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Determination of profiles of occurrence of parabens, triclocarban and elements in select snack foodstuffs from Norway and other countries

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Determination of profiles of occurrence of parabens, triclocarban and elements in select snack foodstuffs from Norway and other countries

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Environmental Toxicology and Chemistry
Submission date: May 2019
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Trondheim, 15.05.2019

Yuki Kimura

Abstract

Processed food stuffs are added chemicals to keep stable quality for long periods. While the additives give positive effect to ordinary life, some of these also possibly cause estrogenic problem for our health. Therefore, determination of the quantity of those chemicals in the food stuffs is a very important task. Among food stuffs, snacks are popular in all generations all over the world, however it has not studied yet. Focusing on the snack food stuffs, thus, would provide useful result for choosing it for especially infants who should be cared for health. Comparing the trend by countries and by food types should be emphasis.

In this study, a liquid chromatography tandem mass spectrometry method was developed and employed for the simultaneous determination of six parabens, five parabens derivatives and an antimicrobial in the snack food stuffs. The target parabens were methyl paraben, ethyl paraben, propyl paraben. butyl paraben, benzyl paraben and heptyl paraben, target parabens derivatives were 4-hydroxybenzoic acid, 3,4-dihydroxybenzoic acid, 4-hydroxy-3-methoxybenzoic acid and ethyl-protocatechuic acid, and target antimicrobial was triclocarban. Methyl paraben and ethyl paraben are well known preservatives, while derivatives are previously suggested transformation process from parabens within an organism. In addition, 62 elements were measured in the snack food samples by ICP-MS analysis in order to account for inorganic pollution sources.

The snack food samples analyzed in this study were collected at the markets in seven countries. Solid-liquid extraction was employed for clean-up and extraction process. For concentration, parabens derivatives were basically much higher than parabens, whereas antimicrobial, triclocarban, was presented very low value over all samples. Methyl paraben and ethyl paraben were the most popular preservatives used, but heptyl paraben was only found in low concentrations. No clear between country patterns were found possibly due to international trade. For categorized characteristics, clear difference was found. Further, in the inorganic analysis, accuracy was ±20 % as certified reference materials and parallel/repeating test. Macromineral elements were presented the highest concentration, then trace elements followed. The result also indicated the snacks contained different ingredients depending on the country.

In the PCA analysis, results were separated by characteristics, form, taste and target age. Na and EtP/OH-EtP were positively correlated, which can be a marker to know how amount of EtP would be contained as seeing the product package.

List of Contents

List of Figures

List of Tables

Abbreviation

Table 0.1: Abbreviations of used chemicals in this study

Chemical	Abbreviation
Methyl paraben	MeP
Ethyl paraben	EtP
Propyl paraben	PrP
Butyl paraben	BuP
Benzyl paraben	BezP
Heptyl paraben	HeP
4-hydrixybenzoic acid	4-HB
3,4-dihydroxybenzoic acid	3,4-DHB
4-hydroxy-3-methoxybenzoic acid	Vanillic acid
Ethyl protocatechuic acid	OH-EtP
Triclocarban	TCC
Methanol	MeOH

1. INTRODUCTION

Nowadays, most consumer products all over the world are mass produced and packed for long term preservation. To achieve this, several different chemicals are added. Paraben (*p*-hydroxybenzoic acid esters), Triclosan (2,4,4′-trichloro-2-hydroxydisphenyl ether) and Triclocarban (3,4,4′-trichlorocarbanilide) are some of them which are used for long period preservation due to their antimicrobial properties. These are group of chemicals generally used as additives in foodstuffs, beverages, cosmetics, pharmaceuticals and several personal care products (Andersen 2008; Guo and Kannan 2013; Karthikraj and Kannan 2018; Moreta et al. 2015a). Those chemicals have also been considered as pollutants due to their specific property.

Recent studies have focused on the amount of parabens in human urine (Adoamnei et al. 2018; Casas et al. 2011; Honda et al. 2018; Iyer et al. 2018; Zhao et al. 2017). Knowing the pollution level is important to avoid pollutants, as well as improve the principle of pollutant use. While, the possible sources of pollutants were also studied so far; how amounts of parabens contained in the indoor dust, baby goods, foods and pharmaceuticals (Asimakopoulos et al. 2016; Chen et al. 2018b; Liao et al. 2013a, 2013b; Ma et al. 2016; Moreta et al. 2015b). These reported that possible sources where people were exposed to pollutant, and how concentration of them were detected. Among them, especially food analyses are really important subject since we have to ingest for life, however the studies were done by comparing the stuffs in a country. Evaluating the differences between country to country will be useful study to know the trend of use in country and possibly take the first step toward improving the regulations for use of pollutant for our health.

In addition to the above, elemental analysis is also needed as some elements are essential for our health and some are toxicity. Elemental analysis of food have been performed in many countries, but few studies have been carried out with comparing different countries (Chekri et al. 2019; Fátima Barroso et al. 2009; Moreda-Piñeiro et al. 2018), and few studies have been carried out on snacks which are eaten between meals. Therefore, in the present thesis both organic and inorganic chemicals have been determined in a wide variety of popular snacks collected in several countries, with a focus on possible differences between countries and the interrelationships between organic and inorganic components.

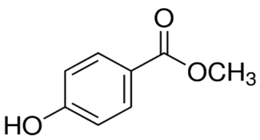
2. THEORY

The theory part begins with the properties of organic chemicals which are target analytes (parabens, its derivatives and microbials) in this study, and possible uses and effects. Then, inorganic chemicals section gives a description of properties of elements, possible sources and effect to human. A brief description of sample preparation follows, as well as analytical techniques which were employed in this study. Thereafter, detailed description is provided for quantification and quality assurance/validation. For the statistical process of data, theory about data transformation, correlations and principal component analysis (PCA) is presented in the last.

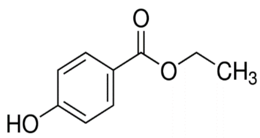
2.1. Organic Chemicals

2.1.1. Parabens

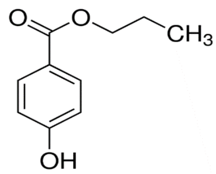
The parabens are the ester compounds of PHBA (4-hydroxy benzoic acid, 4-HB) and there are various kind of substituent which are attached as esters. The alkyl chain and aromatic ring are often put on there. Commonly known parabens are Methyl paraben (MeP), Ethyl paraben (EtP), Propyl paraben (PrP) and Butyl paraben (BuP), Heptyl Paraben (HeP) which are the example of parabens with alkyl chain, while Benzyl paraben (BezP) is representative paraben having aromatic ring (**Figure 2.1**).



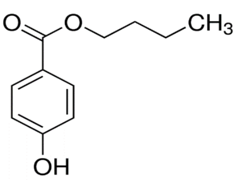
Methyl paraben



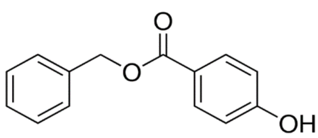
Ethyl paraben



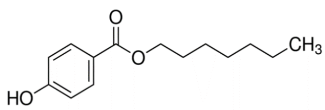
Propyl paraben



Butyl paraben



Benzyl paraben



Heptyl paraben

Figure 2.1: Chemical structure of parabens ring

Parabens are added commonly in foodstuffs because of their properties such as their stable over wide pH, lack of taste and odor, unchanged color, solubility in water and non-volatility (Ito et al. 2015; Soni et al. 2005, 2002). Moreover, the combination of multiple parabens can enhance the antimicrobial activity (Soni et al. 2002). There are several kinds of benefit as additive for products, however weak estrogenic activity attributed to some of them have been indicated. Various bioassays have reported that MeP, EtP, PrP, BuP and BezP possess estrogenic properties(Ahn et al. 2012; Anne Marie Vinggaard et al. 2000; Darbre et al. 2002; Golden et al. 2005; Hossaini et al. 2000; Hu et al. 2013; Miller et al. 2001; Oishi 2002; Okubo et al. 2001; Routledge et al. 1998). From this perspective, an acceptable daily intake (ADI) for the total amount of three parabens, MeP, EtP and PrP, has been set up at <10 mg/kg body weight (bw)/day (JECFA 1974). Further, the use of PrP and BuP for children's product was prohibited in Denmark in 2011 (SCCS 2011).

Other kinds of chemicals with structures similar to parabens are also a focus in this study. 4-hydroxybenzoic acid (4-HB), 3,4-dihydroxy benzoic acid (3,4-DHB), 4-hydroxy-3-methoxybenzoic acid (Vanillic acid) and ethyl-protocatechuic acid (OH-EtP) are showed below (**Figure 2.2**). 3,4-dihydroxy benzoic acid is also known as protocatechuic acid which is a phenolic compound. It is often found in natural products such as flowers, fruits and plants and used as additive due to its applications: antioxidant, antiulcer and antidiabetic. Moreover, antibacterial and antiviral activities are reported as function of 3,4-DHB (Antony and Wasewar 2018). While Vanillic acid is also used for food and drug products as flavoring agent and an intermediate of the vanillin. It is the plant product having cardioprotective, antimicrobial and antioxidant properties (Antony and Wasewar 2018; Rasheeda et al. 2018).

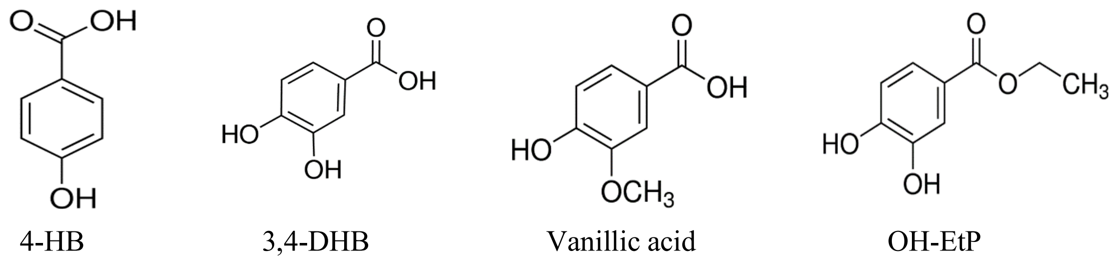
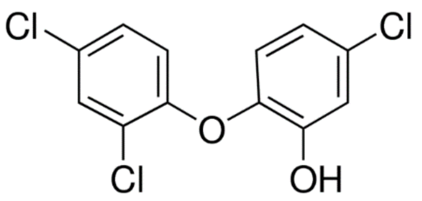


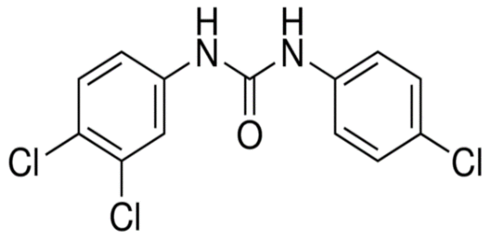
Figure 2.2: Chemical structure of parabens derivatives

2.1.2. Antimicrobials

Triclosan (TCS) and Triclocarban (TCC) are categorized as polychloro phenoxy phenols (**Figure 2.3**). These two compounds are often used as antimicrobials for personal care products (PCPs). Regarding TCS, it has been incorporated into polymeric materials for packaging to reduce or prevent microbial growth (Espitia et al. 2016; de Fátima F Soares et al. 2009). Recent studies have shown the potential health risks which TCS constricts endocrine and immunological ability such as improvement of bacteria resistance and cancer (Dinwiddie et al. 2014; Schweizer 2001). Under these circumstances, TCS has been removed from the EU list of provisional additives for use in food contact materials (Dann and Hontela 2011). As for TCC, it can impair mammalian reproduction and the methemoglobinemia is related with exposing human (Asimakopoulos et al. 2014; Zhou et al. 2012).



Triclosan



Triclocarban

Figure 2.3: Chemical structure of microbials

2.2. Inorganic Chemicals (Heavy Metals)

Heavy metal (Cd, Cr, Cu, Pb, Ni, Hg and Zn) contamination has been getting major concern in worldwide scale because of a serious threat with their duration, concentration and toxicity (Sang et al. 2018; Santorufo et al. 2012). The possibility of heavy metal's accumulation in food crops has been increased due to natural and human activities such as mining and metal smelting, urban development and injudicious use of agricultural chemicals (Doabi et al. 2018; Huang et al. 2007; Wu and Yi 2015). There are mainly three routes which heavy metals are transferred into human body: ingestion, inhalation and dermal contact (Aelion et al. 2008; Doabi et al. 2018; Madrid et al. 2002; Qing et al. 2015; Wu et al. 2015). Due to the serious toxicity, some heavy metals may pose a problem even at low concentrations. In Japan, for instance, cruel incident related heavy metal has occurred around half a century ago. Mercury contaminated effluent was discharged directly to ocean without any cleaning up process, therefore chemicals related mercury had been accumulating in environment. As a result, lots of people were exposed to potent toxicity (Evers et al. 2016; Tomiyasu et al. 2014). The heavy metals are also included in food waste and have effect to waste treatment. Possessing acute toxicity, substantial treatment costs are taken and it has financially stressed to cope with the treatment process in government across different countries (Chu et al. 2019).

2.3. Sample Preparation

Many challenges are involved in trace analysis of samples because there are the complexity of sample matrices and the diversity of interfering compounds (Pérez-Fernández et al. 2017). The performance of selected procedure for sample preparation might have impact due to existence of the matrix: the limit of detection, the limit of quantification, accuracy, precision and linearity might get effect. Because of quite low concentration of environmental samples, enrichment and clean-up process are needed as pre-treatment procedure to achieve suitable concentration level for analysis (Padrón et al. 2014). There are several objectives which should be accomplished for sample extraction toward coming analysis. Primary, the separation of the target chemicals from complex matrix is essential task such as foodstuffs samples to remove interfering compounds. Secondary, in case of trace level analytes, the target chemicals should be condensed to improve instrumental sensitivity applying extraction and concentration steps. Lastly, consideration for the compatibility between the apparatus analysis and the sample matrix is necessary step. Mass spectrometry is the most common technique for organic and inorganic compounds detection (Mitra 2003).

2.3.1. Sample preparation for organic chemical analysis

This section explained the extraction methods for organic analytes, as well as the analytical techniques performed by the earlier researches is given in **Table 2.1**.

2.3.1.1. Liquid-liquid extraction

Liquid-liquid extraction (LLE) is an appropriate method separating between two immiscible solvent such as organic solvent and aqueous solution. In the simplest case, the solute, the carrier liquid and the solvent are involved. This extraction technique is known as safe, reasonable way and environmentally friendly process. The partitioning coefficient K_{LLE} is given by the equation:

$$\boldsymbol{K_{LLE}} = \frac{[\boldsymbol{analyte}]_{\boldsymbol{organic}}}{[\boldsymbol{analyte}]_{\boldsymbol{aqueous}}} \tag{2-1}$$

$[\text{analyte}]_{\text{organic}}$ and $[\text{analyte}]_{\text{aqueous}}$ are showing the concentration of the analyte in the immiscible phase (Lundanes et al. 2014; Marsousi et al. 2019).

2.3.1.2. Solid-liquid extraction

Solid-liquid extraction (SLE) is similar to LLE except that the solute dispersed in a solid phase rather than in a carrier liquid. This classical extraction method can separate analyte from solid samples into liquid phase then solid sample is removed by filtration. The efficiency of this extraction technique is mainly affected by solvent, time of contact, temperature, solid/liquid ratio (Ballesteros et al. 2013; Lepojević et al. 2017).
In recent years, there are several assisting techniques for increasing efficiency of extraction procedure such as ultrasound-assisted and pressure-enhanced methods. Ultrasound-assisted is an effective and time-saving extraction method. It is suitable way for temperature-sensitive components since it can reduce the operating temperature. Whereas, pressure-enhanced can increase the extract yields with shorter time at lower temperature and enhance mass transport process. It has also been recognized as an environmentally friendly technology (Baranowska 2016; Xi and Luo 2015).

Table 2.1: Previous studies on analytical methods for determination of the parabens

Analytical technique	Analyte	Sample	Extraction technique	Column	Solvent	Reference
HPLC-MS/MS	Parabens	Food stuffs	SPE	Strata® NH_2	Acetonitrile	Liao et al. 2013a
HPLC-MS/MS	Parabens Metabolite	Pet food	SLE	-	Ethyl acetate	Karthikraj et al. 2018
HPLC-UV	Parabens	Paste, Juice	SOE, DLLME	-	Acetonitrile	Alshana et al. 2015
CapLC-UV	Parabens	Food, Cosmetics Pharmaceutical Products	VA-DLLME-SFO, SA-CPE	-	1-undecanol Triton X-114	Chen et al. 2018a
UPLC-MS/MS	Parabens	Pharmaceutical Products	SLE	-	Methyl *tert* butyl ether	Ma et al. 2016
HPLC-ESI-MS/MS	Parabens	Pharmaceutical Products	SPE	Strata® NH_2 Oasis® HLB	Methanol	Moreta et al. 2015a
LC-MS/MS	Preservatives Biogenic amines	Meat, Fish Processed products	SLE	-	Mixture of methanol, acetonitrile and water	Molognoni et al. 2018
HPLC-TOF/MS	Parabens	Beverage	SPE	Oasis® HLB	Mixture of methanol and water	Li et al. 2008
UPLC-MS/MS	Parabens	Urine	DLLME	-	Mixture of acetone and trichloromethane	Adoamnei et al. 2018
UPLC-MS/MS	Parabens	Urine	LLE	-	Ethyl acetate	Honda et al. 2018
UPLC-HR/MS	Parabens	Urine	USAEME	-	Ethyl acetate	Zhou et al. 2018
UPLC-MS/MS	Parabens	Plasma	LLE	-	*tert*-butyl methyl ether	Kolatorova Sosvorova et al. 2017
UPLC-MS/MS	Parabens	Urine	LLE	-	Mixture of methyl tert-butyl ether and ethyl acetate	Zhao et al. 2018
HPLC-MS/MS	Parabens	Food stuffs	SPE	Strata® NH_2	Acetonitrile	Liao et al. 2013b
UPLC-DAD	Parabens	Food stuffs	SLE	-	Methanol	Sugiura and Nakajima 2017

2.3.2. Sample preparation for elemental analysis

A decomposition is essential process for inorganic analysis to put the original sample into a solution where the analyte is homogeneously distributed prior to instrumental analysis. The principle of an effective procedure is that dissolution must be performed as complete as possible, organic materials have to be absolutely mineralized and inorganic materials should be altered to soluble compounds. Residual matrix components must be removed to prevent them from interfering with the detection (Baranowska 2016). Liquids can be analyzed directly without decomposition provided total dissolved solids (TDS) are below 0.5%, whilst the solids can precipitate in the nebulizer overloaded plasm when TDS is above 0.5%. With solid samples containing the organic matter have hydrogen peroxide added during dissolution step due to the property of H_2O_2 breaking down organic matter efficiently ("Thermo Fisher Scientific" 2019a).

Microwave-assisted acid digestion has been considered as the most suitable method for the decomposition of complex matrices. Taking advantage of several aspects, that sample preparation technique using various combination of acids under high temperature and pressure has become well established and an extensively employed process for digestion of assorted food related matrices to determine the metals (Mullapudi et al. 2019). This process can make digestion time shorter and recovery better even for volatile elements and it decreases the risk of external contamination. The detection limit and the accuracy of the analytical method are improved since even the small amount of acids is enough (Hassan et al. 2007). Nitric acid is strong oxidant which can dissolve all common metals except aluminum and chromium (Skoog et al. 2003).

2.4. Analytical Techniques

2.4.1. LC-MS/MS

2.4.1.1. Principle

A mass spectrometer coupled to HPLC (LC-MS/MS) is a common apparatus to analyze the samples as it has good property of robustness, automation and performance (Lundanes et al. 2014). The combination of LC and MS provides high sensitivity and "fingerprint" of a specific eluent instead of depending on the retention time in HPLC (Skoog et al. 2003). The important part of the LC analysis system is the chromatographic column which the actual separation occurs (**Figure 2.4**). The ability of the column separating the samples in the complex matrices must be considered. The efficiency of the separation of the different analyte from each other is also considerable point to avoid and decrease the background noise in the analysis. Likewise, it is possible to reduce the risk of false positive and negative results (Kuster et al. 2009). The HPLC can separate the compounds relying on the different polarity.

The HPLC system consists of the various components which have different tasks to perform the analysis (**Figure 2.4**). First of all, the mobile phase is pumped up into the injector and the samples are simultaneously introduced into the injector. At there, samples are dissolved into the mobile phase and transferred to the column. The column is the place where the separation of the individual ingredients occurs depending on the different polarity of the components (Lundanes et al. 2014). The important factor to obtain clearly separated peaks in LC is the composition of the mobile phase and the column design/type (Fernando 2013). When the analytes have been separated into individual components, the various kinds of components are detected. After separation, the separated peaks are flowed into the detector. A typical LC column is 15-25 cm in length with 2-5 mm internal diameter (Lundanes et al. 2014). The most popular tube packing for LC consists of the small silica particles which is average 3-10 μm as diameter (Skoog et al. 2003). Effecting the variety of interactions between the components in the sample and the stationary phase in the column, each component elutes at a different speeds and different retention times. Retention time is the time from the sample injected into the mobile phase until selected peaks observed at the detector (Lundanes et al. 2014). To improve the peak shape in chromatography, the acidic condition for the mobile phase is the most effective way with mixture of methanol-water or acetonitrile-water with gradient elution. Furthermore, adding the acetic acid, formic acid or ammonium acetate into the mobile phase to get modification is powerful attempt improving the sensitivity of MS detection (Fernando 2013).

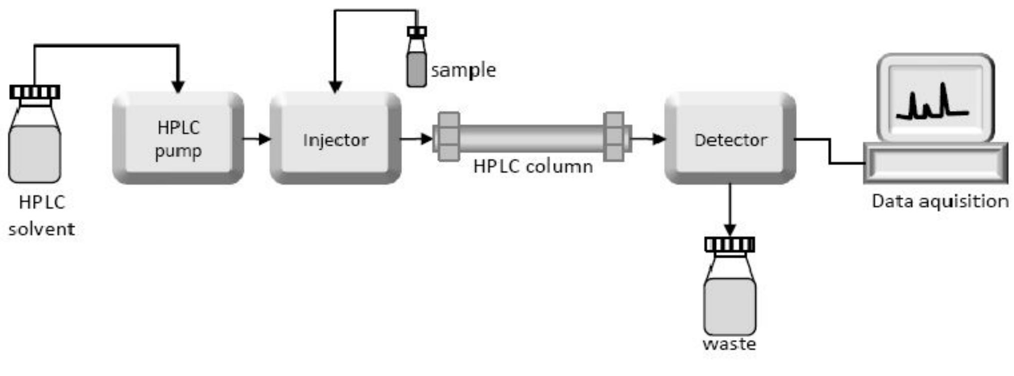


Figure 2.4: General instrumentation of HPLC system (“LaboratoryInfo.com” 2018)

In this experiment, a tandem mass spectrometer (triple quadrupole) was employed for the detection and quantification of target analytes. To identify all the components existing in the chromatogram of effluent, the information of molecular weight and retention times obtained from the total ion chromatogram of a mass spectrometer is usually not enough. However, a LC-MS/MS system can provide a superior sensitivity than can be provided by mass range scan since that system can produce the daughter ions by collision-induced fragmentation of the molecular ion. The fragmentation from the molecular ion to the daughter ions is attributed to the fragment-induced cleavage and rearrangements due to the missing of neutral molecules. Examining the mass intervals and isotopic patterns between product ions, the structure of the daughter ions can be estimated (Marvin C 2005).

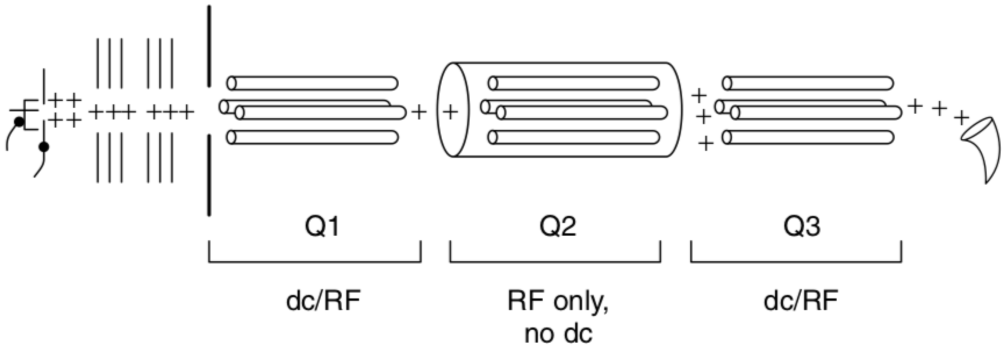


Figure 2.5: Schematic of a triple quadrupole mass spectrometer (Marvin C 2005)

The triple-quad LC-MS/MS (**Figure 2.5**) is designed to cleave ions into their daughter ions. It consists of 3 quadrupoles: a scanning Q1 quadrupole analyzer for separating the original precursor ion, an un-scanned Q2 quadrupole that serves as a collision cell to fragment the ions sent to it by collision with a heavy gas molecule and a scanning Q3 quadrupole analyzer for separating the fragments generated in the Q2 section. The first quadrupole (Q1) is operated in a full-scan or SIM mode to select ions to transfer into the Q2 quadrupole. The middle Q2 is filled with an inert heavy gas like krypton or xenon and the fragmentation is brought on as the transferred ions from Q1 to Q2 where the collision undergoes with the inert heavy gas. The last analyzer Q3, likewise, can be performed in full-scan or SIM mode operation (Marvin C 2005).

There are four possible combination mode of the two analyzers (Q1 and Q3): Q1 for scan/Q3 for SIM that is daughter mode/precursor scanning; Q1 for SIM/Q3 for scan that is parent mode/product scan; both Q1 and Q3 for scan called neutral loss scanning mode; both for SIM referred to multiple reaction monitoring (MRM) mode. The operation with the scan/SIM mode can determine which primary fragments are related each other. The Q1 is scanned over the mass range, then all fragments are transferred to the collision cell (Q2) and cleaved to the secondary fragments. The Q3 focuses on a specific mass/charge position and only primary fragments which break down to a specific secondary m/z value will be detected. The common daughter ion indicates interrelated primary fragments and becomes clue to understand easily which fragment are formed when a large primary fragment cleaves. On the other hand, the SIM/SIM combination is applicable to analysis for the specific components containing very impure mixtures without the complete clean-up process. The analysis can be performed at very high sensitivity as both analyzers detect at different specific single m/z values, and a lot of scans can be summed in determining their positions. When examining the chromatographic peak which are expected to appear, the first quadrupole separates a primary fragment characteristic of the targeted compound, it is passed to the collision cell then, the third quadrupole identifies it by looking for only one of its specific daughter ions at last. As for each analyzed compounds, an individual primary and secondary fragment in a time basis is picked up with corresponding the expected chromatographic retention time (Marvin C 2005).

2.4.1.2. Electrospray ionization

Electrospray ionization (ESI) is one of the well-known techniques for LC-MS and applicable to wide range of analysis. ESI is executed under the atmospheric pressure and mainly eligible for polar compounds. Neutral components either accept or donate a proton to generate positive or negative ions under given conditions. This reaction can occur either in the mobile phase or during the ESI process. The ionization process for acids and bases happens in the mobile phase with pH adjustments (Lundanes et al. 2014).

In this method, the mobile phase containing the analyte moves into the capillary with high voltage (typically +5 or -5 kV). A nebulizing gas (N_2) is mixed with the mobile phase at the outlet of the capillary and it is facilitated to form the droplets. A dry gas is introduced oppositely against the direction of flow. The droplets explode into smaller droplets due to the repulsive forces inside the drop which exceed the surface tension. The mobile phase transforms into the gas phase experiencing this repetitive process. While protonated ions are detected under positive mode, negative mode detects deprotonated ions (Lundanes et al. 2014).

2.4.2. ICP-MS

Inductively coupled plasma-mass spectrometry (ICP-MS) is a technique which can be used for multi element analysis of virtually any materials. ICP-MS has the function to precisely determine the concentration of almost all elements in the periodic table including the refractory elements that are often hard to analyze. Likewise, it can obtain concentrations of analyte elements at very low levels (down to 1-10 ng/L in solution). It is powerful and effective trace analysis apparatus since it runs with a wide linear dynamic work range, high accuracy and precision of measurement, and minimal interference (Taylor 2001).

All atomic spectroscopic techniques need to convert the sample into gas phase atoms and ions as well as atomization of the samples. When the samples are introduced into the atomization source in solution, the equipment makes the analyte species in solution free gas-phase atoms/or elementary ions (West et al. 2014).

Plasma is an electrically neutral gas comprising positive ions and free electrons. It has an enough energy to atomize, ionize and excite almost all element in the periodic table. The inductively coupled plasma (ICP) is the most common ionization method for mass spectrometry. Inert gases are often required to sustain plasma owing to ionization properties and availability in relatively pure form. Argon especially has a useful property leading the minimal chemical reactivity with various analyte species, and less interference with the analytical results (Taylor 2001). When argon ions are formed in plasma, they can absorb sufficient power from external source to keep the fixed temperature at which further ionization maintains the plasma for indefinite period. Thus, the temperature gets achieved as high as 10000 K (West et al. 2014).

Samples can be brought in the ICP with argon flowing through the central quartz tube (**Figure 2.6**). The nebulizer is often used as sample introduction way. Fine droplets of various sizes can be generated by breaking the liquid with high velocity gas, then these droplets are transferred into the plasma (West et al. 2014).

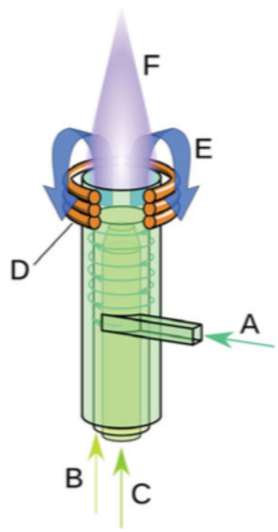


Figure 2.6: The inductively coupled plasma torch. A: cooling gas flow to outer quartz tube. B: discharge gas flow. C: flow of carrier gas. D: induction coil. E: force vectors of the magnetic field. F: the plasma torch (discharge).
Retrieved (15.05.2019) from https://en.wikipedia.org/wiki/File:ICP_torch.svg

The ICP-MS system uses the high temperature argon plasma as the atomic ion source as well as quadrupole as a mass analyzer. The formed ions in plasma enter in the mass analyzer which selects according to the mass-to-charge (m/z) ratio, then sorted ions are detected. Two metal cones usually constitute the interface: the sampler and the skimmer. An attached small orifice (approximately 1 mm) with each cone lets the ions pass through the optics which leads them into the mass analyzer. ICP-MS spectra can identify and quantify the elements present in the sample. For quantitative analysis, calibration curve based on the ratio of the ion signal for the analyte and internal standard is used to calculate (West et al. 2014).

2.5. Quantitation and Quality Assurance

2.5.1. Retention time (RT) and relative retention time (RRT)

The RT of a substance is variable, depending on the applied chromatographic system and it can fluctuate between consecutive injections. The representative factors causing the fluctuation are: instability of the flow rate for mobile phase and in column temperature; column degradation; air bubbles in the mobile phase; the difference of the column length. The difficulty of the comparison absolute RT is attributed to these factors. To resolve it, the RRT is a useful method, which the RRT is the ratio between the RT of the analyte and an internal standard (**Equation 2-2**). Thereby employing the RRT, the fluctuation impact is declined, since the internal standard is also suffered same impact and the proportion should be the same.

$$\boldsymbol{RRT} = \frac{\boldsymbol{RT\ of\ the\ analyte}}{\boldsymbol{RT\ of\ the\ internal\ standard}} \tag{2-2}$$

2.5.2. Relative response (RR)

The relative response (RR) is the factor to compensate for the gap in the signal intensity of a target analyte. This can be result of the differences during sample preparation (e.g. loss of sample volume) in instrumental response. Therefore, a ratio (called relative response) between the signal intensity of the analyte and the internal standard is employed to compensate the variations (**Equation 2-3**).

$$\boldsymbol{RR} = \frac{\boldsymbol{Response\ of\ the\ analyte}}{\boldsymbol{Response\ of\ the\ internal\ standard}} \tag{2-3}$$

2.5.3. Ion ratio (IR%)

The ion ratio is an additional parameter to confirm the target analytes. It is an individual ratio for each chemical in a sample matrix. This value is obtained by calculation: the area of the confirmation ion divided by the area of the quantification ion and multiplied by 100 (**Equation 2-4**).

$$\boldsymbol{IR}\% = \frac{\boldsymbol{Area\ of\ the\ confirmation\ ion}}{\boldsymbol{Area\ of\ the\ quantification\ ion}} \tag{2-4}$$

2.5.4. Repeatability and Reproducibility

Repeatability of measurements refers to the variation in repetition measurement made on the same samples under identical conditions. Whereas, Reproducibility refers to the variation in measurement made on the sample conducted under different conditions (Bartlett and Frost 2008). Herein, the reproducibility of the measurements performed between different days are indicated. A measurement can be run with same condition when this variation is less than a pre-determination acceptance criterion. Reproducibility can be obtained by calculating the standard deviation (**Equation 2-6**) or the relative standard deviation (**Equation 2-7**). The mean value is given as **Equation 2-5**.

$$\overline{\boldsymbol{x}} = \frac{\sum_{i=1}^{n} \boldsymbol{x_i}}{\boldsymbol{n}} \tag{2-5}$$

$$STD = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x})^2}{n-1}} \tag{2-6}$$

$$RSD\% = \frac{STD}{\bar{x}} \times 100\% \tag{2-7}$$

The values such as $x_1, x_2, \ldots, x_n$ are obtained number from the repeated test, $\bar{x}$ is the mean value of the sample, n is the number of samples and n-1 is the degree of freedom. Standard deviation (STD) is employed to measure precision and it provides the amount of variation or dispersion in a data set. Whilst, the relative standard deviation (RSD%) shows the coefficient of variation and also gives a clearer picture of the data quality than STD (Skoog et al. 2003).

2.5.5. Absolute and relative recovery

Recovery is a conception of how an analytical method is effective and used to determine whether analyte detection is affected by the sample preparation process (Meier and Zünd 2005; “Thermo Fisher Scientific” 2019b). The absolute recovery is given as **Equation 2-8** and the relative recovery is given as **Equation 2-9**.

$$Absolute\ recovery\% = \frac{A_{Pre-ext}}{A_{Post-ext}} \times 100\% \tag{2-8}$$

The term of $A_{Pre-ext}$ is the area of analyte in the pre-extraction spiked sample whereas the term of $A_{Post-ext}$ is the area of analyte in the post-extraction spiked sample.

$$Relative\ recovery\% = \frac{A_{Pre-ext}/IS_{Pre-ext}}{A_{Post-ext}/IS_{Post-ext}} \times 100 \tag{2-9}$$

The term of $IS_{Pre-ext}$ is the area of internal standard in the pre-extraction spiked sample whereas the term of $IS_{Post-ext}$ is the area of internal standard in the post-extraction spiked sample (B. K. Matuszewski et al. 2003).

The absolute recovery is the “real” recovery however it is regarded containing the higher uncertainty than its relative recovery. The relative recovery is the “corrected” recovery and it compensates effectively for the analyte losses throughout the sample preparation process.

2.5.6. Limit of detection and lower level of quantification

The limit of detection (LOD) is the smallest value which is clearly distinguished from a blank. While, the lower level of quantification (LLOQ), called (lowest) limit of quantification, is the smallest value which is can be measured with reasonable accuracy (Harris 2010).

The calculation of LODs and LLOQs can vary within a matrix due to matrix effects and it requires "fit the purpose" of the analytical method (Asimakopoulos 2014). In this study, the LLOQ was used to the lowest concentration detected in calibration (same way with Asimakopoulos 2014) and the LOD is obtained from equation below.

$$\boldsymbol{LOD = \frac{LLOQ}{3}} \tag{2-10}$$

2.5.7. Matrix effect

Evaluating matrix effects is the most important process when developing and LC/MS method. There can be coeluting compounds from matrix which can cause either enhancement or suppression. The ionization efficiency of the analyte may also be affected when the matrix compounds and the analyte are introduced simultaneously to the ion source. Thus, the matrix effect can affect both accuracy of the method and the reproducibility. To deal with matrix effect, the isotope labelled internal standard should be used(Van De Steene and Lambert 2008). Matrix factor (MF) expresses the effect on the analytical signal from the other compounds except the main analyte in the matrix (Silvestro et al. 2013).

$$\boldsymbol{MF = \frac{Area_{Post-ext-spike}}{Area_{IS}}} \tag{2-11}$$

The term of $Area_{Post-ext-spike}$ is the area of the post-extraction spiked sample whereas $Area_{IS}$ is the area of analyte in the standard solution (in solvent matrix) corresponding with same concentration as spiked sample (Silvestro et al. 2013). Furthermore, the matrix effect percentage (ME%) can be calculated by **Equation 2-12** (Asimakopoulos 2014).

$$\boldsymbol{ME\% = (MF - 1) \times 100\%} \tag{2-12}$$

2.5.8. Internal standard method

The internal standard method consists of a calibration curve in matrix which is conducted for every target analyte plotted the concentration of the spiked analytes against the proportion of the analyte response and the internal standard response in a set of standard solutions. Validation criteria (i.e. accuracy, reproducibility) can be calculated according to this ratio (Asimakopoulos 2014).

The internal standard is a compound that is very similar however does not correspond with the chemical species of interest in the samples. The signal from the analyte can be compared with the signal from the internal standard and the amount of the analyte present in the sample can be estimated since a known amount of the internal standard is added to the sample. The internal standard method is very useful when apparatus signal varies from run to run, also the results are not effected by any spilled action during sample preparation (Harris 2010).

2.6. Statistics

2.6.1. Correlation

Correlation is popular method to measure the relationship between two variables. The correlation efficient (r) can evaluate the strength of correlation. A r-value is assessed as following rule: from 0.90 to 1 is a very high correlation, 0.70-0.89 is a high correlation, 0.50-0.69 is a moderate correlation, 0.30-0.49 is a low correlation and 0.00-0.29 is little (Asuero et al. 2006). While, the p-value of a correlation shows the probability of finding a correlation if there is none. When the p-value is lower, the probability of "false" correlation should be considered as the lower.

2.6.2. PCA

PCA is a multivariate method, used to analyze the data table which is represented observations described by several dependent variables. The variables in the data table are inter-correlated in general. The aim of PCA is to: (1) extract the most important data from the table; (2) compress the size of the data set by keeping only this data; (3) simplify the description of the data set; (4) analyze the structure of the variables and observations. Besides, by displaying them as points in maps, PCA can show the similarity of the variables and the observations.

To achieve these aims, PCA calculates new variables known as principal components, obtained as linear combinations of the original variables. The first principal component is needed to have the largest possible variance of variables and then it will explicate the majority of variance in the data table. The second principal is that it computes the largest possible variance under the restraint of being orthogonal to the first principal. The values of these new variables obtained aforementioned process is called factor scores. These factor scores can be construed geometrically as projections of the observations on the principal components.

The data table used for PCA analysis is represented by a $\boldsymbol{I} \times \boldsymbol{J}$ matrix ($\boldsymbol{X}$) containing the observations ($\boldsymbol{I}$) described by variables ($\boldsymbol{J}$). The rank of the matrix ($\boldsymbol{X}$) is $\boldsymbol{L}$ ($\boldsymbol{L} \leq \boldsymbol{min}\,\{\boldsymbol{I},\boldsymbol{J}\}$).

The data is mostly pre-processed prior to analysis, almost always by centering the column of $\boldsymbol{X}$ which is subtracted the mean of each variable from the data thus the mean of each column equals to 0. The components in PCA are calculated from singular value decomposition (SVD) of the data table (**Equation 2-13**).

$$\boldsymbol{X} = \boldsymbol{P}\Delta\boldsymbol{Q}^{\boldsymbol{T}} \tag{2-13}$$

The $\boldsymbol{P}$ is the $\boldsymbol{I} \times \boldsymbol{L}$ matrix of left singular vectors (normalized eigenvectors[1] of the matrix $\boldsymbol{X}\boldsymbol{X}^{\boldsymbol{T}}$), whilst $\boldsymbol{Q}$ is the $\boldsymbol{J} \times \boldsymbol{L}$ matrix of right singular vectors (normalized eigenvectors of the matrix $\boldsymbol{X}^{\boldsymbol{T}}\boldsymbol{X}$), and Δ is the diagonal matrix of singular values (square root of the diagonal matrix of the eigenvalues[2] of matrix $\boldsymbol{X}\boldsymbol{X}^{\boldsymbol{T}}$ and $\boldsymbol{X}^{\boldsymbol{T}}\boldsymbol{X}$ (as the same)) (Abdi and Williams 2010).

The main principal component (with the highest variance) is the x-axis as new plot while the other component (with the second highest variance) becomes the y-axis as it sets the orthogonal to the main component. The “plot” is then rotated; hence the x-axis is horizontal, and the y-axis is vertical by means of multiplication the original data due to the eigenvectors which indicate the direction of the principal components. There are two eigenvectors (for each axis) each corresponding to an eigenvalue, the magnitudes of each eigenvalue indicate that the amount of the data’s variability is explained by its eigenvector.

PCA is useful technique to identify patterns within a data set, aiming to cluster similar observations. The goal is to visualize and project the data on a two-dimensional coordinate with a minimal loss of information. To accomplish this, the number of variables is declined to a few linear combinations of the data set with linear combination corresponding to a principal component. The loading plot (shown in **Appendix G**) provides the influential variables for the PCA model and how these variables are correlated. The spots close to each other in the loading plot show similar data profile; the value of one either increases or decreases, it conduce to the same change for proximal components (Asimakopoulos et al. 2016).

[1] Non-zero vector that changes only by a scalar factor, not in direction, when linear transformation is applied to it
[2] Scale factor corresponding to eigenvector

3. MATERIALS and METHODS

3.1. Sample collection

A total of 181 food samples were purchased in 7 countries through 2018: Japan, Switzerland, Greece, Germany, Luxemburg, Spain and Norway. Collected snack food stuffs were purchased from local supermarkets and divided into 7 categories according to the country snacks were sold in: 42 samples from Japan, 13 samples from Switzerland, 7 samples from Greece, 23 samples from Germany, 21 samples from Luxemburg, 22 samples from Spain and 53 samples from Norway. Samples were also categorized according to their physical states and the indications such as sold country (Norway/Japan/others), taste (salty/sweet/others), brand, the visual aspect (solid/liquid/others), the type of snacks (grain/chocolate/others) and target age group. The list of all samples is present in **Table A.1** in **Appendix A**. These samples were stocked in ambient temperature as the supermarket took before treatment.

3.2. Method – Organic

3.2.1. Chemicals and materials

Analytical standards of MeP, EtP (99%), PrP (≧99%), BuP (≧99%), BezP (≧98%), HeP, 4-HB (99%), 3,4-DHB (≧97%), Vanillic acid (97%), OH-EtP (97%) and TCC (99%) were purchased from Sigma-Aldrich. Paraben internal standard mix solution containing $^{13}C_6$-MeP, $^{13}C_6$-EtP, $^{13}C_6$-PrP and $^{13}C_6$-BuP was also obtained from Sigma-Aldrich.

Ammonium acetate, ethyl acetate, MeOH were purchased from Sigma-Aldrich. Milli-Q water was purified by Millipore Water distribution system (Merck Millipore, US).

3.2.2. Standard solutions

3.2.2.1. Internal standard (IS)

For spiking, paraben internal standard mix solution was used. The stock solution was 10 ppm, and to prepare 1 ppm solution, 100 µL of the stock solution was transferred to a glass vial (for LC) by an Eppendorf pipette mixing with 900 µL of MeOH.

3.2.2.2. Standard stock solution

Each standard stock solution in this study was 1000 ppm solution. For most of the standard stock solutions, they were prepared by weighting 10 mg of each chemicals in a 10 mL volumetric flask and dissolved with methanol (MeOH). Actual weight of chemicals and concentration of stock solutions were given in **Table A.1**. From the standard stock solutions, 10 ppm working solutions were prepared. To make the 10 ppm solutions, a calculated amount of standard stock solution was transferred to a 20 mL glass vial by using an Eppendorf pipette prior to diluting up to 10 mL with MeOH. Then, 9 mL of the MeOH were poured by the graduated cylinder, furthermore, the remaining fraction of MeOH was added by an Eppendorf pipette. The calculated amount of standard stock solutions and added MeOH are shown in **Table A.2**. Moreover, the 1 ppm solutions prepared by extracting 1 mL of the 10 mL working solution to 20 mL glass vial, then 9 mL of MeOH was added with an Eppendorf pipette.

3.2.3. Extraction

Before performing the actual experiment, extraction method development has been carried out. A solid-liquid extraction method was used to extract the parabens, their derivatives and antimicrobial from snack food stuffs. Briefly, snack samples were homogenized (solid samples by a hammer), and approximately 1 g for each sample was weighted and transferred into a 15 mL PP tube. Then, 2 mL of 1 M ammonium acetate was added to PP tube. A known concentration of a mixture of labeled IS (10 µL of 1 ppm IS solution prepared in **Section 3.3.2.1.**) was spiked, vortexed and allowed to equilibrate. To the spiked samples, 6 mL of ethyl acetate was added and shaken in a mechanical shaker (KS501 digital, IKA). After 45 min shaking, the PP tubes were centrifuged at 5000 rpm for 5 min, and the supernatant was transferred into another 15 mL PP tube. This extraction process was repeated with 6 mL of ethyl acetate again, then the second supernatant was transferred into same PP tube stored first supernatant (approximately 12 mL in total). To remove the salts, 1mL of Milli-Q water was added to PP tube and shaken. After 5 min shaking, it was centrifuged and removed water. The PP tubes were kept in the freezer at -20 °C over 24 h to separate the lipid layer. After centrifugation, the lipid phase was removed, and the rest of solution (containing the analytes) was concentrated to near dryness in the TurboVap® Classic LV (Biotage). Further, it was reconstituted with 1 mL of methanol, and transferred into vials for UHPLC analysis.

3.2.4. LC-MS/MS

The section of the chromatographic separation was performed using an Acquity UHPLC Thermo system with a column manager, a flow thorough needle manager and binary solvent manager (Waters, Milford, USA). The tandem mass spectrometric system was a Xevo TQ-S (triple quadrupole mass analyzer) with ZSpray ESI (Waters, Milford, USA). The LC column used was Kinetex C18 column (2.1 mm × 50 mm, 1.3 mm; Phenomenex Inc., Torrance, CA, U.S.) connected to a SecurityGuard ULTRA C18 guard column (2.1 mm × sub-2 mm, core-shell column; Phenomenex Inc.). Determinations of the mass spectrometry parameters were carried out by direct infusion and the IntelliStart software (Waters, Milford, USA) (**Appendix D**). The parent and fragment ions of each target chemicals are shown in **Table 3.1**.

Table 3.1: Analyte specific MS/MS parameters

Component	Quantification transition (CE^a [eV])	Confirmation transition (CE^a [eV])	CV^b (V)
MeP	151>92 (20)	136 (14)	36
EtP	165>92 (20)	137 (14)	38
PrP	179>92 (20)	136 (16)	28
BuP	193>92 (24)	137 (14)	46
BezP	227>92 (22)	136 (14)	14
HeP	235>92 (24)	136 (20)	20
4-HB	137>93 (14)	-	30
3,4-DHB	153>109 (14)	-	30
Vanillic acid	167>152 (20)	108 (18)	20
OH-EtP	181>108 (22)	153 (14)	18
TCC	313>160 (12)	126 (24)	8

a: Collision energy b: Cone voltage

Chromatographic separation was performed by Kinetex® C18 column. Chromatographic analyses were carried out using a gradient elution program with water (acidified with 0.1 % v/v formic acid) and methanol as binary mobile phase mixture at a flow rate of 200 µL/min. The gradient elution started with 1 %(v/v) water and increased linearly to 75 % water in 0.4 min. Then, it increased again to 95 % water for 0.4 min (total 0.8 min) and it was held for 1.7 min (until 2.5 min). After holding, it started to increase again up to 99 % for 0.05 min, and then kept 99 % for 0.75 min (until 3.3 min). The gradient elution reverted to 1 % at 3.5 min and re-equilibrated for 0.5 min (totally 4 min). The electrospray ionization voltage was applied at +1.8 kV. The collision gas flow rate was set at 0.15 mL/min. The source temperature was set at 150 °C and the desolvation gas temperature was set at 350 °C. The injection volume was 3 µL. Data were acquired with the MassLynx and TargetLynx software packages (version 4.1 SCN871, Waters, Milford, USA). Data treatment was carried out with Excel (Microsoft Office, 2019).

3.3. Method – Inorganic

3.3.1. Sample preparation

Pre-treatment process for 181 samples was carried out before ICP-MS analysis.
All samples were weighted approximately 400-500 mg and transferred to PTFE-Teflon vials (18 mL). Then, 8 mL of nitric acid HNO_3 (UltraPure grade, distilled with Milestone SubPur, 50% v/v) was added to each sample. After that, samples were put on a high-pressure microwave system (Milestone UltraClave, EMLS, Leutkirch, Germany) and carried out according to a temperature profile which increases gradually from ambient temperature up to 245 °C within 1 hour. Besides, approximately 1 hour was taken to cool temperature down to initial temperature (**Table 3.2**). After cooling step, the digested samples were diluted with Milli-Q water up to roughly 90 mL in polypropylene vials to accomplish a final HNO_3 concentration (0.6 M). For the certified reference sample, cigarette leaf powder was weighted about 270 mg and transferred to PTFE-Teflon vials (18 mL) mixed with 8 mL of HNO_3 (50% v/v) prior to Ultraclave process. After decomposition, it was diluted to approximately 90 mL with Milli-Q water and transferred to polypropylene vial.

Table 3.2: Steps in Ultraclave decomposition

Step	Time (min)	Temp 1(°C)	Temp 2 (°C)	Press (bar)	Energy (Watt)
1	5	50	60	160	1000
2	10	50	60	160	1000
3	10	100	60	160	1000
4	8	110	60	160	1000
5	15	190	60	160	1000
6	5	210	60	160	1000
7	15	245	60	160	1000
8	10	245	60	160	1000

3.3.2. ICP-MS

High resolution inductivity coupled plasma mass spectrometer (HR-ICP-MS) analyses were carried out with a Thermo Finnigan model Element 2 instrument (Bremen, Germany). 1350W as the radio frequency power was set. The samples were automatically introduced by the combination with equipped autosampler SC2 DX (with ULPA filter dust cover) and PrepFAST injection analysis system (ESI, Elemental Scientific, Inc. Omaha, NE), with total flow of 200 μL/min. The apparatus was installed nebulizer (PFA-ST), spray chamber (PFA Barrel 35mm), demountable torch, quarts standard injector and Aluminum type X-skimmer. By adding the methane gas to the sample gas, the sensitivity of Se and As is increased as oxide is lower level. **Appendix F** is showing more details about this instrumentation.

Certified calibration solution can verify the accuracy of the ICP-MS instrument. PS-70 and PS-ClBrI were employed for this study as calibration solution (CS) and each of them was prepared two types which were delivered by ESI from independent producers. The solutions from the one producer was used as a CS while the other from the other producer was used as quality solution (QS). To cover the all elements, both of PS-70 and PS-ClBrI were employed since PS-70 is the primary solution containing 70 elements and PS-ClBrI contains chlorine, bromine and iodine which cannot be mixed into PS-70 due to the matrix of HCl. The precision was obtained from RSD% values which are calculated from three consecutive scans of each sample. The quantification limits (QL) were considered by taking the concentration giving approximately 25 % of RSD, uncorrected of baseline whilst the detection limits (DL) was calculated from QL, corrected of baseline and total measurement uncertainly (MU). The total MU is obtained by **Equation 3-1**.

$$\boldsymbol{MU = \sqrt{DL^2 + DL'^2}} \tag{3-1}$$

DL'^2 is the DL with baseline correction.

3.4. Data treatment

Statistical analysis and correlations were performed by SPSS Statistics (IBM, version 25) and principal component analysis (PCA) was carried out by the statistical software R.

4. RESULTS and DISCUSSION

4.1. Quality assurance and method validation

4.1.1. Organic analysis

The precision of the tandem LC-MS/MS method is given in **Table 4.1**. All of the ion ratios (*IR%*) satisfy the criteria of tolerance announced by Commission Decision 2002/657/EC (European Commission 2002).

Table 4.1: Ion ratios (*IR%*), Retention times (*RT*) and Relative retention times (*RRT*) (RSD%, N=3 highest calibration points)

	IR%	*RT*	*RRT*
MeP	59.3 (5.07)	1.61 (0.29)	1.00 (0.29)
EtP	97.2 (1.62)	1.80 (0.00)	1.00 (0.00)
PrP	18.3 (1.53)	1.98 (0.24)	1.00 (0.24)
BuP	38.8 (2.26)	2.16 (0.22)	1.00 (0.00)
BezP	78.1 (0.12)	2.15 (0.22)	0.995 (0.001)
HeP	23.1 (0.80)	2.62 (0.00)	1.21 (0.22)
4-HB	-	1.21 (0.39)	0.75 (0.39)
3,4-DHB	-	0.99 (0.47)	0.62 (0.47)
Vanillic acid	53.8 (9.00)	1.27 (0.37)	0.79 (0.37)
OH-EtP	72.8 (1.49)	1.61 (0.00)	1.006 (0.00)
TCC	7.79 (2.67)	2.59 (0.18)	1.20 (0.18)

The recoveries for this method are shown in **Table 4.2**. The absolute recoveries in the majority of target analyte are more than 70 %. Regarding the parabens (MeP, EtP, PrP, BuP, BezP and HeP), the recoveries of the target analyte are similar to previous studies (Alshana et al. 2015; Jain et al. 2013; Liao et al. 2013b, 2013a; Molognoni et al. 2018; Prapainop et al. 2019). This is the first work for the determination of 4-HB, 3,4-DHB, vanillic acid, OH-EtP and TCC especially in the snacks. The recoveries of 4-HB and 3,4-DHB at 20 ng/mL were quite high value compared to other concentration. It might get produced during preparation process. For OH-EtP and TCC, there showed good recoveries with 81.0 % and 79.5 % for absolute and 99.5 % and 112.3 % for relative in total value respectively. However, the recoveries of 4-HB, 3,4-DHB and vanillic acid in total value were low values thus these compounds were semiquantified.

Table 4.2: Recoveries% (RSD%, N=4; 10[ng/mL], N=3; 20[ng/mL], N=4; 25[ng/mL], N=4; 50[ng/mL]) of target analytes.

	Absolute recovery					Relative recovery				
	10	20	25	50	Total*	10	20	25	50	Total*
MeP	82.2 (6.39)	54.3 (17.7)	87.7 (6.46)	87.6 (2.52)	88.7	95.8 (12.3)	69.6 (24.8)	122 (9.06)	107 (7.87)	108.6
EtP	84.3 (4.62)	78.3 (5.86)	87.0 (7.71)	85.5 (2.51)	85.6	107 (5.74)	114 (7.63)	110 (5.55)	106 (2.34)	104.9
PrP	85.2 (2.23)	78.6 (4.33)	87.6 (6.41)	84.6 (2.29)	84.2	107 (3.76)	95.6 (3.37)	114 (3.84)	109 (1.95)	108.8
BuP	83.8 (2.55)	74.4 (4.27)	84.6 (6.85)	80.8 (1.84)	79.9	104 (3.81)	97.0 (6.65)	116 (2.31)	106 (2.07)	105.4
BezP	81.6 (2.46)	72.5 (5.43)	79.3 (7.48)	76.8 (1.93)	75.6	101 (3.87)	94.1 (2.43)	108 (1.77)	101 (2.46)	99.9
HeP	80.6 (3.16)	66.8 (5.54)	83.2 (9.16)	81.1 (3.64)	81.1	100 (8.90)	87.0 (9.14)	113 (5.37)	106 (4.39)	107.2
4-HB	79.9 (13.3)	119 (4.74)	46.6 (8.74)	36.7 (6.06)	11.9	93.2 (21.9)	150 (6.73)	64.2 (8.94)	45.1 (11.4)	14.4
3,4-DHB	22.5 (2.27)	144 (11.9)	11.8 (3.09)	9.68 (5.02)	5.4	26.5 (11.2)	181 (13.2)	16.3 (5.81)	11.9 (13.5)	6.8
Vanillic acid	93.9 (4.65)	94.5 (8.34)	84.8 (7.48)	48.3 (20.0)	3.4	125 (11.7)	92.6 (6.66)	113 (13.8)	54.4 (13.4)	19.4
OH-EtP	71.7 (6.40)	69.7 (15.1)	71.2 (5.03)	78.6 (2.01)	81.0	83.7 (8.63)	96.7 (10.1)	98.6 (5.03)	96.7 (11.0)	99.5
TCC	77.9 (4.71)	63.8 (11.1)	72.9 (5.83)	78.7 (4.83)	79.5	99.9 (9.14)	78.7 (5.48)	105 (7.62)	109 (6.73)	112.3

*: calculated from the slope of SP and MM.

Table 4.3 demonstrates the reproducibility of the method and **Table 4.4** provides the limit of quantification and detection calculated under the process of **section 2.5.6**. Concentrations detected less than LOD were cleared away from the data sets. The matrix factors and matrix effects analyzed by LC-MS/MS are presented in **Table 4.5**.

Table 4.3: Reproducibility (RSD%, N=4; 10[ng/mL], N=3; 20[ng/mL], N=4; 25[ng/mL], N=4; 50[ng/mL]) of target analytes.

	Absolute				Relative			
	10	20	25	50	10	20	25	50
MeP	6.39	17.7	6.46	2.52	12.3	24.8	9.06	7.87
EtP	4.62	5.86	7.71	2.51	5.74	7.63	5.55	2.34
PrP	2.23	4.33	6.41	2.29	3.76	3.37	3.84	1.95
BuP	2.55	4.27	6.85	1.84	3.81	6.65	2.31	2.07
BezP	2.46	5.43	7.48	1.93	3.87	2.43	1.80	2.46
HeP	3.16	5.54	9.16	3.64	8.90	9.14	5.37	4.39
4-HB	13.3	4.74	8.74	6.06	21.9	6.74	8.94	11.4
3,4-DHB	2.27	11.9	3.09	5.02	11.2	13.2	5.81	13.5
Vanillic acid	4.65	8.34	7.48	20.0	11.7	6.66	13.8	13.4
OH-EtP	6.40	15.1	5.03	2.01	8.63	10.1	5.03	11.0
TCC	4.71	11.1	5.83	4.83	9.14	5.48	7.62	6.73

Table 4.4: Lower limits of quantification and limits of detection [ng/g]

	LLOQ	*LOD*
MeP	0.10	0.03
EtP	0.10	0.03
PrP	0.10	0.03
BuP	0.10	0.03
BezP	0.10	0.03
HeP	0.10	0.03
4-HB	0.10	0.03
3,4-DHB	0.10	0.03
Vanillic acid	0.20	0.07
OH-EtP	0.20	0.07
TCC	0.10	0.03

Table 4.5: Matrix factors (MF) and matrix effects (ME%)

	MF	*ME%*
MeP	0.71	-28.9
EtP	0.82	-18.5
PrP	0.86	-14.3
BuP	0..42	-58.4
BezP	0.33	-67.3
HeP	0.30	-69.8
4-HB	0.67	-32.5
3,4-DHB	1.33	32.6
Vanillic acid	0.87	-13.2
OH-EtP	1.25	25.3
TCC	0.42	-58.3

4.1.2. Inorganic analysis

Almost all elements in snack food stuffs used for discussion (**Table 4.10**) have been detected above the quantification limits. The detection limit for all elements are given in **Table C.1** in **Appendix C**. The process of calculations for detection limits for ICP-MS is written in **Section 3.3.2**. Each individual sample was analyzed for 3 times for seeing precision. Furthermore, some samples were also used for repeating test in order to confirm its validity. 10 parallels have been analyzed as replication as well. Accuracies (analyzed/certified values) were ± 20 % maximum which was verified against certified reference material.

4.2. Concentration of parabens and elements in snack samples

4.2.1. Parabens

Figure 4.1 shows the overall proportion of parabens, parabens derivatives and all analytes in the snack food samples (n=181).

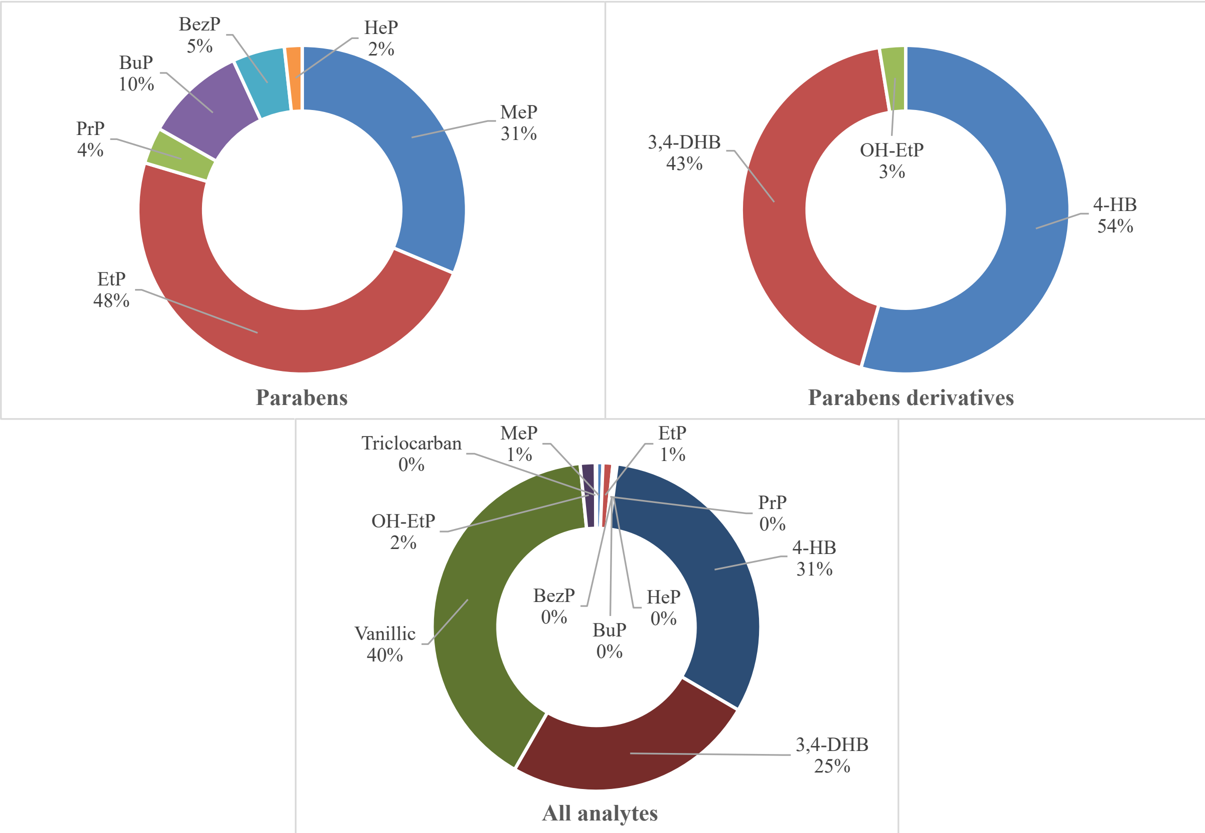


Figure 4.1: Distribution profiles of the amount of target analytes leached from snack food stuffs (based on median concentrations)

Among the parabens, EtP and MeP are the highest and the second highest percentage respectively, and 4-HB and 3,4-DHB account 97% of parabens derivatives. By contrast, PrP, BezP and HeP are very low ratio. Considering the all target analytes, 4-HB, 3,4-DHB and vanillic acid are abundant and occupies 96%. Parabens are significantly poor rate compared to the parabens derivatives. This indicates that parabens derivatives are formed by chemical reactions of parents parabens through the manufacture or storage processes, as mentioned by Asimakopoulos et al. (2016). Alkyl protocatechuates that were found in food samples were potentially formed from parent parabens by photo-oxidation. The process of light-induced hydroxylation of MeP transforming to OH-MeP has been studied, then the relationship between EtP and OH-EtP is also considered as following similar way (Okamoto et al. 2008). The reaction mechanism of 4-HB and 3,4-DHB from parabens in food, however, is still insufficient, while the transformation process of 4-HB and 3,4-DHB from paraben in organism has been proved in human and animal studies (Aubert et al. 2012; Liu et al. n.d.; Ste-Marie et al. 1999; Wang and Kannan 2013). Vanillic acid has been reported that it is a phenolic derivative of edible plants and fruit, as well as an intermediate of vanillin which is common non-toxic food additive and confers the odor and vanilla taste (Noubigh and Abderrabba 2016; Sayavongsa et al. 2007). The ingredients of plenty of samples used this study are plant-derived such as grain, chocolate, fruit and vegetable (see **Table 4.8**, **4.9**). This, therefore, makes it reasonable to presume that vanillic acid accounts large ratio of the distribution profiles.

The concentrations of the food samples from different countries are shown in **Table 4.6** and **Table 4.7**. The highest median concentration of total target analyte is the snacks sold in Switzerland (660 ng/g) and the lowest one is the snacks bought in Spain (93.4 ng/g). It is almost seven times difference. Furthermore, the samples from Switzerland and Spain are also the highest and lowest concentrations of parabens (Σ Parabens) and parabens derivatives (Σ Parabens derivatives). Focusing on individual analytes, maximum concentration of MeP in Japan and Luxembourg and PrP in Luxembourg were 292, 5109 and 1198 ng/g respectively, which were extremely higher concentration than what of median concentration (0.86, 1.38 and 0.17 ng/g respectively). This result was found only at MeP and PrP among parabens, hence these parabens were considered having substantially wide variability. Besides, 4-HB and vanillic acid are always high concentration, while HeP and TCC are very low concentration in all samples. Vanillic acid in Japanese samples is remarkably high concentration (298 ng/g) and it is nine times larger than Spanish samples which are the lowest concentration (32.2 ng/g). TCC is not often used for the food stuffs according to the **Table 4.6** and **4.7**, the number of detected samples are below half samples with very low concentration.

The distribution of the individual parabens (**Figure 4.2**.) indicates that MeP and EtP are the major components in the all countries except Luxembourg where PrP is the second major components instead of EtP. On the other hand, HeP is rarely used as preservative for snack food stuffs, as well as there are very low number of samples detected HeP in **Table 4.6** and **4.7** compared to the other parabens. HeP was also seldom used for food items from China, as frequencies were nearly 0 % (Liao et al. 2013a). PrP, BuP and BezP are still detected in many samples although the composition rates are low (below 4.0 % except two points). For the partition of parabens derivatives (**Figure 4.3**), 4-HB and 3,4-DHB are the major components, further, 3,4-DHB accounts for over the greater part in all countries. While, OH-EtP is not almost contained in the food stuffs from all countries although it was detected over the half of samples (**Table 4.6** and **4.7**).

Table 4.6: Concentrations of the target analytes in the food samples from each country [ng/g]

	Japan (n=42)				Switzerland (n=13)				Greece (n=7)				Germany (n=23)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
MeP	0.86	0.07	292	78.6	0.69	0.03	24.1	100	2.69	0.06	47.9	85.7	2.56	0.11	11.6	91.3
EtP	1.37	0.03	9.53	78.6	7.69	0.04	33.4	100	3.28	0.11	35.6	85.7	4.78	0.04	36.0	91.3
PrP	0.06	0.03	1.38	50.0	0.18	0.05	0.59	38.5	0.56	0.08	0.89	57.1	0.11	0.03	0.95	60.9
BuP	0.11	0.03	2.60	28.6	0.48	0.05	2.02	61.5	0.15	0.05	1.83	71.4	0.66	0.04	1.61	65.2
BezP	0.05	0.03	1.60	38.1	0.17	0.05	1.03	61.5	0.29	0.05	12.2	85.7	0.25	0.14	0.57	60.9
HeP	0.06	0.04	0.10	9.52	-	-	-	0	-	-	-	0	0.06	0.03	0.27	17.4
Σ Parabens	2.00	0.00	292	100	15.4	0.54	42.6	100	6.06	0.12	76.6	100	6.09	0.05	49.7	100
4-HB	59.8	4.60	514	100	40.4	5.16	317	100	57.4	13.2	323	100	50.7	4.88	608	95.7
3,4-DHB	6.54	0.05	3425	90.5	503	2.71	2003	100	21.4	0.06	5408	100	157	2.10	2136	100
OH-EtP	0.32	0.07	4.34	64.3	3.68	0.13	13.1	76.9	2.59	0.13	10.6	57.1	4.30	0.04	6.97	65.2
Σ Parabens derivatives	76.1	4.70	3583	100	536	8.35	2052	100	57.4	21.7	5600	100	343	2.10	2251	100
Vanillic acid	298	2.36	17418	100	95.2	21.3	1715	92.3	59.2	13.4	392	100	47.9	1.77	395	91.3
TCC	0.10	0.03	0.86	45.2	0.13	0.04	1.81	46.2	-	-	-	0	0.16	0.03	1.36	52.2
Σ All	594	12.9	17877	100	660	34.9	2149	100	109	35.2	6068	100	417	12.7	2424	100

*: detection rate [%]

Table 4.7: Concentrations of the target analytes in the food samples from each country [ng/g] (continued)

	Luxembourg (n=21)				Spain (n=22)				Norway (n=53)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
MeP	1.38	0.07	5109	85.7	0.68	0.04	235	95.5	0.46	0.03	39.2	83.0
EtP	5.51	0.08	17.3	85.7	1.05	0.04	11.6	86.4	0.20	0.03	36.6	75.5
PrP	0.17	0.04	1198	42.9	0.09	0.04	0.13	31.8	0.13	0.03	1.65	22.6
BuP	0.38	0.22	0.93	47.6	0.23	0.06	0.48	27.3	0.18	0.06	1.19	32.1
BezP	0.18	0.06	0.81	85.7	0.11	0.03	0.62	68.2	0.15	0.03	2.92	64.2
HeP	-	-	-	0	-	-	-	0	0.05	0.03	0.14	11.3
Σ Parabens	8.62	0.00	6307	100	2.27	0.17	236	100	0.93	0.03	74.8	100
4-HB	32.4	0.67	288	100	29.7	5.08	192	100	45.9	0.50	745	98.1
3,4-DHB	122	1.20	1035	100	16.2	0.04	1676	95.5	47.3	0.03	3099	98.1
OH-EtP	2.65	0.09	5.87	76.2	2.50	0.18	4.08	36.4	3.75	0.14	7.27	20.8
Σ Parabens derivatives	175	1.87	1115	100	53.1	10.6	1868	100	152	4.42	3506	100
Vanillic acid	32.3	0.85	216	95.2	32.2	0.87	340	95.5	42.2	0.48	914	98.1
TCC	0.16	0.04	1.90	38.1	0.43	0.07	1.36	18.2	0.25	0.03	1.97	24.5
Σ All	273	2.72	6430	100	93.4	20.9	1970	100	247	8.14	3577	100

*: detection rate [%]

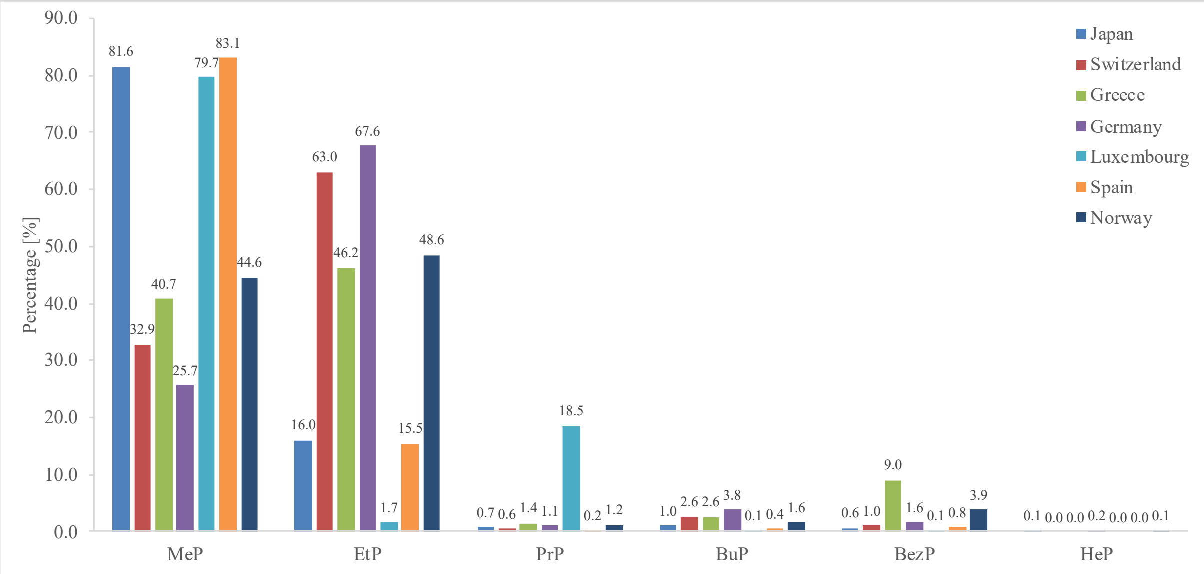


Figure 4.2: Distribution of parabens categorized by country, compared to Σ Parabens (based on median concentrations)

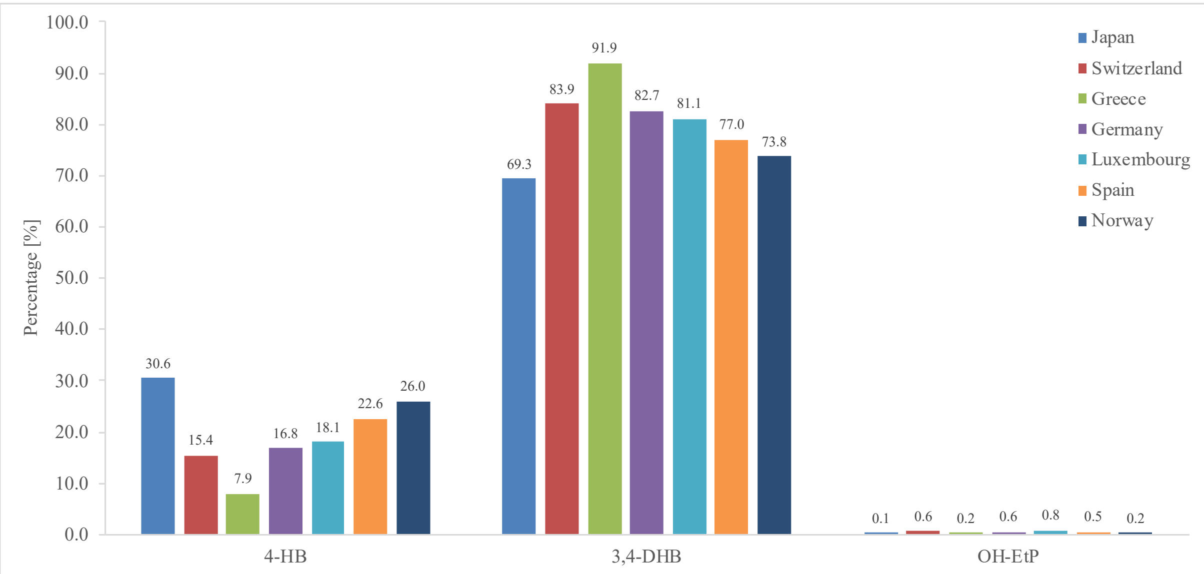


Figure 4.3: Distribution of parabens derivatives categorized by country, compared to Σ Parabens derivatives (based on median concentrations)

Table 4.8 and **4.9** provide the concentrations of the target analytes in the food stuffs classified into 8 categories depending on the characteristics. Seafood is 1225 ng/g (median value) in total analytes, which is the highest concentration among 8 categories. On the contrary, Sugar results the lowest concentration (15.6 ng/g) though it consists of just 2 samples. The second lowest concentration is 38.1 ng/g found in Gelatin, which is approximately 30 times less than Seafood. 4 analytes were detected in Sugar products, and the Vegetable products were detected 6 out of 11 analytes although almost all analytes were detected in the other categorized products except HeP. It indicates that Sugar products are made up with mainly sugar with very low additives, and Vegetable products is apparently reluctant to be added other additives. Fruit showed the highest concentration of total of paraben derivatives. It is presumed that Fruit has originally contained those, and it may have enhancement for proceeding the metabolite reaction stated in previous study. Chocolate contained relatively large amounts of parabens (13.7 ng/g). It seems to have been added many preservatives as one of ingredients is dairy product likely to be spoiled; the combining the parabens is expected to demonstrate better antimicrobial property than only one use. The TCC was detected over half samples in Gelatin, Seafood and Meat. According this result, it is considered that these products need to prevent microbial growth.

Figure 4.4 and **4.5** show the distribution of parabens and parabens derivatives against Σ Parabens and Σ Parabens derivatives respectively. In every category except sugar, MeP and EtP are the main compositions. This is also reported in Liao et al. (2013a, 2013b) that MeP, EtP and PrP are the predominant analogs found in food samples. The composition pattern of parabens in this study is quite similar to what was reported for human blood and urine (MeP >> PrP > EtP) (Calafat et al. 2010; Frederiksen et al. 2011), however, it is similar with food analysis (Liao et al. 2013a, 2013b). BezP occupies 24.6 %, 8.9 % and 3.5 % in Vegetable, Meat and Grain respectively, which are especially higher percentage than other categories (almost 0 %). Likewise, PrP and BuP are higher percentage at 2 categories, then other kinds of snacks scarcely comprise them. To my far knowledge, this is first study to analyze parabens derivatives in food stuffs but due to aforementioned reason, 4-HB and 3,4-DHB are really high distribution.

Table 4.8: Concentrations of the target analytes in the food samples sorted by characteristics [ng/g]

	Grain (n=102)				Gelatin (n=10)				Seafood (n=9)				Meat (n=4)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
MeP	0.75	0.03	292	87.3	8.13	0.09	38.2	80.0	0.61	0.07	4.07	88.9	0.48	0.07	1.67	75.0
EtP	0.92	0.03	33.4	78.4	4.46	0.07	36.6	60.0	1.68	0.17	4.65	88.9	0.11	0.08	0.99	75.0
PrP	0.08	0.03	0.94	34.3	0.19	0.03	1.15	40.0	0.05	0.03	1.38	44.4	0.05	0.04	0.06	50.0
BuP	0.18	0.03	0.99	26.5	0.11	0.07	0.26	60.0	1.33	0.05	2.60	22.2	0.30	0.30	0.30	25.0
BezP	0.15	0.03	12.2	58.8	0.07	0.04	0.08	40.0	0.04	0.04	0.05	22.2	0.19	0.18	0.19	75.0
HeP	0.07	0.03	0.07	2.94	0.05	0.04	0.10	50.0	-	-	-	0	0.03	0.03	0.03	25.0
Σ Parabens	1.64	0.00	292	98.0	4.29	0.12	74.8	100	2.00	0.22	7.44	100	0.74	0.07	2.66	100
4-HB	42.3	0.50	608	98.0	21.5	4.60	514	100	126	67.1	224	100	60.2	11.4	288	100
3,4-DHB	12.7	0.04	1676	96.1	1.89	0.08	191	80.0	47.9	0.18	3425	100	33.3	7.63	91.7	100
OH-EtP	0.50	0.04	13.1	40.2	0.15	0.10	0.19	20.0	0.32	0.07	0.63	100	0.45	0.46	0.45	25.0
Σ Parabens derivatives	57.6	1.87	1868	100	22.9	4.70	706	100	214	67.4	3583	100	112	67.4	3583	100
Vanillic acid	61.8	0.48	17418	94.1	17.3	1.48	3958	100	624	94.0	1601	100	79.6	47.1	316	100
TCC	0.17	0.03	1.80	24.5	0.11	0.06	0.86	100	0.12	0.07	0.17	66.7	0.76	0.05	0.81	75.0
Σ All	169	2.72	17877	100	38.1	12.9	4319	100	1225	234	3943	100	262	72.3	518	100

*: detection rate [%]

Table 4.9: Concentrations of the target analytes in the food samples sorted by characteristics [ng/g] (continued)

	Chocolate (n=39)				Fruit (n=11)				Vegetable (n=4)				Sugar (n=2)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
MeP	3.29	0.03	5109	89.7	0.16	0.09	39.2	90.9	0.09	0.05	0.27	75.0	-	-	-	0
EtP	10.3	0.17	36.0	97.4	0.13	0.03	7.58	90.9	0.19	0.11	0.29	75.0	0.12	0.07	0.17	100
PrP	0.18	0.05	1198	66.7	0.03	0.03	0.03	9.09	-	-	-	0	-	-	-	0
BuP	0.53	0.10	2.02	89.7	0.06	0.06	0.07	18.2	-	-	-	0	-	-	-	0
BezP	0.22	0.03	0.52	92.3	0.06	0.03	0.19	36.4	0.12	0.05	0.16	75.0	-	-	-	0
HeP	0.05	0.04	0.27	12.8	-	-	-	0	-	-	-	0	-	-	-	0
Σ Parabens	13.7	0.42	6307	100	0.24	0.03	46.9	100	0.37	0.10	0.50	100	0.12	0.07	0.17	100
4-HB	45.5	4.39	207	100	106	11.9	745	100	57.7	22.4	451	100	7.18	6.52	7.84	100
3,4-DHB	334	0.03	5408	100	303	46.6	3099	100	46.4	17.5	86.4	100	0.13	0.10	0.17	100
OH-EtP	4.39	0.12	10.6	92.3	0.16	0.14	0.18	18.2	-	-	-	0	-	-	-	0
Σ Parabens derivatives	384	4.42	5600	100	664	152	3506	100	97.7	75.4	514	100	7.31	6.61	8.01	100
Vanillic acid	42.2	1.01	8973	100	102	13.1	706	100	58.4	19.6	148	100	8.14	3.14	13.1	100
TCC	0.16	0.03	1.97	43.6	0.07	0.07	0.07	9.09	-	-	-	0	-	-	-	0
Σ All	612	8.14	9238	100	772	203	3577	100	152	105	663	100	15.6	9.83	21.3	100

*: detection rate [%]

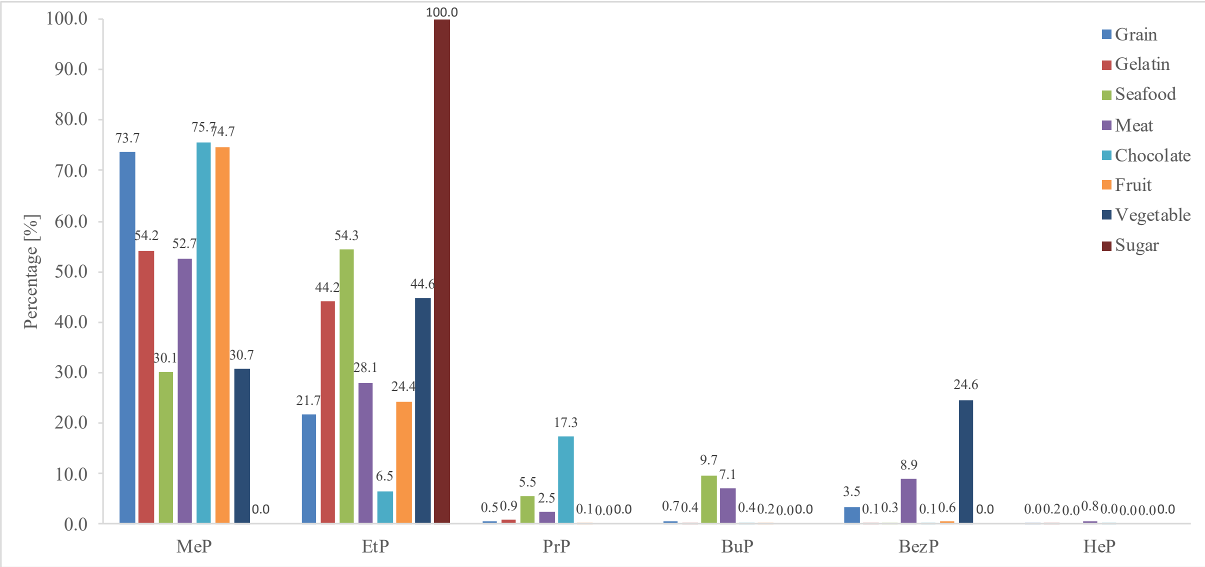


Figure 4.4: Distribution of parabens categorized by characteristics, compared to Σ Parabens (based on median concentrations)

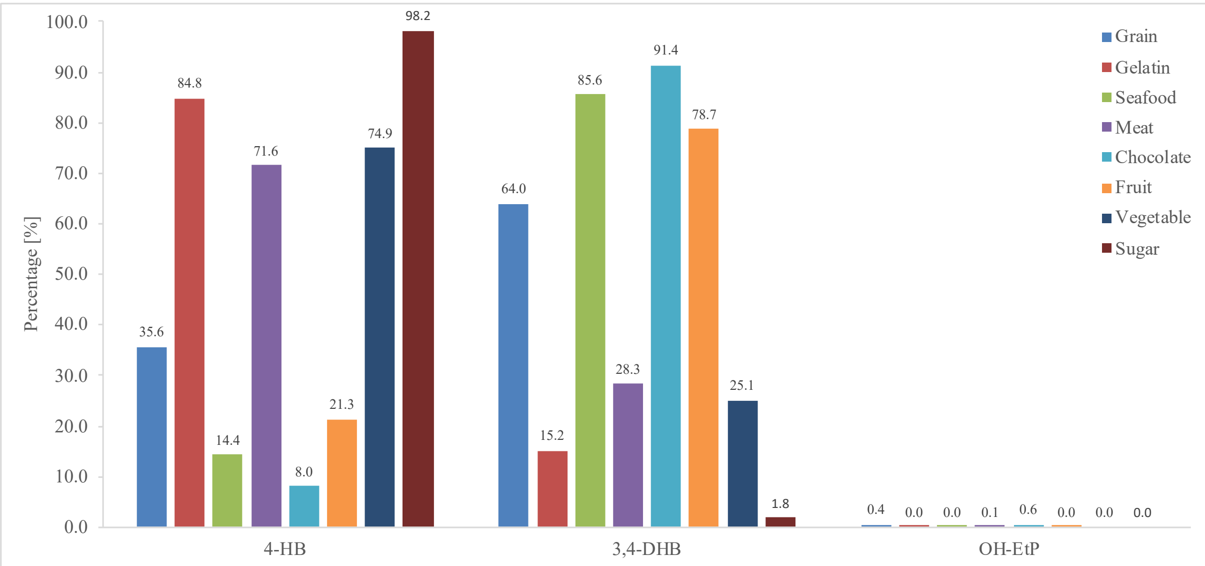


Figure 4.5: Distribution of parabens derivatives categorized by characteristics, compared to Σ Parabens derivatives (based on median concentrations)

4.2.2. Elements

The concentrations of elements detected in the snack food samples are given in **Table 4.10**.6 The macromineral elements, which are potassium, sodium, phosphorous, sulfur, magnesium and calcium, are the highest six elements in concentrations (median) and detected almost all samples. Then, essential trace elements for human health and beneficial bioactive trace elements are following the macromineral elements. According to **Table 4.10**, the elements needed for keeping human health are contained in the commercial products even though the snack food stuffs (Berdanier et al. 2013; Michigan Medicine 2018). **Table 4.10** also supports that the macromineral elements were contained at larger levels of concentration in food stuffs than trace elements (Chevallier et al. 2015; Moreda-Piñeiro et al. 2018). Majority of elements shown the table were detected at high detection rate, however, there were some elements detected relatively low rate, such as Ga (16.6 %), Ge (16.6 %), Sc (14.4 %), and in particular Ir no-detected (0 %).

Table 4.11 provides the differences between countries at the concentrations of selected elements. Full table of it can be found in **Table C.2** in **Appendix C**. Many kinds of elements were contained in Japanese and Norwegian snacks at the lowest concentrations although Japanese snacks had the highest level (5792860 ng/g at Na) in the **Table 4.11**. It is considered that lots of salt are contained in the snacks. The principal difference of snacks between Japan and European countries is use of soy sauce as condiment, since rise crackers collected in Japan often contained soy sauce however European snacks did not it. The amount of soy sauce is one of the factor to show this result (Mandl 2017). Large number of snacks which contained the highest level at each element were from Switzerland, following Germany and Greece. Whereas, the products from Luxembourg and Spain showed moderate concentrations at each element. The element having the largest gap between countries is Na, Japanese snacks are approximately 12 times larger than the lowest concentration (469317 ng/g, Norway) though the other gaps are less than about 2 ~ 6 times. Any other obvious differences apparently are not shown, as many collected samples are produced in international company and those are often imported and exported. Thus, there is not clear border which divides countries based on their elemental contents.

Table 4.10: Concentrations of elements in food samples (decreasing order at median, n=181) [ng/g]

	Median	*Average*	*Min*	*Max*	*%**		*Median*	*Average*	*Min*	*Max*	*%**		*Median*	*Average*	*Min*	*Max*	*%**
K	2373485	3394683	27753	38392218	100	Co	23.0	51.2	4.05	524	85.1	U	0.85	2.77	0.30	70.6	70.2
Na	2048429	4554580	10087	43738392	96.1	Cd	13.5	24.4	0.81	394	87.3	Nb	0.80	2.51	0.10	111	93.9
P	1183308	1372173	658	6867038	100	V	13.4	29.7	2.03	355	84.5	Dy	0.78	1.46	0.52	13.1	33.7
S	656426	796736	7139	3707384	99.4	Li	10.5	16.5	5.03	180	74.0	Ag	0.76	1.10	0.31	7.00	79.6
Mg	377074	568052	1506	3363116	100	Pb	8.45	13.5	2.11	100	84.0	Yb	0.67[3]	1.02	0.40	5.58	22.1
Ca	351877	740587	6695	7684211	100	As	5.92	503	3.02	35999	76.8	Pr	0.60	1.04	0.11	17.4	86.7
Si	37281	92980	10170	1917301	72.9	Ga	5.89[3]	9.32	4.01	50.0	16.6	Be	0.49	0.68	0.31	5.74	50.8
Fe	12802	20699	152	180476	100	Cs	5.32	10.0	0.90	247	96.7	Gd	0.49	0.86	0.10	15.1	91.2
Zn	8899	10690	42.2	58793	100	Ce	4.12	8.48	0.20	148	98.9	Sm	0.42	0.77	0.10	12.9	84.5
Mn	4024	5709	10.8	25049	100	Hg	3.34	6.00	1.02	60.1	81.8	Bi	0.38	1.46	0.05	23.1	86.7
Al	3104	10063	209	189993	97.2	Sn	3.23	25.4	0.34	2400	72.9	Er	0.29	0.54	0.10	7.78	66.9
Rb	1930	3472	19.7	36881	100	Ge	2.86[3]	3.48	2.01	8.85	16.6	Hf	0.17[3]	0.28	0.09	1.78	40.3
Cu	1819	2906	32.6	24508	98.9	La	2.56	4.73	0.31	70.1	93.9	Ho	0.16[3]	0.28	0.09	2.68	39.2
Sr	1310	4028	27.0	238298	98.9	W	2.05	37.2	0.50	649	85.6	Ta	0.14[3]	0.28	0.07	4.97	37.0
B	1300	3526	50.3	75662	96.7	Nd	1.97	3.78	0.25	71.0	93.9	Au	0.12	0.15	0.04	0.73	79.0
Ba	626	921	16.3	7776	98.3	Y	1.95	5.09	0.30	126	91.2	Tb	0.09	0.16	0.03	2.30	70.2
Ni	265	627	16.8	9110	96.1	Sc	1.70[3]	2.33	1.02	13.1	14.4	Tm	0.06[3]	0.11	0.03	1.13	42.5
Ti	192	1522	20.5	114123	95.0	Sb	1.61	2.16	0.62	10.8	85.1	Lu	0.04	0.08	0.02	0.91	60.8
Mo	125	238	21.9	3187	90.6	Tl	1.36	1.70	0.31	7.75	59.7	Pt	0.04	0.10	0.01	4.53	90.1
Cr	86.3	198	20.0	1672	79.6	Th	1.12[3]	1.80	0.50	14.2	42.0	Ir	-	-	-	-	0
Se	48.1	82.0	30.4	455	55.2	Zr	1.10	3.66	0.002	70.5	98.3						

*: detection rate [%] (n=181)

3 Calculated from the values above detection limit so possibly median would be below detection limit if calculation includes all detected values.

Table 4.11: Concentrations of selected elements categorized by countries [ng/g]

	Japan (n=42)		Switzerland (n=13)		Greece (n=7)		Germany (n=23)		Luxembourg (n=21)		Spain (n=22)		Norway (n=53)	
	Median	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**
K	1241961	100	3605620	100	4303315	100	3803891	100	3501158	100	2574732	100	1961775	100
Na	5792860	100	733177	92.3	4179561	100	1790474	95.7	1880148	100	3161191	100	469317	90.6
P	716323	100	1850486	100	962860	100	1881276	100	1943836	100	1222874	100	726782	100
S	772393	100	651007	100	909612	100	695228	100	685456	100	603229	100	500771	98.1
Mg	266792	100	734204	100	328312	100	604214	100	571940	100	375851	100	342344	100
Ca	248455	100	792592	100	327678	100	1053061	100	439451	100	335363	100	244054	100
Si	17802	59.5	34408	76.9	63083	100	47329	82.6	30513	76.2	47793	86.4	38882	67.9
Fe	7133	100	18131	100	16074	100	23977	100	19471	100	14366	100	11250	100
Zn	7682	100	12673	100	6727	100	10315	100	11110	100	8077	100	7058	100
Mn	4030	100	7484	100	4287	100	3794	100	5358	100	4464	100	2146	100
Al	1677	95.2	7370	100	5223	100	5410	100	5555	100	4405	100	2304	94.3
Rb	834	100	4237	100	3025	100	5047	100	3442	100	2174	100	1314	100
Cu	1244	97.6	3538	100	2124	100	3290	100	2692	100	2107	100	1232	98.1
Sr	1278	97.6	3480	100	1356	100	2058	100	1527	100	1777	100	896	98.1
B	875	95.2	2428	100	3027	100	2074	95.7	1129	95.2	1337	95.5	1291	98.1
Ba	471	95.2	1186	100	807	100	858	100	850	100	847	100	375	98.1
Ni	135	95.2	667	100	179	100	678	100	596	100	264	100	190	90.6
Ti	120	92.9	443	92.3	253	100	441	95.7	361	100	224	100	124	92.5
Mo	105	90.5	179	100	114	100	151	100	114	90.5	133	100	103	79.2
Cr	61.0	81.0	96.6	84.6	178	71.4	241	73.9	200	100	72.4	90.9	95.1	69.8
Se	51.8	71.4	49.1	69.2	34.9	71.4	52.5	65.2	43.4	66.7	41.2[4]	45.5	53.6[4]	32.1
Co	13.4	83.3	66.7	100	32.7	85.7	54.4	91.3	55.9	90.5	25.6	86.4	15.3	77.4
Cd	19.5	92.9	18.9	100	21.9	85.7	10.5	95.7	14.5	100	14.0	81.8	6.54	73.6
V	16.7	90.5	13.6	84.6	24.2	100	24.5	87.0	17.9	85.7	13.2	90.9	8.03	73.6
Li	13.5	71.4	7.44	100	11.5	100	11.1	78.3	7.47	95.2	10.6	68.2	12.2	58.5

*: detection rate [%]

The differences between characteristics are given in **Table 4.12**. Full table of concentrations of all elements detected in the snack food stuffs can be found in **Table C.3** in **Appendix C**.

Among macrominerals, meat products had the highest concentrations at K, P and S, which elements are mainly from meats stated in Michigan Medicine (2018). Meat, Chocolate and Grain were high concentration at K, since these categories are known as the main sources of it. Likewise, the categories containing the high concentrations of other macrominerals are also main sources of those elements. According to previous study, the amount of potassium in chocolate was 167-170 mg/100g, which was lower than what of this study (362 mg/100g, converted unit), oppositely grains were approximately 500 mg/100g in previous study, which was higher than what of this study (213 mg/100g, converted unit) (The Office of Disease Prevention and Health Promotion 2015). The largest gap between the highest and lowest is present at Na, the highest is 23597279 ng/g at Seafood and the lowest is 39336 ng/g at Fruit. Seafood has approximately 600 times higher concentration than what Fruit has. All fruit flavor snacks are not salty, hence the fact that Fruit contains few Na is consider as appropriate result. For trace elements, the categories having the highest concentrations also followed previous study. Fe, Zn and Mn, for instance, were rich in Chocolate, Meat and Grain respectively. Fe is often contained in the cereals (e.g. cacao), meats have lots of Zn and plant foods include plenty of Mn (Berdanier et al. 2013; Michigan Medicine 2018).

Almost all elements were detected in each category, but some elements were detected in very low frequency. Mo, Cr, Se, Co and Cd in Gelatin were less than 50 % detection rate. Moreover, some of these elements were also relatively low percentage (less than 80 %) compared to Macrominerals at Grain and Fruit. In particular, Si demonstrated unique detection rate. Although Si showed relatively high concentrations among elements, the detection rate was especially low rate in comparison with elements presented high concentration. Furthermore, Vegetable and Sugar did not contained Si. Some kinds of vegetables did not also detect in the previous study (Powell et al. 2005) though other samples analyzed in its article contained even few amount. For Sugar products, it provided poor concentrations of almost all elements except Mg which was the highest among the 8 categories. Many elements were not detected in Sugar; it was scarcely added any other additives, and this also supports discussion at **Section 4.2.1** about Sugar.

Table 4.12: Concentrations of selected elements categorized by characteristics [ng/g]

	Grain (n=102)		Gelatin (n=10)		Seafood (n=9)		Meat (n=4)		Chocolate (n=39)		Fruit (n=11)		Vegetable (n=4)		Sugar (n=2)	
	Median	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**	*Median*	*%**
K	2137814	100	69452	100	1293631	100	4672683	100	3620261	100	1625590	100	1522719	100	46134	100
Na	3466593	98.0	150537	100	23597279	100	18101957	100	739476	100	39336	54.5	104484	100	5249765	100
P	1130802	100	25075	100	1182755	100	2842934	100	1831749	100	263389	100	257616	100	2117	100
S	734198	100	113164	100	2285038	100	2758364	100	568465	100	123165	100	226341	100	7139	50.0
Mg	367956	100	36954	100	290672	100	282146	100	602678	100	124713	100	90055	100	808883	100
Ca	298938	100	58241	100	251712	100	148999	100	1196614	100	108108	100	117178	100	11656	100
Si	38141	72.5	31723	80.0	14166	77.8	43571	50.0	39482	89.7	34566	54.5	-	0	-	0
Fe	13176	100	1608	100	7851	100	18614	100	28557	100	6076	100	4643	100	3970	100
Zn	8641	100	547	100	7830	100	42433	100	10812	100	1239	100	3352	100	54.5	100
Mn	5481	100	191	100	2564	100	2505	100	3763	100	2146	100	618	100	93.1	100
Al	2734	96.1	3104	100	1654	100	1158	100	10382	100	930	100	896	100	379	50.0
Rb	1582	100	56.7	100	602	100	5486	100	5102	100	1314	100	922	100	26.3	100
Cu	1842	100	225	90.0	1158	100	1204	100	3542	100	669	90.9	405	100	582	100
Sr	1232	99.0	609	90.0	1606	100	291	100	2058	100	505	100	963	100	86.2	100
B	1142	96.1	163	80.0	1300	100	286.4	100	1866	100	2291	100	1512	100	853	100
Ba	652	100	316	80.0	356	100	147.2	100	1095	100	237	100	380	100	22.9	50.0
Ni	207	98.0	60.4	60.0	153.9	100	43.5	100	678	100	163	100	55.0	100	20.1	50.0
Ti	160	94.1	137	100	142	100	148.7	100	734	100	52.4	81.8	72.2	75.0	31.1	100
Mo	159	100	24.4[4]	30.0	86.1	100	35.9	50.0	111	97.4	64.3	63.6	43.2	75.0	-	0
Cr	61.4	74.5	53.5[4]	40.0	86.0	100	62.7	100	241	100	171	81.8	87.3	75.0	-	0
Se	44.0	58.8	49.5[4]	10.0	238	88.9	237	100	42.2	66.7	39.1	9.09	-	0	-	0
Co	18.6	84.3	15.7[4]	40.0	21.6	100	4.71	75.0	74.6	100	8.69	90.9	7.73	75.0	-	0
Cd	14.2	92.2	5.48[4]	40.0	31.4	100	2.04	100	11.8	94.9	2.14	63.6	2.90	75.0	-	0
V	10.2	81.4	12.7	80.0	37.0	100	5.54	75.0	30.2	100	8.42	63.6	2.94	50.0	13.8	100
Li	10.5	66.7	10.9	70.0	17.6	100	7.64	75.0	7.61	94.9	16.5	54.5	11.2	100	-	0

*: detection rate [%]

4 Calculated from the values above detection limit so possibly median would be below detection limit if calculation includes all detected values.

4.3. PCA

The PCA analysis is powerful tool to show a "fingerprint" of the sample matrices. The PCA makes the samples grouped or separated based on the variation in the samples. The samples become the groups together under same relationships between the components analyzed. It is possible to use it to analyze an unknown sample matrix for the same components, as well as distinguish the matrix depending on the placement in the PCA score plot. There are figures edited to capture the features in this section and the original figures are presented in **Appendix G**.

It can be found the relationships with chemicals in **Figure 4.6**. Red line went through among MeP, EtP, BuP and OH-EtP, likewise blue line went through among BezP, 4-HB and 3,4-DHB. It was considered that these elements were very similar property each other; the elements nearly red line were parabens with alkyl chain and OH-EtP was derivative of EtP, the elements nearly blue line were parabens derivatives and BezP having additional aromatic ring unlike other parabens. Besides, PrP was present between red and blue line, hence it would have similar property. Apart from these elements, vanillic acid and triclocarban were present absolutely different area. It is presumed to appropriate result since vanillic acid is slightly different structure from parabens and triclocarban is antimicrobial substance.

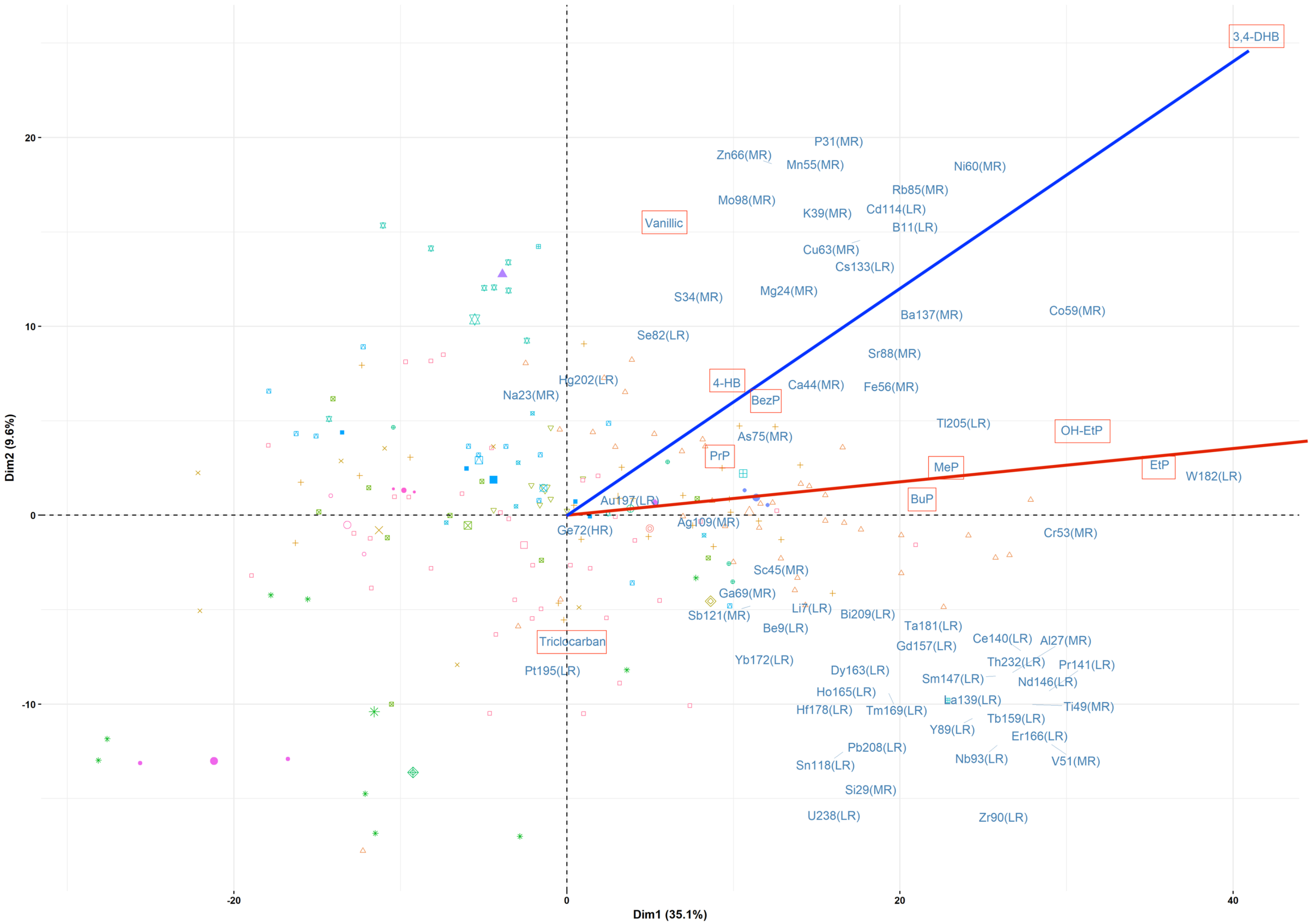


Figure 4.6: The relationship between target analytes

Figure 4.7 provides the PCA analysis result based on characteristics. It was possible to separate Meat, Vegetable, Seafood, Chocolate and Gelatin but it was not completely. Grain spread widely overlapping with 5 categories, and Fruit also contained all Vegetable; it is natural to consider that Vegetable has relationship with Fruit as these are same plant food. Furthermore, it can be seen that Gelatin covered over Sugar; Gelatin products are often sweet snacks (e.g. jelly) so the points were present similar area, however Chocolate as absolute sweet snack was in completely different area.

There were clear separations between forms in **Figure 4.8**. Gel, Liquid and Gum were grouped completely, however Solid was widespread and over Gel group. Generally, Gel is defined as mostly liquid, but it often behaves like solid. Based on this, Gel group was considered that they were present really close to Solid area. Although the property of Gum is assumed to nearly solid than what of Gel, it was exhibited far from Solid. For elements distribution, the majority of elements were present near Solid and partly Gel; Liquid and Gum were apart. Therefore, Solid products tend to contain various kind of elements than Liquid and Gum products.

For the **Figure 4.9**, Sour and Neutral taste were clearly separated, however Sweet and Salty taste covered Sour and Neutral taste. Ideally, Sweet&Salty and Sweet&Sour should be in the area overlapped with Sweet-Salty and Sweet-Sour respectively, but these were only in the Sweet taste area. Regarding element, Na, which constructs salt, was in the area of Salty. This is strong evidence that the taste and element would have relationship obviously.

Three age groups (All, Child and Infant) were set to find relationships in **Figure 4.10**. There were not exactly separations between each age, but it could be found that rough age groups. The snacks for Infant and Child were grouped with subtly overlapping; it is reasonable result that some products did not displayed clearly for suitable age. As far as seeing **Figure 4.10**, the snacks for All were near in the various kind of elements and organic target analytes, while the snacks for Child were relatively far from elements and analytes, then for Infant was present apart from them. Hence, it is thought that the snacks suitable for infant were scarcely added any additives which are often used for food products.

Unlike above PCA results, it is difficult to make groups for country in **Figure 4.11**. Every mark was dispersed on the figure; it is due to the active international trade. The samples collected for this study were classified as where it was purchased not where it was produced. Therefore, samples could not be grouped depending on the countries.

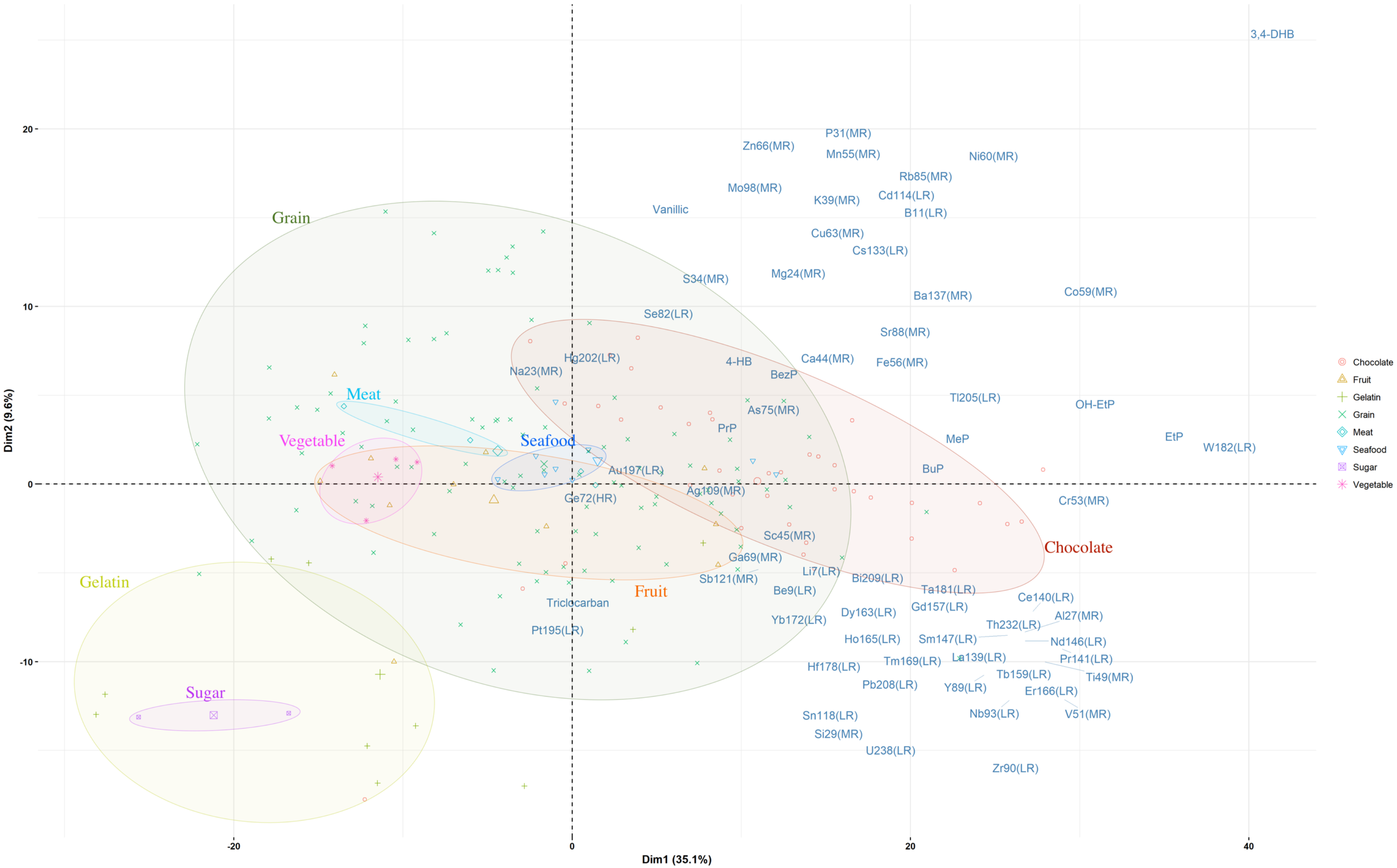


Figure 4.7: PCA of parabens, their derivatives and elements based on characteristics

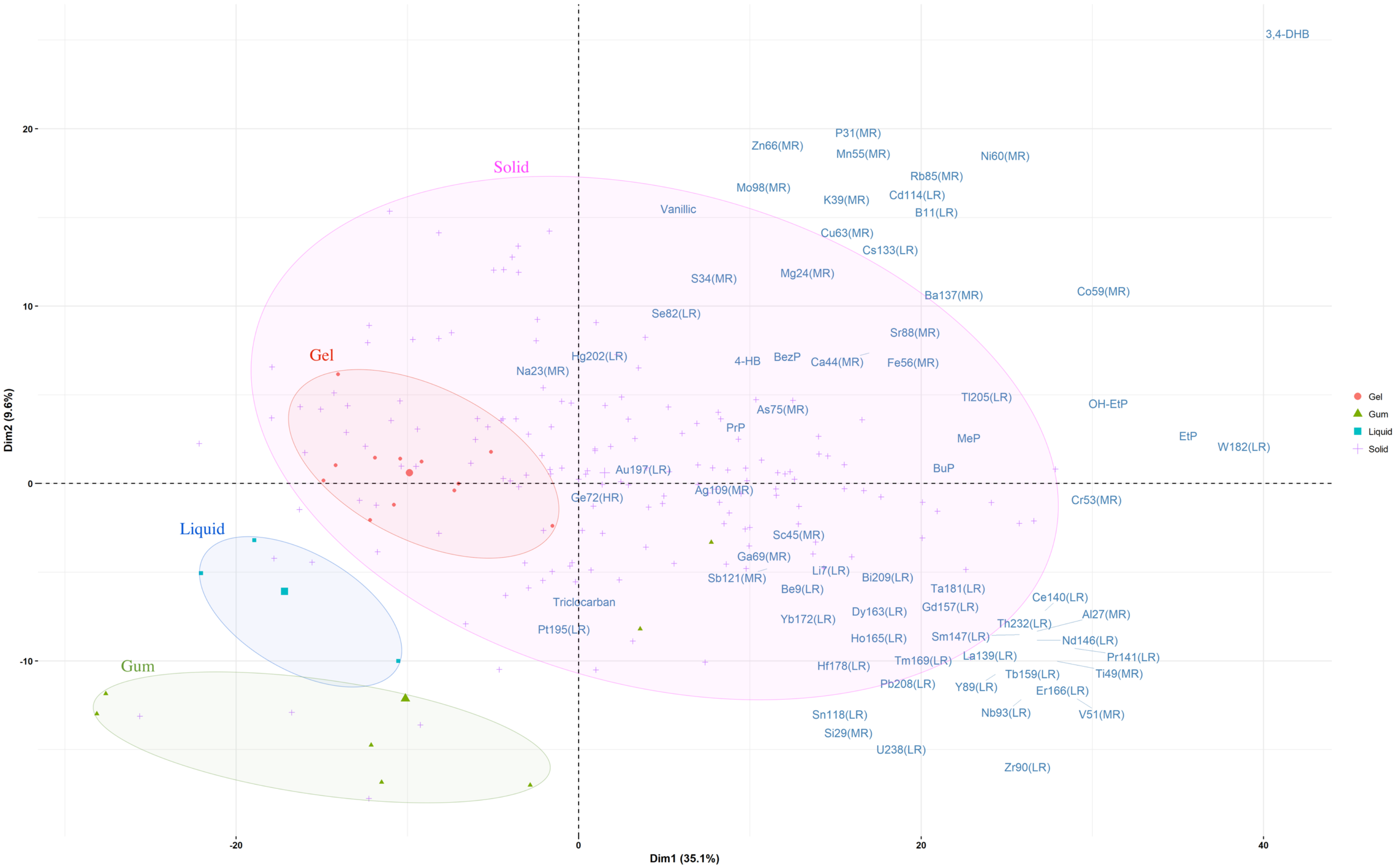


Figure 4.8: PCA based on form

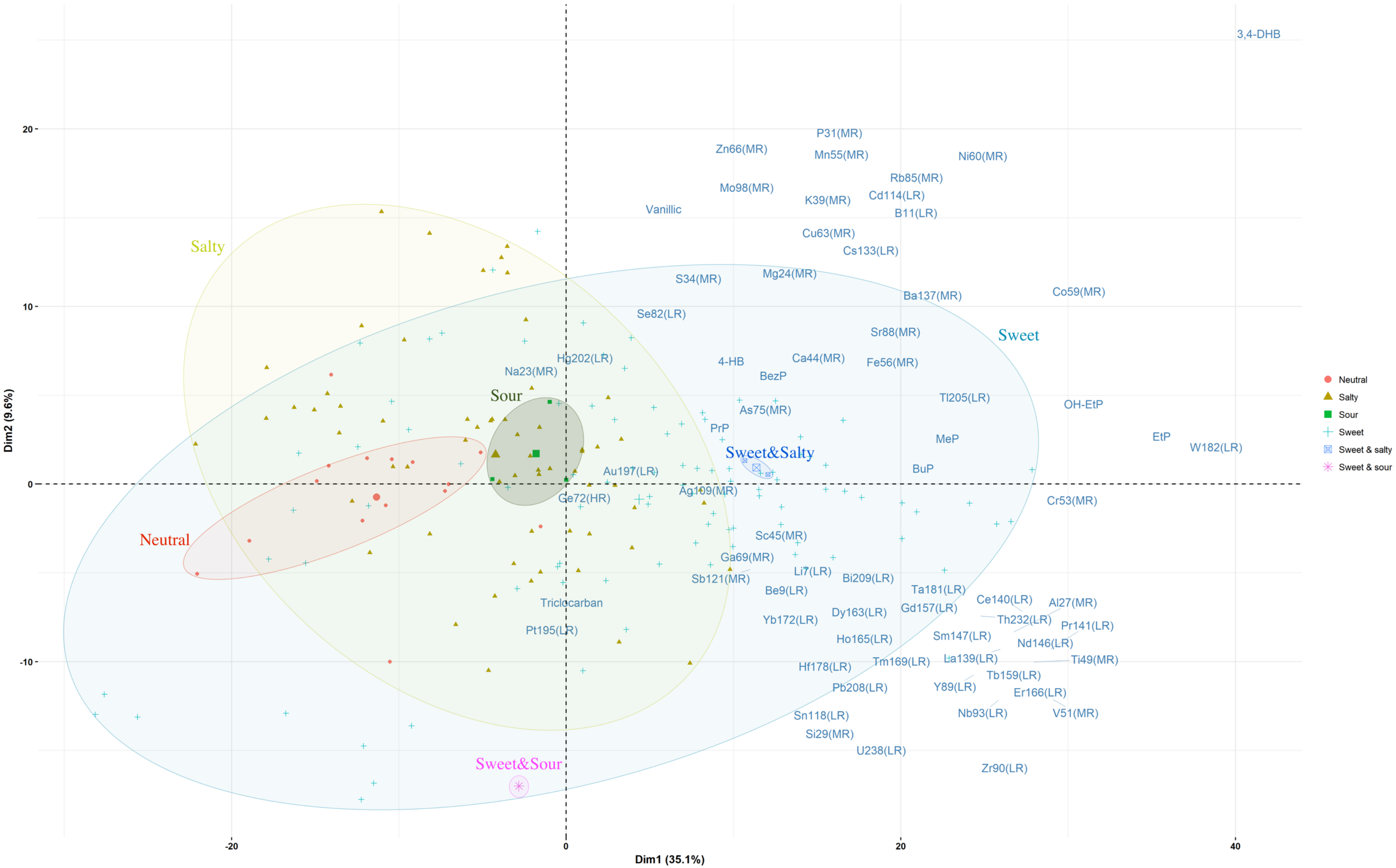


Figure 4.9: PCA based on taste

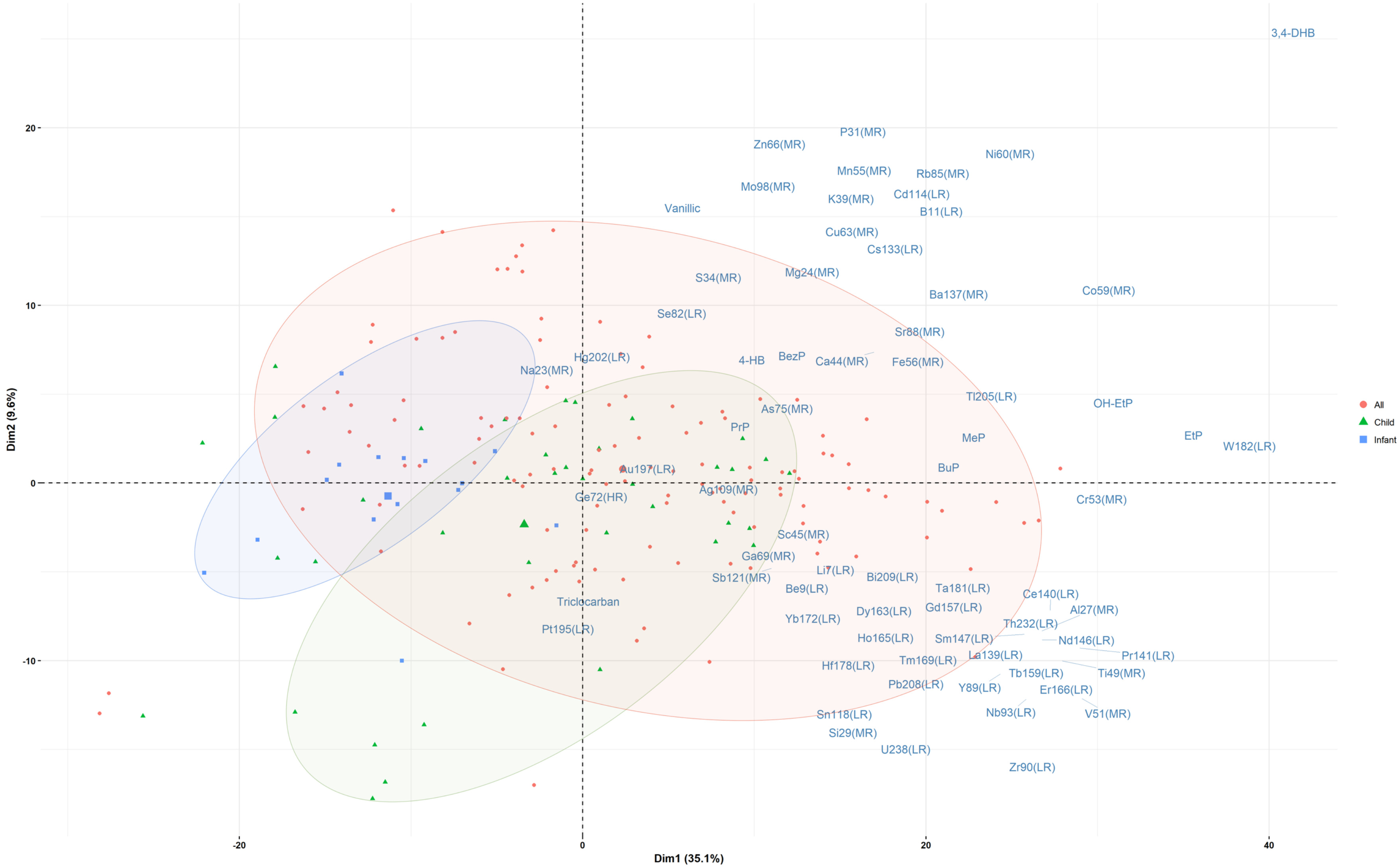


Figure 4.10: PCA based on target age group

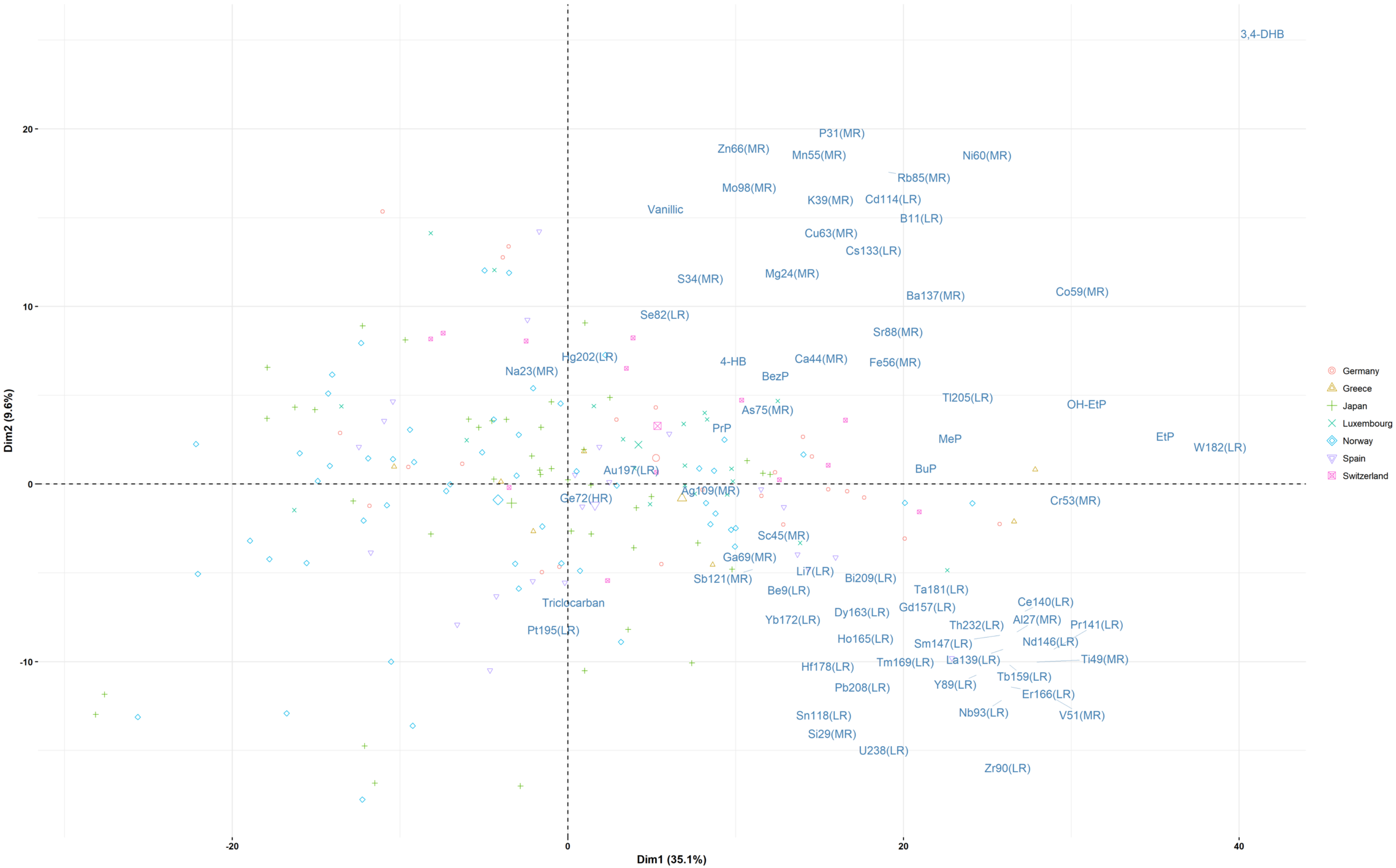


Figure 4.11: PCA based on country

Figure 4.12 showed correlation between elements and target analytes. Full of the correlation is given in **Table G.6** in **Appendix G**. There were noticeable correlations with organic analytes; it was Na. It can be seen negative relationships with Na & EtP and Na & OH-EtP. It means that as higher concentration of Na, EtP/OH-EtP would be lower concentration. 3,4-DHB had lots of positive correlations between elements and also parabens which are parent chemicals of 3,4-DHB. Vanillic acid and 4-HB apparently did not have relationships, and the other organic analytes had slight correlations with elements.

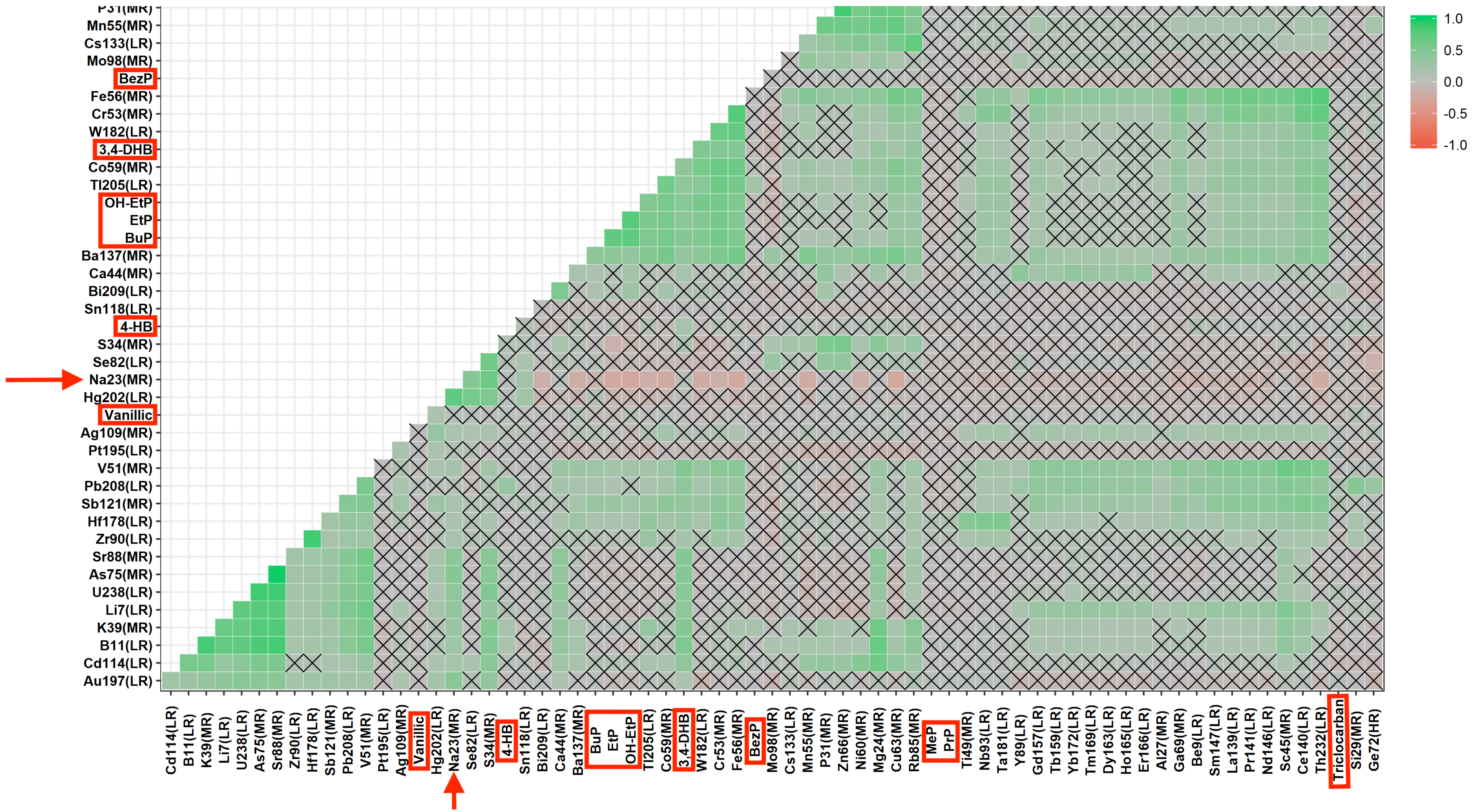


Figure 4.12: A part of correlations between elements and organic analytes

5. CONCLUSIONS

The extraction method employed in this study, solid-liquid extraction (SLE), worked well for separating the organic target analytes from snack food samples, with good reproducibility and high recoveries for parabens. Parabens derivatives, 4-HB and 3,4-DHB, and vanillic acid, demonstrated very low recoveries, interpreting more appropriate to take semi-quantification for these analytes. Another parabens derivative, OH-EtP, and triclocarban as antimicrobial, indicated high recoveries as well. All the organic target analytes were detected in the snack food stuffs though only HeP was extremely low detection rate through the whole. HeP was also hardly ever detected in previous study. Hence, it can be said that the employed extraction method is strong way to derive analyte from snacks.

The parabens derivatives, particularly 4-HB and 3,4-DHB, generally showed higher concentration than parabens, their parent chemicals. This is a reasonable result because 4-HB and 3,4-DHB were the metabolites of parabens; it is considered that the derivatives were resulted of the chemical reaction while storage period from production process. However, the actual process/reaction of it during storage period in snack food stuffs was not investigated in this study. For parabens, the noteworthy result is about HeP as stated above. Not only low detection rate, but it showed very low concentration in spite of having long alkyl chain which has stronger antimicrobial property than detected organic analytes having shorter alkyl chain. The popular parabens often used for snacks were MeP and EtP, which occupied approximately 80 % of all parabens added to snacks. The simplest parabens demonstrating relatively weaker antimicrobial property are generally selected for snacks aiming to preserve it for long period. Although HeP expected to be capable for antimicrobial activity were not often employed for snacks, the parabens with short alkyl chain were usually used for snacks with combination of various parabens expected more antimicrobial property than single used.

No clear trends were found when categorizing the samples by country. It is presumed that every snack/ingredient are often imported/exported so it is regarded as no border for stuffs. While, there were some analytes which were not detected in a specific category. Sugar products, which is one of those characteristics, contained absolutely low concentrations of target analytes, as well as the number of detected analytes were 4 out of 11 analytes. This is independent result than any other analytes.

For elemental analysis, the 6 macromineral elements had much higher concentrations than the other elements. The essential elements for keeping human health were also contained with high concentrations in even snack food stuffs, which are usually known as discretionary food (unessential for life). Almost all target elements were detected with high percentage, whilst some elements were determined with low percentage, further Ir was not detected. Japanese samples often contained Na which demonstrates the existence of salt. It is considered that there is the difference of ingredients between European country and Japan (possibly Asia). The categories having high concentration of macromineral elements and trace elements were almost same with the source of those stated in previous studies.

Regarding PCA analysis, it was possible to make different snack samples grouped depending on the characteristic, form, taste and suitable age. However, it was impossible to separate them as country, which might be aforementioned reason. Besides, target organic analytes were also shown as similar structure/property in the way on the same line. Vanillic acid and triclocarban were located in different areas than those element on the line. Every PCA results demonstrating the group have seemingly appropriate reason, however there are large differences between a number of collected samples where were purchased in or what were characteristics. The relationships were found between organic and inorganic analytes; it can be useful to know the how amount of organic analyte contained when seeing the nutritional information on the package of products.

In conclusion, this is the first study that successfully determined 4-HB, 3,4-DHB, vanillic acid, OH-EtP and TCC in snack food stuffs. The concentrations of parabens often used for preservation of snack food stuffs were generally much lower than those of paraben derivatives since it would be attributed to transformation process from parabens. HeP having long alkyl chain was scarcely used as food additive contrary to strong antimicrobial activity. MeP and PrP were present the wide variability. Many elements were detected, and the result implied the difference of ingredients depending on area, however snacks contained essential elements at higher concentration for human health.

In the present study, a very wide variety of snacks were analyzed, with a low number of each type of snack. Future studies should focus on specific types of snacks collecting higher number of samples. The study emphasizes the value of simultaneous analysis of both organic and inorganic analytes, to evaluate results from a multidirectional view, to study differences by countries and by snack characteristics, and to possibly comment upon positive or negative health effects.

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Appendices

Appendix A

Data of collected samples

Table A.1: Sample information

Sample	Country	Brand	Characteristics	Taste	Type	Target age
1	Japan	SANKO SEIKA	Grain	Salty	Solid	All
2	Japan	SANKO SEIKA	Grain	Salty	Solid	All
3	Japan	SANKO SEIKA	Grain	Salty	Solid	All
4	Japan	SANKO SEIKA	Grain	Salty	Solid	All
5	Japan	SANKO SEIKA	Grain	Salty	Solid	All
6	Japan	SANKO SEIKA	Grain	Salty	Solid	All
7	Japan	SANKO SEIKA	Grain	Salty	Solid	All
8	Japan	SANKO SEIKA	Grain	Salty	Solid	All
9	Japan	YAOKIN	Grain	Salty	Solid	Child
10	Japan	YAOKIN	Grain	Salty	Solid	Child
11	Japan	YAOKIN	Grain	Salty	Solid	Child
12	Japan	Calbee	Grain	Salty	Solid	All
13	Japan	OYATSU COMPANY	Grain	Salty	Solid	All
14	Japan	Calbee	Grain	Salty	Solid	All
15	Japan	DENROKU	Grain	Salty	Solid	All
16	Japan	SAKATABEIKA	Grain	Salty	Solid	Child
17	Japan	KADO	Grain	Salty	Solid	Child
18	Japan	KADO	Grain	Salty	Solid	Child
19	Japan	KADO	Grain	Salty	Solid	Child
20	Japan	DENROKU	Grain	Sweet	Solid	All
21	Japan	KAMEDA SEIKA	Grain	Salty	Solid	All
22	Japan	Glico	Grain	Sweet	Solid	Child
23	Japan	Morinaga	Gelatin	Sweet	Gum	All
24	Japan	UHA Mikakuto	Gelatin	Sweet	Gum	All
25	Japan	Kyoshin	Gelatin	Sweet	Gum	Child
26	Japan	Kyoshin	Gelatin	Sweet	Gum	Child
27	Japan	Kyoshin	Gelatin	Sweet	Gum	Child
28	Japan	Kanro	Gelatin	Sweet & sour	Gum	All
29	Japan	Meiji	Gelatin	Sweet	Gum	All
30	Japan	IWATSUKA CONFECTIONERY	Grain	Salty	Solid	All
31	Japan	YAOKIN	Seafood	Sweet & salty	Solid	Child
32	Japan	YAOKIN	Seafood	Sweet & salty	Solid	Child
33	Japan	KADO	Seafood	Salty	Solid	Child
34	Japan	KADO	Seafood	Sour	Solid	Child
35	Japan	KADO	Seafood	Sour	Solid	Child
36	Japan	KADO	Seafood	Salty	Solid	Child
37	Japan	KADO	Seafood	Salty	Solid	Child
38	Japan	KADO	Seafood	Salty	Solid	Child
39	Japan	KADO	Seafood	Sour	Solid	Child
40	Japan	YAGAI	Meat	Salty	Solid	All
41	Japan	FUJIYA	Grain	Sweet	Solid	All
42	Japan	YURAKU CONFECTIONERY	Chocolate	Sweet	Solid	All
43	Switzerland	Lindt	Chocolate	Sweet	Solid	All
44	Switzerland	Lindt	Chocolate	Sweet	Solid	All
45	Switzerland	Lindt	Chocolate	Sweet	Solid	All
46	Switzerland	Lindt	Chocolate	Sweet	Solid	All
47	Switzerland	ALNATURA	Grain	Sweet	Solid	All

Appendix A. Data of collected samples

Sample	Country	Brand	Characteristics	Taste	Type	Target age
48	Switzerland	ALNATURA	Grain	Sweet	Solid	All
49	Switzerland	Roland	Grain	Sweet	Solid	All
50	Switzerland	MIGROS	Grain	Sweet	Solid	All
51	Switzerland	Lindt	Chocolate	Sweet	Solid	All
52	Switzerland	ALNATURA	Grain	Sweet	Solid	All
53	Switzerland	unknown	Grain	Sweet	Solid	All
54	Switzerland	Dahli	Grain	Sweet	Solid	All
55	Switzerland	MIGROS	Grain	Sweet	Solid	All
56	Greece	Elite	Grain	Salty	Solid	All
57	Greece	Elite	Grain	Salty	Solid	All
58	Greece	Elite	Grain	Salty	Solid	All
59	Greece	Astir	Chocolate	Sweet	Solid	All
60	Greece	unknown	Chocolate	Sweet	Solid	All
61	Greece	unknown	Fruit	Sweet	Solid	All
62	Greece	unknown	Grain	Salty	Solid	All
63	Germany	ja!	Chocolate	Sweet	Solid	All
64	Germany	REWE	Chocolate	Sweet	Solid	All
65	Germany	REWE	Chocolate	Sweet	Solid	All
66	Germany	Kinder	Chocolate	Sweet	Solid	Child
67	Germany	Alpia	Chocolate	Sweet	Solid	All
68	Germany	ZENTIS	Chocolate	Sweet	Solid	All
69	Germany	IronMaxx	Chocolate	Sweet	Solid	All
70	Germany	Wurzener Extra	Chocolate	Sweet	Solid	All
71	Germany	Fulfil	Chocolate	Sweet	Solid	All
72	Germany	Cadbury	Chocolate	Sweet	Solid	All
73	Germany	ETi	Grain	Sweet	Solid	All
74	Germany	IronMaxx	Grain	Sweet	Solid	All
75	Germany	LU	Grain	Salty	Solid	All
76	Germany	Funny Frisch	Grain	Salty	Solid	All
77	Germany	Lorenz	Grain	Salty	Solid	All
78	Germany	ETi	Grain	Sweet	Solid	All
79	Germany	ja!	Chocolate	Sweet	Solid	All
80	Germany	ja!	Grain	Sweet	Solid	All
81	Germany	Lays	Grain	Salty	Solid	All
82	Germany	ültje	Grain	Salty	Solid	All
83	Germany	FARMER'S SNACK	Grain	Salty	Solid	All
84	Germany	DIOFARM	Grain	Salty	Solid	All
85	Germany	Bahlsen	Grain	Sweet	Solid	All
86	Luxembourg	m&m's	Chocolate	Sweet	Solid	All
87	Luxembourg	MinusL	Chocolate	Sweet	Solid	All
88	Luxembourg	Cadbury	Chocolate	Sweet	Solid	All
89	Luxembourg	Mars	Chocolate	Sweet	Solid	All
90	Luxembourg	Cadbury	Chocolate	Sweet	Solid	All
91	Luxembourg	Cadbury	Chocolate	Sweet	Solid	All
92	Luxembourg	Nestle	Chocolate	Sweet	Solid	All
93	Luxembourg	Reece's Pieces	Chocolate	Sweet	Solid	All
94	Luxembourg	LU	Grain	Sweet	Solid	All
95	Luxembourg	LU	Grain	Sweet	Solid	All
96	Luxembourg	Lotus	Grain	Sweet	Solid	All
97	Luxembourg	LU	Grain	Sweet	Solid	All
98	Luxembourg	Bahlsen	Grain	Sweet	Solid	All
99	Luxembourg	Bahlsen	Grain	Sweet	Solid	All
100	Luxembourg	Lotus	Grain	Sweet	Solid	All
101	Luxembourg	LAMBERTZ	Grain	Sweet	Solid	All
102	Luxembourg	Lorenz	Grain	Salty	Solid	All
103	Luxembourg	Hosta Meltis	Grain	Sweet	Solid	All
104	Luxembourg	Lorenz	Grain	Salty	Solid	All

Appendix A. Data of collected samples

Sample	Country	Brand	Characteristics	Taste	Type	Target age
105	Luxembourg	Aoste	Meat	Salty	Solid	All
106	Luxembourg	Bifi	Meat	Salty	Solid	All
107	Spain	snatt's	Grain	Salty	Solid	All
108	Spain	Tosfrit	Grain	Salty	Solid	All
109	Spain	Wise	Grain	Salty	Solid	All
110	Spain	Tosfrit	Grain	Salty	Solid	All
111	Spain	Tosfrit	Grain	Salty	Solid	All
112	Spain	Tosfrit	Grain	Salty	Solid	All
113	Spain	unknown	Grain	Salty	Solid	All
114	Spain	Dia	Grain	Sweet	Solid	All
115	Spain	Schar	Grain	Sweet	Solid	All
116	Spain	gullon	Grain	Sweet	Solid	All
117	Spain	Bahlsen	Grain	Sweet	Solid	All
118	Spain	VALOR	Chocolate	Sweet	Solid	All
119	Spain	Kranch	Chocolate	Sweet	Solid	All
120	Spain	Lotus	Grain	Sweet	Solid	All
121	Spain	Cuetara	Grain	Sweet	Solid	All
122	Spain	idilia	Grain	Sweet	Solid	All
123	Spain	Dia	Grain	Sweet	Solid	All
124	Spain	Hero	Grain	Sweet	Solid	All
125	Spain	Hero	Grain	Sweet	Solid	All
126	Spain	BORGES	Grain	Sweet	Solid	All
127	Spain	Xanos	Grain	Sweet	Solid	All
128	Spain	Alesto	Grain	Salty	Solid	All
129	Norway	Totenflak	Grain	Salty	Solid	All
130	Norway	Totenflak	Grain	Salty	Solid	All
131	Norway	POPPA	Grain	Salty	Solid	All
132	Norway	HiPP	Grain	Salty	Solid	Child
133	Norway	MAARUD	Grain	Salty	Solid	All
134	Norway	Orkla	Grain	Salty	Solid	All
135	Norway	Coop	Grain	Salty	Solid	Child
136	Norway	Coop	Grain	Salty	Solid	Child
137	Norway	MAARUD	Grain	Salty	Solid	All
138	Norway	MAARUD	Grain	Salty	Solid	All
139	Norway	Oreo	Grain	Sweet	Solid	All
140	Norway	Saetre	Grain	Sweet	Solid	All
141	Norway	Korni	Grain	Sweet	Solid	All
142	Norway	minde	Chocolate	Sweet	Solid	All
143	Norway	Nidar	Chocolate	Sweet	Solid	All
144	Norway	Nidar	Chocolate	Sweet	Solid	All
145	Norway	Nidar	Chocolate	Sweet	Solid	All
146	Norway	Nidar	Chocolate	Sweet	Solid	All
147	Norway	Kinder	Chocolate	Sweet	Solid	Child
148	Norway	Malaco	Chocolate	Sweet	Solid	All
149	Norway	Freia	Chocolate	Sweet	Solid	All
150	Norway	Kinder	Grain	Sweet	Solid	Child
151	Norway	Nestle	Grain	Sweet	Solid	Child
152	Norway	Nestle	Grain	Sweet	Solid	Child
153	Norway	Nestle	Chocolate	Sweet	Solid	Child
154	Norway	Malaco	Chocolate	Sweet	Solid	Child
155	Norway	Kiddylicious	Fruit	Sweet	Solid	Child
156	Norway	Kiddylicious	Fruit	Sweet	Solid	Child
157	Norway	saetre	Grain	Sweet	Solid	Child
158	Norway	smasulten	Grain	Salty	Solid	All
159	Norway	smasulten	Grain	Salty	Solid	All
160	Norway	smasulten	Grain	Salty	Solid	All
161	Norway	Toms	Gelatin	Sweet	Solid	Child

Appendix A. Data of collected samples

Sample	Country	Brand	Characteristics	Taste	Type	Target age
162	Norway	Toms	Gelatin	Sweet	Solid	Child
163	Norway	Mattias Lundin	Meat	Salty	Solid	All
164	Norway	Cloetta	Gelatin	Sweet	Solid	Child
165	Norway	FIZZERS	Sugar	Sweet	Solid	Child
166	Norway	Treasure Island Sweets	Sugar	Sweet	Solid	Child
167	Norway	Nestle	Fruit	Neutral	Gel	Infant
168	Norway	Nestle	Fruit	Neutral	Gel	Infant
169	Norway	Ella's kitchen	Fruit	Neutral	Gel	Infant
170	Norway	Ella's kitchen	Fruit	Neutral	Gel	Infant
171	Norway	Ella's kitchen	Fruit	Neutral	Gel	Infant
172	Norway	Semper	Vegetable	Neutral	Gel	Infant
173	Norway	Semper	Vegetable	Neutral	Gel	Infant
174	Norway	Semper	Fruit	Neutral	Gel	Infant
175	Norway	Semper	Fruit	Neutral	Gel	Infant
176	Norway	Semper	Vegetable	Neutral	Gel	Infant
177	Norway	Semper	Vegetable	Neutral	Gel	Infant
178	Norway	Semper	Grain	Neutral	Gel	Infant
179	Norway	Nestle	Grain	Neutral	Liquid	Infant
180	Norway	Nestle	Grain	Neutral	Liquid	Infant
181	Norway	Nestle	Fruit	Neutral	Liquid	Infant

Appendix B

Experimental calculations for organic analysis

Table B.1: Weight of chemical used for stock solutions and ppm per standard stock solution.

Chemical	Weight [g]	ppm
MeP	0.0101	1010
EtP	0.0101	1010
PrP	0.0102	1020
BuP	0.0098	980
BezP	0.0098	980
HeP	0.0099	990
4-HB	0.0110	1100
3,4-DHB	0.0105	1050
Vanillic acid	0.0099	990
OH-EtP	0.0140	1400
TCC	0.0104	1040

Table B.2: Calculated amount of extracted chemical for making 10 ppm working solution (10 mL) and MeOH added with graduated cylinder and pipette.

Chemical	μL extracted	μL MeOH
MeP	99.0	9901.0
EtP	99.0	9901.0
PrP	98.0	9902.0
BuP	102.0	9898.0
BezP	102.0	9898.0
HeP	101.0	9899.0
4-HB	90.9	9909.1
3,4-DHB	95.2	9904.8
Vanillic acid	101.0	9899.0
OH-EtP	71.4	9928.6
TCC	96.1	9903.9

Appendix C

Data tables

Table C.1: Quantification levels for elements analyzed with ICP-MS in different matrices [µg/g]

Element	QL	Element	QL
Ag	0.0003	Mo	0.02
Al	0.2	Na	10
As	0.003	Nb	0.0001
Au	0.00004	Nd	0.0002
B	0.05	Ni	0.015
Ba	0.013	P	0.4
Be	0.0003	Pb	0.002
Bi	0.00005	Pr	0.0001
Ca	2	Pt	0.00001
Cd	0.001	Rb	0.012
Ce	0.0002	S	5
Co	0.004	Sb	0.0006
Cr	0.02	Sc	0.001
Cs	0.0005	Se	0.03
Cu	0.03	Si	10
Dy	0.0005	Sm	0.0001
Er	0.0001	Sn	0.001
Fe	0.02	Sr	0.025
Ga	0.004	Ta	0.00007
Gd	0.0001	Tb	0.00003
Ge	0.002	Th	0.0005
Hf	0.00009	Ti	0.02
Hg	0.001	Tl	0.0003
Ho	0.00009	Tm	0.00003
Ir	0.0005	U	0.0003
K	1	V	0.002
La	0.0003	W	0.0005
Li	0.005	Y	0.0003
Lu	0.00002	Yb	0.0004
Mg	0.1	Zn	0.025
Mn	0.006	Zr	0.0004

Table C.2: Concentrations of the elements in the food samples categorized by countries [ng/g]

	Japan (n=42)				Switzerland (n=13)				Greece (n=7)				Germany (n=23)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
K	1241961	27753	38392218	100	3605620	1356809	6014509	100	4303315	1230209	9662192	100	3803891	921890	8603698	100
Na	5792860	10087	43738392	100	733177	123731	7521223	92.3	4179561	21725	7599023	100	1790474	20575	11577069	95.7
P	716323	11256	4164903	100	1850486	788764	5927859	100	962860	784296	2965044	100	1881276	549242	6867038	100
S	772393	59585	3707384	100	651007	456633	1457998	100	909612	401136	1474171	100	695228	321180	2290473	100
Mg	266792	1506	3201266	100	734204	196821	1434592	100	328312	230978	2408941	100	604214	144600	3363116	100
Ca	248455	13450	5349192	100	792592	263794	7684211	100	327678	298574	755011	100	1053061	52775	2776653	100
Si	17802	10170	1917301	59.5	34408	10974	88187	76.9	63083	10801	156279	100	47329	17629	251267	82.6
Fe	7133	152	46108	100	18131	5804	57576	100	16074	6893	180476	100	23977	2880	74274	100
Zn	7682	176	21334	100	12673	6362	38924	100	6727	2259	32753	100	10315	3192	58793	100
Mn	4030	10.8	10994	100	7484	1556	20420	100	4287	1940	24291	100	3794	827	25049	100
Al	1677	209	124483	95.2	7370	414	19237	100	5223	1282	51134	100	5410	334	39911	100
Rb	834	21.6	15730	100	4237	808	8157	100	3025	891	22824	100	5047	471	36881	100
Cu	1244	67.5	5930	97.6	3538	1654	8849	100	2124	1391	19601	100	3290	513	24508	100
Sr	1278	27.0	238298	97.6	3480	608	7315	100	1356	713	10006	100	2058	175	9260	100
B	875	50.3	75662	95.2	2428	230	9198	100	3027	80.8	18905	100	2074	117	28117	95.7
Ba	471	37.8	2285	95.2	1186	459	7776	100	807	237	6870	100	858	24.3	3868	100
Ni	135	16.8	1307	95.2	667	65.5	2105	100	179	61.8	4444	100	678	35.8	9110	100
Ti	120	20.5	975	92.9	443	31.5	1831	92.3	253	83.1	3552	100	441	27.4	4119	95.7
Mo	105	23.2	3187	90.5	179	86.2	641	100	114	21.9	194	100	151	61.4	820	100
Cr	61.0	21.4	267	81.0	96.6	29.9	786	84.6	178	42.4	1637	71.4	241	20.0	1269	73.9
Se	51.8	30.8	455	71.4	49.1	31.3	113	69.2	34.9	30.4	53.6	71.4	52.5	33.4	189	65.2
Co	13.4	4.63	107	83.3	66.7	4.05	251	100	32.7	4.29	453	85.7	54.4	4.74	218	91.3
Cd	19.5	0.81	256	92.9	18.9	3.07	99.7	100	21.9	13.4	74.2	85.7	10.5	1.48	394	95.7
V	16.7	3.11	355	90.5	13.6	5.07	38.5	84.6	24.2	3.33	164	100	24.5	2.30	110	87.0
Li	13.5	5.55	180	71.4	7.44	5.27	54.9	100	11.5	8.41	30.2	100	11.1	5.42	48.8	78.3
Pb	9.71	2.11	100	90.5	7.63	2.57	23.7	84.6	12.0	2.16	46.4	100	10.9	2.13	34.6	78.3
As	50.3	3.02	35999	92.9	5.63	3.04	25.5	100	6.22	3.57	25.3	85.7	5.48	3.07	16.8	87.0
Ga	5.75	4.33	10.4	11.9	4.79	4.29	6.02	84.6	15.9	5.18	20.1	42.9	5.86	4.01	11.8	39.1
Cs	3.99	0.94	38.5	92.9	9.60	2.51	33.4	69.2	4.42	2.08	46.1	100	11.2	0.93	90.1	100
Ce	2.66	0.23	31.3	95.2	6.40	0.64	45.5	23.1	6.05	1.61	56.9	100	6.68	0.47	82.0	100
Hg	4.20	1.09	60.1	85.7	2.67	1.46	5.85	100	4.13	1.93	7.01	85.7	2.74	1.46	9.35	69.6
Sn	3.28	1.22	2400	81.0	5.04	1.11	20.1	100	2.24	1.44	19.3	100	2.90	1.11	17.3	78.3
Ge	3.04	2.01	6.15	23.8	2.41	2.31	8.82	23.1	2.61	2.61	2.61	14.3	3.74	3.44	4.03	8.70

	Japan (n=42)				Switzerland (n=13)				Greece (n=7)				Germany (n=23)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
La	1.71	0.31	27.8	83.3	3.02	0.36	21.2	100	3.29	0.77	24.0	100	3.49	0.32	34.7	95.7
W	0.79	0.50	53.1	76.2	4.89	1.26	342	92.3	1.44	0.75	649	100	18.4	0.58	282	95.7
Nd	1.40	0.35	18.3	85.7	2.05	0.33	15.3	100	2.73	0.62	19.6	100	2.99	0.34	28.4	95.7
Y	1.69	0.33	126	88.1	2.30	0.32	7.08	92.3	2.08	0.46	12.3	100	2.65	0.38	13.6	95.7
Sc	1.72	1.06	4.15	11.9	1.13	1.04	1.50	23.1	3.18	2.18	4.08	42.9	1.67	1.02	3.04	30.4
Sb	1.57	0.62	8.21	90.5	2.00	0.87	4.30	84.6	1.24	1.11	5.98	71.4	1.68	0.63	7.38	73.9
Tl	0.66	0.32	6.53	33.3	2.00	0.46	5.24	69.2	3.54	0.82	7.75	57.1	1.65	0.33	5.88	69.6
Th	1.06	0.52	1.52	14.3	0.87	0.50	4.18	46.2	5.18	1.26	6.57	42.9	1.44	0.53	6.82	69.6
Zr	0.56	0.01	70.5	97.6	0.66	0.04	6.58	100	2.84	0.28	15.8	100	2.11	0.00	9.55	100
U	1.28	0.37	70.6	69.0	0.76	0.30	1.69	61.5	1.53	0.43	2.45	100	1.00	0.33	36.0	69.6
Nb	0.55	0.14	4.65	90.5	1.35	0.18	7.43	100	1.04	0.45	18.7	100	2.39	0.12	14.1	91.3
Dy	1.24	0.56	7.50	33.3	0.94	0.70	1.47	38.5	2.00	1.71	2.54	42.9	0.76	0.53	2.63	47.8
Ag	0.89	0.38	6.99	83.3	0.93	0.39	2.09	84.6	1.40	0.63	2.41	85.7	0.69	0.31	3.26	69.6
Yb	0.83	0.44	4.35	28.6	0.67	0.40	0.74	23.1	1.00	0.97	1.56	42.9	0.54	0.42	0.94	30.4
Pr	0.39	0.12	4.27	83.3	0.69	0.11	4.00	92.3	0.71	0.17	5.11	100	0.78	0.15	7.74	91.3
Be	0.47	0.32	2.36	42.9	0.49	0.31	0.99	61.5	1.10	0.51	1.57	42.9	0.53	0.33	1.03	56.5
Gd	0.35	0.11	7.07	85.7	0.39	0.16	2.52	100	0.44	0.12	3.69	100	0.72	0.17	5.31	95.7
Sm	0.31	0.11	3.95	85.7	0.57	0.11	1.93	84.6	0.47	0.13	2.80	100	0.55	0.14	5.04	100
Bi	0.25	0.06	4.58	92.9	1.31	0.21	23.1	100	0.44	0.05	0.57	100	0.58	0.06	13.0	91.3
Er	0.26	0.10	5.94	69.0	0.33	0.15	0.70	69.2	0.96	0.15	1.33	71.4	0.37	0.11	1.22	73.9
Hf	0.14	0.10	1.78	42.9	0.17	0.10	0.31	46.2	0.17	0.10	0.63	71.4	0.15	0.10	0.36	47.8
Ho	0.23	0.10	2.02	35.7	0.16	0.10	0.25	53.8	0.39	0.10	0.42	57.1	0.16	0.09	0.52	56.5
Ta	0.15	0.08	0.27	11.9	0.13	0.08	0.46	53.8	0.39	0.07	0.68	57.1	0.14	0.07	0.53	65.2
Au	0.13	0.04	0.73	78.6	0.15	0.06	0.31	92.3	0.17	0.12	0.18	71.4	0.11	0.05	0.27	91.3
Tb	0.08	0.03	1.22	64.3	0.11	0.03	0.26	69.2	0.16	0.03	0.44	85.7	0.10	0.03	0.61	82.6
Tm	0.07	0.03	0.77	42.9	0.07	0.04	0.11	38.5	0.19	0.14	0.23	42.9	0.06	0.03	0.23	52.2
Lu	0.06	0.02	0.60	52.4	0.04	0.03	0.11	69.2	0.08	0.02	0.21	71.4	0.05	0.02	0.21	73.9
Pt	0.06	0.01	4.53	97.6	0.04	0.02	0.08	100	0.03	0.01	0.05	100	0.03	0.01	0.07	91.3
Ir	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0

Table C.3: Concentrations of the elements in the food samples categorized by countries [ng/g] (continued)

	Luxembourg (n=21)				Spain (n=22)				Norway (n=53)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
K	3501158	967294	5865525	100	2574732	723862	13276811	100	1961775	28624	14151496	100
Na	1880148	42081	17436490	100	3161191	34098	13775574	100	469317	14582	18767423	90.6
P	1943836	528648	3341229	100	1222874	382593	4536027	100	726782	658	4315103	100
S	685456	380039	3051414	100	603229	194393	1972754	100	500771	7139	3034503	98.1
Mg	571940	144045	1854104	100	375851	119693	2090806	100	342344	6690	2121275	100
Ca	439451	82236	1959054	100	335363	61486	1343076	100	244054	6695	2785798	100
Si	30513	13560	152948	76.2	47793	13786	581151	86.4	38882	10324	552159	67.9
Fe	19471	6664	61649	100	14366	2187	109496	100	11250	882	141176	100
Zn	11110	4506	51133	100	8077	2050	29172	100	7058	42.2	41433	100
Mn	5358	2553	19809	100	4464	490	20698	100	2146	44.6	19563	100
Al	5555	384	189993	100	4405	349	178239	100	2304	217	40032	94.3
Rb	3442	348	7457	100	2174	484	22956	100	1314	19.7	26926	100
Cu	2692	927	8170	100	2107	383	10879	100	1232	32.6	16707	98.1
Sr	1527	133	4137	100	1777	403	5904	100	896	45.9	6100	98.1
B	1129	90.2	16460	95.2	1337	186	16715	95.5	1291	67.4	18882	98.1
Ba	850	43.0	4112	100	847	33.8	2273	100	375	16.3	3843	98.1
Ni	596	26.8	8488	100	264	18.2	3022	100	190	19.6	6478	90.6
Ti	361	25.6	114122	100	224	25.4	12159	100	124	21.5	2701	92.5
Mo	114	66.8	2637	90.5	133	40.1	1613	100	103	25.6	936	79.2
Cr	200	23.7	1005	100	72.4	21.6	855	90.9	95.1	25.5	1672	69.8
Se	43.4	31.0	244	66.7	41.2	31.7	200	45.5	53.6	31.1	229	32.1
Co	55.9	4.71	121	90.5	25.6	4.13	144	86.4	15.3	4.15	524	77.4
Cd	14.5	1.55	88.4	100	14.0	1.31	198	81.8	6.54	1.34	95.0	73.6
V	17.9	2.42	93.7	85.7	13.2	2.22	300	90.9	8.03	2.03	96.3	73.6
Li	7.47	5.03	13.4	95.2	10.6	5.22	104	68.2	12.2	5.16	70.2	58.5
Pb	7.21	2.98	28.7	100	5.90	3.01	53.5	86.4	7.94	2.13	50.7	71.7
As	5.32	3.59	14.3	76.2	5.71	3.87	67.1	86.4	5.79	3.14	43.5	56.6
Ga	8.20	5.04	24.4	14.3	5.38	4.23	50.0	22.7	10.6	7.64	13.6	3.77
Cs	8.86	0.90	32.5	100	4.79	1.01	24.4	100	4.38	0.92	247	94.3
Ce	6.17	0.45	39.4	100	5.27	0.80	148	100	2.46	0.20	56.0	100
Hg	1.82	1.06	11.0	81.0	4.74	1.02	10.4	90.9	3.25	1.02	10.8	75.5
Sn	3.37	1.29	9.78	81.0	3.79	1.03	18.5	59.1	3.22	0.34	67.5	56.6
Ge	2.53	2.25	3.34	14.3	3.27	2.62	4.62	18.2	2.71	2.07	8.85	13.2

	Luxembourg (n=21)				Spain (n=22)				Norway (n=53)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
La	2.71	0.35	14.5	100	2.86	0.60	70.1	100	1.65	0.31	23.8	94.3
W	22.3	0.63	217	100	2.25	0.51	201	81.8	2.29	0.50	210	81.1
Nd	2.45	0.25	10.91	100	2.39	0.43	71.0	100	1.33	0.27	17.9	92.5
Y	1.82	0.30	6.97	95.2	2.17	0.37	67.6	100	1.39	0.35	23.8	84.9
Sc	1.45	1.02	1.88	9.52	1.87	1.08	13.1	18.2	2.10	1.53	2.68	3.77
Sb	2.06	0.72	3.53	95.2	1.62	0.63	8.10	86.4	1.44	0.64	10.8	83.0
Tl	0.99	0.33	3.92	85.7	1.43	0.48	3.00	63.6	1.23	0.31	5.50	62.3
Th	1.11	0.58	4.09	61.9	1.10	0.51	14.2	54.5	0.82	0.51	6.50	37.7
Zr	1.65	0.00	20.9	100	1.82	0.01	38.4	100	0.98	0.05	31.9	96.2
U	0.43	0.30	2.84	71.4	1.00	0.32	10.8	72.7	0.67	0.34	5.49	67.9
Nb	1.50	0.19	111	90.5	1.35	0.17	15.3	100	0.56	0.10	14.6	94.3
Dy	0.71	0.52	1.36	23.8	0.71	0.55	13.1	45.5	0.74	0.52	2.23	24.5
Ag	0.55	0.31	3.12	90.5	0.61	0.32	4.08	90.9	0.71	0.32	4.15	69.8
Yb	0.57	0.47	0.99	14.3	0.48	0.42	5.58	27.3	0.87	0.44	1.48	11.3
Pr	0.67	0.15	2.99	90.5	0.61	0.13	17.4	95.5	0.45	0.13	5.03	79.2
Be	0.53	0.31	1.69	47.6	0.48	0.35	5.74	59.1	0.48	0.33	2.08	50.9
Gd	0.56	0.14	1.95	95.2	0.55	0.10	15.1	100	0.43	0.11	3.11	84.9
Sm	0.46	0.13	1.64	85.7	0.60	0.15	12.9	90.9	0.37	0.10	2.43	71.7
Bi	0.99	0.06	12.7	90.5	0.42	0.06	2.20	81.8	0.39	0.06	18.2	75.5
Er	0.21	0.12	0.85	76.2	0.31	0.15	7.78	72.7	0.27	0.10	1.54	54.7
Hf	0.18	0.11	1.35	28.6	0.21	0.09	0.96	36.4	0.17	0.10	0.69	35.8
Ho	0.11	0.09	0.28	23.8	0.15	0.09	2.68	50.0	0.13	0.09	0.52	30.2
Ta	0.13	0.07	4.97	57.1	0.14	0.08	0.56	54.5	0.14	0.07	0.65	22.6
Au	0.10	0.05	0.23	81.0	0.12	0.05	0.46	77.3	0.12	0.04	0.38	71.7
Tb	0.08	0.04	0.25	76.2	0.12	0.03	2.30	81.8	0.09	0.03	0.40	60.4
Tm	0.04	0.03	0.15	42.9	0.06	0.04	1.13	63.6	0.06	0.03	0.25	30.2
Lu	0.03	0.02	0.11	71.4	0.04	0.03	0.91	77.3	0.04	0.02	0.21	47.2
Pt	0.04	0.01	0.05	66.7	0.03	0.01	0.11	81.8	0.04	0.01	0.54	92.5
Ir	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0

Table C.4: Concentrations of the elements in the food samples categorized by characteristics [ng/g]

	Grain (n=102)				Gelatin (n=10)				Seafood (n=9)				Meat (n=4)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
K	2137814	432083	14057198	100	69452	27753	5138627	100	1293631	775790	38392218	100	4672683	4148399	5732487	100
Na	3466593	33548	14582087	98.0	150537	10087	1023308	100	23597279	20953957	43738392	100	18101957	16426719	18927129	100
P	1130802	382593	6867038	100	25075	7798	1432903	100	1182755	868914	1652444	100	2842934	2253346	4164903	100
S	734198	162391	1972754	100	113164	24238	851242	100	2285038	1519219	3707384	100	2758364	2286702	3051414	100
Mg	367956	63445	3363116	100	36954	1506	1773375	100	290672	179887	3201266	100	282146	216358	339344	100
Ca	298938	10785	7684211	100	58241	13450	2011560	100	251712	192572	4798031	100	148999	82236	1424497	100
Si	38141	10170	581151	72.5	31723	10265	1917301	80.0	14166	10742	20739	77.8	43571	40593	46549	50.0
Fe	13176	1569	109496	100	1608	152	42805	100	7851	5680	10176	100	18614	15809	27537	100
Zn	8641	1598	58793	100	547	42.2	11148	100	7830	2941	10058	100	42433	21334	51133	100
Mn	5481	322	25049	100	191	10.8	6972	100	2564	908	4119	100	2505	1826	2591	100
Al	2734	217	178239	96.1	3104	209	15387	100	1654	1208	82091	100	1158	508	6191	100
Rb	1582	348	36881	100	56.7	21.6	2931	100	602	331	15730	100	5486	3748	8488	100
Cu	1842	52.1	24508	100	225	67.5	4680	90.0	1158	291	1348	100	1204	1003	1333	100
Sr	1232	94.6	19479	99.0	609	27.0	1310	90.0	1606	994	238298	100	291	133	1675	100
B	1142	77.9	28117	96.1	163	50.3	7089	80.0	1300	693	75662	100	286.4	90.2	338	100
Ba	652	16.3	7776	100	316	89.3	1138	80.0	356	238	1250	100	147.2	43.0	819	100
Ni	207	18.2	9110	98.0	60.4	16.8	453	60.0	153.9	71.2	201	100	43.5	26.8	77.5	100
Ti	160	20.5	4034	94.1	137	21.5	489	100	142	56.7	300	100	148.7	68.0	316	100
Mo	159	25.6	3187	100	24.4	23.2	544	30.0	86.1	55.5	122	100	35.9	26.6	45.2	50.0
Cr	61.4	20.0	855	74.5	53.5	32.8	108	40.0	86.0	37.4	266	100	62.7	54.5	72.9	100
Se	44.0	30.4	455	58.8	49.5	49.5	49.5	10.0	238	39.7	319	88.9	237	202	308	100
Co	18.6	4.05	180	84.3	15.7	4.63	524	40.0	21.6	12.5	30.6	100	4.71	4.15	5.94	75.0
Cd	14.2	1.31	394	92.2	5.48	1.19	13.1	40.0	31.4	19.5	256	100	2.04	0.81	3.07	100
V	10.2	2.22	300	81.4	12.7	2.40	53.9	80.0	37.0	6.56	355	100	5.54	3.16	7.36	75.0
Li	10.5	5.03	104	66.7	10.9	6.02	70.2	70.0	17.6	12.8	180	100	7.64	5.12	12.2	75.0
Pb	7.53	2.11	53.5	81.4	53.8	11.9	92.2	60	6.13	4.99	100	100	8.74	4.03	20.5	100
As	5.68	3.02	368	82.4	3.96	3.50	8.94	70	348	115	35999	100	4.43	3.59	8.18	75.0
Ga	5.75	4.23	50.0	10.8	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Cs	4.01	0.90	247	100	1.57	1.33	9.85	70	4.45	2.59	22.8	100	29.0	22.6	38.5	100
Ce	3.96	0.20	148	99.0	1.52	0.27	7.55	90	2.03	1.11	31.3	100	1.24	0.45	7.08	100
Hg	3.63	1.02	12.6	90.2	1.51	1.29	5.24	30	42.6	6.80	60.1	100	8.78	5.78	12.1	100
Sn	2.53	1.03	20.1	66.7	35.2	1.54	64.1	70	3.54	1.74	2400	100	4.09	1.96	16.9	100
Ge	2.73	2.01	8.82	20.6	4.11	3.55	6.15	40	0.00	0.00	0.00	0	0.00	0.00	0.00	0

	Grain (n=102)				Gelatin (n=10)				Seafood (n=9)				Meat (n=4)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
La	2.57	0.31	70.1	92.2	0.79	0.31	16.8	80	1.37	0.75	5.95	100	1.68	0.35	3.37	100
W	1.93	0.50	342	81.4	1.03	0.65	2.62	70	0.75	0.51	1.11	88.9	1.49	1.01	2.29	100
Nd	2.05	0.33	71.0	92.2	0.95	0.37	10.4	70	1.19	0.89	4.31	100	0.93	0.25	3.16	100
Y	1.85	0.30	126	92.2	2.05	0.84	49.0	60	2.18	0.98	9.14	100	1.62	0.49	4.70	75.0
Sc	1.46	1.02	13.1	5.88	1.72	1.72	1.72	10	3.18	2.20	4.15	22.2	0.00	0.00	0.00	0
Sb	1.33	0.62	8.10	79.4	1.69	0.70	6.32	100	3.93	1.13	8.21	100	1.62	1.38	2.89	100
Tl	1.21	0.31	6.53	50.0	1.07	0.55	1.59	20	0.44	0.43	0.78	33.3	0.82	0.70	4.06	100
Th	0.81	0.51	14.2	36.3	0.82	0.52	1.11	20	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Zr	0.76	0.00	38.4	97.1	1.05	0.01	7.10	100	1.12	0.45	27.8	100	0.88	0.22	70.5	100
U	0.76	0.30	10.8	64.7	2.98	0.97	5.91	50	1.16	0.61	70.6	100	1.71	0.63	2.84	75.0
Nb	0.76	0.12	13.6	89.2	0.58	0.10	1.05	100	0.57	0.33	1.10	100	0.62	0.21	1.14	100
Dy	0.77	0.52	13.1	32.4	0.61	0.58	3.50	30	0.67	0.56	0.78	22.2	0.00	0.00	0.00	0
Ag	0.74	0.32	6.99	85.3	0.74	0.52	4.15	60	2.22	0.58	5.63	100	0.71	0.67	0.73	75.0
Yb	0.71	0.40	5.58	19.6	0.49	0.44	1.76	30	0.77	0.66	0.89	22.2	0.00	0.00	0.00	0
Pr	0.60	0.12	17.4	84.3	0.43	0.16	2.44	60	0.31	0.18	0.92	100	0.27	0.15	0.66	75.0
Be	0.49	0.31	5.74	49.0	0.48	0.32	2.36	50	0.39	0.34	0.51	44.4	0.43	0.43	0.43	25.0
Gd	0.47	0.10	15.1	93.1	0.41	0.18	3.49	60	0.33	0.18	0.88	100	0.50	0.14	0.52	75.0
Sm	0.40	0.10	12.9	87.3	0.22	0.12	2.25	70	0.28	0.14	0.63	88.9	0.45	0.25	0.65	50.0
Bi	0.23	0.05	23.1	79.4	0.28	0.11	11.4	90	0.30	0.12	1.03	100	0.39	0.30	1.84	100
Er	0.30	0.11	7.78	63.7	0.26	0.11	2.33	60	0.16	0.10	0.67	100	0.18	0.10	0.26	50.0
Hf	0.17	0.09	0.96	31.4	0.14	0.10	0.32	50	0.12	0.10	0.79	66.7	1.78	1.78	1.78	25.0
Ho	0.15	0.09	2.68	39.2	0.15	0.14	0.67	30	0.15	0.10	0.20	22.2	0.10	0.10	0.10	25.0
Ta	0.11	0.07	0.56	36.3	0.00	0.00	0.00	0	0.00	0.00	0.00	0	0.07	0.07	0.07	25.0
Au	0.12	0.04	0.73	75.5	0.08	0.05	0.38	60	0.16	0.07	0.69	100	0.22	0.16	0.40	100
Tb	0.10	0.03	2.30	69.6	0.09	0.04	0.52	40	0.06	0.03	0.12	77.8	0.07	0.07	0.08	50.0
Tm	0.06	0.03	1.13	44.1	0.07	0.06	0.26	30	0.05	0.03	0.12	44.4	0.00	0.00	0.00	0
Lu	0.04	0.02	0.91	60.8	0.06	0.03	0.17	40	0.04	0.03	0.19	66.7	0.04	0.03	0.05	50.0
Pt	0.03	0.01	0.11	87.3	0.13	0.04	4.53	90	0.06	0.01	3.55	100	0.05	0.03	0.06	100

Table C.5: Concentrations of the elements in the food samples categorized by characteristics [ng/g] (continued)

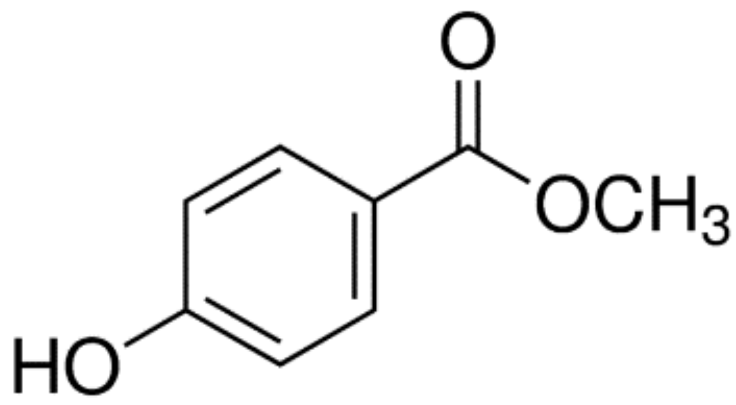
	Chocolate (n=39)				Fruit (n=11)				Vegetable (n=4)				Sugar (n=2)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
K	3620261	35864	7666939	100	1625590	716761	14151496	100	1522719	1369063	1843221	100	46134	28624	63644	100
Na	739476	20575	7733680	100	39336	14582	447816	54.5	104484	60569	287432	100	5249765	3073560	7425970	100
P	1831749	7852	3020335	100	263389	51251	984471	100	257616	123536	637672	100	2117	658	3576	100
S	568465	79955	2290473	100	123165	22430	1474171	100	226341	63066	391659	100	7139	7139	7139	50.0
Mg	602678	113459	2408941	100	124713	40896	1144479	100	90055	79716	115337	100	808883	468907	1148860	100
Ca	1196614	14540	2785798	100	108108	51287	757326	100	117178	95813	557977	100	11656	6695	16616	100
Si	39482	10973	187341	89.7	34566	22795	306162	54.5	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Fe	28557	2591	180476	100	6076	1015	18787	100	4643	1622	10811	100	3970	882	7058	100
Zn	10812	392	32753	100	1239	205	9362	100	3352	1117	7963	100	54.5	43.4	65.6	100
Mn	3763	45.8	24291	100	2146	307	10459	100	618	367	780	100	93.1	53.3	133	100
Al	10382	1549	189993	100	930	445	15836	100	896	535	1264	100	379	379	379	50.0
Rb	5102	28.2	22824	100	1314	534	6372	100	922	448	1347	100	26.3	19.7	32.9	100
Cu	3542	116	19601	100	669	333	4578	90.9	405	335	566	100	582	32.6	1131	100
Sr	2058	45.9	10006	100	505	165	2192	100	963	612	1337	100	86.2	48.5	124	100
B	1866	68.0	9412	100	2291	701	18905	100	1512	662	2345	100	853	675	1031	100
Ba	1095	40.2	6870	100	237	72.7	1393	100	380	129	494	100	22.9	22.9	22.9	50.0
Ni	678	30.0	4444	100	163	19.6	462	100	55.0	50.4	77.4	100	20.1	20.1	20.1	50.0
Ti	734	109	114122	100	52.4	36.5	1361	81.8	72.2	53.5	73.7	75.0	31.1	21.9	40.4	100
Mo	111	26.0	670	97.4	64.3	21.9	221	63.6	43.2	28.6	58.4	75.0	0.00	0.00	0.00	0
Cr	241	24.4	1672	100	171	27.8	598	81.8	87.3	69.0	95.3	75.0	0.00	0.00	0.00	0
Se	42.2	31.3	130	66.7	39.1	39.1	39.1	9.09	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Co	74.6	8.66	453	100	8.69	4.99	19.9	90.9	7.73	5.12	8.28	75.0	0.00	0.00	0.00	0
Cd	11.8	1.34	99.7	94.9	2.14	1.56	18.0	63.6	2.90	1.59	3.80	75.0	0.00	0.00	0.00	0
V	30.2	4.70	164	100	8.42	3.73	35.4	63.6	2.94	2.03	3.84	50.0	13.8	9.26	18.4	100
Li	7.61	5.16	34.8	94.9	16.5	6.31	29.6	54.5	11.2	9.54	46.9	100	0.00	0.00	0.00	0
Pb	12.0	2.13	50.7	94.9	9.50	2.26	45.2	72.7	3.86	2.48	11.2	100	2.80	2.80	2.80	50.0
As	5.82	3.04	25.3	76.9	5.92	3.29	9.96	45.5	6.44	6.44	6.44	25.0	0.00	0.00	0.00	0
Ga	6.41	4.01	24.4	46.2	5.18	5.18	5.18	9.09	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Cs	12.1	2.39	46.1	97.4	5.12	0.92	20.6	100	5.93	1.30	9.93	100	0.00	0.00	0.00	0
Ce	9.61	1.19	82.0	100	1.91	0.48	10.7	100	1.24	1.16	2.46	100	0.91	0.70	1.12	100
Hg	2.61	1.40	7.91	79.5	1.38	1.02	1.86	36.4	1.59	1.34	2.31	75.0	1.91	1.38	2.45	100
Sn	4.14	1.11	67.5	89.7	2.16	0.34	45.4	63.6	4.58	4.58	4.58	25.0	8.37	8.37	8.37	50.0
Ge	2.53	2.25	2.61	7.69	0.00	0.00	0.00	0	5.73	2.61	8.85	50.0	0.00	0.00	0.00	0

	Chocolate (n=39)				Fruit (n=11)				Vegetable (n=4)				Sugar (n=2)			
	Median	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**	*Median*	*Min*	*Max*	*%**
La	4.45	0.46	34.7	100	1.69	0.51	5.86	90.0	0.98	0.60	2.59	100	0.66	0.50	0.82	100
W	44.0	0.56	649	100	1.11	0.50	3.75	100	2.93	2.34	3.53	50.0	0.69	0.69	0.69	50.0
Nd	3.54	0.36	28.4	100	0.79	0.27	4.75	100	0.60	0.56	1.11	100	0.69	0.31	1.07	100
Y	2.93	0.32	13.6	100	1.03	0.35	8.16	81.8	0.47	0.44	0.57	75.0	1.16	0.94	1.38	100
Sc	1.60	1.02	4.08	41.0	2.18	2.18	2.18	9.09	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Sb	2.68	0.72	7.38	97.4	0.94	0.69	1.74	72.7	0.91	0.90	0.91	50.0	6.63	2.51	10.8	100
Tl	1.72	0.45	7.75	97.4	0.54	0.33	4.74	90.0	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Th	1.99	0.50	6.82	82.1	0.70	0.51	1.26	45.5	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Zr	2.75	0.11	23.6	100	0.61	0.12	31.9	100	0.12	0.06	0.28	100	1.76	0.28	3.24	100
U	0.90	0.30	36.0	82.1	0.73	0.38	2.45	63.6	0.54	0.39	0.58	75.0	1.08	0.52	1.63	100
Nb	2.49	0.44	111	100	0.55	0.12	2.30	100	0.27	0.19	0.40	100	0.13	0.11	0.15	100
Dy	0.85	0.55	2.63	53.8	1.18	0.66	1.71	18.2	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Ag	0.71	0.31	4.08	79.5	0.97	0.39	2.41	45.5	0.42	0.38	0.47	50.0	0.93	0.93	0.93	50.0
Yb	0.62	0.42	1.56	33.3	0.70	0.44	0.97	18.2	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Pr	0.98	0.11	7.74	100	0.33	0.13	1.15	81.8	0.16	0.13	0.30	100	0.16	0.16	0.16	50.0
Be	0.55	0.31	1.69	59.0	0.55	0.33	1.68	63.6	0.49	0.49	0.49	25.0	0.34	0.34	0.34	50.0
Gd	0.82	0.16	5.31	100	0.37	0.12	1.22	72.7	0.12	0.11	0.14	75.0	0.14	0.13	0.14	100
Sm	0.83	0.15	5.04	94.9	0.27	0.17	1.23	72.7	0.12	0.12	0.12	25.0	0.10	0.10	0.10	50.0
Bi	1.77	0.16	18.2	100	0.45	0.07	3.85	90.9	0.51	0.09	0.94	100	0.19	0.19	0.19	50.0
Er	0.35	0.11	1.33	84.6	0.35	0.12	0.96	45.5	0.15	0.15	0.15	25.0	0.00	0.00	0.00	0
Hf	0.18	0.10	1.35	66.7	0.17	0.10	0.27	27.3	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Ho	0.17	0.09	0.52	53.8	0.11	0.09	0.36	36.4	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Ta	0.18	0.07	4.97	71.8	0.14	0.14	0.14	9.09	0.00	0.00	0.00	0	0.00	0.00	0.00	0
Au	0.11	0.05	0.27	89.7	0.06	0.05	0.13	81.8	0.13	0.12	0.14	50.0	0.08	0.08	0.08	50.0
Tb	0.10	0.03	0.61	94.9	0.09	0.05	0.23	45.5	0.04	0.04	0.04	25.0	0.00	0.00	0.00	0
Tm	0.07	0.03	0.23	53.8	0.07	0.06	0.14	27.3	0.00	0.00	0.00	0	0.03	0.03	0.03	50.0
Lu	0.04	0.02	0.21	79.5	0.07	0.04	0.08	36.4	0.00	0.00	0.00	0	0.02	0.02	0.02	50.0
Pt	0.04	0.01	0.10	89.7	0.05	0.01	0.08	100	0.06	0.04	0.08	100	0.02	0.01	0.02	100

Appendix D

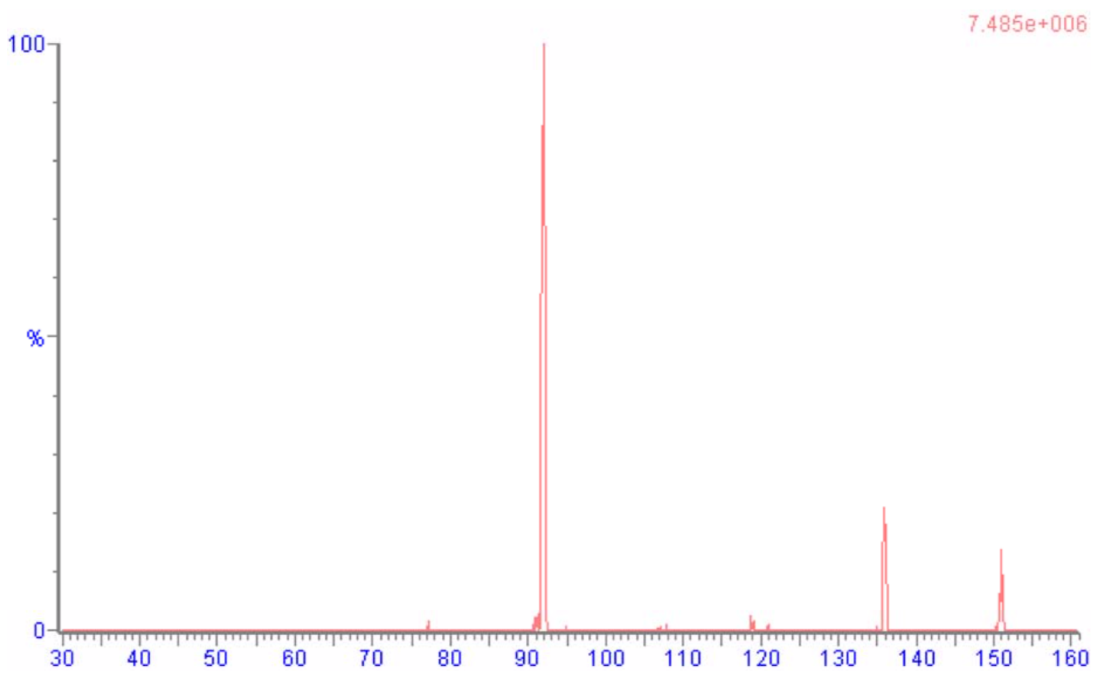
MS/MS Fragmentation under Negative Ionization Mode

MeP - *Methyl paraben*



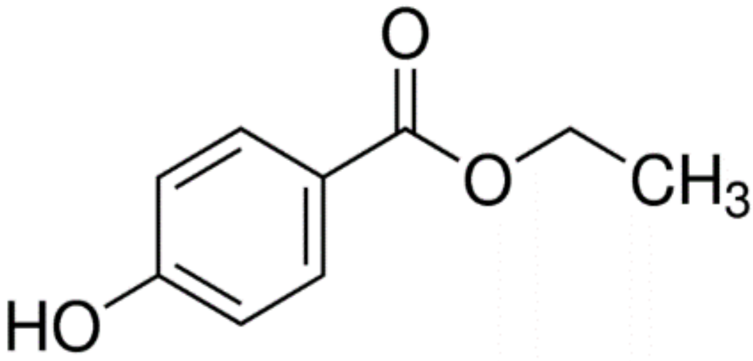
Methyl-4-hydroxybenzoate

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
MeP	C8H8O3	1	151.02	36	92.05	20	ES-
		2	151.02	36	135.98	14	ES-
		3	151.02	36	119.02	16	ES-



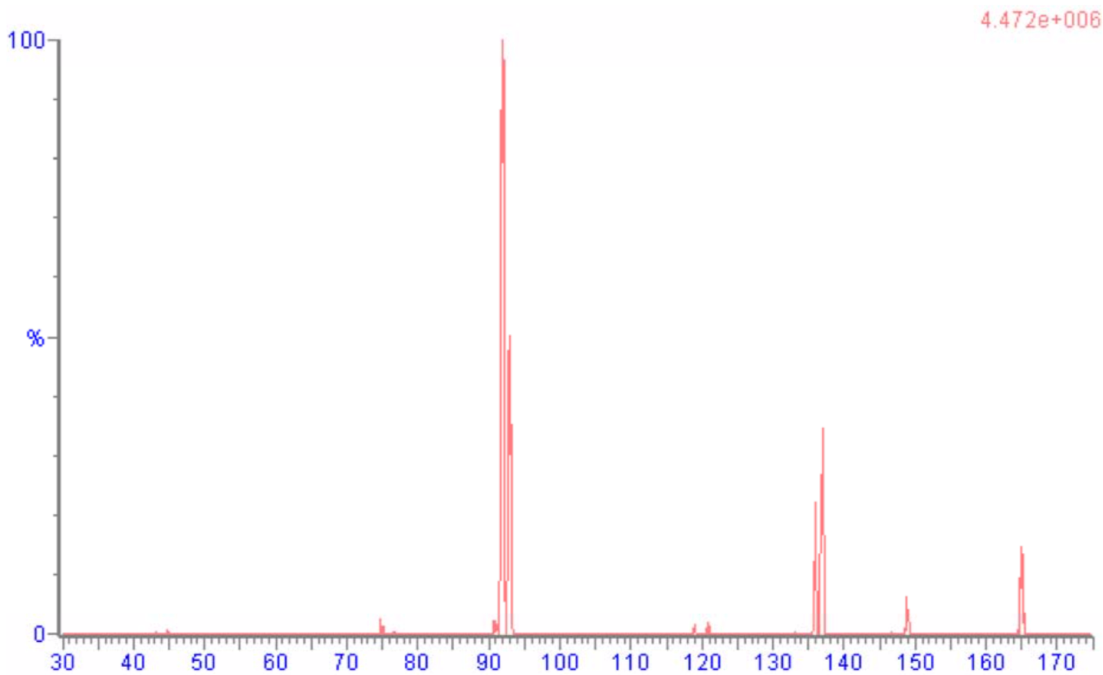
Optimized Daughter Spectrum (at Collision Energy 20eV)

EtP - *Ethyl paraben*



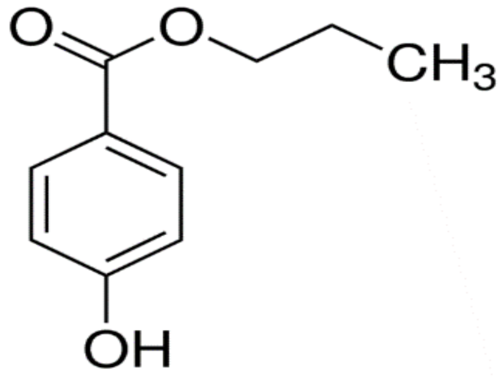
Ethyl-4-hydroxybenzoate

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
EtP	C9H10O3	1	165.03	42	92.13	20	ES-
		2	165.03	42	136.92	14	ES-
		3	165.03	42	74.91	36	ES-



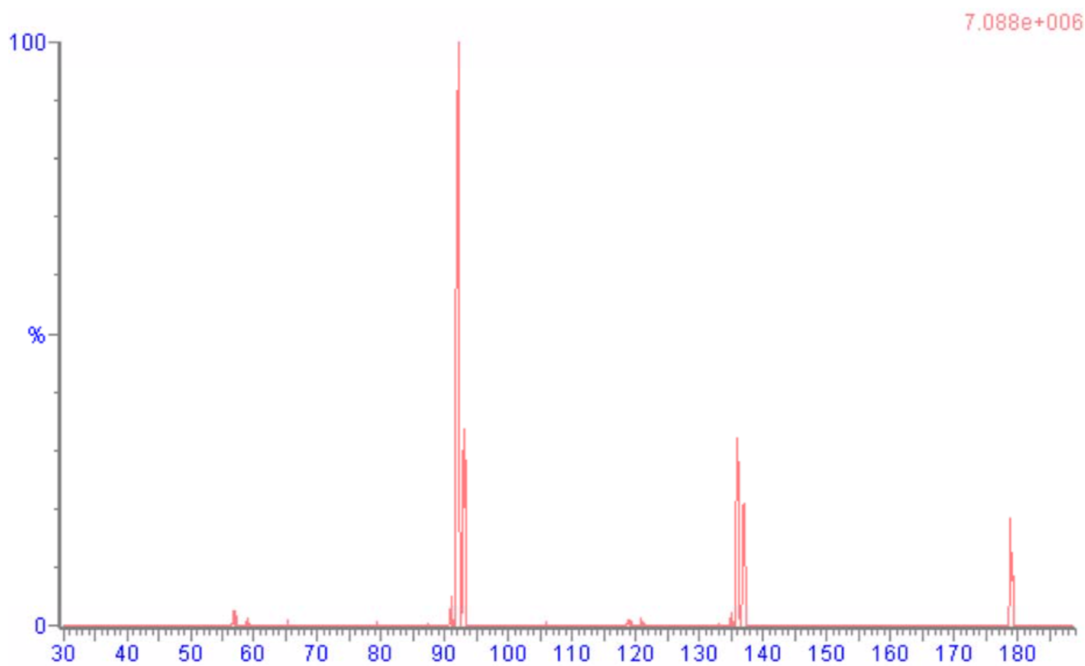
Optimized Daughter Spectrum (at Collision Energy 20eV)

PrP - *Propyl paraben*



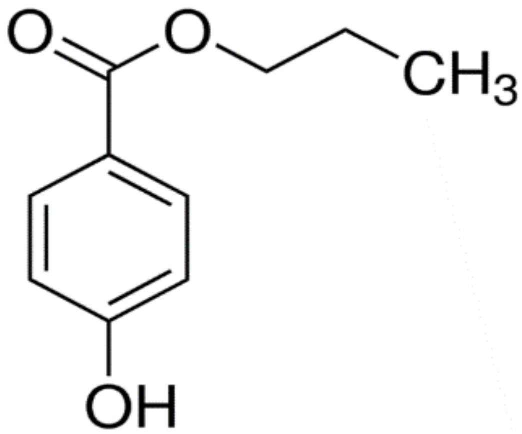
Propyl-4-hydroxybenzoate

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
PrP	C10H12O3	1	179.05	28	92.12	20	ES-
		2	179.05	28	136.24	16	ES-
		3	179.05	28	57.03	30	ES-



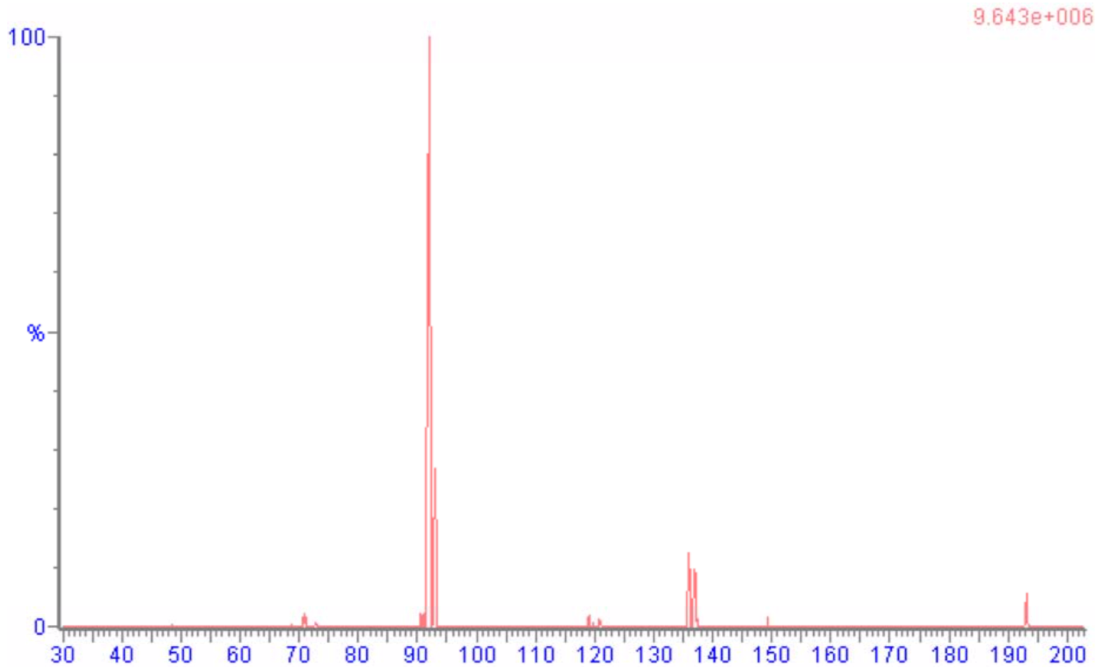
Optimized Daughter Spectrum (at Collision Energy 20eV)

BuP - *Butyl paraben*



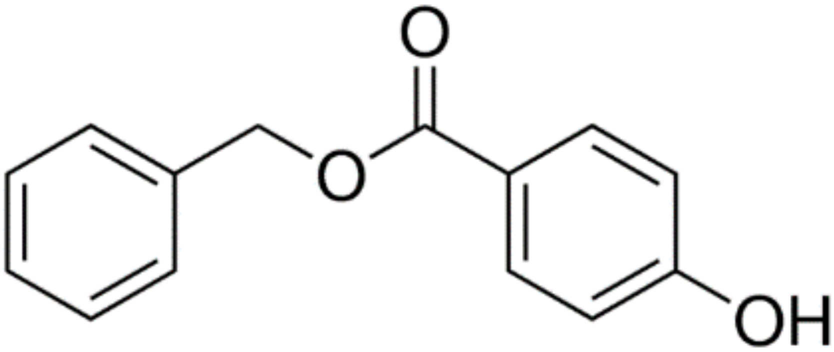
Butyl-4-hydroxybenzoate

Compound	**Formula/Mass**		**Parent m/z**	**Cone Voltage (V)**	**Daughters**	**Collision Energy (eV)**	**Ion Mode**
BuP	C11H14O3	1	193.06	46	92.11	24	ES-
		2	193.06	46	136.76	14	ES-
		3	193.06	46	70.99	32	ES-



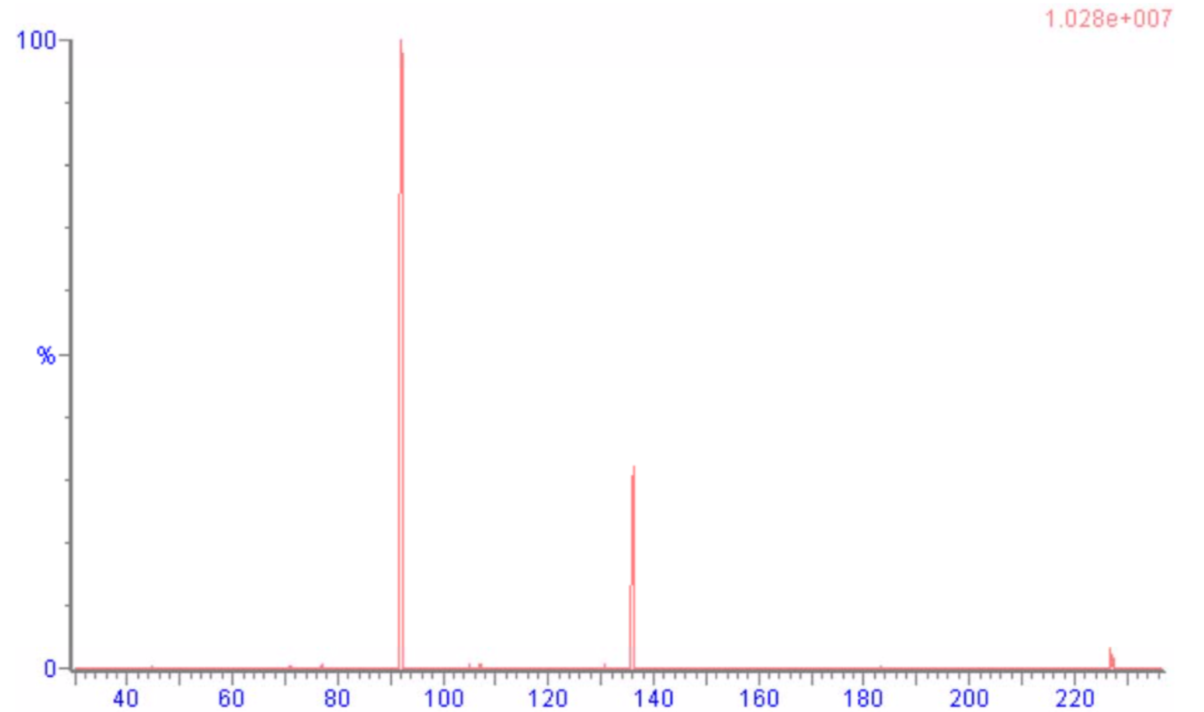
Optimized Daughter Spectrum (at Collision Energy 24eV)

BezP - *Benzyl paraben*



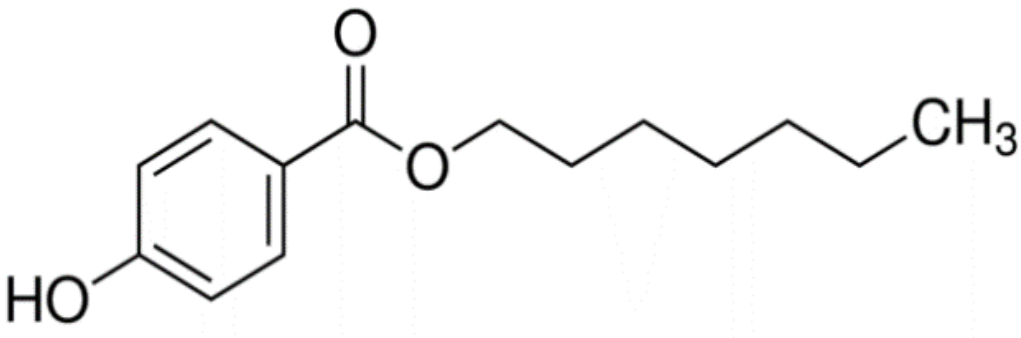
Benzyl-4-hydroxybenzoate

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
BezP	C14H12O3	1	227.05	14	91.99	22	ES-
		2	227.05	14	135.99	14	ES-
		3	227.05	14	183.12	12	ES-



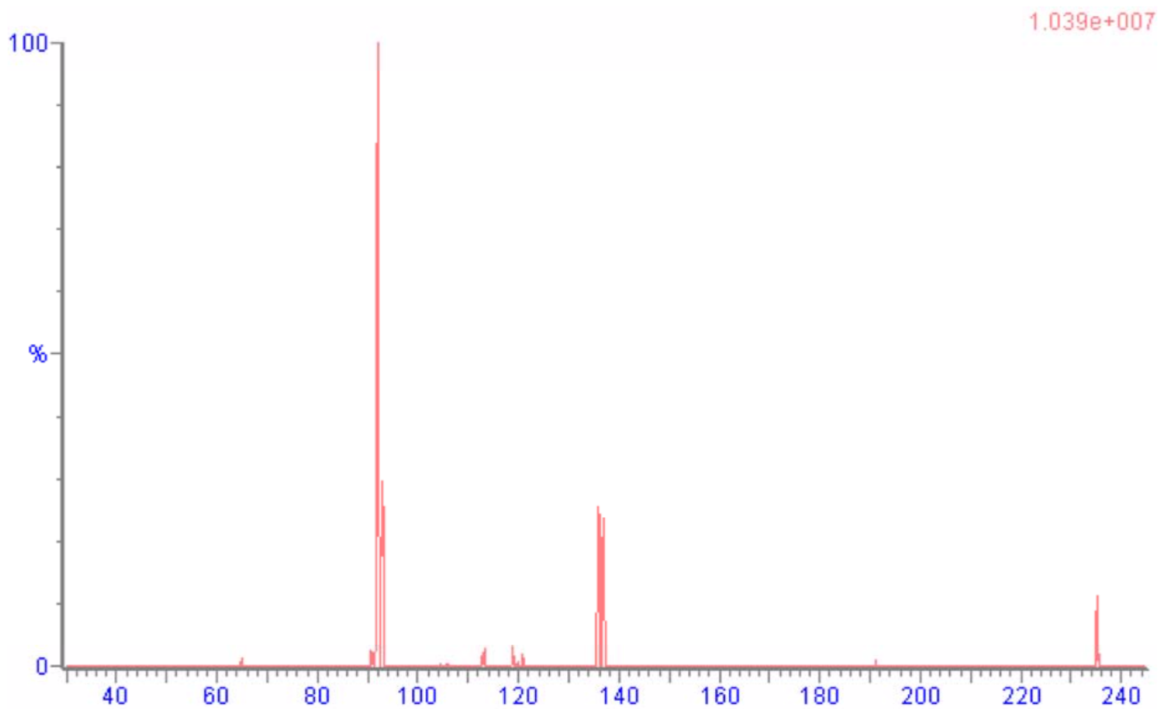
Optimized Daughter Spectrum (at Collision Energy 22eV)

HeP - *Heptyl paraben*



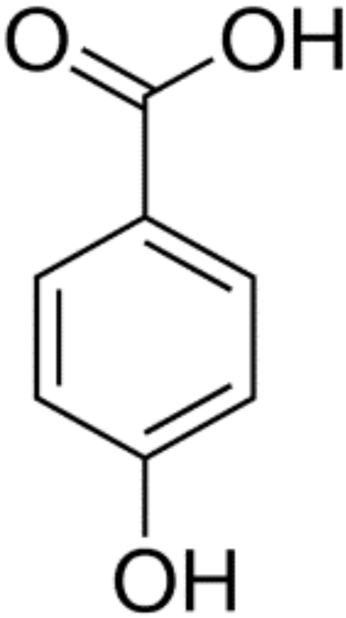
Heptyl-4-hydroxybenzoate

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
HeP	C14H20O3	1	235.11	20	92.12	24	ES-
		2	235.11	20	136.18	20	ES-
		3	235.11	20	113.12	34	ES-



Optimized Daughter Spectrum (at Collision Energy 24eV)

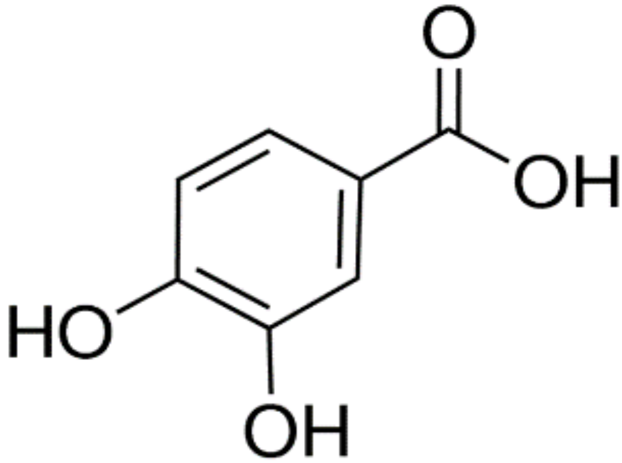
4-HB - *4-Hydroxybenzoic acid*



4-Hydroxybenzoic acid

Compound	**Formula/Mass**		**Parent m/z**	**Cone Voltage (V)**	**Daughters**	**Collision Energy (eV)**	**Ion Mode**
4-HB	C7H6O3	1	136.94	36	92.98	14	ES-

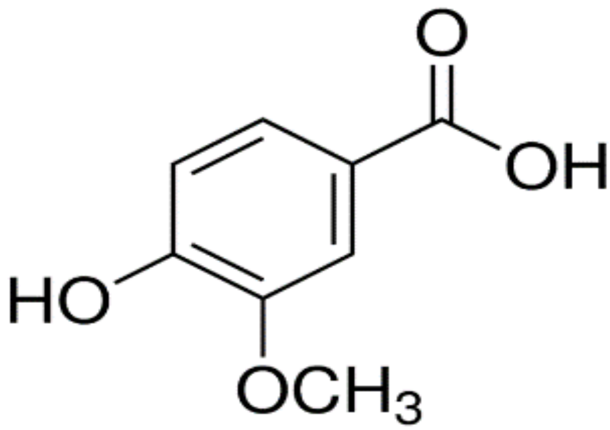
3,4-DHB - *3,4-dihydroxybenzoic acid*



3,4-dihydroxybenzoic acid/Protocatechuic acid

Compound	**Formula/Mass**		**Parent m/z**	**Cone Voltage (V)**	**Daughters**	**Collision Energy (eV)**	**Ion Mode**
3,4-DHB	C7H6O4	1	152.99	34	108.97	14	ES-

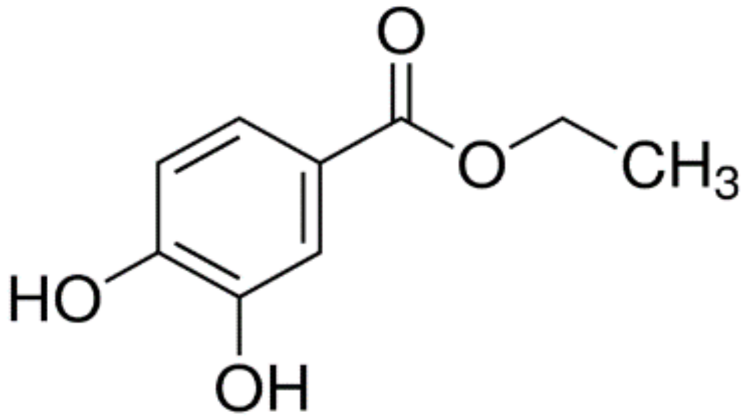
Vanillic acid - *4-hydroxy-3-methoxybenzoic acid*



4-hydroxy-3-methoxybenzoic acid

Compound	Formula/Mass		Parent m/z	Cone Voltage (V)	Daughters	Collision Energy (eV)	Ion Mode
Vanillic acid	C8H8O4	1	167.01	20	151.97	12	ES-
		2	167.01	20	107.98	18	ES-

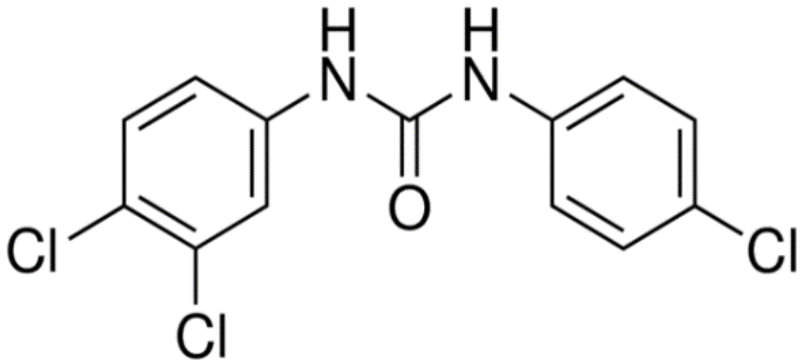
OH-EtP - *Ethyl protocatechuic acid*



Ethyl 3,4-dihydroxybenzoate

Compound	**Formula/Mass**		**Parent m/z**	**Cone Voltage (V)**	**Daughters**	**Collision Energy (eV)**	**Ion Mode**
OH-EtP	C9H10O4	1	181.03	18	108.12	22	ES-
		2	181.03	18	152.91	14	ES-

TCC - *Triclocarban*



3-(4-Chlorophenyl)-1-(3,4-dichlorophenyl) urea

Compound	**Formula/Mass**		**Parent m/z**	**Cone Voltage (V)**	**Daughters**	**Collision Energy (eV)**	**Ion Mode**
TCC	C13H9Cl3N2O	1	312.88	8	159.95	12	ES-
		2	312.88	8	126.42	24	ES-
		3	312.88	8	125.96	22	ES-

Appendix E

Calibration curves

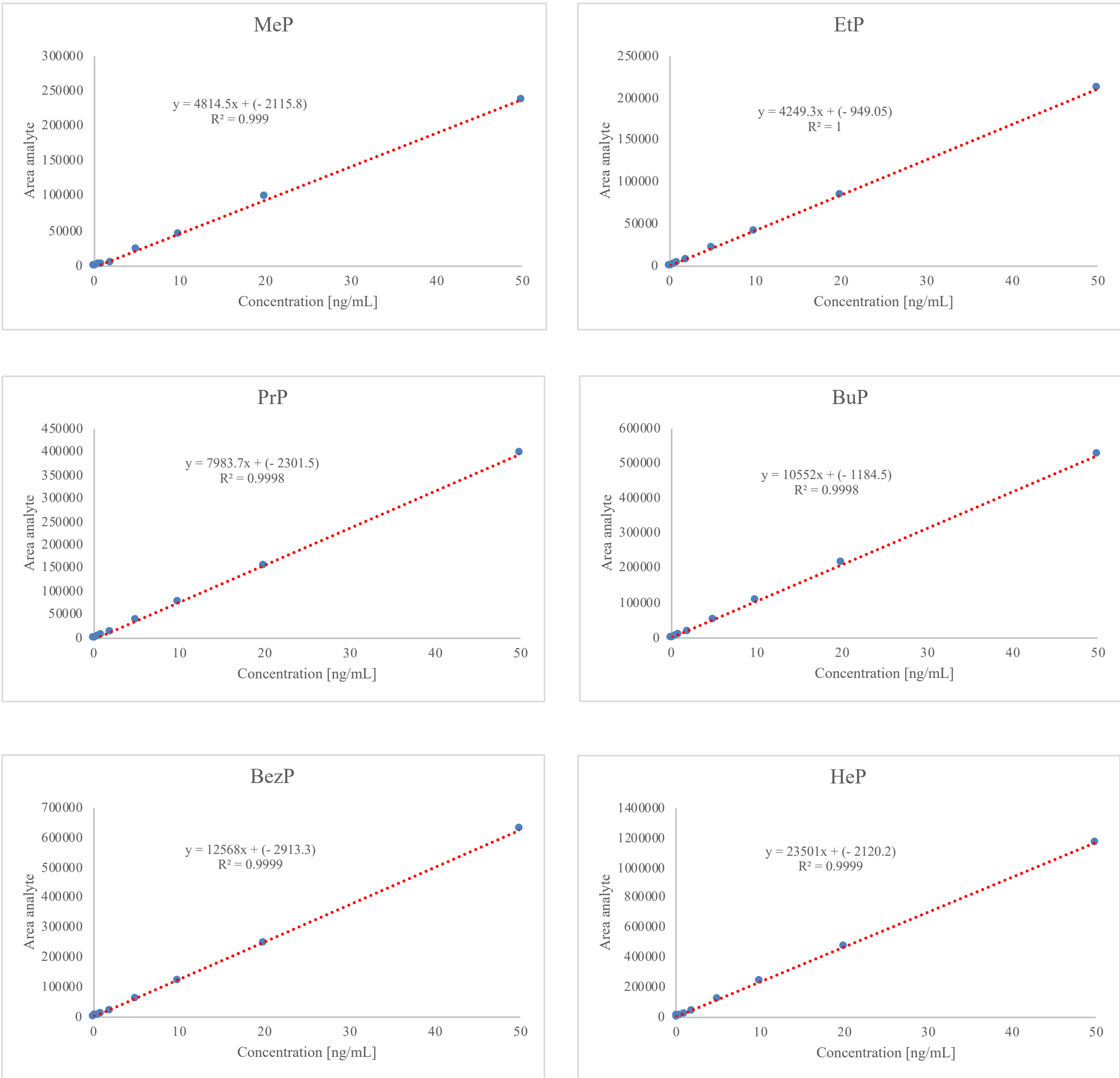


Figure E.1: Absolute calibration curves

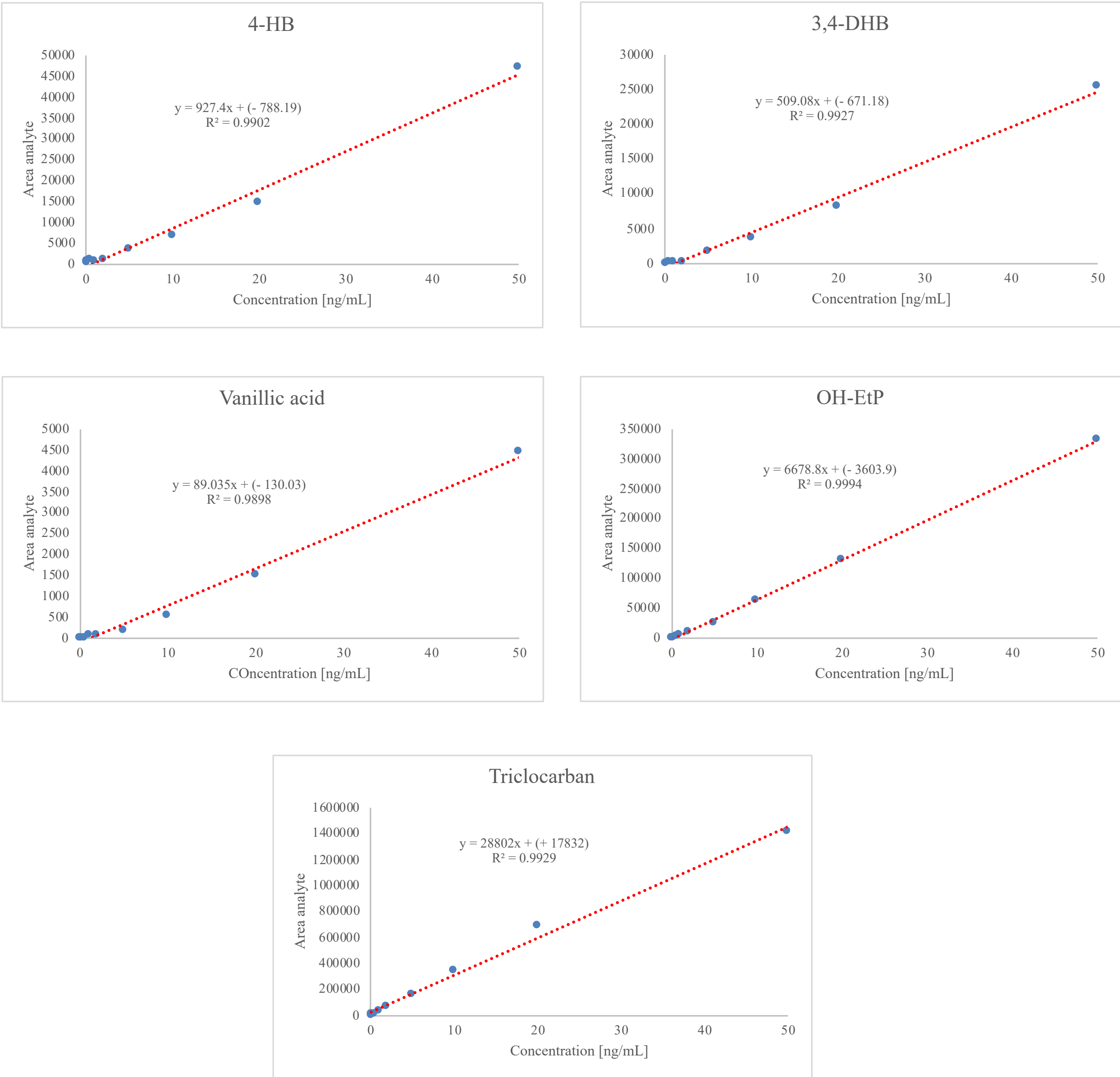


Figure E.2: Absolute calibration curves (continued)

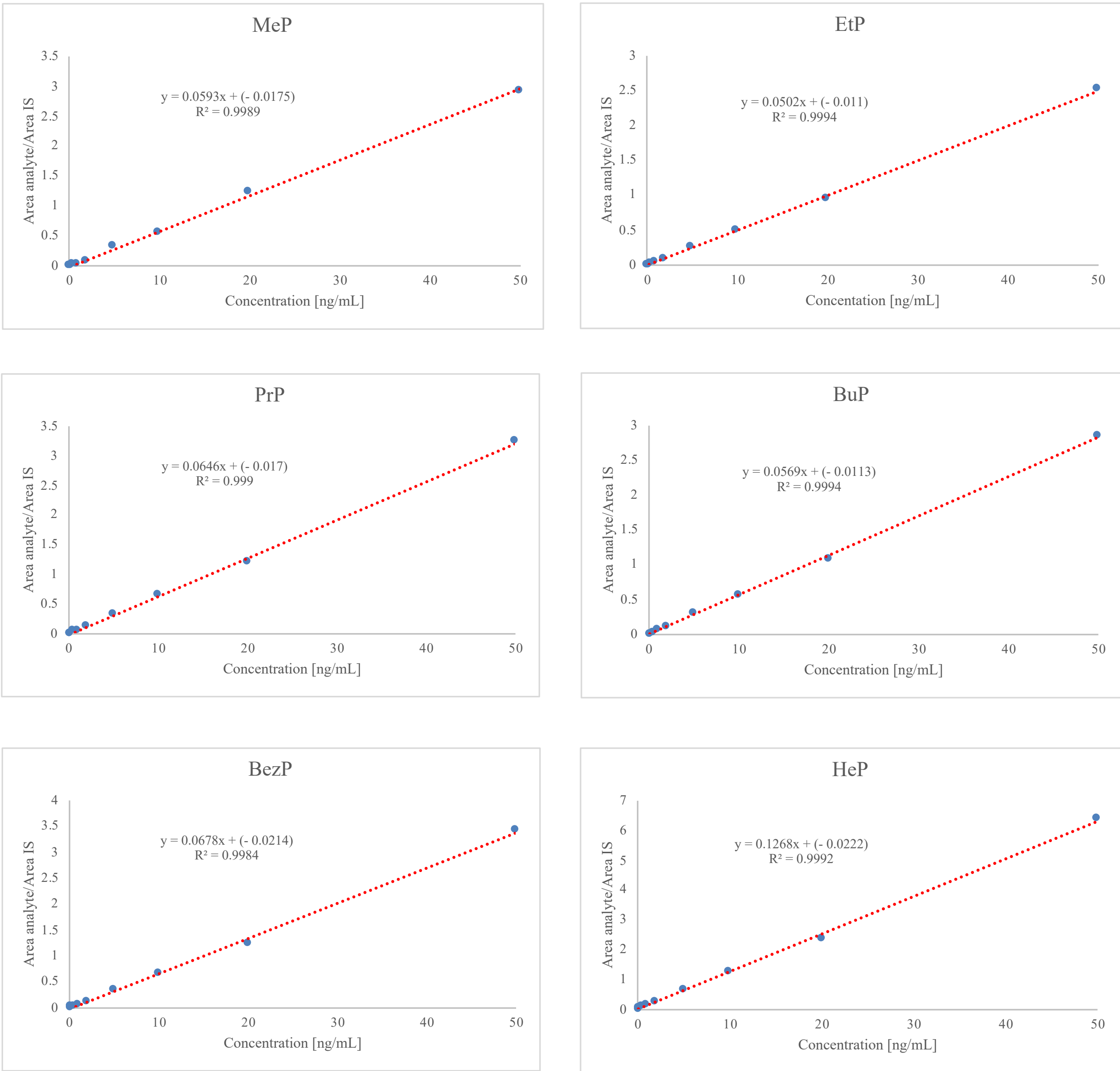
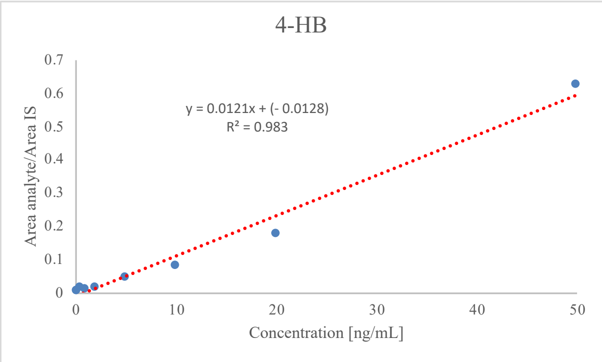
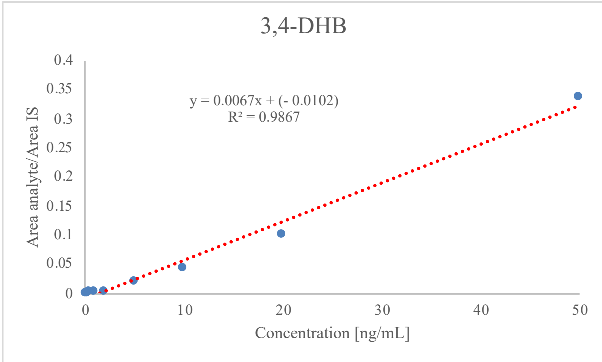
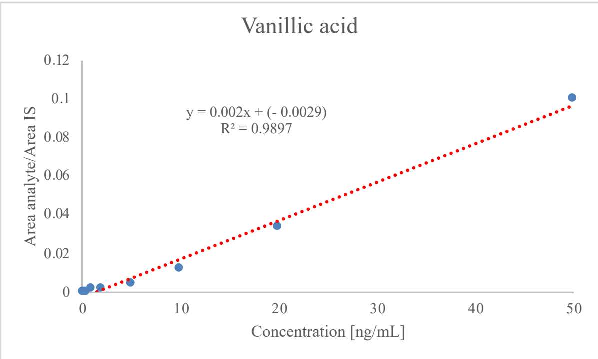
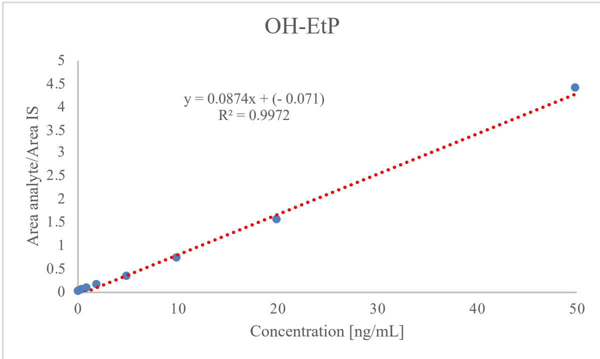


Figure E.3: Relative calibration curve









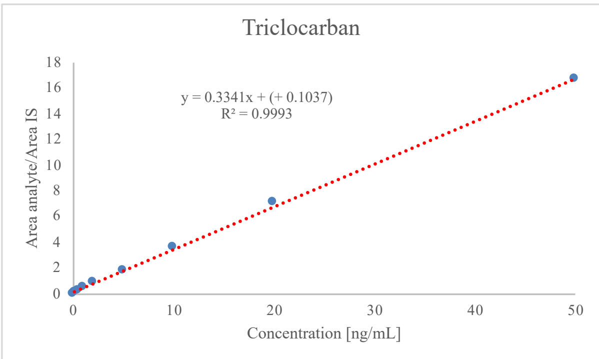


Figure E.4: Relative calibration curve (continued)

Appendix F

ICP-MS parameters

Table F.1: Specifications for ICP-MS, Element 2 from Thermo Scientific

Instrument	**Specification**
Autosampler	SC2 DX equipped with a dustcover with ULPA filter
Sample injector	prepFAST
Nebulizer	PFA-ST with approximately volume range 50 – 700 µL/min
Spray chamber	Quarts baffled micro cyclonic with dual gas inlet type (ESI-ES-3452-111-11)
Cooling	PC^{3x} – Peltier cooling and heated inlet system
Torch	Quarts Demountable with o-rings
Injector	Quarts 2.5 mm with o-rings (ES-1024-0250)
Sample cone	Aluminum (ES-3000-18032)
Skimmer cone	Aluminum type X-skimmer (ES-3000-1805 X)
Radio frequency - power	1350 W

Table F.2: Gas flow setting for ICP-MS

Gas type	**Flow [L/min]**
Cool gas	15.5
Auxiliary gas	1.1
Sample gas 1 (nebulizer)	0.75
Sample gas 2 (T-connection)	0.55
Additional gas	0.0004 corresponds to approximately 0.04% (10 % methane in Argon) in the sample

Appendix G

Principal component analysis (PCA) data

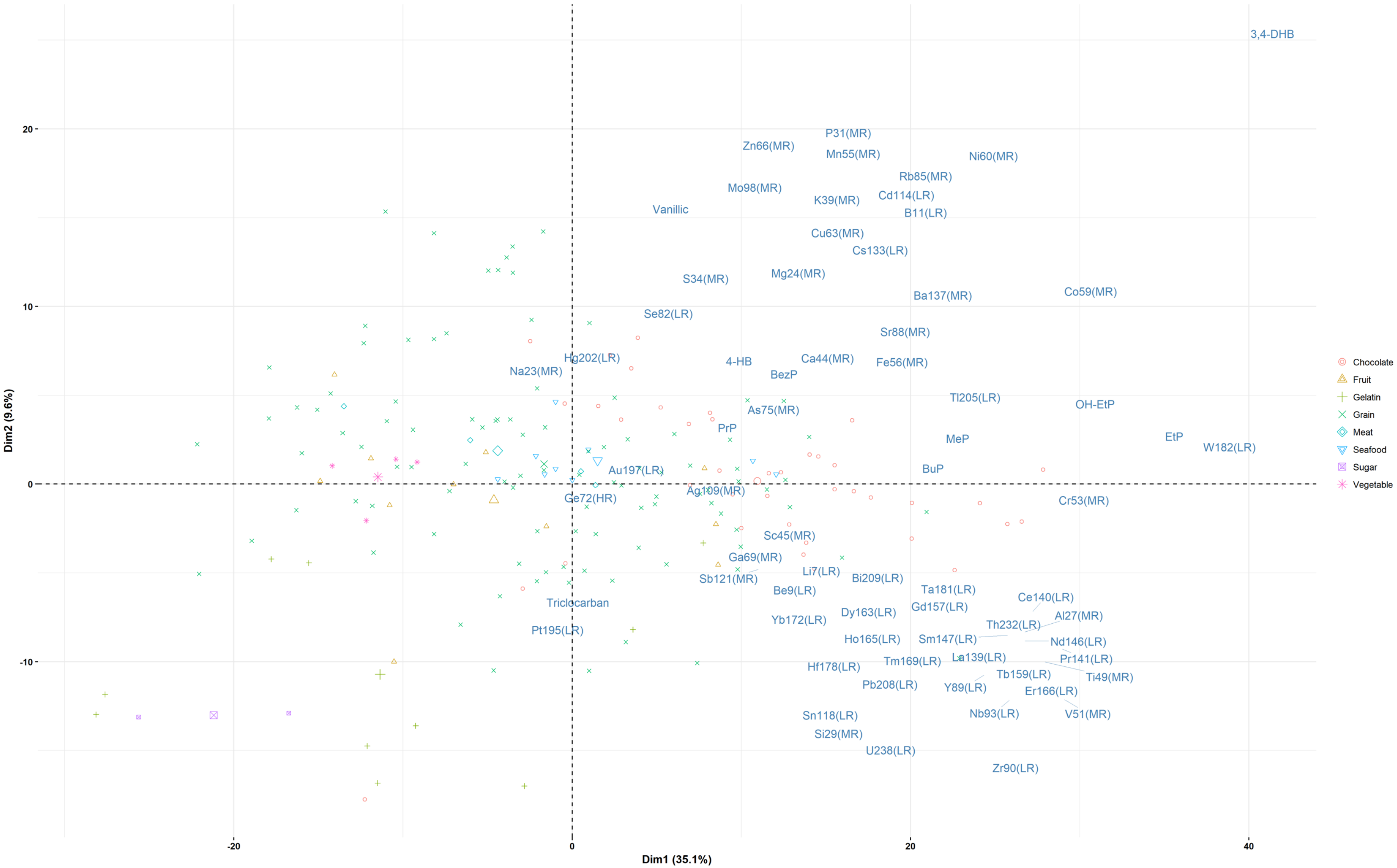


Figure G.1: PCA of organic analytes and elements grouped by characteristics

Appendix G. Principal component analysis (PCA) data

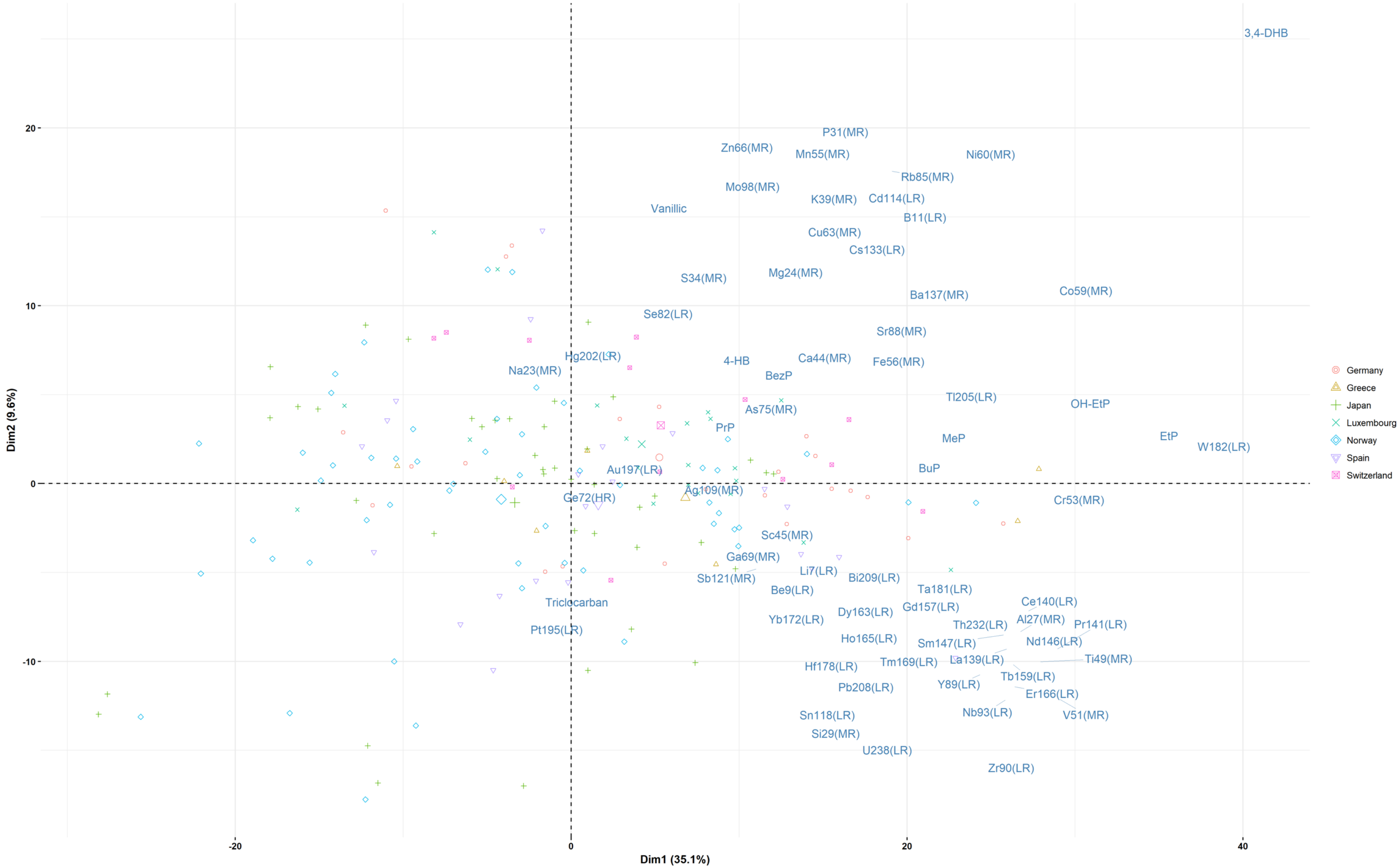


Figure G.2: PCA of organic analytes and elements grouped by countries

Appendix G. Principal component analysis (PCA) data

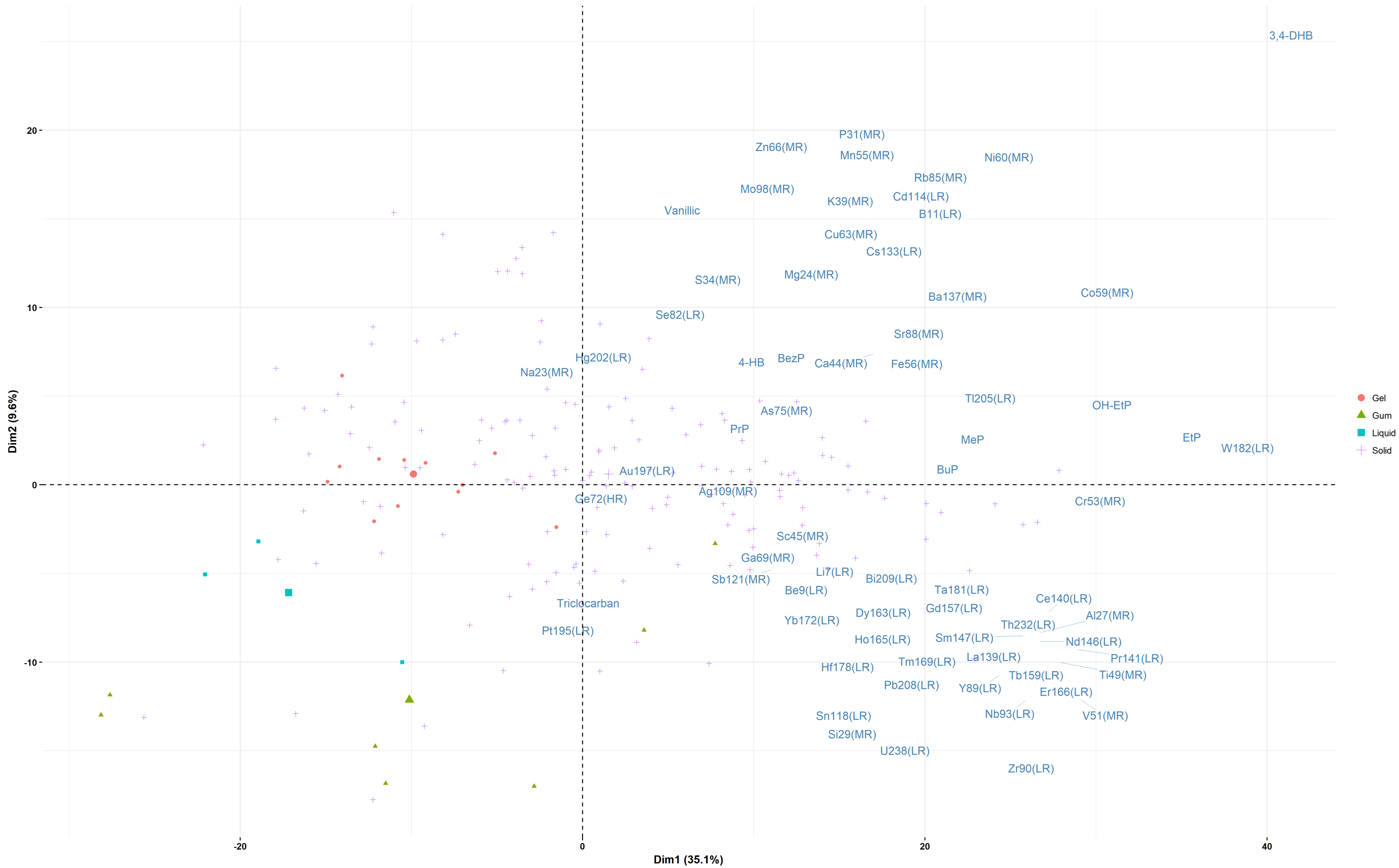


Figure G.3: PCA of organic analytes and elements grouped by forms

Appendix G. Principal component analysis (PCA) data

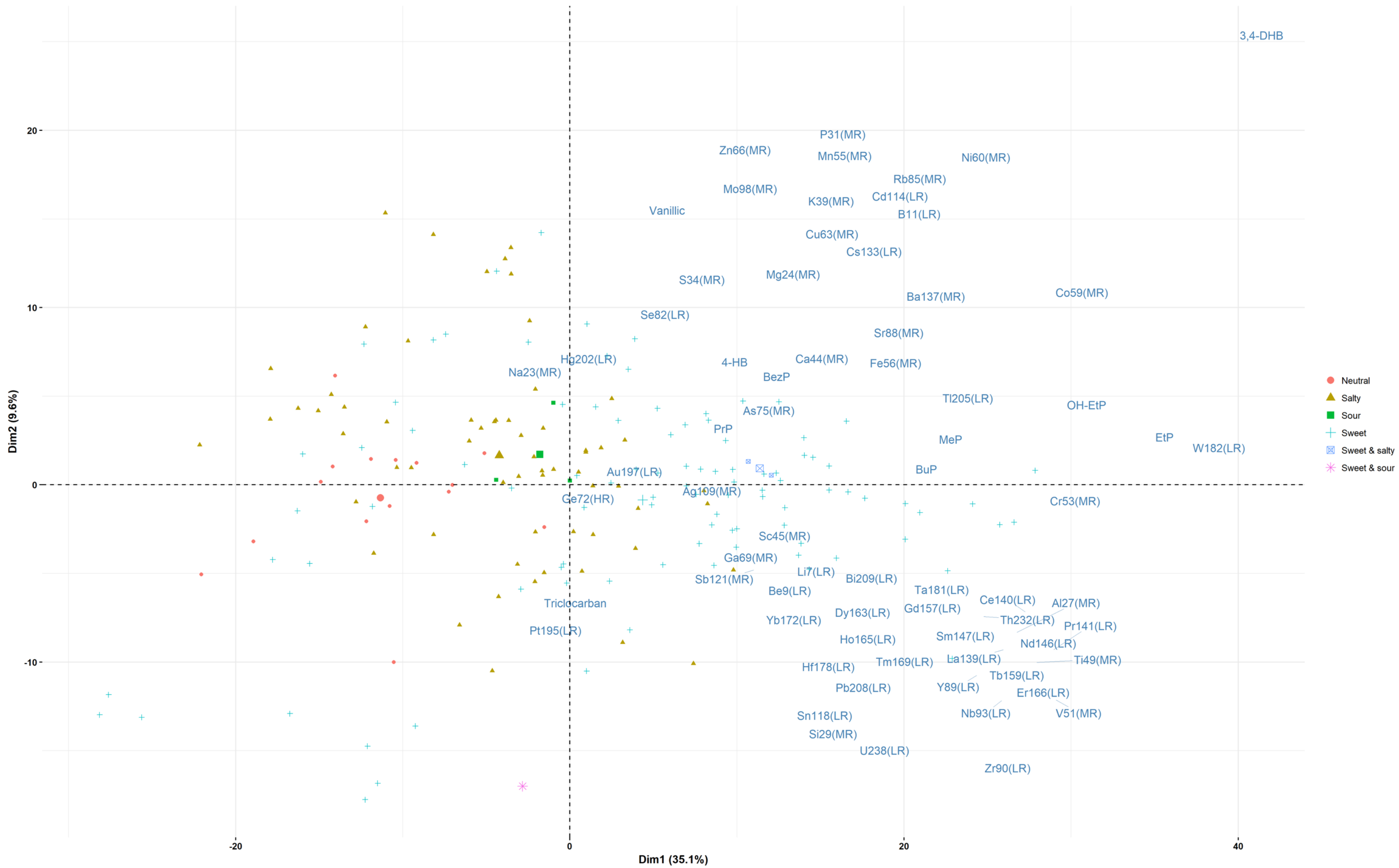


Figure G.4: PCA of organic analytes and elements grouped by tastes

Appendix G. Principal component analysis (PCA) data

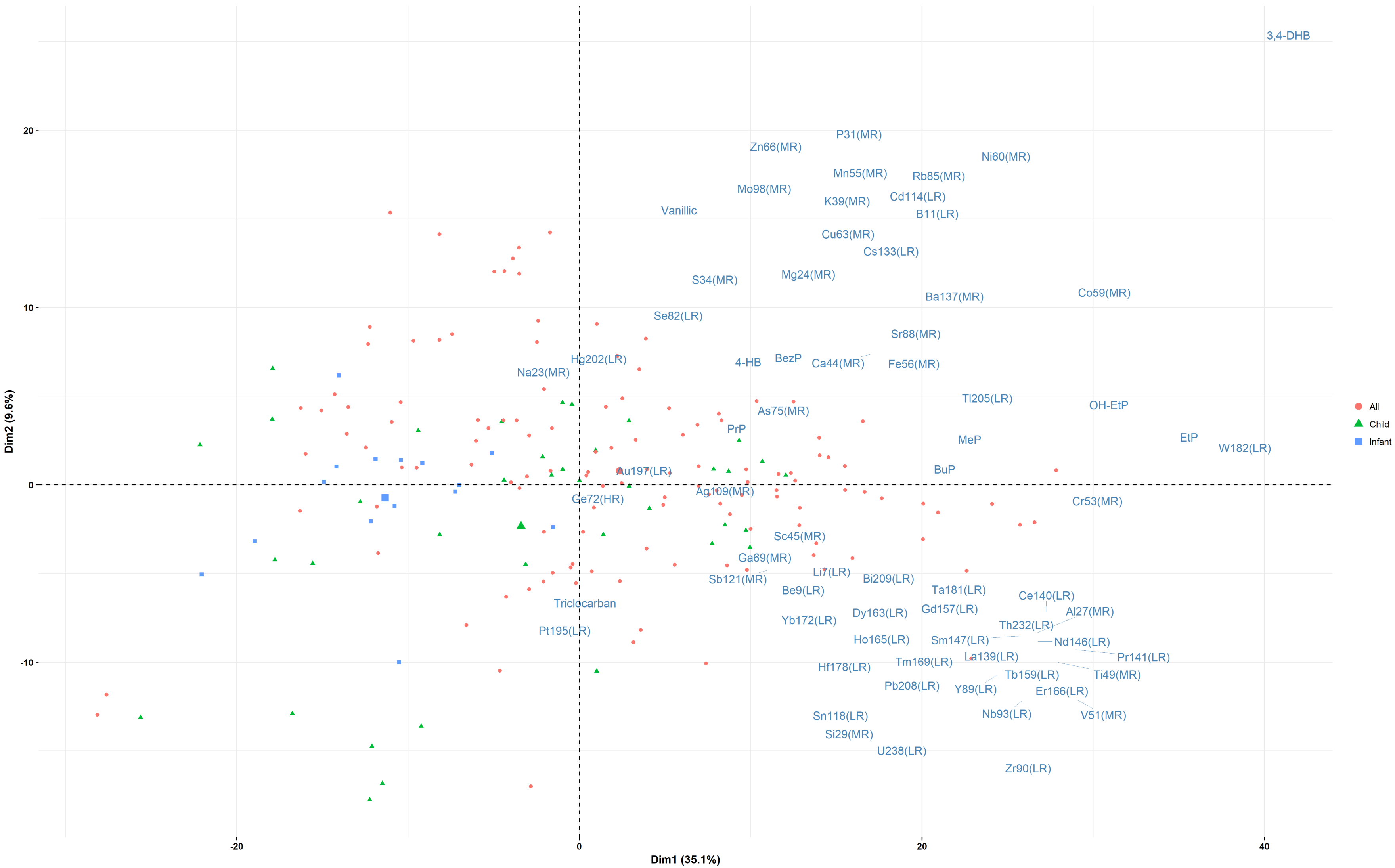


Figure G.5: PCA of organic analytes and elements grouped by suitable ages

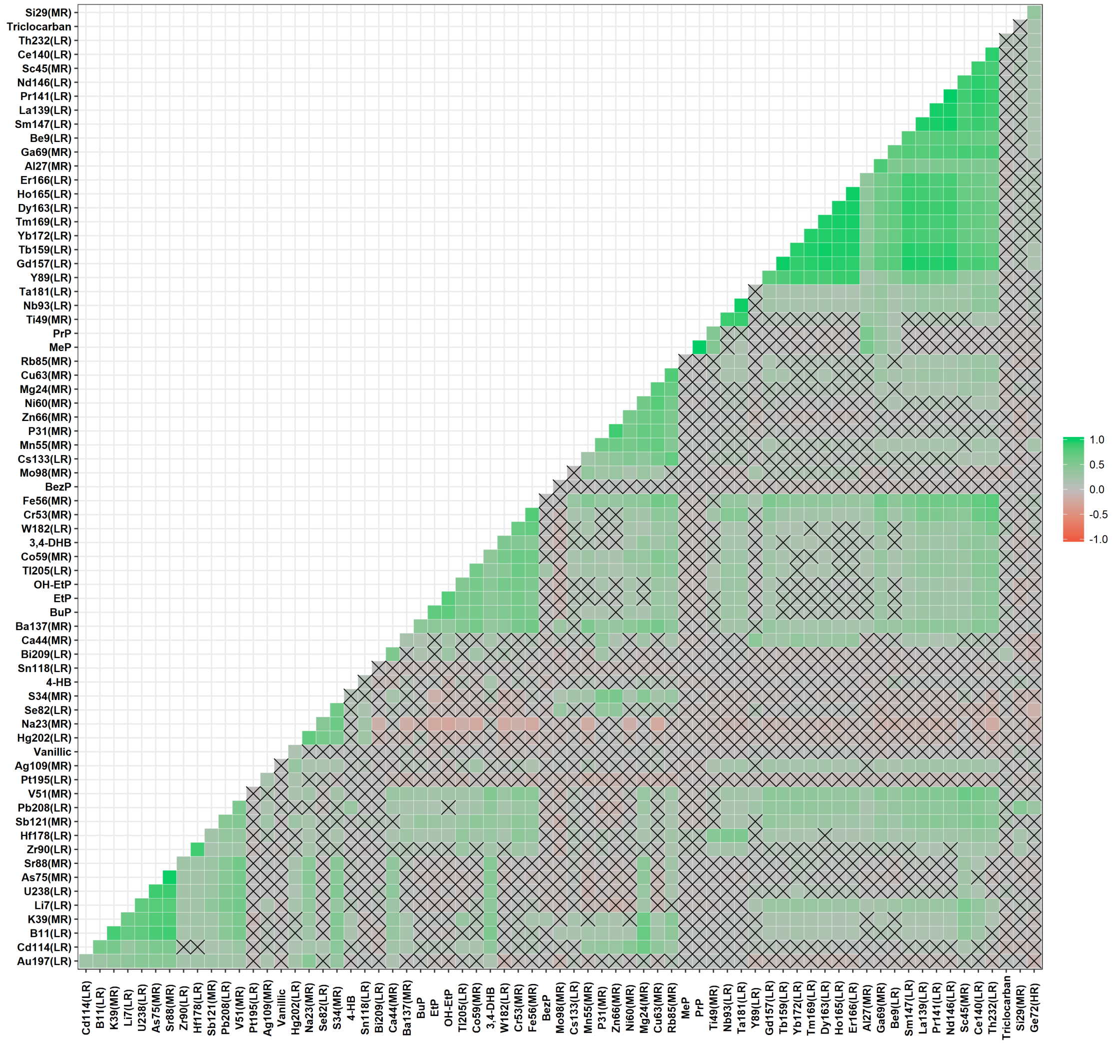


Figure G.6: Correlations of concentration of organic analytes and elements used for PCA