Acid	1.94	0.96	1.45	1.75	0.08	0.18	0.19	0.48	0.57	2.68	0.78	0.28	1.49	2.46
GLYCOLIC-DITMS	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00
3-Ketobutyric-Acid	36.15	0.90	14.40	0.00	1.05	1.19	1.12	2.22	0.27	11.28	0.08	3.70	4.45	1.48
3-Ketobutyric-AcidtriTMS	0.00	0.00	0.00	0.00	1.05	0.00	0.00	0.00	0.00	0.00	0.00	1.18	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	1.44	2.03	0.00	0.00	2.86	0.00	0.18	0.00	2.32	0.00	1.23	1.38
N-Acrylglycine	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oxalic-Acid	5.02	15.95	5.14	6.10	2.30	6.45	6.11	6.46	0.69	14.16	6.22	3.28	34.33	3.60
3-Methylglutaconic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.04	0.00	0.05
3-Hydroxyisobutyric-Acid	2.43	1.71	3.20	2.85	7.96	0.73	2.81	0.89	0.00	2.06	1.42	6.17	0.66	2.19
3-Hydroxyisovaleric-Acid	0.00	0.00	0.00	4.92	0.35	0.79	0.00	0.00	1.15	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.26	0.00	0.00	0.00	0.21	0.00	0.00	0.22	0.00	0.00	0.00	0.35	0.00	0.23
2-Hydroxyisocaproic-Acid	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisovaleric-Acid	0.16	0.00	0.00	0.29	0.11	0.00	0.05	0.00	0.00	0.00	0.00	0.05	0.00	0.00
2-Keto-3-Methylvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	1.40	0.12	1.21	4.80	0.61	0.00	0.06	0.34	0.00	0.50	6.33	0.00	0.86
4-Hydroxyphenyllactic-Acid	3.28	6.39	1.61	0.45	0.63	0.59	0.53	2.32	2.51	3.46	0.07	0.60	5.73	0.83
N-Acetyltyrosine	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.31	0.00	0.00	4.24	5.09	0.00	2.00	0.00	0.00	0.00	3.68	4.65	0.00	1.65
3-Hydroxypropionic-Acid	1.57	0.87	7.33	3.25	9.70	0.79	5.43	0.68	0.42	1.48	4.98	7.02	4.16	3.98
Methylmalonic-Acid	0.00	0.27	0.00	29.62	0	0.00	0.00	0.00	72.50	0.00	0.00	0	175.90	0.00
Methylmalonic-Acid-Tritms	0.56	0.21	0.50	0.00	0.00	0.00	0.00	0.39	0.45	0.63	0.00	0.00	0.74	0.00
N-Propionylglycine	0.00	35.23	16.69	10.97	46.85	75.06	20.25	0.00	14.39	17.38	4.56	20.23	64.96	12.84
N-Isobutyrylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	25.38	0.00	0.00	0.00	0.00	0.00

Glutaric-Acid	1.90	0.00	0.40	0.72	0.43	0.00	0.00	0.00	0.00	0.59	0.66	0.58	4.25	0.52
2-Ketobutyric-Acid	0.61	1.42	1.79	0.00	1.47	1.15	4.44	5.38	0.85	11.50	0.57	2.00	1.85	0.25
2-Hydroxybutyric-Acid	0.00	0.00	1.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Phenylacetylglycine	2.91	0.33	0.00	0.00	0.00	1.00	0.00	2.04	0.00	0.00	0.00	0.00	4.24	0.00
Cyclohexanecarboxylic-Acid	0.00	0.00	4.36	0.00	2.40	0.00	0.00	0.14	0.00	0.00	0.00	1.76	0.00	0.00
2-Hydroxyglutaryllactone	1.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methylglutaconic-Acid-triTMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.74	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.00	0.38	0.21	0.04	0.40	0.00	0.20	0.08	0.47	0.48	0.00	0.35	2.21	0.00
4-Hydroxyphenylacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.00
Phenylacetic-Acid	0.00	2.45	0.00	0.00	0.00	0.39	0.97	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.36	0.00	0.00	0.00
N-Acetyltyrosine	0.00	0.09	0.00	0.00	0.00	0.11	0.13	0.34	0.21	0.45	0.00	0.00	0.11	0.00
Pyroglutamic-Acid	181.18	228.83	0.00	99.27	150.08	137.99	174.31	157.36	200.67	9.17	108.21	132.58	677.18	189.29
Uracil	4.11	4.96	172.25	0.00	0.00	2.13	1.44	1.73	2.44	0.08	0.00	0.00	8.14	1.39
Pyrimidinedione	0.88	0.00	0.93	1.45	0.52	0.00	0.12	0.00	0.00	1.35	0.99	0.31	0.84	0.20
5-Methylpyrimidine-2,4-Diol	0.29	1.47	0.60	0.00	0.00	0.00	0.00	0.12	0.00	1.16	0.00	0.00	3.52	0.00
3-Hydroxy-3-Methylglutaric-Acid	0.07	0.31	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	125.37	68.22	0.00	0.00	0.00	0.00	0.00	409.66	105.99
Benzoic-Acid	0.45	0.00	0.99	2.87	0.84	0.46	0.00	0.31	0.00	0.34	1.72	0.00	0.00	0.71
Hippuric-Acid	6.84	3.13	1.03	1.68	0.00	1.46	0.00	4.76	2.30	1.69	2.03	0.00	4.16	1.94
1-(4-hydroxyphenyl)ethanone	0.00	8.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.47	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.03	3.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxypropanoic-Acid	1.05	2.17	0.73	0.05	0.58	1.07	1.01	0.00	1.79	0.78	0.32	0.41	6.32	0.60
2,4-Dihydroxybenzoic-Acid	0.00	0.09	0.52	0.00	0.00	0.00	1.14	0.00	0.28	0.02	0.00	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0	0	0	2.07	0.00	0.00	0.00	0.00	0.00	3.06	0.85	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	0.25	20.88	0	3.07	0.00	0.00	0.00	6.81	34.08	39.1	0.19	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	2.05	151.87	0	0	0.27	0.00	0.10	0.11	167.91	0	0.00	0.00	0.00	0.04
3-(4-Hydroxy-2,5-Dioxoimidazolidin-4-yl)pr	0	0	0	0.04	0.00	0.00	0.00	0.00	0.00	2.5	0	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0	0	1.18	0.6	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0	0	0.15	0	3.08	6.47	0.90	0.00	0	0.31	0	1.43	21.48	0.55
3-Hydorxybenzoic-Acid	0.13	1.51	0.25	0.05	0.00	0.00	0.53	0.07	0.41	0.34	0.06	0.10	0.41	0.00
4-Hydroxbenzoic-Acid	0.65	2.22	0.6	0.69	0.18	0.34	0.31	0.96	0.23	0.82	0.8	0.21	1.15	0.43
4-Hydroxymandelic-Acid	1.65	0.14	1.89	0.74	0.00	0.00	0.00	2.38	1.98	2.07	0.88	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0	0	0.06	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
5-Hydroxyhydantoin	0.03	0	0	0.06	0.00	0.00	0.00	0.00	0	0	0.01	0.00	0.00	0.03
4-Hydroxyphenylacrylic-Acid	0	0.14	2.08	0	0.02	0.04	0.10	0.09	0	0	1.01	0.00	0.13	0.07
Erythro-Pentonic-Acid	0	79.4	0.13	0	0.00	0.00	0.00	0.00	80.35	0.19	0	0.00	45.38	0.00
Citraconic-Acid	0.49	1.59	0	0.7	0.00	0.00	0.00	0.97	0.54	0	0.39	0.00	0.00	0.00

Citramalic-Acid	0.16	0.21	0.11	0	0.00	0.00	0.00	0.24	0.31	0	0	0.00	0.00	0.00
Maleic-Acid	0.86	0.45	1.29	0.59	0.00	0.63	0.65	0.20	1.64	0.45	0.3	0.00	0.56	0.72
Parabanic-Acid	0.06	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.04	0.00
Pantothenic-Acid	0.00	0	0	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
2-Isopropyl-3-Ketobutyric-Acid	0.00	0	0	0.22	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Pantoyllactone	0.56	0.7	5.83	2.26	3.73	0.00	0.00	0.14	0	0	1.81	3.51	0.00	0.00
Pentadecanoic-Acid	0.38	0.53	0.75	0.77	0.00	0.75	0.14	0.33	1.11	0.91	0.25	0.12		0.61
Pyrrole-2-Carboxylic-Acid	0.00	0	0	0	0.00	0.00	0.00	0	0.00	0	0.99	0.00	0.00	0.00
Urea	11.36	2.78	0	0	0.00	0.00	0.00	5.88	0.64	0	0	0.00	0.00	0.00
Vanillic-Acid	0.00	0	0	0.3	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	1.91	0.97	449.57	5.31	380.48	1.59	0.00	1.77	1.05	0.02	2.03	522.47	5.32	0.00
2,4,6-Trihydroxy-1,3,5-Triazine	0.00	0.00	0.33		0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
2,3-Dihydroxybenzoic-Acid	0.07	0	0.06	0.54	0.00	0.00	0.00	0.03	0.59	4.11	0.01	0.00	0.40	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	73.84	0.00	0.00	0.00	0.03	0.00	0.93	0	0.00	0.00	0.00	0.00
2,3,3-Trihydroxy-2-Propenoic-Acid	0.00	0.37	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
1,2,3-Trihydroxypropane	3.77	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0	0.66	0.13	0.00	0.00
2-Methyl-2-Propylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.1	0	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.72	0.00	0.00	0.00	2.86	0.00	0.00	0	0	0	0.00	0.00	0.00
1,3-Benzenedicarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.01	0	0	0.00	0.00	0.13
2-Hydroxycinnamic-Acid	0.00	0.00	0.91	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.1	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.28	0.00	0.00	0.00
4-Methoxymandelic-Acid	0.00	0.00	4.71	0.00	0.00	0.00	0.00	0.00	7.47	0	0	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0	0.00	0.00	0.00	0.00	0.00	0.00	0.2	0.00	0	0	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.11	0.00	0.39	0.88	0.54	0.00	0.00	0.00	0.00	0.72	2.41	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	0.00	2.78	0.00	0.83	0.74	0.00	0.00	0.00	0.00	2.39	2.18	0.00	0.00	0.00
3,4-Dihydroxy-3,7,11-Trimethyldodecanoic	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
3-Methoxymandelic-Acid	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
2-Methyl-4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.92	3.48	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenyldecanoic-Acid	0.00	0.00	0.00	0.00	0.56	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.64	0.00	0.00	0.00	0.00	0.00	0	0.90	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	6.20	0.00
2-(Hydroxymethyl)phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00
4-(Hydroxymethyl)Phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00
N-Acrylylglycine	0.00	0.00	17.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.12
Ethylmethylmalonic-Acid	82.96	29.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	41.63	0.00	0.00	0.00	0.00
Glyoxylic-Acid	2.35	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
1,2-Butanediol	0.00	0.00	0.00	0.33	0.51	0.00	0.00	0.00	0.00	0	0.04	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.34	0.00	0.00	0.09	0.00	0.00	0.00	0.25	0.00	0	0.22	0.00	0.00	0.00
Cyclopentanecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.29	0.00	0.00	0.00

2,3-Dihydroxybutane	0.11	2.85	33.66	13.63	2.04	1.45	1.50	0.00	2.05	175.71	0.73	1.15	435.17	1.09
1,2-Dihydroxypropane	0	0.00	0.00	0.00	0.00	0.00	0.00	0	1.06	0.24	0	0.00	0.00	0.00
2,4-Dihydroxy-4-Methyl-2-Pentene	0	4.57	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	1.32	0.00	0.00	0.00
1,4-Dihydroxy-2-Butene	0	0.00	0.00	0.00	0.00	0.29	0.00	0	0.00	0	0	0.00	0.90	0.00
1,4-Dihydroxybutane	0	0.00	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0	0	0.02	0.00	1.18
4-Phenol	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0	0.04	0.00	0.00
1,13-Dihydroxytridecane	0	0.00	0.51	0.00	0.00	0.00	0.00	0	0.00	0	0	0.00	0.00	0.00
1,3-Dihydroxy-2-Ketopropane	0	0.00	1.83	0.00	0.21	0.00	0.00	0	0.00	0	0	0.00	0.00	0.00
1,2-Dihydroxybenzene	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0	0.06	0.00	0.00	0.00
1,2-Dihydroxy-3-Methylbutane	0	0.00	0.00	0.44	0.00	0.00	0.00	0	0.00	0	1.38	0.00	0.00	0.00
1,2-Dihydroxyethane	0	0.65	1.72	0.71	0.10	0.31	0.00	0.31	0.00	1.92	0	0.13	0.00	0.00
1,2-Dihydroxycyclohexene	50.69	225.69	40.02	0.00	0.71	1.90	0.00	0.5	205.51	2.31	31.77	0.41	0.00	0.00
1,3-Dihydroxy-2-Ethylpropane	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
Galactopyranose-Alpha-D	0.74	2.16	0.94	0.00	0.00	0.00	0.00	0.81	0.53	1.04	0	0.00	0.00	0.00
Glucopyranose	0.88	1.31	1.02	0.00	0.00	0.42	0.00	0.00	0.00	1.17	0	0.00	1.04	0.00
Fucose	1.64	0.00	0.55	0.10	0.00	0.00	0.13	0.78	0.38	0	0.04	0.00	0.00	0.00
Arabinitol	0.00	0.00	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
Arabinose	0	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	1.16	0	0.00	0.00	0.00
Rhamnose	0.00	0.00	0.03	0.34	0.00	0.00	0.21	0.00	0.38	0	0	0.00	0.91	0.08
Ribose	0.00	0.00	0.73	0.00	0.00	0.00	0.00	0.00	0.00	2.09	0	0.00	0.00	0.00
Galactose	1.18	0.00	0.00	0.00	0.00	0.61	0.00	0.92	0.00	0	0	0.00	0.00	0.00

	3-bromopyruvate (3.75 mM) and Rotenone (10 nM)							3-bromopyruvate (5.2 mM) and Rotenone (1000 nM)						
	Repeat number							Repeat number						
Organic acid	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	0.00	0.00	0.00	0.87	0.00	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
Octanoic-Acid	0.00	0.00	0.00	0.00	0.05	0.05	0.00	0.00	0.00	0.00	0.05	0.10	0.00	0.00
Hexanoic-Acid	0.00	0.00	0.00	0.00	0.09	0.00	0.00	3.13	0.00	0.00	0.00	0.00	0.00	0.00
NoAcid	0.23	0.04	0.25	0.31	0.17	0.21	0.04	14.38	0.00	0.24	0.32	0.35	0.31	0.11
DecAcid	0.17	0.21	0.28	0.19	0.03	0.00	0.00	1.05	0.00	0.13	0.16	0.08	0.00	0.00
EicAcid	0.39	0.16	0.00	0.09	0.00	0.05	0.11	2.95	0.03	0.30	0.10	0.00	0.12	0.11
Dodecanoic-Acid	0.62	1.17	0.57	1.75	0.39	0.00	0.91	8.26	0.57	0.09	0.28	0.48	0.00	1.10
Tetradecanoic-Acid	3.21	2.64	0.37	7.50	0.74	2.11	1.64	40.45	1.77	1.11	1.28	1.25	1.90	2.40
Palmitic-Acid	62.73	94.43	69.41	83.83	16.51	40.71	40.40	935.88	64.66	47.05	34.38	17.86	33.65	39.27
Heptadecanoic-Acid	1.27	2.68	1.63	1.61	0.19	1.06	0.87	17.94	2.06	1.42	0.58	0.14	0.85	0.73
Octadecanoic-Acid	10.12	80.64	46.06	75.30	9.56	33.98	32.85	636.82	46.52	32.93	26.13	8.88	25.43	35.71
6-Octadecenoic-Acid	0.00	1.47	0.00	0.66	0.00	0.00	0.00	4.54	0.00	0.00	0.00	0.00	0.00	0.00
Isovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.52	0.00	0.11	0.12	0.00	0.00
Docosanoic-Acid	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.02
3-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.03
2-Hydroxyoctadecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.08	0.21	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.36	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.00	0.48	0.00	0.00	0.00	0.04	0.00	1.72	0.00	0.15	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	29.88	0.00	1.53	0.00	0.00	0.27	0.00	1.78	0.12	0.00	0.00	0.00	0.00	4.61
2-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.33	0.00	0.00	478.23	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	31.51	40.42	37.54	12.93	6.57	0.00	21.71	208.37	35.16	22.38	13.43	5.47	0.00	20.46
2-Hydroxyundecanoic-Acid	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.93	0.00	0.00	0.00	0.00
2-Hydroxyhexacosanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00
3-Hydroxylauric-Acid	0.42	0.00	0.21	0.00	0.05	0.05	0.00	0.00	0.00	0.00	0.00	0.02	0	0.08
2-Hydroxysebacic-Acid	1.40	0.00	2.26	0.10	0.00	0.40	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	0.00	0.00	0.00	25.47	0.00	0.00	0.00	0.00	0.00	0.00	18.27	0.00
Palmitelaidic-Acid	1.19	1.06	1.60	0.22	0.43	1.23	0.86	8.97	1.43	0.96	0.33	0.32	0.94	0.78
Oleic-Acid	5.69	0.00	6.72	12.81	6.36	5.24	4.09	397.16	0.00	21.59	13.78	5.50	3.71	3.90
2-Undecenoic-Acid	0.42	0.00	0.21	0.00	0.05	0.05	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.08
11-Octadecenoic-Acid	31.51	40.42	37.54	12.93	6.57	25.47	21.71	208.37	35.16	22.38	13.43	5.47	18.27	20.46
Arachidonic-Acid	3.39	5.96	0.00	1.39	0.45	3.15	1.99	40.06	4.84	2.41	1.80	0.17	1.56	2.25
Linolenic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	13.47	0.00	0.00	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	1.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	8.96	14.58	11.18	3.62	1.26	5.53	3.62	134.73	13.63	6.76	3.96	0.93	3.52	3.82
Pimelic-Acid	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00

Suberic-Acid	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hexenedioic-Acid	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	1.75	0.00	0.00	1.32	0.00	0.00	0.00	0.79	0.00	0.00	0.00
Azelaic-Acid	5.58	0.00	0.00	0.00	0.00	0.64	1.22	16.24	0.00	0.00	0.00	0.00	0.58	1.37
11-Eicosenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00
Tetradecanedioic-Acid	0.02	0.06	0.26	0.01	0.07	0.00	0.00	0.00	11.17	0.00	0.03	0.00	0.00	0.00
Malonic-Acid	0.26	0.87	1.04	2.02	0.30	37.34	1.24	5.65	0.76	0.87	0.31	0.52	0.55	0.00
Citric-acid	5.96	17.03	17.29	2.54	0.43	3.36	1.83	0.00	15.56	5.94	1.61	2.18	1.52	1.45
Aconitic-Acid	0.15	0.20	0.46	0.30	0.00	0.15	0.00	0.00	0.57	0.09	0.20	0.00	0	0.00
2-Ketoglutaric-Acid	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Succinic-Acid	53.06	61.21	62.19	40.81	27.31	44.17	38.95	2.72	52.48	54.38	39.80	27.47	39.73	34.57
Fumaric-Acid	1.26	3.60	3.26	0.89	0.80	0.92	1.07	0.00	2.32	1.26	1.45	0.99	1.03	1.24
Malic-Acid	1.90	3.54	6.48	0.92	2.60	7.19	3.30	0.00	2.70	1.46	3.33	2.15	3.16	1.66
Lactic-Acid	177.38	148.16	219.66	487.92	348.09	516.00	86.26	98.56	122.28	175.81	384.79	381.42	461.25	111.62
Lactyllactate	0.00	0.00	0.00	0.00	0.00	0.49	0.00	0.00	0.00	0.00	0.08	0.00	0.13	0.00
Pyruvic-Acid	0.82	5.95	15.50	1.18	0.46	0.65	3.16	74.52	0.45	7.31	1.37	0.41	0.36	0.21
GLYCOLIC-DITMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	5.90	0.40	11.83	1.00	0.37	10.77	0.42	233.10	0.33	24.82	1.04	0.00	11.79	0.54
3-Hydroxybutyric-Acid	0.00	0.15	0.37	2.94	3.26	4.38	1.19	0.00	0.00	0.00	2.28	0.00	4.87	2.05
Oxalic-Acid	19.90	38.76	57.76	5.18	53.54	5.79	75.24	11.85	19.80	16.04	29.86	58.58	25.01	66.84
3-Methylglutaconic-Acid	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00
3-Hydroxyisobutyric-Acid	1.20	0.00	1.70	1.06	0.00	3.89	0.71	0.00	1.46	0.56	0.00	0.00	0.00	0.91
3-Hydroxyisovaleric-Acid	0.00	0.00	0.13	2.10	0.00	0.00	0.00	0.00	0.00	0.00	3.00	2.79	0.00	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.00	0.00	0.00	0.42	0.07	0.22	0.00	0.00	0.00	0.37	0.00	0.65	0.00	0.00
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.15	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Keto-3-Methylvaleric-Acid	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.00	1.33	1.12	2.78	2.29	0.00	0.00	0.00	0.00	0.00	3.32	0.00	0.00
4-Hydroxyphenyllactic-Acid	0.57	1.33	2.19	0.00	0.20	0.50	0.00	0.00	1.61	0.51	0.18	0.13	0.42	0.00
3-Hydroxyvaleric-Acid	0.00	0.00	1.22	0.00	2.20	1.44	0.00	0.00	1.56	0.00	4.87	0.00	2.27	0.97
3-Hydroxypropionic-Acid	8.83	9.68	14.03	89.43	51.02	67.58	7.93	80.65	15.00	17.28	85.26	57.43	113.55	17.94
Methylmalonic-Acid	3.44	41.91	2.97	0.00	0.00	0.00	0.00	0.00	0.69	0.15	2.20	0.00	35.85	0.00
Methylmalonic-Acid-Tritms	0.44	0.15	1.13	0.23	0.00	0.00	0.00	28.44	0.46	0.25	0.36	0.00	0.00	0.00
N-Propionylglycine	0.00	0.00	0.00	0.00	1.08	2.96	0.70	0.00	0.90	0.00	0.00	1.81	1.37	1.05
N-Isobutyrylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.81	0.00	0.00	0.00	0.00	0.00
Propionic-acid	0.04	0.00	0.00	0.10	0.00	0.00	0.00	1.02	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.00	0.56	0.00	0.35	0.00	0.00	0.39	0.00	0.18	0.73	1.96	0.00	0.20	0.41
Glutaconic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00
2-Ketobutyric-Acid	7.76	2.58	18.59	3.82	3.98	11.65	3.39	423.54	4.57	13.14	2.45	3.93	0.94	7.38
2-Hydroxybutyric-Acid	0.00	0.73	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

2-Methyl-3-Ketobutyric-Acid	0.00	0.00	0.11	0.00	0.00	0.00	0.00	2.26	0.00	0.05	0.00	0.00	0.04	0.00
N-Phenylacetylglycine	2.41	0.45	0.49	0.65	0.00	0.00	0.00	0.00	1.15	8.20	0.82	0.00	0.00	0.00
Cyclohexanecarboxylic-Acid	0.00	0.00	0.00	0.00	5.91	4.76	0.00	0.00	0.00	0.00	0.00	4.33	4.54	0.00
2-Hydroxyglytaric-Acid	0.30	0.27	0.00	0.08	0.29	0.45	0.00	0.00	0.09	0.16	0.02	0.01	0.50	0.00
4-Hydroxyphenylacetic-Acid	0.23	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00
Phenylacetic-Acid	2.47	1.00	2	0.00	0.00	3.36	0.11	0.00	1.67	4.56	0.00	0.00	3.08	0.21
Phenylpyruvic-Acid	0.00	0.50	0.06	0.00	0.00	0.96	0.00	0.00	0.00	21.28	23.59	0.00	0.00	0.00
4-Hydroxybutyric-Acid	0.00	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
N-Acetyltyrosine	0.75	0.14	0.00	0.00	0.00	0.26	0.00	0.00	0.00	0.50	0.00	0.00	0.06	0.10
N-Acetylaspartic-Acid	0.00	0.00	0.00	0.00	0.00	0.48	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	4.14	252.20	21.56	201.66	179.39	223.10	217.00	0.00	257.71	152.15	136.28	172.40	181.71	185.04
Uracil	2.02	0.96	0.78	0.00	0.00	0.50	0.45	0.00	0.91	0.50	0.00	0.09	0.32	0.26
Pyrimidinedione	39.90	9.29	5.97	30.34	7.12	12.46	16.13	0.00	27.11	64.37	36.35	32.04	19.12	27.44
2-Hydroxyhippuric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00
3-Hydroxy-3-Methylglutaric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0	0.09	0.00	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.11	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	96.42	58.54	0.00	0.00	0.00	0.00	0.00	53.87	58.05
Benzoic-Acid	0.53	0.00	0.00	1.97	0.00	0.00	0.55	0.00	0.00	0.24	0.96	0.00	1.04	0.00
Hippuric-Acid	5.44	5.71	2.56	2.27	0.00	2.11	1.11	5.93	3.25	4.17	2.41	0.00	1.57	1.10
2,4,6-Trihydroxybenzoic-Acid	0	0.00	0.00	0.00	0.01	0.12	0.17	0	0.19	0.00	0.00	0.00	0.39	0.07
2,4,5--Trihydroxybenzeneacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxypropanoic-Acid	25.56	30.24	49.50	34.37	19.40	18.69	11.26	0	38.00	37.97	37.31	25.43	21.69	16.00
2,4-Dihydroxybenzoic-Acid	0.00	0.1	0.69	0.11	0.00	0.00	0.00	1.01	0.91	0.27	0.00	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0	0	0	0.09	0.00	0.00	0.03	0	0	0.17	0	0.00	0.00	0.00
2,6-Dihydroxypyrimidinecarboxylic-Acid	0.00	0	64.26	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	5.95	31.21	0	7.16	0.00	0.00	0.00	26.48	19.38	71.61	0.7	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	0.64	184.32	61.54	0.31	0.13	0.05	0.18	0.00	0	0.66	0	0.00	0.46	0.08
2-Hydroxyisobutyric-Acid	0	0.52	0.00	0	0.76	1.89	0.00	0.00	0	0	0	0.00	2.69	0.00
3,4-Dihydroxybutyric-Acid	0	0	0.21	0.15	2.31	2.25	0.38	2.03	0	0	0	2.20	1.48	0.19
3-Hydorxybenzoic-Acid	0.16	0.21	0.42	0.21	0.00	0.00	0.38	52.60	0.67	0.2	0.12	0.05	0.00	0.00
4-Hydroxbenzoic-Acid	0	0.92	0.52	1.54	0.26	0.00	0.00	0.00	0.52	0	0.94	0.09	0.36	1.24
4-Hydroxymandelic-Acid	3.02	2.4	2.31	1.34	0.00	0.00	0.00	47.53	1.98	1.5	1.14	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.00	0	0.21	0.15	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
5-Hydroxyhydantoin	0.00	0.26	0	0.07	0.00	0.00	0.05	7.24	0	0.64	0.03	0.00	0.00	0.03
4-Hydroxyphenylacrylic-Acid	0.05	0	0	0	0.01	0.00	0.00	0.00	0.08	1.2	0	0.00	0.00	0.00
Dimethylmalonic-Acid	0	0	0	0	0.00	0.00	0.33	0.00	0	2.44	0	0.39	0.00	0.00
Erythro-Pentonic-Acid	0	0	0.12	0	0.00	0.15	0.00	0.88	129.53	0	0	0.00	0.00	0.00
Citraconic-Acid	0.88	0.85	0	0.93	0.00	0.00	0.00	75.57	1.27	0	0.81	0.00	0.00	0.00
Citramalic-Acid	0.13	0.00	0	0	0.00	0.00	0.00	0	0.00	0.11	0	0.00	0.00	0.00

Threitol	0	0	0	0	0.00	0.00	0.00	1.21	0	0	0	0.00	0.00	0.00
Maleic-Acid	0.59	0	1.13	1.36	2.88	0.03	0.48	63.22	44.14	0.08	0.06	0.01	0.00	0.97
Parabanic-Acid	0	0	0	0	0.00	0.00	0.00	0	0	0.61	0	0.00	0.00	0.00
2-Isopropyl-3-Ketobutyric-Acid	0.00	0.00	0	0	0.00	0.00	0.00	0.00	0	1.99	0.36	0.00	0.00	0.00
Pantoyllactone	0.27	0	1.95	2.54	4.62	4.48	0.00	3.67	0.49	1.36	2.95	4.10	6.35	0.00
Pentadecanoic-Acid	0.81	1.27	1.3	1.26	0.18	0.46	0.57	0	0.84	0.66	0.36	0.37	0.42	0.49
Pyrrole-2-Carboxylic-Acid	2.58	0	5.35	0	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
Urea	9.81	0.9	0.00	0	0.00	0.00	0.00	298.34	0	0	0	0.00	0.00	0.00
Vanillic-Acid	0.00	0	0.00	0.05	0.00	0.00	0.00	0.00	0	0	0	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	1.78	555.26	1.86	2.36	24.39	0.00	1.41	0.00	0.98	1.7	1.37	1.43	0.00	0.00
4-Methylmandelic-Acid	0.00	0.00	2.77	0	0.00	0.00	0.00	0.00	0.00	0	0	0.00	0.00	0.00
2,3-Dihydroxybenzoic-Acid	0.38	0	0.19	3.59	0.00	0.11	0.04	0.00	0.15	0.07	0	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	144.29	2.72	0.00	84.49	0.00	0.00	0.00	0.00	79.99	0.00	0.00	0.00	0.00
2-Methyl,2,3-Dihydroxypropanoic-Acid	0.00	0.00	0	0.23	0.00	0.00	0.00	0.00	1.32	0.00	0.1	0.03	0.00	0.00
2,3,3-Trihydroxy-2-Propenoic-Acid	0.51	4.29	0.67	1.43	2.51	0.29	1.23	0.00	4.36	0.78	1.52	2.30	0.00	1.82
2,3-Dihydroxyacrylic-Acid	0.25	0.16	3.26	0.20	0.20	2.01	0.00	0.00	0.00	0.51	0.11	0.14	1.12	0.00
1,2,3-Trihydroxypropane	3.23	0.00	2.89	2.09	0.00	0.00	0.00	370.98	0.00	0.00	2.29	0.00	0.00	0.00
2-Methyl-2-Propylmalonic-Acid	0.06	0.03	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0	0.00	0.00	0.00	0.00	1.49	0.00	0.00	0.00	0.00	0.00	0.10
Citrazinic-Acid	0.03	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03
1,3-Benzenedicarboxylic-Acid	0.40	0.00	0	0.94	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.24	0.12
2-Hydroxycinnamic-Acid	0.40	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.00	0.00	0	0	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00
3-Hydroxymandelic-Acid	0.62	0.40	0	0	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.9	0.00	0.57	0	0.00	0.00	0.00	28.65	0.00	0.49	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.00	0	0.2	0.00	0.00	0.00	276.64	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	1.70	0.00	0	0.00	0.00	0.00	0.00	26.72	2.62	1.18	0.29	0.00	0.00	0.00
2-Methoxymandelic-Acid	0.00	0.00	0	0.00	0.00	0.00	0.00	68.78	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxy-3,7,11-Trimethyldodecanoi	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00
2-Methyl-4-Hydroxybutyric-Acid	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00
2-Keto-3-Methylbutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00
4-Hydroxproline	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.94	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.41	1.06	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	1.35	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Hydroxymalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.58	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05
2-Methyl-1,2-Dihydroxubutane	0.00	0.00	0	0.00	0.00	0.00	0.00	47.15	0.00	0.00	0.00	0.00	0.00	0.00
Glyoxylic-Acid	1.85	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylhexanoic-Acid	0.00	0.00	0	0.00	0.00	0.00	0.00	13.10	0.00	0.00	0.00	0.00	0.00	0.00

1,2-Butanediol	0.00	0.00	1.14	0.23	0.00	0.00	0.00	1.92	0.00	0.00	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.38	0.00	0.33	0.10	0.00	0.00	0.00	0.00	0.00	0.09	0.12	0.00	0.00	0.00
Tiglic-Acid	0.00	0.48	0	0.00	0.00	0.00	0.00	0.00	0.00		0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.18	2.51	0.38	0.00	1.39	3.85	0.00	9.64	3.42	0.41	0.00	2.07	4.18	0.00
Phenylhydracrylic-Acid	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylsuccinic-Acid	0.00	0.00	0.00	20.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxypropane	0.00	0.00	1.67	0.00	0.00	0.00	0.00	0.00	0	0.23	0.00	0.00	0.00	0.00
1,4-Dihydroxybutane	0.58	3.39	0.57	2.68	3.75	4.01	0.77	0.00	1.93	1.19	3.51	4.39	10.88	1.57
4-Phenol	0	0.00	0	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0	0.02	0.00	0.00
1,13-Dihydroxytridecane	0.85	0.00	1.74	0.00	0.00	0.00	0.00	1.53	0.00	0.00	1.13	0.00	0.00	0.00
1,3-Dihydroxy-2-Ketopropane	0.15	0.00	0	0.00	0.22	0.12	0.04	0	0.00	0.00	0.00	0.39	0.32	0.20
1,2-Dihydroxy-3-Methylbutane	0	0.00	0	0.25	0.00	0.00	0.00	399.13	0.00	0.00	0.16	0.00	0.00	0.00
1,2-Dihydroxyethane	5.77	0.00	4.3	0.19	0.58	0.00	0.00	25.76	0	0.99	0.00	0.00	0.26	0.00
1,2-Dihydroxycyclohexene	22.71	1.27	4.7	20.12	0.00	0.38	0.28	51.95	0.91	95.83	50.54	0.29	0.39	0.00
1,6-Dihydroxyhexaan	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	1.29	0	0	0.00	0.00	0.00
1,3-Dihydroxy-2-Ethylpropane	0	0.00	1.69	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0	0.00	0.00	0.00
Galactopyranose-Alpha-D	2.29	0.53	4.33	0.00	0.00	0.00	0.00	25.21	0.64	1.78	0.5	0.00	0.47	0.00
Galactopyranose-Beta-D	0	0.00	0	0.00	0.00	0.00	0.00	11.79	0.00	0	0	0.00	0.00	0.00
Glucopyranose	0.00	0.00	0	0.20	0.00	0.77	0.00	0.00	0.93	0	0	0.00	0.57	0.00
Glucono-1,5-Lactone	0.61	0.00	0	0.00	0.00	0.00	0.00	40.00	0	0	0	0.00	0.00	0.00
Mannonic1,4-Lactone	1.36	0.00	0	0.00	0.00	0.00	0.00	1.95	0.00	0.66	0	0.00	0.02	0.00
Mannitol	0.00	0.00	0	0.00	0.00	0.00	0.00	43.14	0.00	0	0	0.00	0.00	0.00
Erythronic-Acid	0.04	0.00	0	0.16	0.00	0.00	0.00	0.00	0.00	0	0.16	0.00	0.00	0.00
Fucose	2.95	0.33	0	0.33	0.00	0.00	0.11	27.89	1.23	0	0.36	0.00	0.00	0.00
Rhamnose	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.56	0	0	0.00	0.00	0.00
Ribose	0.00	0.78	0	0.00	0.00	0.00	0.00	2.06	0.00	1.24	0	0.00	0.00	0.00
Galactose	0	0.00	0	0.00	0.00	1.23	0.00	15.76	0.00	0	0	0.00	0.64	0.00

Organic acid	Rotenone (10 nM)							Rotenone (1000 nM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
NoAcid	0.36	0.00	0.00	0.00	0.34	0.05	0.50	0.20	0.00	1.39	0.00	0.45	0.12	0.09
EicAcid	0.22	0.00	0.37	0.00	0.00	0.04	0.07	0.15	0.05	0.00	0.00	0.00	0.15	0.11
Dodecanoic-Acid	0.62	0.27	0.27	0.28	0.64	1.83	1.05	0.55	0.33	8.49	0.29	0.93	3.07	0.86
Tetradecanoic-Acid	1.99	1.85	0.37	1.15	0.78	1.55	1.10	2.14	2.28	11.42	1.09	1.21	4.17	1.38
Palmitic-Acid	27.82	47.21	66.55	16.26	13.58	27.90	20.36	41.16	71.64	381.82	22.15	16.49	76.91	25.42
Heptadecanoic-Acid	0.61	1.31	2.31	0.24	0.14	0.66	0.34	0.70	1.88	1.79	0.27	0.12	1.69	0.47
Octadecanoic-Acid	20.80	38.70	58.82	11.94	9.76	26.02	22.68	30.50	46.18	69.20	19.85	7.58	62.53	28.27
Docosanoic-Acid	0.00	0.00	0.03	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00
3-Methylpimelic-Acid	0.00	0.00	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.08	0.00	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00
3-Hydroxycapric-Acid	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.39	0.21
5-Hydroxyvaleric-Acid	0.00	0.00	2.50	7.60	0.00	0.00	0.08	0.57	3.67	133.62	4.63	0.00	0.00	4.46
2-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.16	0.12	0.00	0.00
2-Hydroxytetradecanoic-Acid	11.23	22.38	0.00	0.29	2.45	0.00	9.96	12.20	35.07	72.91	7.69	0.65	0.00	10.78
2-Hydroxyheptanoic-Acid	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetracosanoic-Acid	0.00	0.00	0.21	0.00	0	0.00	0.00	0.00		0.00	0.00	0	0.00	0.00
2-Keto-Octanoic-Acid	0.00	0.00	0.91	0.00	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00	0.00
3-Methyladipic-Acid	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.06	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.00	0.00	0.00	0.12	0.00	0	0.00	0.07	0.00	0.00	0.00	0.00	0	0.00
2-Hydroxysebacic-Acid	0.00	0.00	3.56	0.00	0.00	0	0.00	0.49	0.00	0.00	0.00	0.00	0	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	37.94	0.00	0.00	14.98	0.00	0.00	0.00	0.00	0.00	0.00	33.04	0.00
Palmitelaidic-Acid	0.20	0.55	1.87	0.00	0.09	0.33	0.20	0.32	1.35	0.00	0.21	0.00	1.51	0.21
Oleic-Acid	11.12	3.94	7.68	3.06	4.77	2.33	1.96	12.37	34.98	0.00	7.65	3.39	6.01	1.82
2-Undecenoic-Acid	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00
11-Octadecenoic-Acid	11.23	22.38	37.94	0.29	2.45	14.98	9.96	12.20	35.07	72.91	7.69	0.65	33.04	10.78
Arachidonic-Acid	0.54	1.87	7.32	0.06	0.13	1.73	0.51	0.71	4.55	0.00	0.28	0.00	1.86	0.62
Linolenic-Acid	0.00	0.00	2.84	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	39.88	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	3.29	6.99	18.05	0.45	0.81	3.48	1.72	3.19	12.51	0.00	1.97	0.47	7.87	1.90
Pimelic-Acid	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.09	0.00	0.30	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.94	0.00	0.00	1.43	0.00	0.00	0.00	0.00	0.00	0.00	24.48	0.00	0.00	0.00
Azelaic-Acid	0.91	0.00	0.00	1.01	0.00	0.00	0.75	0.00	0.00	0.00	0.00	0.00	0.00	0.81
Tetradecanedioic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.65	0.00	0.00	0.00	0.00

Malonic-Acid	2.78	0.73	0.24	1.20	0.13	0.00	0.20	1.27	0.94	3.89	2.62	2.77	0.44	0.00
Citric-acid	22.34	40.59	41.71	4.45	7.14	22.67	4.74	17.62	33.16	0.00	2.63	9.61	14.65	4.93
Aconitic-Acid	0.22	0.85	2.82	0.97	0.20	0.32	0.27	0.08	0.79	0.00	0.40	0.21	0.94	0.00
Succinic-Acid	48.76	56.88	108.59	35.39	30.87	57.80	31.08	41.59	55.56	225.90	32.91	25.38	130.23	34.06
Fumaric-Acid	2.20	5.06	8.37	3.28	2.94	3.47	1.51	2.50	5.97	7.41	2.61	1.28	5.61	1.69
Malic-Acid	7.13	6.00	12.31	5.09	5.06	7.89	1.88	4.70	7.64	23.77	11.33	5.77	19.37	4.16
Lactic-Acid	60.18	397.66	771.48	317.70	388.19	1179.88	920.32	377.82	278.97	540.78	95.14	108.72	1219.10	611.90
Lactyllactate	12.13	0.28	0.73	261.19	0.09	15.86	15.33	55.27	0.16	0.00	198.72	0.03	4.77	1.38
Pyruvic-Acid	0.43	0.15	0.41	0.54	0.41	0.50	0.32	1.29	0.40	3.18	0.62	0.17	0.83	0.55
GLYCOLIC-DITMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.26	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	2.85	0.41	0.48	0.23	0.91	1.36	11.13	0.00	0.42	10.12	0.00	0.00	3.98	0.42
3-Ketobutyric-AcidtriTMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	1.78	0.84	1.15	4.83	0.00	4.53	1.77	0.00	1.57	1.15	0.00	0.00	1.62
N-Acrylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.42	0.00
Oxalic-Acid	2.50	9.09	12.16	13.46	24.60	4.96	1.55	1.12	1.06	23.55	18.26	36.64	60.31	2.65
2-Methyl-3-Hydroxybutyric-Acid	0.21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methylglutaconic-Acid	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyisobutyric-Acid	2.14	0.86	2.88	1.06	3.12	3.08	3.31	0.00	0.00	0.00	1.05	4.48	0.55	0.39
3-Hydroxyisovaleric-Acid	1.50	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	3.56	2.28	0.00	0.00
2-Ethyl-3-Hydroxypropionic-Acid	0.00	0.00	0.00	0.00	0.25	0.00	0.15	0.00	0.00	2.26	0.00	0.06	0.00	0.00
2-Hydroxyisocaproic-Acid	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.29	0.00	0.00	0.00	0.00	0.97	0.00	0.09	0.00	0.00
2-Keto-3-Methylvaleric-Acid	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	1.37	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.00	0.00	0.23	2.56	0.00	0.00	0.00	0.00	0.00	0.25	1.23	0.00	0.10
4-Hydroxyphenyllactic-Acid	0.77	2.90	2.00	0.17	0.39	1.06	0.48	0.85	3.65	0.00	0.47	0.46	2.82	0.46
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.07	0.00	2.35	1.68	0.00	0.00	0.00	0.00	0.00	1.85
3-Hydroxypropionic-Acid	2.31	0.43	2.33	1.33	5.92	0.00	3.99	2.86	7.98	7.21	1.68	5.79	4.77	2.97
Methylmalonic-Acid	3.90	51.18	0.20	0.00	0.00	0.00	0.00	33.94	0.00	0.00	4.34	0.85	0.00	0.00
Methylmalonic-Acid-Tritms	0.11	0.21	0.34	0.00	0.10	0.00	0.23	0.00	0.00	7.63	0.28	0.09	0.00	0.00
N-Propionylglycine	0.00	18.76	36.09	4.96	37.54	0.00	11.08	0.00	14.28	35.80	8.87	22.28	66.10	13.76
Propionic-acid	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.00	0.26	1.83	1.00	0.00	0.62	0.20	0.80	0.92	0.00	1.70	0.00	1.84	0.12
Glutaconic-Acid	0.00	0.00	20.48	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketobutyric-Acid	0.43	1.16	5.29	0.21	2.72	3.66	10.77	3.24	0.93	3.69	0.96	0.11	3.59	3.79
2-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	3.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methylglutaric-Acid	0.00	0.00	0.00	0.00	0	108.70	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00
N-Phenylacetylglycine	2.73	0.62	5.20	0.00	0.00	0.00	0.41	2.30	5.16	0.00	1.39	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.07	0.26	0.68	0.00	0.19	0.00	0.00	0.12	0.32	2.97	0.05	0.00	1.45	0.00
4-Hydroxyphenylacetic-Acid	0.00	0.00	1.46	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Phenylacetic-Acid	0.00	0.28	0.31	0.00	0.69	2.36	2.13	0.86	0.75	0.00	1.22	0.43	1.35	1.26
Phenyllactic-Acid	0.12	0.00	0.06	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylpyruvic-Acid	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.39	728.81	0.00	0.00	0.21	7.33	0	0.00	0.00	0.00
N-Acetyltyrosine	0.22	0.00	0.80	0.00	0.00	0.08	0.05	0.13	0.08	3.00	0.00	0.00	0.00	0.02
N-Acetylaspartic-Acid	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	136.45	317.04	440.79	66.98	166.89	205.68	129.83	88.95	228.74	302.33	118.35	139.52	587.81	146.92
Uracil	2.86	1.98	3.29	0.00	0.90	2.68	2.30	1.86	2.61	0.00	0.00	0.00	6.60	1.11
Pyrimidinedione	1.19	0.26	0.00	0.00	0.19	0.14	0.11	0.90	0.40	0.00	0.00	0.00	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.39	0.29	0.00	0	0.00	0.21	0.00	0.22	0.00	0	0.00	0.00	0.00	0.00
3-Hydroxy-3-Methylglutaric-Acid	0.10	0	0.42	0.00	0.00	0.00	0.00	0.00	0.00	0.61	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.11	0.00	0.00	0	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	240.09	0.00	0.00	132.13	71.73	0.00	0.00	0.00	0.00	0.00	285.70	71.86
Benzoic-Acid	0.46	0.00	0.00	0.73	0.00	1.07	1.24	0.42	0.00	5.49	0.75	0.46	1.47	0.58
Hippuric-Acid	5.43	2.23	2.59	0.95	0.00	1.83	1.22	3.19	3.70	1.70	2.18	0.00	2.13	0.95
Depakin-Glucuronide	1.37	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00
1-(4-hydroxyphenyl)ethanone	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0	0.00	0.00	0	0.00	0.00	0.25	0.00	0.02	0.07	0
2,3-Dihydroxypropanoic-Acid	0.38	1.96	1.13	0.28	0.34	2.84	0.77	0.00	2.40	0.00	0.00	0.43	5.57	1.06
2,4-Dihydroxybenzoic-Acid	0.05	0.18	0.00	0.00	0.00	0.00	0.00	0.09	0.11	12.07	0.15	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0	0	0.00	8.58	0.00	0.00	0	0.82	0	15.08	0	0.02	0.00	0
2,6-Dihydroxybenzoic-Acid	9.68	32.33	0.00	0	0.00	0.00	0.00	18.79	33.96	706.59	7.9	0.00	0.00	0.00
2-Piperidinecarboxylic-Acid	3.03	0.95	0.00	45.22	0.00	154.93	0.06	0.00	0	101	0	0.00	12.69	0
2,3,4-Trihydroxybutyric-Acid-Lactone	0.09	0	0.00	0	0.00	0.00	0.00	0.03	0	0	0	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0	0	0.00	0.14	1.98	0.00	0.00	0.00	0	0	0	0.00	1413.76	0.00
3,4-Dihydroxybutyric-Acid	0	0	3.91	0	1.99	2.94	0.33	0.00	0	0	0	1.66	0.00	1.61
4-Hydroxbenzoic-Acid	0.72	0	1.49	0.44	0.21	0.00	0.32	0.52	0.61	3.97	0.68	0.12	0.16	0.26
4-Hydroxymandelic-Acid	1.73	1.01	0.00	1.15	0.00	0.00	0.00	1.34	0.55	10.42	1.28	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.00	0	0.00	0	0.00	0.00	0.00	0.00	0	1.02	0	0.00	0.00	0.00
5-Hydroxyhydantoin	0.46	0	0.78	0.02	0.03	0.11	0.00	0.03	0	0	0	0.00	0.00	0
4-Hydroxyphenylacrylic-Acid	4.95	0.15	0.00	0	0.00	0.06	0.00	0.00	0.74	0.26	0	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.06	0	0.34	0	0.00	0.00	0.00	0.00	0	1.06	0	0.00	0.40	0.00
Citraconic-Acid	0.93	0.19	0.92	0.64	0.00	0.79	0.00	2.32	1.65	0	0.71	0.00	0.00	0.00
Citramalic-Acid	0.48	0.16	9.81	0	0.00	0.00	0.00	3.48	0.00	0	0	0.00	0.00	0.00
Threitol	0	0.12	0.14	0	0.00	0.00	0.00	0	0	0.04	0	0.00	0.00	0.00
Levulinic-Acid	0	0	0.00	0	0.00	0.00	0.00	0	0	0.2	0	0.00	0.00	0.00
Maleic-Acid	0.62	0.2	0.34	0.42	0.03	0.05	0.00	0.21	0.25	0.97	6.55	0.04	0.00	0.16
Parabanic-Acid	0.17	0	0.00	0	0.00	0.00	0.00	0	0	0	0	0.00	0.00	0.00
Mandelic-acid	0	0	0.00	0	0.00	0.00	0.00	0	0	0	0.56	0.00	0.00	0.00

Pantoyllactone	0.54	0	0.65	1.8	5.25	0.94	0.89	0.58	0	0	0.51	2.60	0.00	0.00
Pentadecanoic-Acid	0.37	0.47	1.10	0.08	0.28	0.25	0.32	0.71	0.8	8.8	0.25	0.31	0.72	0.31
Urea	4.04	2.26	15.72	0	0.00	2.43	0.00	0.00	0.74	0	0	0.00	0.00	1.62
3-Methyl-4-Hydroxybutyrate	425.67	642.06	2.94	496.28	7.01	7.95	0.66	1.51	1.37	610.44	2.25	4.21	5.08	142.19
2,3-Dihydroxybenzoic-Acid	12.63	8.25	0.07	0.01	0.00	0.00	0.00	0.00	0.07	0.14	0.18	0.00	0.00	0.09
2-Ketopyrrolidine-1-Carboxylic-Acid	2.73	8.2	0.00	0.00	0.00	0.31	0.00	0.00	0.00	119.68	0.00	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.00	0	0.19	390.60	0.15	0.00	0.00	0.00	0.00	0	0.00	0.28	0.00	9.46
2,3,4-Trihydroxybenzoic-Acid	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.89	0.00	0.03	0.00	0.13
1,3-Benzenedicarboxylic-Acid	0.58	0	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.28	0.00	0.00
3-Hydroxyacetophenone	0.00	0	0.00	7.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0	0.00	0.71	0.00	0.00	0.00	0.00	0.85	0.00	0.79	0.00	0.00	0.00
2-Ethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dimethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methoxymandelic-Acid	2.04	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dimethyl-3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.00	0	0.93	0.00	0.00	0.00	0.00	0.00	0.00	3.11	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.15	0.00	2.50	0.68	0.00	0.00	0.08	0.00	0.00	0.39	0.32	0.00	0.00
2-Hydroxyphenylpropionic-Acid	1.45	2.87	0.00	0.00	0.00	0.00	0.00	0.00	3.94	0.00	1.91	0.00	0.00	0.00
2-Methoxymandelic-Acid	4.28	5.96	0.00	0.00	0.00	0.00	0.00	2.49	9.86	0.00	0.00	0.00	0.00	0.00
4-Methylcinnamic-Acid	0.00	0	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxyphenylheptanoic-Acid	0.00	0	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00
3-Methoxymandelic-Acid	0.00	0	0.00	0.00	0.00	0.00	0.00	4.86	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxproline	0.00	0.00	2.38	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.59	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Treonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00
Phenylhexanoic-Acid	0.00	0	0.00	0	0.00	0.00	0.00	0.00	0.00	3.30	0.00	0.00	0.00	0.00
1,2-Butanediol	2.03	0	2.07	0.26	0.00	0.00	0.00	0.00	0.00	0.20	0.15	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.30	0	0.00	0.13	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.90	1.86	2.69	0.17	0.06	11.27	1.34	0.10	2.81	4.66	0.27	1.28	1005.82	1.93
2,4-Dihydroxy-4-Methyl-2-Pentene	2.03	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,4-Dihydroxybutane	0.00	0	0.00	0.00	0.00	0.19	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00
Sarcosine	0	0	0.00	0.71	0.00	0.00	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxyethane	0.23	0	0.00	0.28	0.00	0.00	0.00	0	0.32	0.00	0.00	0.00	0.55	0.00
1,2-Dihydroxycyclohexene	0.17	1.26	8.89	27.64	13.15	0.00	0.12	0.05	2.23	0.00	68.15	1.24	1.80	0.26
1,6-Dihydroxyhexaan	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.90	0.00	0.00	0.00
1,3-Dihydroxy-2-Ethylpropane	1.9	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,4-Dihydroxybutane	0	0	0.00	0.00	0.00	0.00	0.00	4.04	0.00	0.00	0.00	0.00	0.00	0.00
Galactopyranose-Alpha-D	1.52	0.69	0.00	0.00	0.00	0.42	0.00	0.79	0.00	13.84	0.00	0.00	1.19	0.00

Galactopyranose-Beta-D	0	0	1.56	0.00	0.00	0.00	0.00	0.13	0.00	3.12	0.00	0.00	0.00	0.00
Glucopyranose	1.57	0.55	1.95	0.00	0.00	0.00	0.00	0.59	0.54	3.11	0.00	0.00	0.00	0.28
Mannonic1,4-Lactone	1.02	0	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00
Erythronic-Acid	0.00	0	0.29	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fructofuranose	0.00	0	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.05	0.69	0.00	0.00	0.00	0.00	0.00	0.58	0.00	0.00	0.00	0.00	0.00	0.00
Arabinitol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.32	0.00	0.00	0.00	0.00
Arabinose	0.11	0.38	0.05	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00
Rhamnose	1.06	0	1.27	0.00	0.00	0.38	0.13	0.72	0.00	0.00	0.07	0.00	0.00	0.00
Ribose	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00	11.12	0.00	0.00	0.00	0.00
Galactose	1.56	0.35	0.00	0.00	0.00	0.00	0.00	0.66	0.18	0.00	0.00	0.00	1.54	0.00
Monomyristoylglycerol	0.00	0	0.00	15.96	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Monohexadecanoylglycerol	0.00	0.00	0.48	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00
2-Monostearylglycerol	0.00	0.00	0.40	0.00	0	0.00	0.00	0.00	0.00	0.00	0.00	0	0.00	0.00

Organic acids in the cell lysates

Organic acid	Control (PDHc)							Control (Complex I)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Hexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04
Octanoic-Acid	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
NoAcid	0.43	0.27	0.00	0.14	0.45	0.29	0.33	0.61	0.24	0.00	0.57	0.34	9.56	0.88
DecAcid	0.00	0.09	0.06	0.11	0.08	0.00	0.00	0.00	0.00	0.03	0.10	0.08	0.00	0.00
EicAcid	0.12	0.00	0.00	0.00	0.00	0.01	0.00	0.22	0.00	0.12	0.19	0.00	0.00	0.00
Dodecanoic-Acid	0.98	0.00	0.39	0.24	0.05	0.74	0.57	0.89	0.39	0.13	0.48	0.05	38.67	0.71
Tetradecanoic-Acid	7.37	2.16	2.11	3.07	0.00	1.96	0.87	7.75	1.18	3.76	7.55	0.00	155.88	0.93
Palmitic-Acid	114.87	40.25	42.22	59.17	3.19	32.17	9.95	138.49	45.42	74.85	108.61	1.18	2343.27	8.56
Heptadecanoic-Acid	1.10	0.32	0.49	0.44	0.00	0.22	0.00	1.13	0.35	1.15	3.11	0.00	14.97	0.00
Octadecanoic-Acid	46.41	18.44	15.63	33.11	0.39	13.25	6.17	57.11	23.74	31.79	71.82	0.00	954.11	4.03
2-Methylbutyric-Acid	0.00	0.00	0.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6-Octadecenoic-Acid	0.26	3.94	0.00	15.32	0.00	0.00	0.00	51.90	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	0.11	0.00	0.00	0.00	0.00	0.00	0.00	1.07	2.01	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	53.81	16.16	20.85	22.77	0.00	9.18	0.00	0.00	15.18	45.96	38.36	0.00	1101.27	0.86
3-Hydroxylauric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.44	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxysebacic-Acid	0.00	0.00	0.00	0.37	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	67.52	0.00	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	8.06	1.79	2.53	2.92	0.00	0.97	0.00	12.05	0.96	8.57	3.42	0.00	211.72	0.00
Oleic-Acid	0.00	17.09	19.58	20.91	0.00	2.91	1.37	0.00	15.74	0.00	44.96	0.00	382.74	0.99
2-Undecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.44	0.00	0.00	0.00	0.00	0.00	0.00
11-Octadecenoic-Acid	53.81	16.16	20.85	22.77	0.00	9.18	0.00	67.52	15.18	45.96	38.36	0.00	1101.27	0.86
Arachidonic-Acid	4.83	1.74	2.29	2.80	0.00	0.00	0.00	5.50	1.38	5.04	1.75	0.00	27.15	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.61	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	15.25	5.25	6.06	7.31	0.00	0.28	0.09	20.09	4.55	14.06	7.52	0.00	139.14	0.05
Pimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hexenedioic-Acid	0.00	0.84	0.00	0.00	0.00	0.00	0.00	0.00	1.67	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	0.80	0.00	0.00	0.00	0.00	0.00	0.00	0.80	0.00	0.00	0.00
Azelaic-Acid	0.75	0.21	0.00	0.30	0.00	0.00	0.40	1.82	0.58	0.00	0.13	0.00	0.00	0.10
11-Eicosenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00
Sebacic-Acid	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanedioic-Acid	0.14	0.60	0.07	0.05	0.03	0.00	0.00	0.53	0.32	0.00	0.13	0.00	0.00	0.00
Malonic-Acid	0.09	0.70	0.78	0.36	0.00	0.00	0.00	0.00	44.27	1.23	0.00	0.01	0.00	0.04

Citric-acid	12.95	6.26	2.62	0.08	0.00	0.00	0.00	12.91	7.58	0.00	0.02	0.00	0.00	0.00
Aconitic-Acid	0.14	0.08	0.09	0.00	0.00	0.00	0.00	0.39	0.32	0.00	0.00	0.00	0.00	0.00
2-Ketoglutaric-Acid	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00
Succinic-Acid	21.46	14.36	10.45	2.88	2.24	0.65	4.23	32.31	15.85	0.11	2.94	1.68	62.22	5.27
Fumaric-Acid	1.35	0.57	0.26	0.56	0.14	0.00	0.00	1.58	0.15	0.00	0.25	0.05	0.00	0.00
Malic-Acid	11.61	3.17	3.79	1.74	0.47	0.00	0.78	8.73	2.89	0.00	0.00	0.25	0.00	1.84
Lactic-Acid	134.22	416.64	362.94	38.50	40.62	7.86	41.83	168.90	257.10	7.59	36.40	54.15	460.92	49.46
Lactyllactate	0.00	1.10	1.49	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00	0.00	0.00	0.00
Pyruvic-Acid	0.50	1.87	0.83	0.18	0.00	0.00	0.09	0.95	0.95	0.34	0.08	0.00	5.26	0.00
GLYCOLIC-DITMS	1.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Acrylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.00	0.00	0.00	0.00	0.00
Oxalic-Acid	5.61	0.68	2.15	1.90	7.51	0.00	0.67	4.89	1.00	2.96	2.94	7.95	0.00	5.70
2-Ketoisovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.20	0.10	0.00	0.00	0.00	0.00	0.18	0.00	0.00
4-Hydroxyphenyllactic-Acid	0.78	0.31	0.16	0.00	0.00	0.00	0.00	1.57	0.57	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.27	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	1.42	2.76	4.55	2.10	7.18	1.77	4.28	2.21	1.86	6.82	2.21	7.76	486.74	3.21
Methylmalonic-Acid	0.00	0.00	0.00	1.91	0.00	0.49	0.00	0.00	1.57	0.00	0.00	0.00	3.31	0.00
N-Propionylglycine	0.00	0.00	0.62	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Propionic-acid	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.00	0.00	0.00	0.00	0.03	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.02
2-Ketobutyric-Acid	0.00	2.68	1.09	0.03	0.00	0.00	0.00	0.12	0.91	1.68	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.06	0.03	0.01	0.00	0.00	0.00	0.01	0.29	0.00	0.00	0.00	0.00	0.00	0.03
4-Hydroxybutyric-Acid	0.00	0.00	29.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00
N-Acetylaspartic-Acid	0.16	0.03	0.06	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	52.39	28.71	29.41	0.33	0.00	0.00	0.00	86.13	47.97	0.00	0.00	0.00	0.00	0.00
Uracil	0.21	0.47	0.06	0.00	0.00	0.00	0.00	0.63	0.27	0.17	0.00	0.00	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.06	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	25.02	1.62	0.00	0.00	0.00	0.00	0.00	2050.38	0.60
Benzoic-Acid	0.48	0.45	1.73	0.00	0.24	0.00	0.08	0.00	0.36	0.09	0.30	0.05	0.00	0.13
Hippuric-Acid	0.62	0.22	0.04	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00
1-(4-hydroxyphenyl)ethanone	0.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.54	0.22	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.26	0.41	0.37	0.00	0.28	0.00	0.00	0.32	0.00	0.00
2,3-Dihydroxypropanoic-Acid	0.00	0.00	0.21	0.09	0.14	0.00	0.12	0.82	0.00	0.00	0.00	0.12	4.63	0.28
2,4-Dihydroxybenzoic-Acid	0.54	0.00	0.15	0.13	0.00	0.00	2.44		0.04	0.08	0.38	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0.05	0.00	0.00	0.00	0.00	0.00	0.00	3.11	0.00	0.00	3.14	0.00	0.00	0.00
2,6-Dihydroxypyrimidinecarboxylic-Acid	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	82.05	2.62	2.91	1.45	0.03	0.00	0.00	170.37	7.95	3.01	8.37	0.00	0.00	0.00

2-Piperidinecarboxylic-Acid	0.00	0.47	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0.00	0.94	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.24	0.09	0.02	0.09	1.51	1.15	1.21	0.34	0.16	0.23	0.02	1.98	183.07	2.05
3-Hydorxybenzoic-Acid	0.27	0.12	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.87	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.33	0.08	0.10	0.14	0.00	0.06	0.00	0.86	0.00	0.00	0.18	0.00	0.00	0.00
4-Hydroxymandelic-Acid	3.61	1.30	1.13	1.23	0.00	0.00	0.00	5.13	2.01	0.57	1.64	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	1.27	0.00	0.00	0.00	0.00	0.00	0.00	1.21	0.00	0.00	0.00	0.00	0.00	0.00
4-Ketovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.12	0.04	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.14	0.01	0.04	1.22	0.00	0.00	0.00	0.04	0.00	1.28	0.00	0.00	0.00	0.00
Dimethylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Citramalic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00
Maleic-Acid	0.12	0.15	0.07	0.50	0.19	0.00	0.02	2.34	0.62	0.15	0.81	0.11	0.00	0.03
Pantoyllactone	0.00	0.50	0.58	0.00	0.00	0.00	0.00	0.28	0.30	0.00	0.19	0.00	0.00	0.00
Dimethylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pentadecanoic-Acid	1.60	0.39	0.45	0.62	0.00	0.46	0.00	2.24	0.51	1.04	0.95	0.00	0.00	0.00
Urea	0.54	1.79	0.00	0.00	0.00	0.00	0.00	3.50	0.00	0.82	0.00	0.00	0.00	0.00
1,3-Dicarboxylic-5-Hydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02
3,3-Dihydroxy-7,11-Dimethyldodecanoic-A	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.61	0.00	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	72.47	0.76	0.00	0.00	5.41	0.00	0.00	283.80	253.22	0.00	0.00	11.73	0.00	0.00
4-Methylmandelic-Acid	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybenzoic-Acid	0.03	0.03	0.01	0.00	0.00	0.00	0.06	0.00	0.02	0.21	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	21.62	0.00	0.53	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxyacrylic-Acid	0.00	0.00	0.00	1.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.24	0.21	0.47	1.54	0.10	0.00	0.00	0.00	0.00	0.43
1,3-Benzenedicarboxylic-Acid	0.00	0.89	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxy-2-Methylbutyric-Acid	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyacetophenone	0.59	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyacetophenone	0.00	0.00	0.00	16.97	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	1.23	0.19	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.11	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	3.66	2.29	0.00	0.93	0.00	0.00	0.00	3.95	2.67	0.00	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	26.35	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Butanediol	1.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.03	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.11	0.19	0.16	0.00	1.45	0.76	0.76	0.17	0.00	0.41	0.00	1.85	118.13	1.99
1,2-Dihydroxypropane	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.57	0.00	0.00	0.00	0.00	0.00	0.00

1,4-Dihydroxy-2-Butene	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00
1,4-Dihydroxybutane	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.13	0.09	0.00	2.29	0.00
2-Methyl-1,3-Dihydroxybutane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	42.57	0.00
1,13-Dihydroxytridecane	0.00	0.00	0.00	0.45	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00
1,2-Dihydroxy-2-Propane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00
1,2-Dihydroxyethane	0.26	0.09	0.78	0.00	0.00	0.00	0.00	0.00	1.70	0.00	1.77	0.05	0.00	0.25
1,2-Dihydroxycyclohexene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	14.60	0.00	0.00	218.18	0.00
Galactopyranose-Alpha-D	0.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.54	0.00	0.00	0.00	0.00	0.00
Glucopyranose	0.21	0.23	0.27	0.00	0.00	0.00	0.00	0.00	0.80	0.00	0.00	0.00	0.00	0.00
Mannonic1,4-Lactone	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.44	0.00	0.00	0.00	0.00	0.00
Fucose	0.46	0.26	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00
Rhamnose	0.00	0.20	0.19	0.00	0.00	0.00	0.00	0.00	0.46	0.00	0.00	0.00	0.00	0.00
Ribose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00
Galactose	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.79	0.47	0.00	0.00	0.00	0.00	0.00
Monohexadecanoylglycerol	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	3.51	0.00

Organic acid	Moniliformin (110.2 µM)							Moniliformin (220.4 µM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Hexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.85
Valeric-Acid	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Octanoic-Acid	0.00	0.06	0.04	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.21
NoAcid	1.08	0.46	0.27	0.14	0.26	0.47	0.18	0.75	0.30	0.00	23.96	0.22	0.38	0.65
DecAcid	0.25	0.08	0.08	0.05	0.03	0.00	0.00	0.22	0.05	0.07	2.90	0.00	0.00	0.00
EicAcid	0.27	0.07	0.09	0.15	0.00	0.10	0.00	0.44	0.10	0.08	0.00	0.00	0.04	0.00
Dodecanoic-Acid	1.07	0.36	0.21	0.32	0.56	0.77	0.77	0.70	0.31	0.37	12.71	0.16	0.80	0.77
Tridecanoic-Acid	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanoic-Acid	8.15	0.33	3.19	2.61	0.37	2.03	0.00	2.55	1.84	2.16	73.55	0.13	1.95	1.44
Palmitic-Acid	120.34	28.50	60.53	49.47	4.04	31.23	64.20	95.84	33.76	48.42	1192.58	1.23	30.81	12.35
Heptadecanoic-Acid	1.61	0.36	0.41	0.48	0.00	0.21	0.00	1.69	0.53	0.56	8.00	0.00	0.18	0.23
Octadecanoic-Acid	54.08	16.58	24.13	28.35	2.68	15.46	14.79	53.41	15.68	20.55	692.56	0.07	15.76	10.43
2-Methylbutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.54	0.00	0.00	0.00	0.00	0.00	0.00
Isovaleric-Acid	0.00	0.28	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
2-Ethylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.50	0.00	0.00	0.19
5-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.71	0.57	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	1.34	34.66	15.91	7.87	10.09	0.00	0.00	4.49	21.90	466.50	0.00	9.39	0.00
3-Methylpimelic-Acid	0.00	0.21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methyladipic-Acid	0.18	0.07	0.00	0.00	0.00	0.00	0.02	0.18	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.32	0.00	0.00	0.00
2-Hydroxysebacic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	1.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	55.39	0.00	0.00	0.00	0.00	0.00	0.00	43.08	0.00	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	3.49	0.24	4.34	1.00	0.00	0.71	0.00	1.60	1.51	2.12	47.85	0.00	0.59	0.00
Oleic-Acid	0.00	6.01	10.98	15.06	0.81	0.00	0.18	39.69	15.96	23.93	90.47	0.00	2.92	1.60
2-Undecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.32	0.00	0.00	0.00
11-Octadecenoic-Acid	55.39	1.34	34.66	15.91	7.87	10.09	0.00	43.08	4.49	21.90	466.50	0.00	9.39	0.00
Arachidonic-Acid	3.73	0.72	4.36	1.21	0.00	0.00	0.00	2.40	2.56	2.96	49.59	0.00	0.24	0.00
Linolenic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	15.41	1.82	10.15	3.62	0.00	0.80	0.00	10.06	6.66	6.86	133.46	0.00	0.83	0.00
Pimelic-Acid	0.19	0.11	0.00	0.00	0.00	0.00	0.12	0.08	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	1.39	0.29	0.00	0.00	0.17	0.00	0.84	0.45	0.04	0.00	0.00	0.00	0.14	0.00

Adipic-acid	0.00	0.24	0.00	0.64	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Azelaic-Acid	6.46	1.55	0.00	0.13	0.15	0.37	1.30	4.07	0.38	0.22	0.00	0.00	0.86	0.46
11-Eicosenoic-Acid	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sebacic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanedioic-Acid	0.02	0.00	0.01	0.14	0.00	0.00	0.07	9.04	0.01	0.04	32.30	0.00	0.00	0.06
Malonic-Acid	0.24	0.12	20.73	0.00	0.03	0.00	0.27	1.13	0.18	0.33	0.00	0.00	0.00	0.10
Citric-acid	17.28	3.57	1.90	0.00	0.00	0.00	0.27	6.98	7.75	1.45	0.00	0.00	0.00	0.00
Aconitic-Acid	0.30	9.35	0.09	0.00	0.00	0.00	0.00	0.15	27.13	0.22	0.00	0.00	0.00	0.00
Succinic-Acid	24.33	21.18	12.31	3.39	1.56	4.12	5.73	15.23	19.24	11.78	0.00	2.11	4.85	3.56
Fumaric-Acid	0.32	0.31	0.21	0.39	0.05	0.04	0.63	0.00	0.60	0.00	0.00	0.04	0.00	0.23
Malic-Acid	4.15	1.01	1.24	0.00	1.56	1.45	1.84	3.08	1.56	1.09	0.00	0.24	1.75	1.44
Lactic-Acid	55.11	111.93	229.65	27.27	45.32	27.94	72.32	118.61	176.60	160.69	47.13	49.77	23.70	99.62
Lactyllactate	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
Pyruvic-Acid	0.53	0.22	0.69	0.00	0.00	0.00	0.00	0.15	0.11	0.10	15.68	0.00	0.00	0.77
2-Methyl-3-Ketobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.20	0.00	0.00	0.00
3-Ketobutyric-Acid	0.00	0.10	0.17	0.00	0.00	0.00	0.00	0.00	0.18	0.12	0.00	0.02	0.00	0.00
3-Ketobutyric-AcidtriTMS	0.00	12.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.64	0.00	0.10	0.00	0.00	0.00	0.05	0.34	0.00	0.00	0.00	0.00	0.00	0.08
Oxalic-Acid	16.78	1.39	4.12	2.93	9.10	1.14	7.84	4.02	3.79	3.92	13.85	3.03	2.15	0.43
3-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisocaproic-Acid	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00
4-Hydroxyphenyllactic-Acid	1.01	0.16	0.19	0.00	0.00	0.00	0.01	0.42	0.37	0.13	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	0.49	0.94	1.34	3.55	9.57	4.17	5.95	0.78	1.04	0.99	23.70	6.92	4.34	9.97
Methylmalonic-Acid	15.08	1.16	0.00	0.00	0.00	0.00	0.00	0.13	0.31	0.00	0.00	0.00	0.00	0.00
Methylmalonic-Acid-Tritms	3.49	0.00	0.00	0.00	0.00	0.00	0.00	2.01	0.00	0.00	0.00	0.00	0.00	0.00
N-Propionylglycine	0.00	2.52	1.75	0.00	0.00	0.00	1.20	0.00	2.52	1.71	0.00	0.00	0.00	0.00
Propionic-acid	0.11	0.36	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	3.17	0.23	0.00	0.41	0.00	0.02	0.06	0.23	0.00	0.00	0.00	0.06	0.03	0.03
2-Ketobutyric-Acid	0.28	0.00	1.09	0.18	0.00	0.00	0.00	0.00	5.37	0.74	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.30	0.13	0.03	0.00	0.01	0.08	0.10	0.17	0.11	0.01	0.00	0.00	0.15	0.09
2-Hydroxyphenylacetic-Acid	0.00	0.41	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacetic-Acid	0.00	0.59	0.00	0.00	0.00	0.00	0.17	0.00	0.81	0.00	0.00	0.00	0.00	0.05
Phenyllactic-Acid	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	87.50	27.37	21.38	0.00	0.00	0.00	0.74	35.95	38.55	31.07	0.00	0.00	0.00	0.85
Uracil	0.67	0.65	0.48	0.00	0.00	0.00	0.00	0.14	0.78	0.16	2.54	0.00	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.00	0.00	0.00	0.42	0.00	0.00	0.00	0.00	0.00	0.00	14.34	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	18.33	0.34	0.00	0.00	0.00	0.00	0.00	7.00	0.61
Benzoic-Acid	0.00	0.56	0.33	0.37	0.30	0.07	0.07	0.25	0.26	0.24	7.11	0.06	0.00	0.59

Hippuric-Acid	0.72	0.53	0.00	0.00	0.00	0.00	0.00	0.46	0.23	0.00	0.00	0.00	0.00	0.00
1-(4-hydroxyphenyl)ethanone	22.78	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.37	0.00	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.02	0.14	0.00	0.13	0.00	0.00	0.00	0.00	0.24	0.00	0.05
2,3-Dihydroxypropanoic-Acid	0.54	0.18	0.12	0.14	0.16	0.24	0.67	0.00	0.22	0.29	0.00	0.10	0.00	0.33
2,4-Dihydroxybenzoic-Acid	0.23	0.08	0.01	0.00	0.00	0.00	0.00	0.01	0.00	0.00	3.65	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0.10	0.88	0.00	0.00	0.00	0.01	0.00	0.09	0.00	0.00	0.00	0.00	0.01	0.00
2,6-Dihydroxybenzoic-Acid	37.76	0.25	0.77	4.58	0.00	0.00	0.00	40.37	0.10	0.52	37.05	0.00	0.00	0.07
2-Piperidinecarboxylic-Acid	0.00	0.11	0.17	0.00	0.00	0.00	0.00	0.00	0.45	25.55	0.00	0.00	0.00	0.02
3-(4-Hydroxy-2,5-Dioxoimidazolidin-4-y	0.00	0.23	0.00	0.00	0.00	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.25	0.00	0.05	0.03	2.22	1.98	4.63	0.13	0.24	0.03	0.00	1.57	2.11	2.62
3-Hydorxybenzoic-Acid	5.24	0.22	0.08	0.18	0.01	0.06	0.00	0.29	0.18	0.00	0.00	0.00	0.00	0.00
3-Hydroxycinnamic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
3-Hydroxyphenylpropionic-Acid	0.00	0.63	0.03	0.00	0.00	0.00	0.00	0.00	2.75	0.00	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	1.87	0.60	0.18	0.29	0.06	0.08	0.38	0.33	0.74	0.19	0.00	0.00	0.10	0.12
4-Hydroxycinnamic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
4-Hydroxymandelic-Acid	4.85	1.23	1.68	1.34	0.00	0.00	0.00	0.71	0.10	1.40	30.72	0.00	0.00	0.00
3-Methoxy-4-hydroxycinnamic-acid	0.00	0.28	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00
3-Methoxy-4-Hydroxyphenylpropionic-A	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-(Hydroxymethyl)Furan-2-Carboxylic-A	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.00	0.04	0.03	0.00	0.00	0.00	0.00	0.02	0.06	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.17	0.37	0.03	1.27	0.00	0.00	0.00	0.00	0.00	0.00	18.27	0.00	0.00	0.02
Dimethylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.02
Erythro-Pentonic-Acid	0.00	0.04	0.00	0.00	0.00	0.00	0.10	0.07	0.95	0.01	0.00	0.00	0.00	0.00
Citraconic-Acid	0.00	0.00	0.04	0.06	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.11	0.00	0.00
Citramalic-Acid	0.13	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.52	0.00	0.00	0.00	0.00	0.00
Levulinic-Acid	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Maleic-Acid	1.19	0.30	0.92	1.00	0.37	0.00	0.24	0.24	0.40	0.00	0.00	0.07	0.00	1.19
Parabanic-Acid	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Mandelic-acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.08	0.00
Pentadecanoic-Acid	2.33	0.38	0.76	0.45	0.01	0.51	0.07	1.63	0.42	0.55	10.41	0.00	0.36	0.02
Tricarballylic-Acid	0.00	1.32	0.00	0.00	0.00	0.00	0.00	0.00	0.62	0.00	0.00	0.00	0.00	0.00
Urea	3.31	7.47	0.69	0.00	0.00	0.00	0.00	1.28	7.61	0.92	0.00	0.00	0.00	0.00
Vanillic-Acid	0.00	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxycinnamic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	107.77	0.24	0.00	1.52	4.49	0.00	0.00	113.77	64.45	63.47	0.00	7.47	0.00	0.00
2,4,6-Trihydroxy-1,3,5-Triazine	0.00	1.75	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylmandelic-Acid	0.21	0.00	0.00	0.04	0.12	0.00	0.03	0.08	0.00	0.00	0.00	0.02	0.00	0.17
2,3-Dihydroxybenzoic-Acid	2.64	0.12	0.01	1.89	0.00	0.00	0.00	0.02	0.00	0.00	4.22	0.00	0.00	0.00

3,4-Dihydroxycinnamic-Acid	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,4-Dihydroxy-4-Methyl-2-Pentene	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	19.53	0.00	0.00	0.00
2-(Hydroxymethyl)phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.33
4-(Hydroxymethyl)Phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.47
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.05	0.37	0.11	1.70	0.00	0.00	2.89	0.00	0.28	0.00
1,3-Benzenedicarboxylic-Acid	0.00	7.21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.00
2-Hydroxyacetophenone	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.91	0.00	0.00	0.00	0.00	0.00	0.00
Thiodiglycol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.64	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.52	0.00	0.00	0.00	0.00	0.00	0.00	18.67	0.00	0.00	0.00
4-Hydrocinnamic-Acid	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00
4-Methoxy-3-Hydroxycinnamic-Acid	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	0.00	0.00	0.00
4-Methoxymandelic-Acid	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Phosphonobutanoic-Acid	0.00	0.00	0.00	0.00	11.55	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.74	0.00	0.00	0.00	0.00
1,13-Dihydroxytridecane	0.00	0.00	0.21	0.00	0.00	0.00	0.00	0.00	0.58	0.00	3.07	0.00	0.00	0.00
1,2-Dihydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.57	0.00	0.00	0.00
1,2-Dihydroxyethane	0.21	0.03	0.12	0.00	0.06	0.00	0.00	0.64	0.12	0.08	0.00	0.14	0.10	0.00
1,2-Dihydroxycyclohexene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	1061.43	0.00	0.00	0.00
1,6-Dihydroxyhexaan	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	37.07	0.00	0.00	0.00
Galactopyranose-Alpha-D	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.63	0.00	0.00	0.00	0.00	0.00
Glucopyranose	0.00	0.14	0.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Mannonic1,4-Lactone	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.26	0.11	0.00	0.00	0.00	0.00	0.00	0.22	0.16	0.25	0.00	0.00	0.00	0.00
Rhamnose	0.30	0.22	0.82	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00
Ribose	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactose	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.42	0.00	0.00	0.00	0.00	0.00
Monostearylglycerol	0.00	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.00	0.13	0.09

Organic acid	3-bromopyruvate (3.75 mM)							3-bromopyruvate (5.2 mM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Hexanoic-Acid	0.00	0.00	0.00	0.00	1.42	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Octanoic-Acid	0.00	0.05	0.06	0.00	0.45	0.00	0.00	0.00	0.00	0.00	0.31	0.00	0.00	0.00
NoAcid	1.00	0.13	0.00	2.01	1.22	0.00	0.19	13.34	0.46	0.00	1.20	0.09	0.00	0.28
DecAcid	0.12	0.04	0.06	2.51	0.20	0.00	0.00	0.00	0.16	0.00	0.40	0.00	0.00	0.00
EicAcid	0.36	0.00	0.05	0.00	0.00	0.00	0.00	7.30	0.04	0.01	0.00	0.00	0.00	0.00
Dodecanoic-Acid	0.00	0.23	0.20	6.32	0.69	0.55	0.58	6.73	0.32	0.23	0.80	0.00	0.51	0.65
Tridecanoic-Acid	4.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanoic-Acid	77.42	0.57	0.90	5.16	1.12	0.83	0.95	48.80	0.48	0.55	3.20	0.00	1.02	1.20
Palmitic-Acid	0.91	14.24	18.75	210.66	0.00	8.58	6.12	889.01	20.31	9.97	32.02	0.00	9.67	6.85
Heptadecanoic-Acid	42.31	0.05	0.19	0.00	0.00	0.00	0.00	1.87	0.12	0.04	0.16	0.00	0.08	0.00
Octadecanoic-Acid	0.00	8.90	10.18	127.75	4.08	5.85	4.26	561.39	14.59	6.16	22.31	0.00	6.16	3.58
6-Octadecenoic-Acid	0.00	0.00	7.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Isovaleric-Acid	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.76	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethylhexanoic-Acid	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	2.96	0.44	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.71	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	23.05	3.50	8.04	1.67	0.00	0.00	0.00	132.77	0.00	1.74	5.35	0.00	0.00	0.00
3-Methyladipic-Acid	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxysebacic-Acid	23.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	3.71	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	0.44	0.19	0.38	0.00	0.00	0.00	0.00	3.14	0.10	0.00	0.00	0.00	0.00	0.00
Oleic-Acid	3.16	0.46	1.55	11.42	0.39	0.63	0.03	136.04	0.87	0.02	5.66	0.00	0.45	0.14
2-Undecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Valerylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00
11-Octadecenoic-Acid	23.05	3.50	8.04	1.67	0.00	0.00	0.00	132.77	3.71	1.74	5.35	0.00	0.00	0.00
Arachidonic-Acid	0.27	0.18	0.95	0.00	0.00	0.00	0.00	3.50	0.34	0.05	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	3.98	0.49	1.96	0.59	0.00	0.00	0.00	29.00	1.08	0.22	1.47	0.00	0.00	0.00
Suberic-Acid	0.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.19	0.00	0.00	0.00
Azelaic-Acid	3.70	0.27	0.00	0.00	0.26	0.13	0.35	0.00	0.50	0.14	0.11	0.00	0.00	0.00
Tetradecanedioic-Acid	0.06	0.00	0.02	0.00	0.00	0.05	0.09	303.14	0.02	0.08	0.06	0.00	0.00	0.00
Malonic-Acid	0.00	0.17	1.47	3.28	0.00	0.00	0.00	70.63	0.55	5.43	0.52	3.63	0.00	0.00
Citric-acid	4.72	2.33	0.04	0.00	0.00	0.00	0.00	0.00	1.30	0.29	0.00	0.00	0.00	0.00
Aconitic-Acid	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.36	0.09	0.00	0.00	0.00

Succinic-Acid	15.30	7.31	4.58	0.00	2.45	2.97	3.59	7.00	6.19	7.13	1.31	0.00	3.40	2.11
Fumaric-Acid	0.00	0.10	0.00	0.00	0.00	0.19	0.41	0.00	0.00	0.00	0.20	0.00	0.34	0.24
Malic-Acid	0.00	0.45	0.47	0.00	1.18	0.95	1.19	0.00	0.00	0.00	0.00	0.00	1.10	1.89
Lactic-Acid	82.46	32.58	76.62	20.21	30.24	11.87	27.84	180.58	35.05	65.93	3.57	17.60	14.44	25.33
Pyruvic-Acid	0.51	0.26	1.60	3.13	1.40	0.00	0.36	137.24	0.28	1.47	0.13	4.12	0.00	0.00
3-Ketobutyric-Acid	0.00	0.00	0.18	0.00	0.20	0.10	0.00	39.62	0.28	0.00	0.00	0.00	0.04	0.00
3-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00
Oxalic-Acid	13.80	1.72	6.75	3.83	3.53	2.25	5.63	14.61	0.69	10.38	1.08	6.85	1.67	14.26
3-Hydroxyisobutyric-Acid	0.00	4.93	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenyllactic-Acid	0.00	0.02	0.00	0.00	0.00	0.00	0.00	3.03	0.03	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	13.70	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	6.33	2.92	4.92	0.00	12.87	6.26	5.66	32.66	3.58	7.43	1.63	7.65	9.62	7.93
Methylmalonic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.53	1.06	0.00	0.00	0.00	0.00
Methylmalonic-Acid-Tritms	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Propionic-acid	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.00	0.00	0.00	0.00	0.10	0.01	0.01	0.00	0.00	0.00	0.42	0.00	0.01	0.00
2-Ketobutyric-Acid	0.00	1.23	0.40	0.00	0.00	0.00	0.00	44.53	1.27	0.02	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.00	0.00	0.00	0.00	0.03	0.02	0.08	0.00	0.00	0.00	0.00	0.00	0.09	0.13
4-Hydroxyphenylacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.21	0.00	0.00	0.00	0.00	0.00	0.00
Phenylpyruvic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.29	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	67.15	32.64	20.70	0.00	0.00	0.00	0.00	0.00	24.67	33.70	0.00	0.00	0.00	0.17
Uracil	0.05	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Pyrimidinedione	3.72	1.60	0.63	0.00	0.00	0.00	0.00	0.00	3.29	2.48	0.00	0.00	0.00	0.00
2-Hydroxyhippuric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	0.48	0.06	0.00	0.00	0.00	0.00	0.00	0.84	0.04
Benzoic-Acid	0.00	0.32	0.23	0.00	0.29	0.16	0.07	0.00	0.48	0.00	0.99	0.00	0.02	0.12
Hippuric-Acid	0.48	0.15	0.00	0.00	0.00	0.00	0.00	19.63	0.25	0.00	0.00	0.00	0.00	0.00
1-(4-hydroxyphenyl)ethanone	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.06	0.39	0.13	24.38	0.00	0.00	0.05	0.00	0.35	0.00
2,3-Dihydroxypropanoic-Acid	4.83	3.69	0.93	0.00	0.19	0.00	0.86	0.00	4.15	3.61	0.00	0.00	0.35	0.77
2,4-Dihydroxybenzoic-Acid	0.27	0.02	0.05	16.26	0.00	0.00	0.00	3.97	0.15	0.00	0.09	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0.11	0.00	0.00	0.00	0.00	0.00	0.00	29.21	0.00	0.00	0.11	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	95.28	0.11	0.94	56.28	0.00	0.00	0.01	1368.55	0.11	0.37	11.57	0.00	0.04	0.02
2-Hydroxyisobutyric-Acid	64.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.41	0.13	0.11	0.00	3.05	1.36	3.28	0.00	0.01	0.00	0.02	0.06	2.82	4.36
3-Hydorxybenzoic-Acid	0.00	0.22	0.02	0.00	0.00	0.00	0.00	1.41	0.20	0.00	0.06	0.00	0.00	0.00
3-Hydroxyphenylpropionic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.39	0.07	0.10	0.00	0.00	0.04	0.07	5.09	0.16	0.00	0.33	0.00	0.00	0.04

4-Hydroxymandelic-Acid	5.39	1.40	1.50	21.74	0.00	0.00	0.00	78.65	1.31	1.53	0.68	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.39	0.00	0.00	0.00
5-Hydroxyhydantoin	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.35	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.00	0.12	0.06	0.00	0.00	0.00	0.00	1.61	0.00	0.00	0.38	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.22	0.03	0.00	0.00	0.00	0.00	0.05	0.00	0.02	0.07	0.00	0.00	0.00	0.11
Citraconic-Acid	0.39	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.22	0.31	0.00	0.00	0.00	0.00
Citramalic-Acid	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00
Maleic-Acid	1.83	0.11	0.00	0.00	0.00	0.00	0.25	11.07	0.32	0.27	0.53	0.24	0.22	0.00
Pentadecanoic-Acid	1.05	0.07	0.15	0.00	0.04	0.00	0.00	15.19	0.34	0.09	0.34	0.00	0.00	0.02
Urea	0.95	0.75	0.00	0.00	0.00	0.00	0.00	46.85	0.49	1.16	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	0.00	0.00	0.00	0.00	13.39	0.65	0.00	0.00	0.00	0.00	0.00	9.04	0.00	0.00
2,4,6-Trihydroxy-1,3,5-Triazine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
4-Methylmandelic-Acid	0.04	0.00	0.00	0.00	0.02	0.00	0.12	0.00	0.00	0.00	0.09	0.00	0.81	0.00
2,3-Dihydroxybenzoic-Acid	0.40	0.01	0.00	0.57	0.00	0.00	0.00	0.00	0.08	0.04	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxyacrylic-Acid	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.01	0.00	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	8.59	0.00	0.00	0.00	0.00	0.00	0.00
2-(Hydroxymethyl)phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7.55	0.00	0.00	0.00
4-(Hydroxymethyl)Phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.27	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.07	0.44	0.00	0.00	0.41	0.00	0.05	1.22	0.44	0.25
1,3-Benzenedicarboxylic-Acid	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	11.43	0.00	0.00	0.00	0.00	0.00	0.00	0.51	0.00	0.00	0.00
4-Methoxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.89	0.00	0.00	0.00	0.00
Phenylhydracrylic-Acid	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-Ketovaleric-Acid	1.45	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.59	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.00	0.00	9.65	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	8.35	1.21	1.80	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.70
2-Methoxymandelic-Acid	6.47	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.48	5.65	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glyoxylic-Acid	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.00	0.00	0.00	0.00	2.60	3.11	18.34	0.00	0.34	0.00	0.00	0.24	3.07	3.11
1,2-Dihydroxypropane	1.93	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,4-Dihydroxybutane	0.21	0.14	0.00	0.00	0.01	0.10	0.00	0.00	0.00	0.45	0.00	0.00	0.12	0.19
2-Methyl-1,3-Dihydroxybutane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Phenol	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,13-Dihydroxytridecane	2.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00
1,2-Dihydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.13

1,2-Dihydroxy-2-Propane	0.23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxy-3-Methylbutane	0.00	0.00	0.00	0.00	0.00	0.05	0.00	15.99	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxyethane	0.00	0.00	0.00	15.26	0.00	0.00	0.04	0.00	0.02	0.05	0.29	7.41	0.22	0.00
1,2-Dihydroxycyclohexene	0.00	0.00	0.00	0.13	0.00	0.00	0.00	7.10	0.07	2.30	0.00	0.00	0.00	0.00
Galactopyranose-Alpha-D	0.83	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.38	0.00	0.00	0.53	0.00	0.00
Glucopyranose	0.00	0.42	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00
Mannitol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	17.25	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.70	0.39	0.10	0.00	0.00	0.00	0.00	3.66	0.36	0.00	0.00	0.03	0.00	0.00
Arabinose	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Rhamnose	0.74	0.34	0.00	0.00	0.00	0.00	0.00	6.04	0.00	0.26	0.00	0.00	0.00	0.00
Ribose	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactose	0.00	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.29	0.80	0.00	0.00	0.00	0.00
2-Monoisobutyrylglycerol	0.00	0.00	1.30	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Monohexadecanoylglycerol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.34
Monostearylglycerol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.23

Organic acid	Moniliformin (110.2 µM) and Rotenone (10 nM)							Moniliformin (220.4 µM) and Rotenone (1000 nM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Hexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.24	1.26	0.00
Octanoic-Acid	0.00	0.00	0.00	0.00	0.01	0.00	0.10	0.00	0.12	0.00	0.00	0.17	0.00	0.00
NoAcid	0.41	0.21	0.00	0.43	0.13	0.32	0.41	0.67	0.52	0.00	0.26	0.87	18.62	0.27
DecAcid	0.00	0.09	0.07	0.21	0.01	0.00	0.00	0.06	0.11	0.08	0.16	0.16	0.00	0.00
EicAcid	0.30	0.02	0.00	0.00	0.00	0.00	0.00	0.33	0.07	0.00	0.10	0.00	1.96	0.00
Dodecanoic-Acid	1.81	0.20	0.00	0.33	0.00	0.41	0.40	1.44	0.28	0.17	0.66	0.11	64.19	0.79
Tridecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Tetradecanoic-Acid	1.86	1.84	0.93	2.64	0.00	1.14	0.74	5.29	1.39	1.95	3.66	0.28	169.82	1.15
Palmitic-Acid	136.78	37.88	35.25	47.03	0.00	14.30	5.07	77.11	24.32	38.32	39.18	1.19	2045.75	7.45
Heptadecanoic-Acid	2.08	0.44	0.41	0.38	0.00	0.00	0.00	0.67	0.38	0.46	0.10	0.00	7.70	0.00
Octadecanoic-Acid	67.10	18.79	16.08	29.69	0.00	6.95	2.59	45.08	14.32	16.71	27.01	0.17	1036.03	3.96
2-Methylbutyric-Acid	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
6-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.99	1.67	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00
2-Ethylhexanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00
5-Hydroxyvaleric-Acid	0.99	0.42	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	68.77	16.02	19.40	14.61	0.00	3.92	0.00	30.75	0.00	6.26	10.28	0.00	629.91	0.00
3-Methyladipic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	10.94	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	5.30	1.28	1.99	1.07	0.00	0.27	0.00	1.96	0.65	2.27	0.00	0.00	43.32	0.00
Oleic-Acid	0.00	15.85	18.82	16.03	0.00	0.66	0.09	29.39	0.00	20.33	9.27	0.00	178.80	0.13
11-Octadecenoic-Acid	68.77	16.02	19.40	14.61	0.00	3.92	0.00	30.75	10.94	6.26	10.28	0.00	629.91	0.00
Arachidonic-Acid	8.35	1.34	2.22	1.16	0.00	0.00	0.00	2.84	1.20	2.55	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	1.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	22.42	4.27	5.69	3.74	0.00	0.30	0.00	10.07	4.03	6.53	2.24	0.00	87.74	0.00
Pimelic-Acid	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.07	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.26	0.00	0.00	0.00
2-Hexenedioic-Acid	0.00	0.00	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	0.49	0.00	0.00	0.00	0.00	0.00	0.00	1.21	0.00	0.00	0.00
Azelaic-Acid	4.28	0.62	0.00	0.28	0.00	0.00	0.00	1.37	0.40	0.00	0.37	0.00	0.00	2.97
Tetradecanedioic-Acid	0.08	0.02	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.05	0.00	0.00	0.00
Malonic-Acid	3.78	0.18	11.97	1.65	0.05	0.19	0.00	1.80	0.35	7.68	0.00	0.00	0.00	0.00
Citric-acid	8.63	5.44	2.02	0.04	0.00	0.00	0.00	7.59	3.85	0.74	0.00	0.00	0.00	0.00
Aconitic-Acid	0.00	0.43	0.23	0.12	0.00	0.00	0.00	0.00	3.79	0.00	0.38	0.00	0.00	0.00
Succinic-Acid	20.92	8.02	8.70	2.80	1.01	0.60	0.77	17.94	12.27	7.30	1.19	1.24	70.14	3.66

Fumaric-Acid	0.76	0.29	0.16	0.20	0.06	0.00	0.04	0.53	0.15	0.21	0.14	0.02	1.77	0.00
Malic-Acid	1.59	0.83	2.31	1.33	0.35	0.00	0.00	1.95	0.36	1.11	0.00	0.22	0.00	1.70
Lactic-Acid	261.83	135.14	374.24	104.11	55.07	4.66	13.94	173.65	316.34	349.43	66.34	56.24	632.71	52.34
Lactyllactate	0.00	0.00	0.58	0.00	0.00	0.00	0.00	0.00	0.63	0.29	0.00	0.00	0.00	0.00
Pyruvic-Acid	0.48	0.20	0.33	0.08	0.00	0.00	1.86	0.30	0.94	0.04	0.06	0.00	29.09	0.00
GLYCOLIC-DITMS	0.00	0.46	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	0.33	0.19	0.12	0.00	0.00	0.00	0.00	0.00	0.22	0.09	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.10	1.86	0.05
N-Acrylglycine	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Oxalic-Acid	7.82	2.46	3.26	1.72	7.07	0.04	0.00	8.66	2.15	3.30	1.13	7.69	0.00	4.13
3-Hydroxyisobutyric-Acid	0.00	0.00	0.38	0.00	0.00	0.00	0.00	3.90	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisovaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00	0.23	0.00	0.16
4-Hydroxyphenyllactic-Acid	0.55	0.35	0.36	0.00	0.00	0.00	0.00	0.31	0.25	0.13	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	2.01	0.55	1.57	2.60	5.12	4.29	8.86	1.20	1.32	0.48	1.54	7.00	664.02	4.26
Methylmalonic-Acid	0.00	0.15	0.00	0.00	0.04	0.33	0.00	0.26	0.00	0.16	0.69	0.00	27.25	0.00
N-Propionylglycine	0.00	0.00	1.58	0.00	0.00	0.00	0.00	0.00	0.00	0.72	0.00	0.00	0.00	0.00
Glutaric-Acid	0.58	0.00	0.00	0.00	0.05	0.00	0.00	0.32	0.29	0.00	0.00	0.03	0.00	0.09
2-Ketobutyric-Acid	0.00	0.34	1.12	0.00	0.00	0.00	0.00	0.15	0.05	0.91	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.09	0.04	0.03	0.00	0.00	0.00	0.00	0.05	0.03	0.00	0.00	0.00	0.00	0.09
4-Hydroxyphenylacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.42	0.00	0.00	0.00	0.00	0.00
4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.10	0.00	0.00	2.28
N-Acetyltyrosine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00
N-Acetylaspartic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.36
Pyroglutamic-Acid	69.75	31.06	33.02	1.47	0.00	0.00	0.00	81.07	37.19	30.41	1.01	0.00	0.00	0.00
Uracil	0.14	0.17	0.18	0.00	0.00	0.00	0.00	0.05	0.18	0.08	0.00	0.00	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	12.00	0.55	0.00	0.00	0.00	0.00	0.00	1488.47	0.04
Benzoic-Acid	0.00	0.25	0.28	0.15	0.02	0.20	0.18	0.64	0.25	0.25	0.33	0.33	0.00	0.07
Hippuric-Acid	0.94	0.00	0.00	0.00	0.00	0.00	0.00	0.63	0.19	0.00	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.05	0.00	0.32	0.08	0.00	0.00	0.00	0.00	0.00	0.16	0.00	0.18
2,3-Dihydroxypropanoic-Acid	0.00	0.12	0.30	0.00	0.03	0.00	0.12	0.00	0.10	0.12	0.00	0.17	0.00	0.35
2,4-Dihydroxybenzoic-Acid	0.17	0.17	0.06	0.53	0.00	0.00	0.00	0.66	0.00	0.00	0.17	0.00	0.27	0.00
2,5-Furandicarboxylic-Acid	0.00	0.73	0.00	1.96	0.00	0.00	0.00	0.00	0.05	1.38	0.06	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	116.45	0.52	0.16	3.04	0.00	0.00	0.00	23.18	1.30	0.13	7.44	0.00	0.00	0.00
2-Hydroxy-5-Methoxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.96	0.00
2-Piperidinecarboxylic-Acid	0.00	0.09	0.00	1.18	0.00	0.00	0.00	0.00	0.00	23.88	0.00	0.00	0.00	0.00
3-(4-Hydroxy-2,5-Dioxoimidazolidin-4-y	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.83	0.00	0.00	0.00	0.00	0.00

3,4-Dihydroxybutyric-Acid	0.24	0.06	0.00	0.00	1.15	1.12	2.58	0.32	0.04	0.00	0.03	2.21	149.27	3.15
3-Hydorxybenzoic-Acid	0.31	1.30	0.00	0.02	0.00	0.00	0.00	0.06	0.47	1.48	0.59	0.00	0.00	0.00
3-Hydroxycinnamic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
3-Hydroxyphenylpropionic-Acid	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.87	0.00	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.48	0.17	0.00	0.16	0.00	0.00	0.02	0.42	0.41	0.00	0.17	0.00	0.00	0.11
4-Hydroxymandelic-Acid	4.08	0.96	1.30	1.17	0.00	0.00	0.00	6.73	1.40	1.16	0.68	0.00	0.00	0.01
3-Methoxy-4-hydroxycinnamic-acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.03	0.00	0.00	0.60	0.00	0.00	0.00
4-Ketovaleric-Acid	0.00	0.00	0.36	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.07	0.08	0.05	0.00	0.00	0.00	0.00	0.10	0.07	0.14	0.00	0.00	0.00	0.04
Citraconic-Acid	0.00	0.10	0.00	0.00	0.10	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00
Citramalic-Acid	0.00	0.03	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00
Levulinic-Acid	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Maleic-Acid	0.22	0.49	1.68	0.00	0.19	0.00	1.08	0.07	0.14	0.00	0.77	0.22	49.27	0.21
Mandelic-acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.14	0.00	0.03	0.00	0.00
Pantoyllactone	0.00	0.00	0.37	0.00	0.00	0.00	0.00	0.00	0.62	0.00	0.00	0.00	0.00	0.00
Pentadecanoic-Acid	2.19	0.44	0.36	0.42	0.00	0.20	0.00	1.47	0.42	0.44	0.43	0.00	21.27	0.10
Tricarballylic-Acid	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	2.00	0.00	0.00	0.00	0.00	0.00
Urea	0.61	0.00	1.65	0.00	0.00	0.00	0.00	0.86	1.11	0.42	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	0.27	74.60	0.00	0.00	10.90	0.00	0.00	255.84	0.00	169.12	0.00	10.14	0.00	0.00
4-Methylmandelic-Acid	0.00	0.03	0.00	0.00	0.15	0.00	0.04	0.00	0.08	0.00	0.23	0.15	0.00	0.17
2,3-Dihydroxybenzoic-Acid	0.14	0.37	0.16	0.19	0.00	0.00	0.00	0.31	0.13	0.06	0.04	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	22.09	0.00
4-(Hydroxymethyl)Phenol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04
2,3,4-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.11	0.35	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,3-Benzenedicarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.22	0.00	0.00	0.96	0.00	0.00	0.00
2-Hydroxyacetophenone	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	18.83	0.00	0.00	0.00	0.00
1,3-Dihydroxy-2-Methylpropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
2-Hydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.75	0.79	0.00	0.00	0.00	0.19
2-Hydroxyphenylpropionic-Acid	8.76	1.25	1.93	0.00	0.00	0.00	0.00	7.93	0.71	0.00	0.00	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.02	0.00
2-Methoxymandelic-Acid	19.36	0.00	0.00	7.09	0.00	0.00	0.00	0.00	4.80	0.00	0.00	0.00	0.00	0.00
2-Methyl-4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.21	0.16	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.06	0.00	0.83	0.00	0.00	0.00	0.00	0.00	0.53	0.00	0.00	0.00	0.00	0.00
2,4-Dihydroxybutane	0.00	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00

Glyoxylic-Acid	0.00	0.00	0.23	0.00	0.00	0.00	1.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Butanediol	1.54	0.48	0.30	0.00	0.00	0.00	0.00	0.00	0.57	0.00	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.00	0.05	0.00	0.00	1.27	1.08	2.47	0.00	0.00	0.00	0.00	2.12	232.32	2.66
Glucutol	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.25	0.00
1,2-Dihydroxypropane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.07	0.00	0.00
1,4-Dihydroxybutane	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.00	0.00	0.00	0.15	0.00	0.14
1,13-Dihydroxytridecane	2.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.04	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxy-2-Propane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00
1,2-Dihydroxy-3-Methylbutane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.51	0.00
1,2-Dihydroxyethane	8.20	0.82	0.49	0.00	0.00	0.00	0.00	3.61	0.40	0.36	0.00	0.00	0.00	0.07
1,2-Dihydroxycyclohexene	0.00	0.00	0.00	0.00	0.00	13.22	6.64	0.00	0.00	7.08	0.00	0.00	526.26	0.00
1,3-Dihydroxy-2-Ethylpropane	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Galactopyranose-Alpha-D	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.32	0.16	0.09	0.00	0.00	0.00	0.00

Organic acid	3-bromopyruvate (3.75 mM) and Rotenone (10 nM)							3-bromopyruvate (5.2 mM) and Rotenone (1000 nM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Octanoic-Acid	0.00	0.07	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07
NoAcid	0.56	0.39	0.03	0.10	0.23	0.00	0.29	0.76	0.27	0.09	0.11	0.18	0.00	0.28
DecAcid	0.00	0.11	0.07	0.19	0.00	0.00	0.00	0.00	0.16	0.00	0.06	0.00	0.00	0.00
EicAcid	0.40	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.05	0.00
Dodecanoic-Acid	0.00	0.60	0.49	0.52	0.03	1.46	0.35	0.70	0.38	0.26	0.19	0.00	2.01	0.31
Tetradecanoic-Acid	0.58	2.08	1.22	1.28	0.00	2.43	0.75	4.03	1.42	0.85	0.43	0.05	2.70	0.57
Palmitic-Acid	57.26	37.43	22.82	14.02	0.00	25.63	5.50	81.63	19.99	18.97	8.87	0.00	29.12	2.83
Heptadecanoic-Acid	0.65	1.26	0.24	0.00	0.00	0.00	0.00	0.79	0.20	0.15	0.00	0.00	0.00	0.00
Octadecanoic-Acid	38.24	42.29	11.68	11.88	0.00	22.78	3.12	46.51	13.23	9.28	5.00	0.00	26.19	1.58
6-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.02	0.00	0.00	0.00
3-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00
4-Methylpimelic-Acid	0.00	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	0.00	4.72	0.00	0.00	0.00	0.00	0.00	0.00	0.47	0.27	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	12.09	2.95	9.63	0.22	0.00	0.00	0.00	31.32	4.90	7.48	0.00	0.00	0.00	0.00
2-Hydroxyundecanoic-Acid	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	0.30	0.17	0.72	0.00	0.00	0.00	0.00	1.72	0.11	0.45	0.00	0.00	0.00	0.00
Oleic-Acid	15.31	6.44	9.68	0.19	0.00	1.49	0.06	7.26	1.13	0.00	0.00	0.00	1.71	0.00
2-Undecenoic-Acid	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
11-Octadecenoic-Acid	12.09	2.95	9.63	0.22	0.00	0.00	0.00	31.32	4.90	7.48	0.00	0.00	0.00	0.00
Arachidonic-Acid	0.00	0.16	1.20	0.00	0.00	0.00	0.00	1.90	0.43	0.62	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.85	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	1.95	1.81	2.38	0.00	0.00	0.00	0.00	7.21	1.68	0.00	0.00	0.00	0.00	0.00
Pimelic-Acid	0.00	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.00	0.08	0.00	0.00	0.00	0.78	0.00	0.00	0.04	0.00	0.00	0.00	0.67	0.00
Adipic-acid	0.00	0.00	0.00	1.40	0.00	0.00	0.00	1.03	0.00	0.00	0.70	0.00	0.00	0.00
Azelaic-Acid	1.38	1.22	0.00	0.05	0.00	1.80	0.00	0.00	0.51	0.00	0.00	0.00	1.35	0.00
Sebacic-Acid	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00
Tetradecanedioic-Acid	15.35	0.03	0.12	0.18	0.00	0.00	0.00	0.00	0.02	0.06	0.25	0.00	0.00	0.01
Malonic-Acid	0.13	2.68	1.40	0.22	0.00	0.00	0.00	5.09	0.92	0.14	1.66	5.28	0.00	8.25

Citric-acid	6.55	3.44	0.00	0.00	0.00	0.00	0.00	4.67	2.78	0.32	0.00	0.00	0.00	0.00
Aconitic-Acid	0.00	2.61	0.26	0.15	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Succinic-Acid	21.16	10.24	0.60	1.22	0.88	11.71	2.90	21.23	7.28	6.48	0.95	1.12	14.23	2.57
Fumaric-Acid	0.00	0.24	0.00	0.06	0.00	0.00	0.26		0.11	0.00	0.02	0.00	0.00	0.00
Malic-Acid	0.00	0.00	0.00	0.00	0.32	0.27	0.79	2.78	0.00	0.00	0.00	0.13	0.65	0.41
Lactic-Acid	55.76	127.32	3.69	7.28	12.97	13.84	9.83	148.46	110.37	44.22	7.48	15.42	29.94	15.84
Pyruvic-Acid	0.29	0.26	1.80	0.37	0.00	0.00	0.00	0.41	0.81	0.75	0.22	0.00	0.00	0.52
GLYCOLIC-DITMS	0.15	0.00	0.22	0.00	0.00	0.71	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Ketobutyric-Acid	0.00	0.20	0.09	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.35	0.00	0.00	0.01	0.00	0.00	0.00	0.27	0.00	0.00	0.00	0.00	0.00
3-Hydroxyisovaleric-Acid	0.00	0.39	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
Oxalic-Acid	12.19	2.00	0.30	2.91	8.55	15.31	4.60	20.44	1.35	6.70	1.57	9.06	15.46	6.90
3-Hydroxyisobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	5.41	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.00	0.27	0.00	0.00	0.00	0.00	0.10	0.00	0.18	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenyllactic-Acid	0.00	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.49	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	8.20	11.06	3.17	1.99	9.80	2.28	2.72	8.21	11.46	6.18	1.61	10.07	3.90	8.56
Methylmalonic-Acid	0.00	7.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.02	0.00	0.00	0.13
Methylmalonic-Acid-Tritms	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	1.23	0.00	0.00	0.00	0.00	0.00
Propionic-acid	0.28	0.11	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.32	0.00	0.00	0.26	0.01	0.00	0.00	0.00	0.29	0.00	0.28	0.01	0.00	0.01
2-Ketobutyric-Acid	0.00	5.20	2.13	0.00	0.00	0.00	0.00	0.00	0.87	0.05	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.00	0.10	0.00	0.00	0.00	0.00	0.03	0.00	0.04	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacetic-Acid	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.00	0.00	0.00
Phenylpyruvic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.95	2.21	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	119.94	41.05	0.00	0.00	0.00	0.00	0.00	115.99	32.62	32.25	0.00	0.00	0.00	0.36
Uracil	0.00	0.09	0.02	0.00	0.00	0.00	0.00	0.00	0.03	0.00	0.00	0.00	0.00	0.00
Pyrimidinedione	6.71	2.25	0.00	0.00	0.00	0.00	0.00	12.15	4.04	1.71	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	0.91	0.02	0.00	0.00	0.00	0.00	0.00	0.64	0.01
Benzoic-Acid	0.00	1.04	0.27	0.73	0.02	0.15	0.13	0.26	0.69	0.20	0.08	0.00	0.00	0.26
Hippuric-Acid	0.49	1.29	0.00	0.00	0.00	0.00	0.00	0.20	0.18	0.18	0.00	0.00	0.00	0.00
1-(4-hydroxyphenyl)ethanone	0.00	0.00	0.00	0.00	0.00	0.00	0.00	92.55	12.14	0.00	0.00	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.46	0.00	0.19	0.00	0.00	0.00	0.00	0.00	0.28	0.10

2,3-Dihydroxypropanoic-Acid	5.29	2.56	0.00	0.00	0.21	0.00	0.47	11.60	6.24	3.38	0.00	0.11	0.25	0.63
2,4-Dihydroxybenzoic-Acid	0.00	0.07	0.06	0.00	0.00	0.00	0.00	0.82	0.00	0.63	0.00	0.00	2.03	0.24
2,5-Furandicarboxylic-Acid	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	117.58	2.97	0.11	1.51	0.00	0.00	0.00	159.45	0.06	0.11	5.53	0.00	0.00	0.07
2-Piperidinecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00
3-(4-Hydroxy-2,5-Dioxoimidazolidin-4-y	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyisobutyric-Acid	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.77	0.26	0.11	0.00	1.85	2.36	3.38	0.23	0.14	0.15	0.00	2.25	2.63	0.32
3-Hydorxybenzoic-Acid	0.52	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.13	0.00	0.15	0.00
3-Hydroxyphenylpropionic-Acid	0.00	0.24	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.80	0.62	0.00	0.16	0.00	0.00	0.00	0.54	0.49	0.08	0.14	0.00	0.00	0.00
4-Hydroxycinnamic-Acid	0.00	0.00	0.00	0.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxymandelic-Acid	2.80	1.15	0.76	0.00	0.00	0.00	0.00	5.75	1.01	1.75	0.00	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.20	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-(Hydroxymethyl)Furan-2-Carboxylic-/	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.23	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	6.99	0.00	1.06	0.00	0.00	0.00	0.00	0.00	0.19	0.01	0.14	0.00	0.00	0.01
Erythro-Pentonic-Acid	0.00	0.03	0.00	0.00	0.00	0.00	0.05	0.00	0.03	0.03	0.00	0.00	0.00	0.01
Citraconic-Acid	27.58	0.00	2.29	0.00	0.00	0.00	0.00	0.95	0.00	0.24	0.00	0.00	0.00	0.00
Citramalic-Acid	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Levulinic-Acid	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Maleic-Acid	1.24	1.06	1.20	0.00	0.22	0.00	0.12	0.00	0.14	0.27	0.60	0.18	0.00	0.47
Parabanic-Acid	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Dimethylmalonic-Acid	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pentadecanoic-Acid	0.73	0.57	0.24	0.10	0.00	0.00	0.02	0.88	0.32	0.28	0.00	0.00	0.38	0.00
Tricarballylic-Acid	0.00	0.03	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Urea	1.24	1.27	2.56	0.00	0.00	0.00	0.00	0.36	0.34	0.77	0.00	0.00	0.00	0.00
3-Hydroxyphenylhydracrylic-Acid	0.00	0.00	0.00	0.00	0.00	0.81	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	34.81	0.40	0.00	0.00	5.92	0.00	15.28	0.00	0.43	0.00	1.46	6.43	0.00	18.80
4-Methylmandelic-Acid	0.00	0.02	0.00	0.03	0.28	0.65	0.05	0.00	0.00	0.00	0.12	0.10	0.00	0.00
2,3-Dihydroxybenzoic-Acid	0.05	0.08	0.07	0.74	0.00	0.00	0.01	0.00	0.00	0.02	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	29.48	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxyacrylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.00	0.00

2,4-Dihydroxy-4-Methyl-2-Pentene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00
1,2,3-Trihydroxypropane	0.00	0.00	4.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	0.62	0.00	0.00	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.35	0.00	0.00
1,3-Benzenedicarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.67	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.98	0.00	0.83	0.00	0.00	0.00	0.00	0.09	0.90	0.68	0.00	0.00	0.00
4-Methoxy-3-Hydroxycinnamic-Acid	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methoxymandelic-Acid	0.00	3.80	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.00	0.00	2.65	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	91.98	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	4.66	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	11.17	2.68	0.00	0.00	0.00	0.00	0.00	8.96	1.69	2.08	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	22.53	0.00	0.00	0.00	0.00	0.00	0.00	11.16	0.00	0.00	0.00	0.00	0.00	0.00
3,4-Dihydroxy-3,7,11-Trimethyldodecar	0.04	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	7.35	0.00	0.00	0.00	0.00	0.00	0.00
N-Acrylylglycine	0.00	5.62	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glyoxylic-Acid	1.24	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Butanediol	0.00	0.75	0.00	0.00	0.00	0.00	0.00	0.30	0.00	0.44	1.08	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	2.68	0.00	0.00	0.10	2.26	0.00	1.34	0.00	0.00	0.00	0.00	2.09	0.15	10.38
1,4-Dihydroxybutane	0.57	0.61	0.00	0.00	0.00	0.00	0.00	0.36	0.47	0.14	0.00	0.00	0.00	0.03
1,13-Dihydroxytridecane	0.00	0.64	0.00	0.00	0.00	0.00	0.00	0.00	1.10	0.41	0.00	0.00	0.00	0.00
1,2-Dihydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00
1,2-Dihydroxy-3-Methylbutane	0.00	0.00	1.28	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxyethane	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.49	0.00	0.00	0.00	0.00
1,2-Dihydroxycyclohexene	0.00	0.07	0.34	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00
1,6-Dihydroxyhexaan	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.21	0.00	0.00
Galactopyranose-Alpha-D	1.36	0.59	0.00	0.00	0.00	0.00	0.00	1.78	0.47	0.38	0.00	0.00	0.00	0.00
Galactopyranose-Beta-D	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.48	0.00	0.00	0.00	0.00
Glucopyranose	0.00	0.36	0.00	0.00	0.00	0.00	0.00	1.68	0.00	0.34	0.00	0.00	0.00	0.00
Mannitol	0.00	0.00	0.37	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Fructofuranose	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.00
Fucose	0.00	0.00	0.00	0.00	0.00	0.00	0.08	0.00	0.48	0.00	0.00	0.00	0.00	0.07

Organic acid	Rotenone (10 nM)							Rotenone (1000 nM)						
	Repeat number							Repeat number						
	1	2	3	4	5	6	7	1	2	3	4	5	6	7
Valeric-Acid	0.00	0.00	0.00	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00
Octanoic-Acid	0.11	0.00	0.00	0.07	0.22	0.00	0.00	0.00	0.00	0.00	0.12	0.00	0.00	0.00
NoAcid	0.47	0.19	0.00	0.04	0.44	0.00	0.35	0.33	0.00	0.13	0.00	0.11	0.26	0.44
DecAcid	0.03	0.14	0.00	0.33	0.04	0.00	0.00	0.00	0.00	0.07	0.18	0.00	0.00	0.00
EicAcid	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.06	0.00	0.00	0.00	0.00	0.00	0.00
Dodecanoic-Acid	0.99	0.52	0.23	0.00	0.05	1.82	0.77	0.50	1.87	0.38	0.00	0.06	1.73	0.59
Tetradecanoic-Acid	3.01	1.81	1.68	0.80	0.00	2.98	1.47	3.73	5.97	1.07	0.86	0.00	2.96	1.27
Palmitic-Acid	44.90	41.43	46.57	46.05	2.69	26.25	15.81	72.24	89.24	20.13	14.36	0.70	27.57	9.94
Heptadecanoic-Acid	1.00	0.65	0.40	0.15	0.00	0.00	0.07	0.82	0.58	0.07	0.00	0.00	0.00	0.00
Octadecanoic-Acid	35.76	23.16	20.22	23.09	0.43	20.19	9.45	36.91	34.01	10.00	10.62	0.02	23.29	4.72
4-Methylpimelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.18	0.00	0.00	0.00	0.00	0.00	0.00
Nonadecanoic-Acid	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	0.00	19.89	29.49	19.36	0.00	2.76	0.00	35.21	0.00	7.46	0.92	0.00	0.00	0.00
2-Keto-Octanoic-Acid	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Methyladipic-Acid	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxylauric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
2-Hydroxysebacic-Acid	2.18	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxytetradecanoic-Acid	16.61	0.00	0.00	0.00	0.00	0.00	0.00	0.00	24.50	0.00	0.00	0.00	0.00	0.00
Palmitelaidic-Acid	0.39	1.33	2.70	1.23	0.00	0.00	0.00	2.92	1.22	0.45	0.00	0.00	0.00	0.00
Oleic-Acid	18.09	18.59	28.66	6.02	0.00	1.98	3.23	35.72	10.41	0.00	1.08	0.00	1.34	1.25
2-Undecenoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
11-Octadecenoic-Acid	16.61	19.89	29.49	19.36	0.00	2.76	0.00	35.21	24.50	7.46	0.92	0.00	0.00	0.00
Arachidonic-Acid	1.46	2.50	2.51	1.68	0.00	0.00	0.00	2.30	0.00	0.27	0.00	0.00	0.00	0.00
9-Octadecenoic-Acid	0.00	0.00	24.47	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
9,12-Octadecadienoic-Acid	5.24	7.21	8.00	5.92	0.00	0.00	0.99	10.60	1.99	1.99	0.07	0.00	0.00	0.23
Pimelic-Acid	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Suberic-Acid	0.15	0.02	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00
Adipic-acid	0.00	0.00	0.00	0.47	0.00	0.00	0.00	0.00	0.00	0.00	0.46	0.00	0.00	0.00
Azelaic-Acid	2.15	0.00	0.00	0.15	0.00	0.92	1.09	1.40	0.50	0.08	0.00	0.00	0.00	0.10
Tetradecanedioic-Acid	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.05	0.11	0.00	0.19	0.00	0.00	0.00
Malonic-Acid	1.13	0.79	218.50	0.33	0.00	0.00	0.01	0.00	0.00	0.74	0.61	0.00	0.00	6.82
Citric-acid	28.23	5.38	0.91	0.39	0.00	0.00	0.28	10.97	0.00	0.17	0.00	0.00	0.00	0.00
Aconitic-Acid	0.63	0.06	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Succinic-Acid	61.53	9.94	6.53	2.67	1.36	13.63	3.78	20.36	15.07	7.37	1.42	1.68	0.98	3.96

Fumaric-Acid	3.17	0.26	0.00	0.45	0.08	0.77	0.08	0.55	0.00	0.00	0.06	0.09	0.00	0.00
Malic-Acid	9.62	0.83	0.95	1.95	0.24	0.97	1.37	4.23	0.26	1.21	0.00	1.44	0.00	1.29
Lactic-Acid	380.06	123.02	185.50	45.13	58.43	48.51	70.62	344.38	96.90	125.19	33.08	66.29	17.58	52.45
Lactyllactate	1.72	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pyruvic-Acid	0.74	0.49	0.28	0.14	0.00	0.00	0.00	0.53	0.00	0.09	0.12	0.00	0.00	1.94
GLYCOLIC-DITMS	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00
2-Methyl-3-Ketobutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00	0.11	0.00	0.00
3-Ketobutyric-Acid	8.68	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.02	0.00	0.00	0.00	0.00	0.02	0.00	0.01	0.00	0.00
N-Acrylglycine	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.48	0.00	0.00	0.00	0.00	0.00	0.00
Oxalic-Acid	2.15	1.17	0.93	1.55	3.75	2.44	0.58	1.64	5.99	3.34	1.06	8.53	0.00	0.63
3-Hydroxyisobutyric-Acid	1.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketoisovaleric-Acid	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.08
4-Hydroxyphenyllactic-Acid	1.19	0.31	0.20	0.00	0.00	0.00	0.00	1.02	0.00	0.04	0.00	0.00	0.00	0.00
N-Acetyltyrosine	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxyvaleric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.27	0.00	0.00	0.00	0.00
3-Hydroxypropionic-Acid	1.34	0.69	0.84	1.53	6.09	4.05	3.13	1.31	8.74	0.43	2.06	11.91	2.49	5.40
Methylmalonic-Acid	0.32	7.55	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Methylmalonic-Acid-Tritms	0.10	0.00	6.13	0.00	0.00	0.00	0.00	0.17	0.00	0.00	0.00	0.00	0.00	0.00
N-Propionylglycine	7.62	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glutaric-Acid	0.00	0.06	0.00	0.46	0.01	0.06	0.04	0.00	0.00	0.00	0.00	0.01	0.00	0.02
2-Ketobutyric-Acid	0.71	0.00	0.22	0.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00	0.00	0.00
N-Phenylacetylglycine	17.41	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyglytaric-Acid	0.00	0.04	0.00	0.00	0.00	0.00	0.00	0.24	0.00	0.04	0.00	0.00	0.00	0.09
4-Hydroxyphenylacetic-Acid	0.19	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenylacetic-Acid	1.23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Phenyllactic-Acid	0.10	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxybutyric-Acid	2.29	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Acetyltyrosine	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N-Acetylaspartic-Acid	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pyroglutamic-Acid	184.76	36.71	19.83	1.17	0.00	0.00	0.00	93.67	0.00	29.11	0.00	0.00	0.00	0.00
Uracil	2.50	0.15	0.04	0.00	0.00	0.00	0.00	0.51	0.00	0.05	0.00	0.00	0.00	0.00
Pyrimidinedione	1.37	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Methylpyrimidine-2,4-Diol	0.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyhippuric-Acid	0.00	0.54	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyhippuric-Acid	0.16	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cholesterol	0.00	0.00	0.00	0.00	0.00	5.23	0.98	0.00	30.98	0.00	0.00	0.00	2.66	0.55
Benzoic-Acid	0.64	0.00	0.00	0.02	0.15	0.00	0.07	0.00	1.68	0.10	0.10	0.10	0.04	0.25
Hippuric-Acid	6.73	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00	0.00	0.00

1-(4-hydroxyphenyl)ethanone	0.00	0.00	0.00	0.21	0.00	0.00	0.00	49.85	0.00	20.52	0.07	0.00	0.00	0.00
2,4,6-Trihydroxybenzoic-Acid	0.00	0.00	0.00	0.00	0.28	0.42	0.39	0.00	0.86	0.00	0.00	0.50	0.24	0.22
2,3-Dihydroxypropanoic-Acid	0.00	0.00	0.14	0.00	0.13	0.00	0.22	0.00	0.00	0.24	0.00	0.21	0.00	0.15
2,4-Dihydroxybenzoic-Acid	0.19	0.00	0.18	0.00	0.00	0.00	0.00	2.82	0.00	0.38	0.39	0.00	0.00	0.00
2,5-Furandicarboxylic-Acid	0.00	0.00	0.64	0.00	0.00	0.00	0.00	2.60	0.00	0.00	0.00	0.00	0.00	0.00
2,6-Dihydroxybenzoic-Acid	59.54	0.68	13.02	1.23	0.02	0.00	0.00	91.93	0.00	0.35	10.31	0.03	0.00	0.00
2-Hydroxy-5-Methoxybenzoic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.41	0.00	0.00	0.00	0.00
3,4-Dihydroxybutyric-Acid	0.00	0.22	0.00	0.06	1.67	2.52	1.78	0.72	2.19	0.18	0.00	3.49	0.43	1.65
3-Hydorxybenzoic-Acid	0.08	0.00	0.00	0.19	0.00	0.00	0.00	0.20	0.13	0.04	0.21	0.00	0.00	0.00
4-Hydroxbenzoic-Acid	0.85	0.19	0.00	0.08	0.00	0.18	0.00	0.30	0.00	0.04	0.05	0.00	0.28	0.06
4-Hydroxymandelic-Acid	1.69	1.42	0.53	1.24	0.00	0.00	0.00	4.25	0.00	1.43	1.42	0.00	0.00	0.00
3-Methoxycinnamic-Acid,	0.47	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Ketovaleric-Acid	0.00	0.00	0.00	0.23	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
5-Hydroxyhydantoin	0.21	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Hydroxyphenylacrylic-Acid	0.04	0.00	0.02	0.34	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00
Dimethylmalonic-Acid	0.00	0.08	0.00	0.00	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Erythro-Pentonic-Acid	0.25	0.00	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00
Citraconic-Acid	2.50	0.00	0.00	0.08	0.00	0.00	0.00	0.37	0.00	0.00	0.00	0.19	0.00	0.00
Citramalic-Acid	2.29	0.00	0.00	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00
Maleic-Acid	46.58	0.27	0.00	0.00	0.00	0.00	0.33	0.58	0.00	0.59	0.00	0.00	0.00	0.00
Parabanic-Acid	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Pentadecanoic-Acid	0.54	0.45	0.20	0.32	0.00	0.00	0.05	1.00	0.77	0.16	0.02	0.00	0.25	0.00
Urea	0.00	0.32	0.73	0.00	0.00	0.00	0.00	2.06	0.00	0.61	0.00	0.00	0.00	0.00
3-Methyl-4-Hydroxybutyrate	3.19	1.05	0.53	0.00	13.13	0.00	0.00	2.02	0.00	22.62	0.00	21.06	0.00	0.00
4-Methylmandelic-Acid	0.00	0.05	0.00	0.09	0.00	0.00	0.30	0.16	0.52	0.00	0.09	0.05	0.00	0.20
2,3-Dihydroxybenzoic-Acid	0.05	0.00	2.56	0.00	0.00	0.00	0.00	0.57	0.00	0.02	0.04	0.00	0.00	0.00
1,2,3-Trihydroxypropane	2.97	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,4-Trihydroxybenzoic-Acid	0.00	1.02	0.00	0.00	0.08	0.38	0.00	0.00	0.00	0.00	0.00	0.42	0.31	0.00
1,3-Benzenedicarboxylic-Acid	0.32	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3,3-Trihydroxy-2-Propenoic-Acid	0.00	0.00	0.00	0.00	0.00	1.31	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.44	0.66	0.00	0.00	0.00	0.00	0.00	0.00	0.28	0.00	0.00	0.00	0.00
2-Ethyl-3-ketobutyric-Acid-triTMS	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Ketopyrrolidine-1-Carboxylic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	76.97	0.00	0.00	0.00	0.00	0.00	0.00
2,2-Dihydroxyacetic-Acid	0.00	0.00	0.00	0.55	0.00	0.00	0.00	0.16	0.00	0.00	0.00	0.00	0.00	0.00
2-Hydroxyphenylpropionic-Acid	2.95	0.98	0.00	0.00	0.00	0.00	0.00	4.48	0.00	0.40	0.00	0.00	0.00	0.00
2-Hydroxy-3-Methylbutryic_Acid	0.00	0.00	0.00	0.00	0.00	0.09	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2-Methoxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.69	0.00	0.00	0.00	0.00
Parabanic-Acid	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
4-Methylcinnamic-Acid	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

2-Methyl-4-Hydroxybutyric-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.52	0.00	0.00	0.00	0.00	0.00	0.00
3-Hydroxymandelic-Acid	0.00	0.00	0.00	0.00	0.00	0.00	0.00	2.39	0.00	0.00	0.00	0.00	0.00	0.00
4-Pyridinecarboxylic-Acid	0.12	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Cyclopentanecarboxylic-Acid	0.08	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
2,3-Dihydroxybutane	0.64	0.00	0.00	0.00	1.47	0.00	1.55	0.00	3.11	0.00	0.00	4.92	0.00	1.99
Glucuto	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxypropane	0.00	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.13	0.00	0.00	0.00	0.00	0.00
1,4-Dihydroxybutane	0.00	0.00	0.00	0.00	0.04	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.13
4-Phenol	0.05	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
1,13-Dihydroxytridecane	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.24	0.00	0.00	0.00	0.00	0.00	0.00
1,2-Dihydroxybenzene	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.32	0.00
1,2-Dihydroxyethane	0.56	0.00	0.96	1.44	0.00	0.12	0.00	0.00	0.00	0.00	0.00	0.24	0.00	0.00
1,2-Dihydroxycyclohexene	12.62	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.33	0.00
Galactopyranose-Alpha-D	1.85	0.26	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Glucopyranose	2.14	0.47	0.00	0.00	0.00	0.00	0.15	0.00	0.00	0.19	0.00	0.00	0.00	0.00