Chapter 8
Metabolomics: Applications to Food Safety and Quality Research

Farhana R. Pinu

1 Introduction

Food safety is a major concern worldwide, which has gained enormous attention in the last two decades mainly because of the emergence of new food-borne pathogens and other chemical hazards. Additionally, there has been an extreme increase in the food-borne illness incidences along with large-scale outbreaks. Many factors contribute to these growing concerns, including the industrialisation and mass production of agricultural products, the increasing number of imported food products, and changes in food consumption patterns due to consumer lifestyle changes (Motarjemi et al. 2008). Ready-to-eat and fast foods, especially, have gained great popularity, and thus also resulted in many food-borne illness incidences in recent years. Moreover, the tremendous upsurge in global population is also almost forcing producers towards mass production of agricultural products without giving much attention to quality and safety issues (Motarjemi and Lelieveld 2014). The world has already seen an introduction of a massive amount of genetically modified (GM) crops in the last 40 years, in response to the need to feed over 6.5 billion people. Consumers are doubtful about the safety of consuming GM food products; therefore, scientific attention is required to unravel the facts about the safety of eating such foods (Pinu 2015).

In many third-world countries, food quality and safety are often overlooked. In addition, many food vendors deliberately contaminate food products with unwanted materials (e.g. melamine in powdered milk) to increase profits, and others do so

F.R. Pinu (✉)
The New Zealand Institute for Plant and Food Research Limited,
Private Bag, 92169, Auckland 1142, New Zealand
e-mail: farhana.pinu@plantandfood.co.nz

F.R. Pinu
The Liggins Institute, University of Auckland, Private Bag, 92019, Auckland, New Zealand

D.J. Beale et al. (eds.), *Microbial Metabolomics*,
DOI 10.1007/978-3-319-46326-1_8

unintentionally because of their lack of knowledge of food hygiene and safety (Unnevehr 2015). Therefore, insecurity about raw foods and other food products is on the rise because of the deterioration of quality in different food products that are produced in large amounts and the lack of adequate information about their nutritional properties. However, the good news is that consumers around the world are now more aware about the risks and safety of different food products because of the availability of information via the internet and social media (Pinu 2015). Therefore, there is growing interest and a need from both food producers and consumers in implementing proper management of food safety and quality.

Quality control is a routine activity in different food industries, and can ensure the adequate safety of food, helping to maintain the trust of consumers. However, there is a strong demand for the development of techniques that might help to determine the key chemical, microbiological and nutritional features of a food product. Although many technologies are already available for the routine checking of many food products, these can be inadequate and often cannot determine emerging chemical and microbiological hazards present in foods. There is indeed scope for improvement and this is where metabolomics has a potential in food safety and quality research—mainly by introducing, developing and improving techniques to detect contaminants (both microbiological and chemical) present in food products. In this chapter, the ways in which metabolomics can be used (both targeted and non-targeted approaches) to ensure the safety and quality of raw, processed and GM foods and food products will be discussed. The importance of improvement on different analytical approaches that may lead to the management of toxins and food-borne illnesses caused by different microorganisms will also be highlighted.

2 The Concept of Food Safety and Current Practices

Food safety issues around the world are mainly monitored by the World Health Organisation (WHO) and The Food and Agriculture Organisation (FAO) of the United Nations. The Codex Alimentarius Commission (CAC) is an intergovernmental body that is operated under WHO and FAO. In 1997, CAC defined food safety as the assurance that a food or food product will not cause any harm to the consumers when it is prepared and/or eaten according to its intended use. Therefore, a food will only be considered as safe when it will not cause any long- or short-term illness to the consumer. It is the responsibility of food safety management to make sure that a food is safe before it is sold to its intended consumers. The maintenance of food hygiene is another important parameter during industrial food production that can ensure the safety and quality of food products. However, consumers are also responsible for following the instructions provided on the packaging to ensure the post-sale safety of food. Therefore, the key responsibilities that allow the proper maintenance of food safety follow a chain of action from regulators, to producers and then to consumers (Fig. 1).

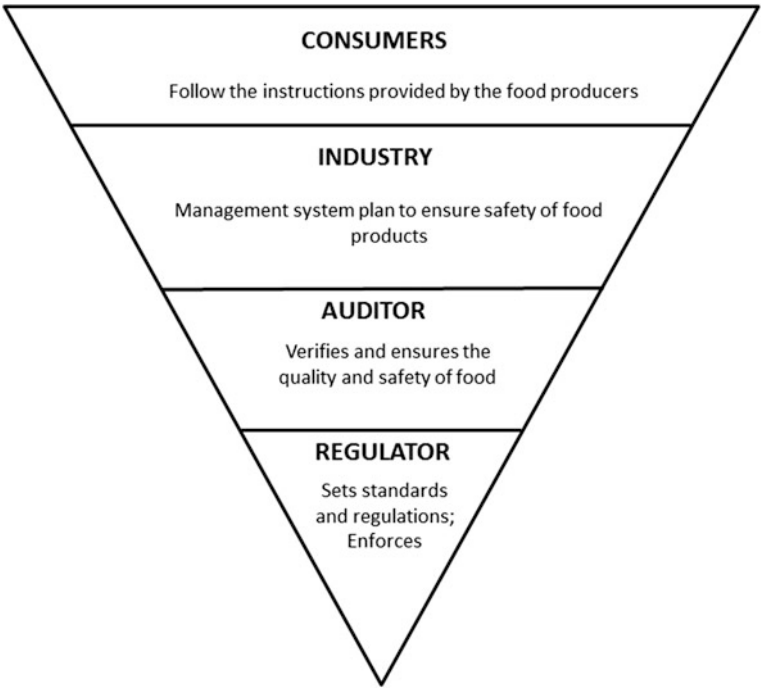

Fig. 1 The food safety regulatory model

The role of regulatory organisations and bodies is of foremost importance (Fig. 1), and relies on the cooperation of different sectors, including government, industry, consumers, and even academia (Motarjemi and Mortimore 2014). While the main task of a government in this area is to foresee all infrastructure and public health services needed for food safety management and to implement and enforce the laws and regulations, the industry is the one that actually ensures the safety of a food product by following all the regulatory protocols. The codes of good practices (CGP) are the first line of defence for any food industry and are a set of principles and measures that have been previously identified, based on past incidences. Generally, CGPs are applicable to most food industries; however, these may vary slightly depending on the type of industries. Hazard Analysis Critical Control Point (HACCP) is the second line of defence, which is also widely implemented in different food industries. There are seven principles under HACCP (Fig. 2) that include identifying the potential hazards or problems, taking measurements and then appropriate precautions to control the situation. Although HACCP is very beneficial in an industrial setting to ensure the safety of the product, industry staff may feel burdened by administrative requirements (Motarjemi 2014). However, the implementation of HACCP rules allows setting up critical control points (CCPs) that can be monitored, and corrective actions that can be undertaken if necessary to avoid any further loss of industrial food production (Fig. 2). Verifications are

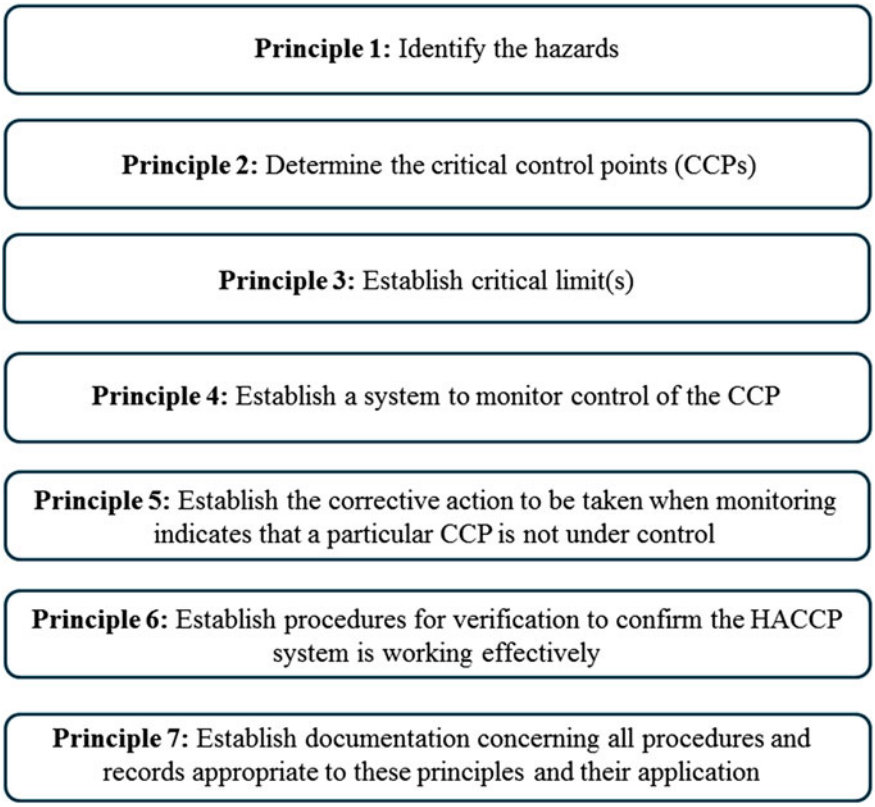

Fig. 2 The seven principles of Hazard Analysis Critical Control Points (HACCP)

carried out to determine the food quality by testing the raw material and the end product, by monitoring the environment before releasing the products. Auditing and consumer complaints handling are also associated with HACCP implementation in an industry.

In addition to regulatory bodies and industries, consumers also play a vital role in maintaining food hygiene and safety. Many consumers prefer to buy inexpensive food materials that do not have appropriate labels and safety information, and consumptions of these foods might pose a health risk (Motarjemi et al. 2001). Moreover, some ignore the instructions provided within the packaging of the food products and some never report defective foods that may cause public health concerns. Therefore, the liability of consumers cannot be overlooked and raising awareness might help to improve current food safety issues. Food safety-related campaigns organised by government and non-governmental organisations and social media can help in raising awareness in consumers.

The role of the scientific community is also important in maintaining food safety and quality. Ongoing research related to food products is always beneficial,

bringing new insight into different food pathogens and chemicals that contaminate food and food products. Moreover, toxicological and ecological knowledge of microbial and chemical spoilage provided by scientists allows us to manage the food safety situation in a better way by undertaking control measurements (Motarjemi and Lelieveld 2014).

3 Food Safety and Quality Research: The Main Problems

The current mass production and industrialisation of different foods and food products have been initiated in order to feed the increasing world population. The 'green revolution' has also taken place in the last decades, enabling production of vast amounts of crops mainly using genetically modified (GM) plants. There is still an insecurity about GM food products, as many believe that long-term consumption of these food materials may cause some deleterious effects on human health including allergies and other immunological disorders (Maghari and Ardekani 2011; Krimsky 2015). However, this is still under question as at least two different groups of scientists exist who either consider GM food as safe or harmful (Krimsky 2015). Due to the lack of long-term and consistent research on the effect of GM food on human health, it is still not possible to come to a conclusion and this is why consumers are even more doubtful about the safety of GM products. In addition, climate change is another key factor that has prompted development of new plants or crop varieties that will withstand the gradual changes in environmental conditions. For instance, many efforts have already been undertaken to develop new rice varieties that can withstand considerably unfavourable conditions including heat stress, drought and high salinity (Nokkoul and Wichitparp 2014; Van Oort et al. 2015; Nguyen et al. 2016). Barley is another crop variety that has been used widely as a model to study and develop climate-resilient crops (Dawson et al. 2015). Therefore, the world has observed huge changes in the quality and type of foods and raw materials, which pose both a significant advantage and sometimes a new threat to food safety and quality. Chemical contaminants and xenobiotic molecules, including pesticide residues and organic halogenated compounds, also pose significant potential impacts on both human health and the environment, as these molecules can take a very long time to break down (over 50 years) in the environment. The effects of pesticides and other xenobiotics on aquatic and other environments (e.g. infertility of sea birds) is well documented, and attempts have already been undertaken to reduce the rate of contamination by banning many known chemical contaminants (Walker 1990; Falkowska and Reindl 2015; Gustafson et al. 2015; Pérez et al. 2015). In addition to chemical hazards, food safety is also threatened by microbial exposure. For instance, overall changes in lifestyle have steadily forced us to adapt to comparatively different food habits, and introduced new types of foods (e.g. raw food). As a result, many new food-borne pathogens have emerged or other pathogens re-emerged because of these newly found transmission vehicles. Thus, many food-borne outbreaks which occurred in

the last 20 years were caused by bacteria, viruses, and protozoa, and many more pathogens are being introduced via food contamination every year. Therefore, there is an ongoing need for a proper risk assessment and management system to control outbreaks or even a pandemic related to any food-borne pathogen.

Major current challenges can be identified as follows:

I. Emergence of new food pathogens and control of outbreaks
II. Potential effects from genetically modified foods
III. Emerging chemical contaminants and xenobiotics
IV. Adulterations of food materials.

4 Current State of the Art of Food Safety and Quality Research

Food safety is not only a public health issue, but also has serious social and economic consequences. Food-borne illness can cause havoc in any country and sometimes worldwide when it is an epidemic that cause loss of many lives. For instance, food- and water-borne diseases are the main reasons of death of over 2.2 million people annually (WHO 2006), children, immunocompromised and elderly populations are often the most affected. This is not only a burden for many poor countries, but also endangers the international developmental efforts that have been undertaken to combat poverty (Kuchenmüller et al. 2009). These food-borne illnesses can be caused by various agents including pathogenic microbes, heavy metals, chemical contaminants and other toxic materials found in different food sources (e.g. toxins in wild mushrooms) (Anater et al. 2016; Signes-Pastor et al. 2016). Among pathogenic microbes, different strains of *Escherichia coli, Listeria monocytenes, Salmonella* spp. and even some food-borne viruses including norovirus and Hepatitis C have gained particular attention because of outbreaks related to contaminated food consumption in many countries (Marušic 2011). Moreover, many incidents were also reported of contamination of foods due to the presence of heavy metals and chemicals. In particular, the presence of arsenic in rice and other crops in many developing countries and melamine in milk products have gained public attention in recent years (Signes-Pastor et al. 2016). Most previous research on food quality and safety have mainly focused on determining the food composition and stress response of food pathogens, and have helped to add knowledge on what should be present in a particular food and how the growth of pathogenic microbes can be controlled using different techniques.

4.1 Study of Food Composition and Its Importance in Food Quality and Safety Research

To know more about the quality of food and food products, it is important to determine the composition, which also allows us to decide whether a given food is safe to consume, by providing information about any potential hazard. Much research has already been undertaken by focusing mainly on food composition of different crops, fresh food materials, and raw ingredients for other food products. Determination of food composition is not only focused on differentiating between different food products to ensure their safety, but is also intended to gain insight about the originality of some speciality foods and fermented food products, e.g. fruit juices, balsamic vinegars, and wines. One of the main reasons for determining originality is to control the adulteration of food material with unwanted ingredients that should not be present in that specific food. For instance, nuclear magnetic resonance (NMR) profiling of fruit juices has been carried out to determine the country of origin and also to discover if those fruit juices were produced using real juice or concentrate (Spraul et al. 2009a, b; Tomita et al. 2015). In addition, volatile compound analysis of balsamic vinegars through the use of gas chromatography and mass spectrometry (GC-MS) allowed determination of the effects of ageing materials or woods on vinegar quality (Chinnici et al. 2009; Callejón et al. 2010). Many studies have also focused on regional or country-specific food products including fresh vegetables, seafood, fish and ready-to-eat foods. This is mainly true for those countries either with low average incomes or where environmental pollution is a considerably bigger problem than in other developed countries. In countries that lack proper implementation of laws, regulations and auditing systems required for maintaining food safety, food stuffs can become deliberately contaminated with unwanted materials by vendors in order to gain more profit (Pinu 2015). In this situation, food composition studies that help to determine the type and diversity of contaminants are very useful. However, there is still a huge scope for improvements to technologies for rapid detection and identification of those food contaminants. Using these technologies, food auditors will be able to manage situations better by analysing food samples in real time while examining a food processing unit. Such technologies are still very limited currently, and research should focus on developing more user-friendly techniques and detectors using cutting-edge technologies.

4.2 Food Safety: Pathogenic Microbes and Their Stress Responses

One of the most demanding areas of research in food safety is the study of food-borne pathogens, which is mainly because of the many outbreaks related to the consumption of food products contaminated with pathogenic microbes. Food is

mostly considered as an ideal growth medium for a wide range of microorganisms, and thus also an ideal vehicle for transmission of food-borne illnesses. Although vast numbers of people from most low-income countries where food hygiene is not maintained properly suffer from food-borne illnesses frequently, few data are available about those illnesses or outbreaks, mainly because of the lack of appropriate reporting systems. Therefore, most of the available data about food-borne outbreaks related to the consumption of contaminated food materials from restaurants to homes are from developed countries, where these cases are well documented. In recent years (2009–2015), a few developed countries, including Germany and the United States, have seen food-borne outbreaks associated with pathogenic *Escherichia coli* strains (O104:H4, O157:H7, O27 and O121) from the consumption of fresh vegetables, sprouted foods, ground beef, chicken salad and chipotle Mexican grill (Raupp 2014; Gelting et al. 2015; Ison et al. 2015; Radosavljevic et al. 2015). Different species of *Salmonella* have also caused food-borne outbreaks in developed countries including the USA and Australia from the consumption of chicken, cucumber, nut butter and raw cashew cheese (OzFoodNet Working 2014; Herman et al. 2015; Laufer et al. 2015; McWhorter et al. 2015). In addition to bacteria, food-borne illnesses associated with viruses, such as norovirus and rotavirus, were also quite common, and caused severe gastroenteritis disorders in many countries (Trivedi et al. 2012; Pacilli et al. 2015).

Food pathogens are very efficient in responding to the environmental changes during the different steps of food processing and they evolve to adapt to these harsh environments, mainly by changing their gene expression or by producing quorum sensing molecules, thus showing potential for causing disease in vulnerable hosts (Humphrey 2004; Begley and Hill 2015; Rul and Monnet 2015). Therefore, many studies have been undertaken to find out the mechanisms of adaptation of pathogenic microbes under various stresses including heat, acid, salt and oxidative stress (Samelis et al. 2001; Humphrey 2004; Koutsoumanis and Sofos 2004; Tiganitas et al. 2009; Shen and Fang 2012; Stackhouse et al. 2012; Alvarez-Ordóñez et al. 2015; O'Leary et al. 2015). For instance, biofilm formation is one of the key adaptation mechanisms that has been observed in many food pathogens, including *Listeria monocytogenes* and *Salmonella enterica* (Rodrigues et al. 2011; O'Leary et al. 2015). Preventive measures include the use of either chemical or physical forces and using bacteriophages that do not allow these food pathogens to form the biofilms, thus diminishing their chances of growing in the food products (Soni and Nannapaneni 2010; Van Houdt and Michiels 2010; Da Silva and De Martinis 2013). Therefore, studies of stress adaptation of food pathogens are very useful in the area of food safety, and generate in-depth knowledge about the molecular mechanisms behind this process. Control measures can be undertaken or developed based on what causes food pathogens to adapt to these adverse situations. Moreover, these may also lead to the development of techniques to detect the microbial contamination in the early stages of growth, thus preventing the infection from being transmitted widely by the consumption of food.

5 Metabolomics and Food Safety and Quality Research

5.1 Food Metabolomics

Metabolomics is one of the most recently introduced 'omics' that aims to analyse small molecules (metabolites) in a given biological sample. Although metabolomics was initially defined as the technical area by which it would be possible to detect and identify all the metabolites produced by a cell or an organism (Fiehn 2002; Bino et al. 2004), this has not been realised, mainly due to the diversity of metabolites. However, metabolomics is already established as a powerful tool for studying the metabolism and physiology of many living organisms, and thus this approach has been applied to a diverse range of research areas, including biomarker and drug discovery, agriculture, nutrition, bioremediation, plant biotechnology and also food science (Anizan et al. 2012; Badilita et al. 2014; Hall and de Maagd 2014; Li et al. 2014; Lima et al. 2014; Booth et al. 2015; El Amrani et al. 2015; Melnik 2015). Metabolomics has been used to study food systems including food ingredients, food processing and food pathogens; it has gained popularity in the last 10 years and numerous studies have already been carried out (Vikram et al. 2004; Badilita et al. 2014; Kusano et al. 2014; Inoue et al. 2015; Le Boucher et al. 2015; Ragone et al. 2015). Therefore, a distinct research area entitled 'food metabolomics' is well established that refers to the application of metabolomics in food system processes, from farm to consumers (Kim et al. 2016). Recently a term 'foodomics' has been introduced within the scientific community that refers to the application of 'omics approaches including genomics, proteomics, transcriptomics and metabolomics in food science (Herrero et al. 2012; Cifuentes and Rutledge 2013; D'Alessandro and Zolla 2013; Ibáñez and Cifuentes 2014; Laghi et al. 2014; Inoue and Toyo'oka 2015). However, food metabolomics deals only with the most downstream product of cell metabolism, metabolites, present in a given food or food system.

The food metabolome is very complex in nature, and also widely variable, depending on the type of food and the raw materials. Therefore, many thousands of metabolites are present in food are highly variable in terms of polarity and molecular weight (Shulaev 2006). The differing concentrations of metabolites in food items pose a major challenge in the development of analytical tools to detect as many metabolites as possible within a single analysis (Kueger et al. 2012). So far, there is no such analytical instrument available; therefore, for the better understanding of the metabolome by analysing as many metabolites as possible, the use of multiple analytical technologies is suggested by many scientists (Hall et al. 2002; Dunn and Ellis 2005; Villas-Bôas et al. 2007; Sumner 2010; Hall and Hardy 2012; Pinu et al. 2014). In addition, one of the major challenges that a food scientist needs to overcome while analysing food is the complex sample matrix. The matrix effect (ME) can create challenges in the detection and quantification of compounds that are present at very low concentrations in different food. ME is also responsible for poor and unreliable data that can affect the reproducibility, repeatability, linearity

and accuracy of the methods used by various analytical instruments (Trufelli et al. 2011). To avoid and reduce the ME, a sample clean-up step using Solid Phase Extraction (SPE) or Solid Phase Microextraction (SPME) or liquid extraction is usually necessary before analysis by other methods (Jiang et al. 2012). More efficient chromatographic separation is also suggested by Trufelli et al. (2011), in which two-dimensional separation techniques (both GC and LC) can also be applied (Marriott et al. 2012; Mondello et al. 2012). However, pre-analytical steps can be time-consuming, arduous and often can cause loss of analytes, which is not appropriate for an unbiased profiling approach (Villas-Bôas et al. 2007; Cappiello et al. 2010; Trufelli et al. 2011). Although metabolomics was initially introduced mainly as an unbiased and non-targeted approach, both targeted and non-targeted analyses are performed for any biological samples to better answer the research questions. Therefore, both targeted and non-targeted metabolomics are gaining popularity for the analysis food products.

A significant improvement has also been achieved in metabolomics workflow, including sample preparation, quenching, metabolite extraction and acquisition of data (Fig. 3). In recent years, many sample preparation protocols have been published that allow better detection of metabolites with a wide range of chemical properties (Anizan et al. 2010; Biais et al. 2012; Teo et al. 2013; Brennan 2014; Chan et al. 2014; Le Gall 2015; Rejczak and Tuzimski 2015). In short, an appropriate quenching method is used to stop the ongoing enzymatic activities after the collection of a food or microbial samples. After quenching, metabolites are extracted using a suitable extraction solvent (e.g. chloroform/methanol/water). However, it is noteworthy that metabolite profiles may vary depending on the metabolite extraction protocols; therefore, it is better to use at least a few extraction protocols to obtain a global metabolite profile of any biological sample (Duportet et al. 2012, Jäpelt et al. 2015). Once metabolites are extracted from the sample, they are ready for analysis by an instrument of choice. The acquired data then needs to be explored using different statistical and chemometric approaches (Aggio et al. 2011, 2014; Gowda et al. 2014; Pluskal et al. 2010; Robotti and Marengo 2016; Smith et al. 2006; Xia et al. 2012): including feature detection, alignment, biomarker identification and chemical structure elucidation (Fig. 3).

5.2 *Recent Advancements of Analytical Instruments in Metabolomics*

Due to advancements in different analytical instruments in the last decade, it is now possible to analyse thousands of metabolites from a food sample in a single analysis. The sample preparation and data handling processes have also been improved tremendously, making it easier for scientists to analyse samples in a short time. Moreover, there are many commercial and in-house metabolite databases available, which is also beneficial for the identification and sometime structural elucidation of

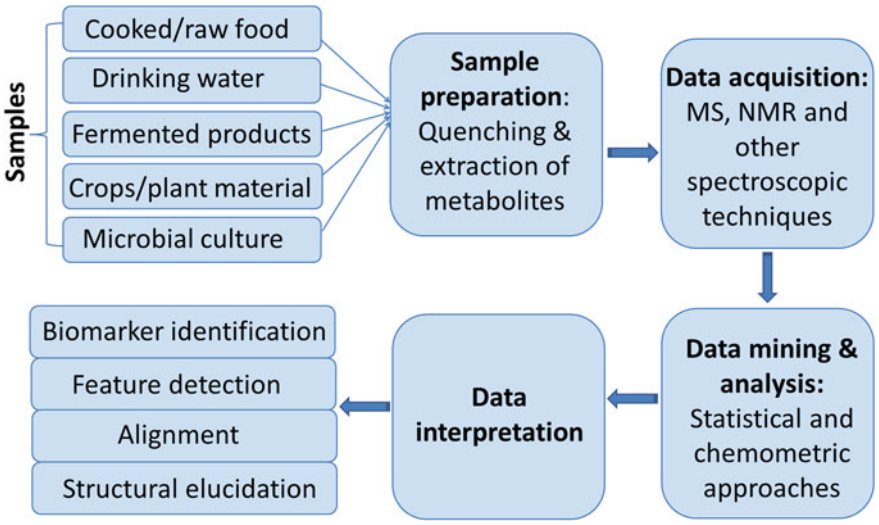

Fig. 3 Workflow for the analysis of the food metabolome. Here, *MS* Mass spectrometry and *NMR* Nuclear Magnetic Resonance spectroscopy

unknown metabolites present in a food. It is well known that powerful detectors are the main factors for the analysis of metabolites. Two technologies, Nuclear Magnetic Resonance (NMR) and Mass Spectrometry (MS) have been employed widely in metabolomics (Shulaev 2006; Villas-Bôas et al. 2007; Dieterle et al. 2011; Herrero et al. 2012; Kueger et al. 2012; Zhang et al. 2012; Balan et al. 2013; Ibáñez et al. 2013; Badilita et al. 2014; Senyuva et al. 2015). However, there are many other instrumental techniques, including Fourier transform infra-red spectroscopy (FTIR), which are available for metabolite profiling of food samples.

NMR has been broadly used for untargeted metabolite profiling of complex mixtures (i.e. fruit juices, wines, spirits, urine and blood) (Ogrinc et al. 2003). NMR spectroscopy is increasingly renowned for its efficacy, non-invasiveness (non-destructive), throughput and linearity (Laghi et al. 2014). Moreover, NMR spectroscopy also provides structural, chemical-kinetics and other information in multidimensional applications (Dieterle et al. 2011). Thus, high resolution NMR spectroscopy along with multivariate data analysis has been used for direct characterisation of fruit juices (Cuny et al. 2008), wine (Lee et al. 2009; Pinu et al. 2014), grape berries (Pereira et al. 2006; Mulas et al. 2011), olive oil (Del Coco et al. 2012; Piccinonna et al. 2016) and beer (Almeida et al. 2006; Rodrigues et al. 2011). To obtain a global metabolite profile of a complex sample, NMR needs to be coupled with another non-targeted analytical approach (e.g. MS). But there are some serious drawbacks to using NMR for metabolome analysis. Different parameters of the sample, e.g. salinity, pH and concentrations of metal ions, can affect the sensitivity of NMR spectrometers and can cause difficulty in bioinformatics-based resonance assignments (Lewis et al. 2012). To avoid these

problems, consistency in sample preparation is required. Moreover, an NMR spectrometer cannot detect metabolites with low concentrations; samples may need to be concentrated before analysing, as well as require larger sample volumes. To dissolve the dried samples, high concentration of deuterated solvents are required and these solvents also cause bias in sample preparation and data analysis (Lewis et al. 2012).

On the other hand, the MS technique has gone through remarkable developments and it is now an important instrument for many researchers (El-Aneed et al. 2009). MS is the most extensively used instrumental approach in metabolomics (Villas-Bôas et al. 2005; Dunn 2011; Vestal 2011; Kueger et al. 2012). It is also considered the technique of choice in metabolite profiling mainly because of its high sensitivity and also its ability to profile a wide range of metabolites in a mixture and within a single analysis (Glinski and Weckwerth 2006). Significant improvements have been achieved in terms of mass analysers, including quadrupole (Q), quadrupole ion-trap (QIT), time of flight (ToF), orbitrap, ion-mobility spectrometry (IMS) and Fourier transform ion cyclotron resonance (FTICR). Quadrupole mass analysers are very robust, low cost and simple to use, but they provide lower mass resolution and accuracy than other mass analysers (Villas-Bôas et al. 2005). ToF, FTICR and orbitrap are considered excellent instruments that offer the highest mass resolution of all mass analysers.

MS is mostly used in combination with a few powerful separation techniques to enhance its identification power. Gas chromatography (GC), liquid chromatography (LC) and capillary electrophoresis (CE) are the most common separating techniques used in combination with MS, which allow maximum separation of metabolites in a complex biological sample (Villas-Bôas et al. 2003; Ramautar et al. 2011; Theodoridis et al. 2012). However, direct infusion (DI) is also widely used for metabolite profiling, which is usually referred to as metabolic footprinting or fingerprinting, depending on whether the analysis is of extra- or intracellular metabolites (Villas-Bôas et al. 2005; Han et al. 2009). Because of the development of interfacing systems such as atmospheric pressure ionisation (API), DI-MS can be used to analyse a sample to obtain mass spectra of the metabolites within a few seconds (Villas-Bôas et al. 2005). The requirement for a small amount of sample is the major advantage of using DI-MS. Moreover, no derivatisation is required for this analysis, and more metabolites are detected by DI-MS than by GC-MS, making this technique best suited for high throughput non-targeted metabolite profiling (Mas et al. 2007). However, DI-MS shows poor reproducibility when analysing complex mixtures because of the matrix effect. The identification of metabolites by DI-MS is also very troublesome, and stereoisomers cannot be resolved using this technique (Villas-Bôas et al. 2005; Glinski and Weckwerth 2006; Pope et al. 2007). GC is one of most efficient separation techniques in metabolomics, allowing the separation of hundreds of metabolites within a single analysis and requiring a very small sample volume (1–2 μL). The coupling of GC with MS is a perfect match because metabolites in an inert gas phase can be ionised much more easily at the

MS ion source, making GC-MS the best combination of separation technique with mass spectrometry detection. The instrumentation has been developed considerably during the last 50 years. GC-MS is a highly sensitive analytical platform, which also provides excellent instrument repeatability, around 5 % or below (Villas-Bôas et al. 2005). However, an extra step of sample derivatisation is required for the analysis of semi- and non-volatile metabolites, and GC-MS has been widely used for the last 50 years for the analysis of a wide range of metabolites present in foods (Table 1). LC is another powerful separation technique that allows rapid analysis of small amounts of sample. The main advantage of this separation technique over GC is that no previous derivatisation of the sample is required to analyse the non-volatile compounds (Scalbert et al. 2009). This technique is often coupled with MS and sometimes also with NMR (Shulaev 2006; Zhou et al. 2012). For LC-MS, a wide range of different detectors is used, ranging from ultra-high resolution MS such as FTICR or orbitrap to low-resolution MS such as ion traps and triple quads and hybrid systems. The most recent addition is the ion-mobility TOF-MS system (Lanucara et al. 2014). The development of methods depends on the nature of the metabolites to be analysed. LC-MS has been applied widely in metabolite profiling (both targeted and non-targeted) of complex biological samples (Berg et al. 2012; Theodoridis et al. 2012). CE is an efficient and rapid technique that can separate a wide range of charged metabolites within a single analytical run (Villas-Bôas et al. 2005). CE is often coupled to MS and it is considered a promising analytical instrument in metabolomics (Shulaev 2006). CE-MS has high resolving power and requires very small volumes of samples (1–20 nL). Thus, it has been used for both targeted and non-targeted high throughput analysis of metabolites (Nevedomskaya et al. 2010; Sato and Yanagisawa 2010; Ramautar et al. 2011). The major drawback for CE-MS is its poor sensitivity; thus the detection limit is several magnitudes higher than those of chromatographic methods (Table 1). The introduction of a small volume of sample is inadequate for the detection of many metabolites (Cai and Henion 1995). Moreover, low recovery and irreversible adsorption of analytes onto the capillary wall also can occur in CE. For these reasons, CE-MS is mostly used in metabolomics as a combination of different protocols targeting different groups of metabolites combined with sample preparation steps to concentrate the metabolites in the samples, making it a lower throughput technology in metabolomics and certainly more suitable for targeted analysis.

Fourier transform infrared spectroscopy (FTIR) is another analytical technique that is extensively applied in the food industry because it is rapid, highly automated, reproducible, non-destructive and cost-effective (Bauer et al. 2008; Versari et al. 2010). Nevertheless, FTIR is insensitive for complex liquid samples and water in the samples often increases the background noise, increasing the limit of detection and reducing linearity (Achá et al. 1998). The data obtained from FTIR are also very complex and there few databases available for assisting with identification of metabolites (Berthomieu and Hienerwadel 2009).

Table 1 Comparisons of different analytical instruments used in food safety and quality research

Analytical technique	Advantages	Disadvantages	Application in food safety and quality research
GC-MS	• High chromatographic resolution • Sensitive and robust • Simultaneous analysis of different groups of metabolites • Large linear range, availability of commercial and in-house MS libraries	• Derivatisation is required for non-volatile metabolites • Unable to analyse thermo-labile compounds	Gilbert-López et al. (2010), Anizan et al. (2012), Canellas et al. (2012), Banerjee et al. (2013), Caligiani et al. (2013), Cao et al. (2014), Guo et al. (2014), Duedahl-Olesen et al. (2015a, b), Giri et al. (2015), Grimalt et al. (2015), Janssens et al. (2015), Walorczyk et al. (2015)
LC-MS	• High sensitivity • Derivatisation not usually required • Large sample capacity • Thermo-stable compounds can be analysed	• Average to poor chromatographic resolution • De-salting may be required • Limited commercial libraries • Tough restrictions on LC eluents • Matrix effects	Da Rosa et al. (2012), García-Gómez et al. (2012), Russo et al. (2012), Gottfried and Herebian (2013), Boutsiadou-Theurillat et al. (2014), Fan et al. (2014), Zeng et al. (2014), Arroyo-Manzanares et al. (2015), Juan-Borrás et al. (2015), Khan (2015), Squadrone et al. (2015), Zhang et al. (2015), Han et al. (2016)
CE-MS	• High resolution, small volume of sample required • Rapid analysis • Usually no derivatisation required	• Poor reproducibility • Poor sensitivity • Buffer incompatibility with MS • Difficulty in interfacing with MS • Limited commercial libraries	Font et al. (2008), Lara et al. (2008), Nevedomskaya et al. (2010)

(continued)

Table 1 (continued)

Analytical technique	Advantages	Disadvantages	Application in food safety and quality research
Direct MS	• High resolution depending on the mass analyser • Sensitive • Rapid analysis	• Interference of salts and strong ions • Limited identification power • Poor reproducibility	Ackerman et al. (2009), Self and Wu (2012), Shen et al. (2012), Farré et al. (2013), Self (2013), Doué et al. (2015)
NMR	• Rapid analysis • Non-destructive • Minimal sample preparation • Quantitative	• Low sensitivity • More than one peak per component • Identification is laborious because of complex matrix	Spraul et al. (2009a, b), Balan et al. (2013), Osselaere et al. (2013), Badilita et al. (2014), Lima et al. (2014), Qi et al. (2015), Ragone et al. (2015), Tomita et al. (2015), Wan et al. (2015)

GC-MS Gas Chromatography and Mass Spectrometry; *LC-MS* Liquid Chromatography and Mass Spectrometry; *CE-MS* Capillary Electrophoresis and Mass Spectrometry and *NMR* Nuclear Magnetic Resonance

6 Application of Metabolomics in Food Safety and Quality Research

Although the main aim of metabolomics is to generate hypotheses based on data using an unbiased and non-targeted approach, both targeted and non-targeted methodologies are frequently applied in food safety and quality research (Table 1). It is especially true when metabolomics has been used for the analysis of chemical contaminants including pesticides in different types of food materials (Forsberg et al. 2011; Arroyo-Manzanares et al. 2015; Chatterjee et al. 2015). However, when the main purpose of a study is to determine biomarkers either for microbial spoilage or other sort of contamination, it is better to choose a non-targeted approach that might help in finding novel compounds or metabolic pathways relevant to a food system. The two main areas in food safety where metabolomics has been widely applied are in determining either chemical or microbiological hazards present in a food or food processing system. However, consumers these days are also concerned about food prepared using GM ingredients, as the long-term effects of consumption of such foods are still not adequately known; therefore, a growing research trend is observed in this area.

6.1 Chemical Food Safety

A large number of chemicals have entered our food chain as a result of the wide application of different growth-promoting agents (e.g. clenbuterol in pigs, recombinant growth hormones in fish and steroids in bovine animals), antibiotics and pesticides that help us to produce large amounts of agricultural products. Therefore, both food ingredients and the environment are facing the burden of chemical exposures, many of which are unwanted and pose a threat to human health. Moreover, deliberate contamination of food ingredients with unwanted chemicals (e.g. melamine) also poses a serious risk to consumers. Therefore, these chemicals should be banned or their use should be limited as set by the regulatory authorities. To achieve this, development of high throughput methods that would enable study of these contaminants is urgently needed. Both targeted and non-targeted metabolomics demonstrate enormous potential in detecting and identifying these chemicals in our food. For instance, targeted analysis using a suitable analytical platform (e.g. NMR and MS) is beneficial for the study of already-known chemical contaminants in food. However, it is more problematic when the contaminants are either not known or are unknown breakdown products of a familiar compound. An untargeted metabolomics approach could be a better way to study those novel compounds and also to determine and validate candidate biomarkers that could be used for tackling illegal practices in food production (Dervilly-Pinel et al. 2012).

Although NMR was initially the method of choice for detecting and identifying chemical contaminants in food because of its capacity to quantify and elucidate the

structure of molecules (Dieterle et al. 2011), MS is currently more popular due to its sensitivity, and robustness of coupling with various separation systems (e.g. GC, LC and CE). Moreover, tandem MS/MS or MS^n experiments can now elucidate the structure of any unknown metabolites, and thus are useful for the development of multi-residue methods to detect and identify chemical contaminants accurately. Many LC-MS-based methods have been published recently that have been used to study chemical contaminants (Table 1) in different crops, including herbal teas, nutraceuticals, rice and maize, and also in animals (Castro-Puyana and Herrero 2013). For instance, 255 veterinary drug residues and other chemical contaminants were determined within 10 min using a UHPLC-MS/MS method (Zhan et al. 2012). In addition, high resolution MS/MS has been widely applied for the analysis of pesticides, toxins and antibiotics. More than 500 pesticides were screened in fruits and vegetables using an orbitrap tandem MS/MS method (Alder et al. 2011). De Dominicis et al. (2012) also reported an orbitrap-MS/MS-based protocol for analysing pesticides and toxins simultaneously in bakery and other foods. In addition to analysing pesticides and other xenobiotic molecules, attempts have also been made to develop methods using LC-MS to identify other contaminants in food, including melamine in infant formula (Inoue et al. 2015). Many other LC-MS/MS protocols have already been published that analysed a wide range of food and fermented products including fruits, vegetables, wine, baby foods and cereals (Lacina et al. 2012; Pérez-Ortega et al. 2012; Fan et al. 2014).

While LC has been the choice of separation technique for the analysis of contaminants in food materials, GC still remains the mostly used system coupled with high resolution MS for the determination of environmental pollutants in food such as polychlorinated biphenyls (PCBs), polycyclic aromatic hydrocarbons (PAHs) or polybrominated diphenyl ethers (PBDEs) in various samples including fruits, vegetables, cereals, teas, fish muscle, dietary supplements and sheep milk (Mastovska and Wylie 2012; Storelli et al. 2012; Banerjee et al. 2013; Cao et al. 2014; Duedahl-Olesen et al. 2015a, b; Walorczyk et al. 2015). For example, Sapozhnikova and Lehotay (2013) accurately quantified over 80 pollutants (PCBs, PAHs and pesticides) in fish within 9 min using a low pressure GC-MS/MS method. In addition to tandem MS used with a GC system, two-dimensional GC (GCxGC) analysis is also gaining popularity for the analysis of pollutants, which allows determination of these compounds in very small amounts (0.1 μg/kg) (Kalachova et al. 2012, 2013; Giri et al. 2015).

Some applications of food safety in terms of chemical contaminant determination also make use of direct MS analysis either as direct analysis in real time (DART) or as desorption electrospray analysis (DESI). Rapid and high throughput analysis of food samples can be obtained using DART-MS, as it directly analyses samples from the surface, thus decreasing sample preparation time significantly compared with those for the other coupled MS systems (Castro-Puyana et al. 2013). DART-MS combined with high resolution analysers has been applied to analyse pesticides in fruits and grains (Schurek et al. 2008; Farré et al. 2013). Similarly, DESI-MS has been used for the determination of pesticides in fruit peels and vegetables (García-Reyes et al. 2009; Zhang et al. 2009).

6.2 Early Detection of Food Pathogens and Food Spoilage Microorganisms

Food pathogens are one of the major threats for food safety, and large numbers of people around the world suffer from diseases including diarrhoea, dysentery and other forms of food poisoning that are directly caused by various food pathogens, such as *Salmonella* spp., *Shigella* spp., *Listeria monocytogenes, Campylobacter jejuni* and *E. coli*. Moreover, food spoilage microorganisms (e.g. *Pseudomonas* spp., *Acinetobacter* spp., *Botrytis* spp.) are not necessarily pathogenic for people, but can cause severe economic damage because of the spoilage of a wide range of food materials. If there was a way to detect these pathogens or spoilage microbes in the early stages of their growth in food products, it would be possible to reduce dramatically the numbers of food-borne outbreaks and subsequent significant losses of food by undertaking appropriate measurements to control their further growth. Traditional identification and cultural methods for pathogens or food spoilage microbes are time consuming, and therefore it is necessary to develop techniques that would enable the rapid detection of microbes soon after the contamination occurred in a food system (Xu et al. 2010). The metabolomics approach has already shown huge potential for developing analytical methods to detect food pathogens in their early stages of growth in a food product (Li et al. 2011; Beale et al. 2014). In this approach, an experiment is performed using both a contaminated and a non-contaminated food, and the metabolites from both are analysed. Multivariate or discriminant analyses are performed to determine a group of potential candidate biomarkers that can distinguish between the two conditions. Once validated, these biomarkers can be used for the determination of pathogens in a real food sample, or a simpler screening technique (e.g. enzymatic or colorimetric) can be developed to be used routinely by food auditors.

GC-MS has been the choice of analytical instrument for determining pathogenic growth in a food, as this technique is very efficient in determining the volatile organic compounds (VOC) produced by microorganisms. Food spoilage microbes generally produce many VOCs as part of their metabolism, and this causes alteration in the sensory properties of the food (Li et al. 2011). VOC analysis is attractive for food sampling and is also advantageous because of rapid and non-invasive sample preparation. Once collected in the headspace using an appropriate SPME cartridge, VOCs produced by spoilage or pathogenic microorganisms are ready to be analysed by GC-MS. Xu et al. (2010) published a VOC-based GC-MS metabolite profiling approach to determine the potential biomarkers of spoilage of pork by *S. typhimurium,* and identified 16 metabolites that clearly distinguished the naturally spoiled from *S typhimurium*-contaminated pork meats. Moreover, Li et al. (2011) demonstrated the capability of metabolomics in assigning biomarkers to the spoilage microbes, *Botrytis allii* and *Burkholderia cepacia,* and they identified 16 volatile metabolites related to post-harvest onion spoilage. In addition to volatile metabolites, other primary metabolites including sugars and amino acids (dextrose, glycine, tyrosine and histidine) were also

characterised as potential biomarkers that could be used for the early detection of *E. coli* O157:H7 and of different strains of *Salmonella* in ground beef and chicken (Cevallos-Cevallos et al. 2011).

Among other MS-based techniques, Matrix-assisted laser desorption/ionisation coupled to time of flight-MS (MALDI-TOF-MS) also has been used to identify different strains of pathogenic microbes in biological samples, including food and beverages (Böhme et al. 2010, 2012; Picariello et al. 2012; Ojima-Kato et al. 2014; Beale et al. 2014; Jadhav et al. 2015). MALDI-TOF-MS is very useful for identifying microbial strains using either whole cells or cell extracts and has been applied to epidemiological studies, biological warfare agents, detection of antibiotic resistance pathogens, detection of water- and food-borne pathogens and enterotoxins (Tsilia et al. 2012). This technique is rapid, sensitive and inexpensive, and thus well received by microbiologists (Singhal et al. 2015). Recently, rapid detection and source tracking of *L. monocytogenes* was carried out using MALDI-TOF-MS in Australian dairy products (Jadhav et al. 2015). *Staphylococcus aureus* strain characterisation was also performed in Italian dairy products using MALDI-TOF-MS fingerprinting (Böhme et al. 2012). However, the main drawback of using this technique is the inability to identify new species, as the identification process depends on the existing spectral database that contains the peptide mass fingerprints of the type strains (Singhal et al. 2015).

6.3 Microbial Food Toxins

In contrast to chemical contaminants, food toxins that pose serious health hazards for consumers are mainly produced naturally by different microorganisms (fungi, algae and others) growing on food substrates or during the food preparation and storage. Many of these toxins are produced as by-products of fungal metabolism (mainly *Penicillium*, *Aspergillus* and *Fusarium*) in contaminated foods including beer, wine, bread, rice and maize, and are thus known as mycotoxins. The determination of mycotoxins is very similar to that of chemical contaminants and mainly carried out by multi-residue analysis (Giacometti et al. 2013; Gottfried and Herebian 2013; Aniołowska and Steininger 2014; Pizzutti et al. 2014; Rodríguez-Carrasco et al. 2015). In addition to mycotoxins, toxins produced by some algae are also of interest for food safety. This type of toxin is usually found in contaminated seafood and fish and may affect people, such as fish and different types of shellfish poisoning (e.g. neurotoxic, paralytic, diarrhoeic and amnesic). It is important to study algal toxins to know about their modes of action and toxic doses in detail, to help to take appropriate precautions to prevent an outbreak. MS-based metabolomics approaches have been developed to detect and quantify several groups of algal toxins, such as ciguatoxins and domoic acid (Yogi et al. 2011; Beach et al. 2014; Stewart and McLeod 2014).

6.4 Study of GM Crops and Food Materials

GM or transgenic crops have gained popularity since the first commercial plantings in 1996. GM technology has allowed us to produce crops and food materials with enhanced nutritional properties, increased yield; and moreover, these crops can be resistant to various pests and diseases, and adverse environments, including drought and salinity (Parrott et al. 2010). A wide range of GM crops are now commercially cultivated around the world, including soybean, maize, cotton, canola, potatoes and tomatoes. Although the new traits in GM crops are mainly from the introduction of small RNAs or some regulatory proteins, it is still unknown if even that small amount of change could cause an overall alteration in other metabolic pathways, and thus adverse modification of cellular downstream products (Delaney 2015). The effects of growing transgenic plants on the environment have also been well documented (Liu et al. 2012; Brookes and Barfoot 2013; Knight et al. 2013), which has in turn raised concerns about the long-term consumption of GM food materials on human and animal health.

As the long-term effects of consuming GM food ingredients are still under question, it is time to do more research on toxicological aspects that could provide assurance to consumers about their safety. A few research projects have already been carried out that addressed the effects of consumption of GM feed ingredients by animal models. For instance, Sheng et al. (2014) evaluated the toxicity and allergenicity of GM rice as expressed in human serum albumin in rats, and Qi et al. (2015) assessed the safety of consumption of similar GM rice by rats using their urine metabolome. Although both sets of authors found significant differences in profiles between GM and non-GM rice-consuming rats, they concluded that GM rice could be considered safe. However, both these studies were performed for a limited period of time (only 90 days), and therefore it is still too soon to conclude if long-term consumption (e.g. 5–10 years) of such GM rice by the rats would have any adverse effects on their health.

Much research has been undertaken in last 10 years to acquire more knowledge regarding the compositional differences between GM and non-GM crops and food materials (Barros et al. 2010; Asiago et al. 2012; Cao et al. 2012; Liu et al. 2012; Clarke et al. 2013; Kusano et al. 2014). This provides valuable insight into the nutritional properties compared with those of conventional crops, and if any unintended chemicals or proteins are present in that given crop that might pose a threat to consumers. Metabolomics (both targeted and non-targeted), especially metabolite profiling, is very useful in this regard, as it allows the generation of data on the comprehensive composition of any GM crop (Rischer and Oksman-Caldentey 2006). For example, Kusano et al. (2014) recently published a study using metabolomics and ionomics approaches to determine the chemical diversity of a soybean lineage representing 35 years of breeding. The authors used different analytical platforms, including CE-TOF-MS, GC-TOF-MS and LC-qTOF-MS, to determine the global metabolite profiles of soybeans, and found that newer varieties are completely different from older ones. However, they found

no significant differences in metabolite composition between conventional and GM soybeans, thus indicating that GM soybeans could be safe as food and feed; their findings were in accordance those of with Clarke et al. (2013). Similar studies have been performed for other GM crops (e.g. maize and potato). Using a hierarchical metabolomics approach, it has been shown that metabolite composition is very similar between conventional and GM potato crops (Catchpole et al. 2005). However, it is noteworthy that compositional differences also exist among conventional crops, depending on their origin, environmental conditions, and genetics (Reynolds et al. 2005; Harrigan et al. 2007). The use of 'omics' approaches, including metabolomics, in determining the safety aspect of GM food materials still has scope for improvement, and more research should be undertaken to highlight the toxicological aspects in addition to the compositional studies.

6.5 *Food Quality and Traceability*

Both targeted and non-targeted metabolomics have been widely applied to determine food quality by analysing any adulteration during food processing, or to confirm authenticity of a food or beverage. Adulteration is usually performed deliberately to gain more profit, using unwanted substances, such as the addition of melamine to milk powder, synthetic dyes in spices, and the use of horsemeat in other meat products (Senyuva et al. 2015). Some of these adulterations might cause serious health issues (Chu and Wang 2013) and some of them are related to economic adulterations to consumers (Everstine et al. 2013). However, in all cases, it is essential to know the overall quality of the food materials and also to determine if the food product is adulterated or not before it can be sold in the market. Authentication of food is a useful step, and attempts have been made to determine potential markers in different food matrices that can differentiate between adulterated and normal food. For example, both targeted and untargeted metabolomics approaches using LC-MS/MS have been used to authenticate Indian citrus fruits, and several metabolites (didymin, rhoifolin, isorhoifolin, neohesperidin, hesperidin, naringin, narirutin, limonin glucoside, and vicenin) were characterised as potential markers (Jandrić et al. 2015). Arias et al. (2016) recently published a metabolomics study using UHPLC–QTof-MS (ESI + mode) to distinguish the control (non-medicated pigs) and pigs treated with ronidazole, dimetridazole and metronidazole where they have identified at least four ionic features that could be used as potential biomarkers of illegal 5-nitroimidazole abuse. GC-MS is another popular analytical platform that has been successfully implemented to determine the quality of various food products. For instance, GC-MS has been used to monitor the kimchi fermentation process (Park et al. 2016). Moreover, fatty acid profiling using GC-MS has also been found to be useful in determining adulteration in flaxseed oil (Sun et al. 2015). Recently, Isotope-ratio MS (IRMS) along with either GC or LC has become another technique that can be used for authentication of foods including wines, essential oils in mandarin, and flavoured strawberry foods (Schipilliti et al. 2010; Guyon et al. 2011;

Schipilliti et al. 2011). In addition to MS-based techniques, other spectroscopic instruments and imaging systems have also been used successfully to authenticate different foods. NMR-based metabolomics was applied to determine adulteration in foods and beverages, including saffron and fruit juice (Balan et al. 2013; Ordoudi et al. 2015). NMR metabolomics approach has also been successfully used to determine the freshness of shucked mussels and a significant increase of many primary metabolites including acetate, lactate, succinate, alanine, branched chain amino acids and trimethylamine was observed during storage of mussels between 0 and 4 °C (Aru et al. 2016). Yang et al. (2016) recently reported the use of both NMR and LC-MS-based metabolomics study of milk adulteration and they identified some metabolites (choline and succinic acid) that can distinguish Holstein milk from that of other cows. Moreover, the use of Raman imaging could also identify the adulteration agents (e.g. melamine and dihydrocyanide) in powdered food (Qin et al. 2014).

One major area where much attention has been paid and which helps to prevent adulteration is the determination of geographic origins of foods and beverages. In many countries, food and condiment preparation is considered an art (e.g. wine-making) and strong regulation already exists to ensure the quality of the product before it can be marketed under protected designation of origin (PDO) or protected geographic indication (PGI). This is especially true for many European food products (balsamic vinegars, olive oils and cheeses). Traditional balsamic vinegars are important product from Italy, produced in many regions; however, Modena is famous for production of balsamic vinegars with PGI certification. GC-MS analysis of volatile compounds was found to be very useful for distinguishing balsamic vinegar samples with PGI (Chinnici et al. 2009; Cirlini et al. 2011). Extra virgin olive oil is another product for which PDO status is very important. Many producers follow fraudulent practices to obtain PDO for low-quality olive oils for which consumers will pay comparatively higher prices. Pizarro et al. (2011) identified volatile markers related to the geographic origin of Spanish extra virgin olive oils using headspace-SPME-GC-MS analysis. GC-MS along with multivariate data analysis has also been used to study the origin and quality of Italian buffalo mozzarella cheese (Pisano et al. 2016). Moreover, different types of NMR experiments (^{1}H, ^{13}C, ^{31}P) have also been successfully employed for quality assessment and authentication of olive oils (Dais and Hatzakis 2013).

7 Conclusion

Metabolomics has already been employed widely in food science, especially to address issues of food safety and quality. Although recent analytical developments allow us to analyse over 1000 metabolites in a single analysis (or using multiple analytical instruments), a big challenge still exists in the handling of large data sets (Skov et al. 2014). This is where all the ‘omics’ approaches currently have major difficulties and, frequently, the huge amount of data generated cannot be

appropriately interpreted biologically because of the inability to analyse the data. Therefore, genuine efforts should be undertaken to improve the data analysis platforms, to improve the overall quality of research in the metabolomics area. In addition, ongoing technical improvement should lead to more cost-effective, user-friendly and high throughput methods that could be used for the analysis of various food matrices. Other aspects that need attention include the creation of more food-based databases to make identification and discrimination of foods much easier. It would be also easier to formulate regulatory actions to maintain the quality and safety of foods and food products. We have already seen a tremendous improvement in food safety and quality research in the last few years, and the application of metabolomics will allow us to look at a holistic overview of the food system, thus improving the overall objectives of ensuring food safety and quality.

Acknowledgements The author would like to thank Dr Damian Martin, Megan Jones and Science and Publishing Office of Plant and Food Research Ltd for their support during the writing of this manuscript.

References

Achá V, Naveau H, Meurens M (1998) Extractive sampling methods to improve the sensitivity of FTIR spectroscopy in analysis of aqueous liquids. Analusis 26:157–163

Ackerman LK, Noonan GO, Begley TH (2009) Assessing direct analysis in real-time-mass spectrometry (DART-MS) for the rapid identification of additives in food packaging. Food Addit Contam Part A 26:1611–1618

Aggio R, Villas-Bôas SG, Ruggiero K (2011) Metab: an R package for high-throughput analysis of metabolomics data generated by GC-MS. Bioinformatics 27:2316–2318

Aggio RBM, Mayor A, Reade S, Probert CSJ, Ruggiero K (2014) Identifying and quantifying metabolites by scoring peaks of GC-MS data. BMC Bioinformatics 15:374

Alder L, Steinborn A, Bergelt S (2011) Suitability of an orbitrap mass spectrometer for the screening of pesticide residues in extracts of fruits and vegetables. J AOAC Int 94:1661–1673

Almeida C, Duarte IF, Barros A, Rodrigues J, Spraul M, Gil AM (2006) Composition of beer by 1H NMR spectroscopy: effects of brewing site and date of production. J Agric Food Chem 54:700–706

Alvarez-Ordóñez A, Broussolle V, Colin P, Nguyen-The C, Prieto M (2015) The adaptive response of bacterial food-borne pathogens in the environment, host and food: implications for food safety. Int J Food Microbiol 213:99–109

Anater A, Manyes L, Meca G, Ferrer E, Luciano FB, Pimpão CT, Font G (2016) Mycotoxins and their consequences in aquaculture: a review. Aquaculture 451:1–10

Aniołowska M, Steininger M (2014) Determination of trichothecenes and zearalenone in different corn (*Zea mays*) cultivars for human consumption in Poland. J Food Compos Anal 33:14–19

Anizan S, Bichon E, Monteau F, Cesbron N, Antignac JP, le Bizec B (2010) A new reliable sample preparation for high throughput focused steroid profiling by gas chromatography-mass spectrometry. J Chromatogr A 1217:6652–6660

Anizan S, Bichon E, Duval T, Monteau F, Cesbron N, Antignac JP, Le Bizec B (2012) Gas chromatography coupled to mass spectrometry-based metabolomic to screen for anabolic practices in cattle: identification of 5α-androst-2-en-17-one as new biomarker of 4-androstenedione misuse. J Mass Spectrom 47:131–140

Arias M, Chevallier OP, Graham SF, Gasull-Gimenez A, Fodey T, Cooper KM, Crooks SRH, Danaher M, Elliott CT (2016) Metabolomics reveals novel biomarkers of illegal 5-nitromimidazole treatment in pigs. Further evidence of drug toxicity uncovered. Food Chem 199:876–884

Arroyo-Manzanares N, Diana Di Mavungu J, Uka V, Malysheva SV, Cary JW, Ehrlich KC, Vanhaecke L, Bhatnagar D, de Saeger S (2015) Use of UHPLC high-resolution Orbitrap mass spectrometry to investigate the genes involved in the production of secondary metabolites in *Aspergillus flavus*. Food Addit Contam Part A 32:1656–1673

Aru V, Pisano MB, Savorani F, Engelsen SB, Cosentino S, Cesare Marincola F (2016) Metabolomics analysis of shucked mussels' freshness. Food Chem 205:58–65

Asiago VM, Hazebroek J, Harp T, Zhong C (2012) Effects of genetics and environment on the metabolome of commercial maize hybrids: a multisite study. J Agric Food Chem 60:11498–11508

Badilita V, Adhikari SS, MacKinnon N, Wallrabe U, Korvink JG (2014) Disposable 1H NMR detectors for food quality monitoring: application to butter and citrus juice discrimination. Chem Biol Microsyst Soc 1710–1712

Balan M, Nicolescu A, Stavarache C, Ciobanu M, Deleanu C (2013) Fast NMR juice identification based on sugars and other plant metabolites from fruits. Rev Roum Chim 58:175–182

Banerjee K, Mujawar S, Utture SC, Dasgupta S, Adsule PG (2013) Optimization of gas chromatography-single quadrupole mass spectrometry conditions for multiresidue analysis of pesticides in grapes in compliance to EU-MRLs. Food Chem 138:600–607

Barros E, Lezar S, Anttonen MJ, van Dijk JP, Röhlig RM, Kok EJ, Engel KH (2010) Comparison of two GM maize varieties with a near-isogenic non-GM variety using transcriptomics, proteomics and metabolomics. Plant Biotechnol J 8:436–451

Bauer R, Nieuwoudt H, Bauer FF, Kossmann J, Koch KR, Esbensen KH (2008) FTIR spectroscopy for grape and wine analysis. Anal Chem 80:1371–1379

Beach DG, Walsh CM, McCarron P (2014) High-throughput quantitative analysis of domoic acid directly from mussel tissue using Laser Ablation Electrospray Ionization—tandem mass spectrometry. Toxicon 92:75–80

Beale DJ, Morrison PD, Palombo EA (2014) Detection of *Listeria* in milk using non-targeted metabolic profiling of *Listeria* monocytogenes: a proof-of-concept application. Food Control 42:343–346

Begley M, Hill C (2015) Stress adaptation in food-borne pathogens. Ann Rev Food Sci Technol 6:191–210

Berg M, Vanaerschot M, Jankevics A, Cuypers B, Breitling R, Dujardin JC (2012) LC-MS metabolomics from study design to data-analysis—using a versatile pathogen as a test case. Comput Struct Biotechnol J 4:e201301002

Berthomieu C, Hienerwadel R (2009) Fourier transform infrared (FTIR) spectroscopy. Photosynth Res 101:157–170

Biais B, Bernillon S, Deborde C, Cabasson C, Rolin D, Tadmor Y, Burger J, Schaffer AA, Moing A (2012) Precautions for harvest, sampling, storage, and transport of crop plant metabolomics samples. Methods Mol Biol 860:51–63

Bino RJ, Hall RD, Fiehn O et al (2004) Potential of metabolomics as a functional genomics tool. Trends Plant Sci 9:418–425

Böhme K, Fernández-No IC, Barros-Velázquez J, Gallardo JM, Calo-Mata P, Cañas B (2010) Species differentiation of seafood spoilage and pathogenic gram-negative bacteria by MALDI-TOF mass fingerprinting. J Proteome Res 9:3169–3183

Böhme K, Morandi S, Cremonesi P, Fernández No IC, Barros-Velázquez J, Castiglioni B, Brasca M, Cañas B, Calo-Mata P (2012) Characterization of *Staphylococcus aureus* strains isolated from Italian dairy products by MALDI-TOF mass fingerprinting. Electrophoresis 33:2355–2364

Booth SC, Weljie AM, Turner RJ (2015) Metabolomics reveals differences of metal toxicity in cultures of *Pseudomonas pseudoalcaligenes* KF707 grown on different carbon. Front Microbiol 6:827

Boutsiadou-Theurillat X, Meier P, Richard C (2014) Development and in-house validation of a rapid LC-MS/MS method for the semi-quantification of eleven mycotoxins in maize samples. Chimia 68:716–720

Brennan L (2014) NMR-based metabolomics: from sample preparation to applications in nutrition research. Prog Nucl Magn Reson Spectrosc 83:42–49

Brookes G, Barfoot P (2013) Key environmental impacts of global genetically modified (GM) crop use 1996-2011. GM Crops Food 4:109–119

Cai J, Henion J (1995) Capillary electrophoresis-mass spectrometry. J Chromatogr A 703:667–692

Caligiani A, Malavasi G, Palla G, Marseglia A, Tognolini M, Bruni R (2013) A simple GC-MS method for the screening of betulinic, corosolic, maslinic, oleanolic and ursolic acid contents in commercial botanicals used as food supplement ingredients. Food Chem 136:735–741

Callejón RM, Torija MJ, Mas A, Morales ML, Troncoso AM (2010) Changes of volatile compounds in wine vinegars during their elaboration in barrels made from different woods. Food Chem 120:561–571

Canellas E, Vera P, Domeño C, Alfaro P, Nerín C (2012) Atmospheric pressure gas chromatography coupled to quadrupole-time of flight mass spectrometry as a powerful tool for identification of non intentionally added substances in acrylic adhesives used in food packaging materials. J Chromatogr A 1235:141–148

Cao S, He X, Xu W, Luo Y, Yuan Y, Liu P, Cao B, Shi H, Huang K (2012) Safety assessment of transgenic *Bacillus thuringiensis* rice T1c-19 in Sprague-Dawley rats from metabonomics and bacterial profile perspectives. IUBMB Life 64:242–250

Cao YZ, Liu YM, Wang N, Ji XX, Yao CC, Li X, Shi LL, Chang QY, Fan CL, Pang GF (2014) Multiresidual determination of 295 pesticides and chemical pollutants in animal fat by gel permeation chromatography (GPC) cleanup coupled with GC-MS/MS, GC-NCI-MS, and LC-MS/MS. In: High-throughput analysis for food safety. Wiley Blackwell, New York, pp 117–166

Cappiello A, Famiglini G, Palma P, Trufelli H (2010) Matrix effects in liquid chromatography-mass spectrometry. J Liq Chromatogr Relat Technol 33:1067–1081

Castro-Puyana M, Herrero M (2013) Metabolomics approaches based on mass spectrometry for food safety, quality and traceability. TrAC Trend Anal Chem 52:74–87

Castro-Puyana M, Mendiola JA, Ibáñez E, Herrero M (2013) MS-based metabolomics approaches for food safety, quality, and traceability. In: Foodomics: advanced mass spectrometry in modern food science and nutrition. Wiley, New York, pp 453–470.

Catchpole GS, Beckmann M, Enot DP et al (2005) Hierarchical metabolomics demonstrates substantial compositional similarity between genetically modified and conventional potato crops. Proc Natl Acad Sci USA 102:14458–14462

Cevallos-Cevallos JM, Danyluk MD, Reyes-De-Corcuera JI (2011) GC-MS based metabolomics for rapid simultaneous detection of *Escherichia coli* O157:H7, *Salmonella typhimurium*, *Salmonella muenchen*, and *Salmonella hartford* in ground beef and chicken. J Food Sci 76: M238–M246

Chan PH, Zhang WL, Lau CH, Cheung CY, Keun HC, Tsim KWK, Lam H (2014) Metabonomic analysis of water extracts from different angelica roots by 1 h-nuclear magnetic resonance spectroscopy. Molecules 19:3460–3470

Chatterjee NS, Banerjee K, Utture S, Kamble N, Rao BM, Panda SK, Mathew S (2015) Assessment of polyaromatic hydrocarbons and pesticide residues in domestic and imported *pangasius* (*Pangasianodon hypophthalmus*) fish in India. J Sci Food Agric 96:2373

Chinnici F, Guerrero ED, Sonni F, Natali N, Marín RN, Riponi C (2009) Gas chromatography-mass spectrometry (GC-MS) characterization of volatile compounds in quality vinegars with protected European geographical indication. J Agric Food Chem 57:4784–4792

Chu CY, Wang CC (2013) Toxicity of melamine: the public health concern. J Environ Sci Health Part C 31:342–386

Cifuentes A, Rutledge D (2013) Foodomics and food analysis in the post-genomics era. TrAC Trend Anal Chem 52:1

Cirlini M, Caligiani A, Palla L, Palla G (2011) HS-SPME/GC-MS and chemometrics for the classification of Balsamic Vinegars of Modena of different maturation and ageing. Food Chem 124:1678–1683

Clarke JD, Alexander DC, Ward DP, Ryals JA, Mitchell MW, Wulff JE, Guo L (2013) Assessment of genetically modified soybean in relation to natural variation in the soybean seed metabolome. Sci Rep 3:3083

Cuny M, Vigneau E, Le Gall G, Colquhoun I, Lees M, Rutledge DN (2008) Fruit juice authentication by 1H NMR spectroscopy in combination with different chemometric tools. Anal Bioanal Chem 390:419–427

D'Alessandro A, Zolla L (2013) Foodomics to investigate meat tenderness. TrAC Trend Anal Chem 52:47–53

Da Rosa JS, Freitas-Silva O, Pacheco S, de Oliveira Godoy RL, de Rezende CM (2012) LC-MS based screening and targeted profiling methods for complex plant: coffee a case study. Curr Drug Metab 13:1244–1250

Da Silva EP, De Martinis ECP (2013) Current knowledge and perspectives on biofilm formation: The case of *Listeria monocytogenes*. Appl Microbiol Biotechnol 97:957–968

Dawson IK, Russell J, Powell W, Steffenson B, Thomas WTB, Waugh R (2015) Barley: a translational model for adaptation to climate change. New Phytol 206:913–931

De Dominicis E, Commissati I, Suman M (2012) Targeted screening of pesticides, veterinary drugs and mycotoxins in bakery ingredients and food commodities by liquid chromatography-high-resolution single-stage Orbitrap mass spectrometry. J Mass Spectrom 47:1232–1241

Delaney B (2015) Safety assessment of foods from genetically modified crops in countries with developing economies. Food Chem Toxicol 86:132–143

Del Coco L, Schena FP, Fanizzi FP (2012) ^{1}H Nuclear magnetic resonance study of olive oils commercially available as Italian products in the United States of America. Nutrients 4:343–355

Dervilly-Pinel G, Courant F, Chéreau S, Royer AL, Boyard-Kieken F, Antignac JP, Monteau F, Le Bizec B (2012) Metabolomics in food analysis: application to the control of forbidden substances. Drug Test Anal 4:59–69

Dais P, Hatzakis E (2013) Quality assessment and authentication of virgin olive oil by NMR spectroscopy: a critical review. Anal Chim Acta 765:1–27

Dieterle F, Riefke B, Schlotterbeck G, Ross A, Senn H, Amberg A (2011) NMR and MS methods for metabonomics. Methods Mol Biol 691:385–415

Doué M, Dervilly-Pinel G, Pouponneau K, Monteau F, le Bizec B (2015) Direct analysis in real time—high resolution mass spectrometry (DART-HRMS): a high throughput strategy for identification and quantification of anabolic steroid esters. Drug Test Anal 7:603–608

Duedahl-Olesen L, Navaratnam MA, Jewula J, Jensen AH (2015a) PAH in some brands of tea and coffee. Polycyclic Aromat Compd 35:74–90

Duedahl-Olesen L, Aaslyng M, Meinert L, Christensen T, Jensen AH, Binderup ML (2015b) Polycyclic aromatic hydrocarbons (PAH) in Danish barbecued meat. Food Control 57:169–176

Dunn WB (2011) Mass spectrometry in systems biology: an introduction. Methods Enzymol 500:15–35

Dunn WB, Ellis DI (2005) Metabolomics: current analytical platforms and methodologies. TrAC Trend Anal Chem 24:285–294

Duportet X, Aggio RBM, Carneiro S, Villas-Bôas SG (2012) The biological interpretation of metabolomic data can be misled by the extraction method used. Metabolomics 8:410–421

El-Aneed A, Cohen A, Banoub J (2009) Mass spectrometry, review of the basics: electrospray, MALDI, and commonly used mass analyzers. Appl Spectrosc Rev 44:210–230

El Amrani A, Dumas AS, Wick LY, Yergeau E, Berthomé R (2015) "Omics" Insights into PAH degradation toward improved green remediation biotechnologies. Environ Sci Technol 49:11281–11291

Everstine K, Spink J, Kennedy S (2013) Economically motivated adulteration (EMA) of food: common characteristics of EMA incidents. J Food Prot 76:723–735

Falkowska L, Reindl AR (2015) Dietary exposure to, and internal organ transfer of, selected halogenated organic compounds in birds eating fish from the Southern Baltic. J Environ Sci Health Part A Toxiic/Hazard Subst Environ Eng 50:1029–1039

Fan S, Zhao P, Yu C, Pan C, Li X (2014) Simultaneous determination of 36 pesticide residues in spinach and cauliflower by LC-MS/MS using multi-walled carbon nanotubes-based dispersive solid-phase clean-up. Food Addit Contam Part A 31:73–82

Farré M, Picó Y, Barceló D (2013) Direct peel monitoring of xenobiotics in fruit by direct analysis in real time coupled to a linear quadrupole ion trap-orbitrap mass spectrometer. Anal Chem 85:2638–2644

Fiehn O (2002) Metabolomics—the link between genotypes and phenotypes. Plant Mol Biol 48:155–171

Font G, Ruiz MJ, Fernández M, Picó Y (2008) Application of capillary electrophoresis-mass spectrometry for determining organic food contaminants and residues. Electrophoresis 29:2059–2078

Forsberg ND, Wilson GR, Anderson KA (2011) Determination of parent and substituted polycyclic aromatic hydrocarbons in high-fat salmon using a modified quechers extraction, dispersive SPE and GC-MS. J Agric Food Chem 59:8108–8116

García-Gómez D, García-Hernández M, Rodríguez-Gonzalo E, Carabias-Martínez R (2012) A fast and reliable method for the quantitative determination of benzimidazoles and metabolites in milk by LC-MS/MS with on-line sample treatment. Anal Bioanal Chem 404:2909–2914

García-Reyes JF, Jackson AU, Molina-Díaz A, Cooks RG (2009) Desorption electrospray ionization mass spectrometry for trace analysis of agrochemicals in food. Anal Chem 81:820–829

Gelting RJ, Baloch MA, Zarate-Bermudez M, Hajmeer MN, Yee JC, Brown T, Yee BJ (2015) A systems analysis of irrigation water quality in an environmental assessment of an *E. coli* O157:H7 outbreak in the United States linked to iceberg lettuce. Agric Water Manag 150:111–118

Giacometti J, Tomljanović AB, Josić D (2013) Application of proteomics and metabolomics for investigation of food toxins. Food Res Int 54:1042–1051

Gilbert-López B, Robles-Molina J, García-Reyes JF, Molina-Díaz A (2010) Rapid determination of BTEXS in olives and olive oil by headspace-gas chromatography/mass spectrometry (HS-GC-MS). Talanta 83:391–399

Giri A, Khummueng W, Mercier F, Kondjoyan N, Tournayre P, Meurillon M, Ratel J, Engel E (2015) Relevance of two-dimensional gas chromatography and high resolution olfactometry for the parallel determination of heat-induced toxicants and odorants in cooked food. J Chromatogr A 1388:217–226

Glinski M, Weckwerth W (2006) The role of mass spectrometry in plant systems biology. Mass Spectrom Rev 25:173–214

Gottfried S, Herebian D (2013) Determination of mycotoxins in food matrices using LC-MS/MS compared with high-resolution orbitrap™ MS technology. Curr Anal Chem 9:99–107

Gowda H, Ivanisevic J, Johnson CH, Kurczy ME, Benton HP, Rinehart D, Nguyen T, Ray J, Kuehl J, Arevalo B, Westenskow PD, Wang J, Arkin AP, Deutschbauer AM, Patti GJ, Siuzdak G (2014) Interactive XCMS online: simplifying advanced metabolomic data processing and subsequent statistical analyses. Anal Chem 86:6931–6939

Grimalt S, Harbeck S, Shegunova P, Seghers J, Sejerøe-Olsen B, Emteborg H, Dabrio M (2015) Development of a new cucumber reference material for pesticide residue analysis: feasibility study for material processing, homogeneity and stability assessment. Anal Bioanal Chem 407:3083–3091

Guo C, Huang XY, Yang MJ, Wang S, Ren ST, Li H, Peng XX (2014) GC/MS-based metabolomics approach to identify biomarkers differentiating survivals from death in crucian carps infected by *Edwardsiella tarda*. Fish Shellfish Immunol 39:215–222

Gustafson KD, Belden JB, Bolek MG (2015) The effects of the herbicide atrazine on freshwater snails. Ecotoxicology 24:1183–1197

Guyon F, Gaillard L, Salagoïty MH, Médina B (2011) Intrinsic ratios of glucose, fructose, glycerol and ethanol 13C/12C isotopic ratio determined by HPLC-co-IRMS: toward determining constants for wine authentication. Anal Bioanal Chem 401:1551–1558

Hall R, Beale M, Fiehn O, Hardy N, Sumner L, Bino R (2002) Plant metabolomics: the missing link in functional genomics strategies. Plant Cell 14:1437–1440

Hall RD, Hardy NW (2012) Practical applications of metabolomics in plant biology. Methods Mol Biol 860:1–10

Hall RD, de Maagd RA (2014) Plant metabolomics is not ripe for environmental risk assessment. Trend Biotechnol 32:391–392

Han J, Datla R, Chan S, Borchers CH (2009) Mass spectrometry-based technologies for high-throughput metabolomics. Bioanalysis 1:1665–1684

Han Y, Song L, Zhao P, Li Y, Zou N, Qin Y, Li X, Pan C (2016) Residue determination of glufosinate in plant origin foods using modified Quick Polar Pesticides (QuPPe) method and liquid chromatography coupled with tandem mass spectrometry. Food Chem 197:730–736

Harrigan GG, Stork LG, Riordan SG et al (2007) Impact of genetics and environment on nutritional and metabolite components of maize grain. J Agric Food Chem 55:6177–6185

Herman KM, Hall AJ, Gould LH (2015) Outbreaks attributed to fresh leafy vegetables, United States, 1973–2012. Epidemiol Infect 143:3011–3021

Herrero M, Simõ C, García-Cañas V, Ibáñez E, Cifuentes A (2012) Foodomics: MS-based strategies in modern food science and nutrition. Mass Spectrom Rev 31:49–69

Humphrey T (2004) *Salmonella*, stress responses and food safety. Nat Rev Microbiol 2:504–509

Ibáñez C, García-Cañas V, Valdés A, Simó C (2013) Novel MS-based approaches and applications in food metabolomics. TrAC Trend Anal Chem 52:100–111

Ibáñez E, Cifuentes A (2014) Foodomics: food science and nutrition in the postgenomic era, vol 64. Elsevier, Amsterdam, pp 395–440

Inoue K, Toyo'oka T (2015) Foodomics, vol 68. Elsevier, Amsterdam, pp 653–684

Inoue K, Tanada C, Sakamoto T, Tsutsui H, Akiba T, Min JZ, Todoroki K, Yamano Y, Toyo'Oka T (2015) Metabolomics approach of infant formula for the evaluation of contamination and degradation using hydrophilic interaction liquid chromatography coupled with mass spectrometry. Food Chem 181:318–324

Ison SA, Delannoy S, Bugarel M, Nightingale KK, Webb HE, Renter DG, Nagaraja TG, Loneragan GH, Fach P (2015) Genetic diversity and pathogenic potential of attaching and effacing *Escherichia coli* O26: H11 strains recovered from bovine feces in the United States. Appl Environ Microbiol 81:3671–3678

Jadhav S, Gulati V, Fox EM, Karpe A, Beale DJ, Sevior D, Bhave M, Palombo EA (2015) Rapid identification and source-tracking of *Listeria monocytogenes* using MALDI-TOF mass spectrometry. Int J Food Microbiol 202:1–9

Jandrić Z, Islam M, Singh DK, Cannavan A (2015) Authentication of Indian citrus fruit/fruit juices by untargeted and targeted metabolomics. Food Control (in press)

Janssens G, Mangelinckx S, Courtheyn D, De Kimpe N, Matthijs B, Le Bizec B (2015) Simultaneous detection of androgen and estrogen abuse in breeding animals by gas chromatography-mass spectrometry/combustion/isotope ratio mass spectrometry (GC-MS/C/IRMS) evaluated against alternative methods. J Agric Food Chem 63:7574–7581

Jäpelt KB, Nielsen NJ, Wiese S, Christensen JH (2015) Metabolic fingerprinting of Lactobacillus paracasei: a multi-criteria evaluation of methods for extraction of intracellular metabolites. Anal Bioanal Chem 407:6095

Jiang H, Cao H, Zhang Y, Fast DM (2012) Systematic evaluation of supported liquid extraction in reducing matrix effect and improving extraction efficiency in LC-MS/MS based bioanalysis for 10 model pharmaceutical compounds. J Chromatogr B Anal Technol Biomed Life Sci 891–892:71–80

Juan-Borrás M, Periche A, Domenech E, Escriche I (2015) Routine quality control in honey packaging companies as a key to guarantee consumer safety. The case of the presence of sulfonamides analyzed with LC-MS-MS. Food Control 50:243–249

Kalachova K, Pulkrabova J, Cajka T, Drabova L, Hajslova J (2012) Implementation of comprehensive two-dimensional gas chromatography-time-of-flight mass spectrometry for the simultaneous determination of halogenated contaminants and polycyclic aromatic hydrocarbons in fish. Anal Bioanal Chem 403:2813–2824

Kalachova K, Pulkrabova J, Cajka T, Drabova L, Stupak M, Hajslova J (2013) Gas chromatography-triple quadrupole tandem mass spectrometry: a powerful tool for the (ultra)trace analysis of multiclass environmental contaminants in fish and fish feed. Anal Bioanal Chem 405:7803–7815

Khan MR (2015) Influence of food condiments on the formation of carcinogenic heterocyclic amines in cooked chicken and determination by LC-MS/MS. Food Addit Contam Part A Chem Anal Control Expo Risk Assess 32:307–314

Kim S, Kim J, Yun EJ, Kim KH (2016) Food metabolomics: from farm to human. Curr Opin Biotechnol 37:16–23

Knight JG, Clark A, Mather DW (2013) Potential damage of GM crops to the country image of the producing country. GM Crops Food 4:151–157

Koutsoumanis KP, Sofos JN (2004) Comparative acid stress response of *Listeria monocytogenes*, *Escherichia coli* O157:H7 and *Salmonella Typhimurium* after habituation at different pH conditions. Lett Appl Microbiol 38:321–326

Krimsky S (2015) An illusory consensus behind GMO health assessment. Sci Technol Human Values 40:883–914

Kuchenmüller T, Hird S, Stein C, Kramarz P, Nanda A, Havelaar AH (2009) Estimating the global burden of foodborne diseases—a collaborative effort. 14(18). pii: 19195

Kueger S, Steinhauser D, Willmitzer L, Giavalisco P (2012) High-resolution plant metabolomics: from mass spectral features to metabolites and from whole-cell analysis to subcellular metabolite distributions. Plant J 70:39–50

Kusano M, Baxter I, Fukushima A et al (2014) Assessing metabolomic and chemical diversity of a soybean lineage representing 35 years of breeding. Metabolomics 11:261–270

Lacina O, Zachariasova M, Urbanova J, Vaclavikova M, Cajka T, Hajslova J (2012) Critical assessment of extraction methods for the simultaneous determination of pesticide residues and mycotoxins in fruits, cereals, spices and oil seeds employing ultra-high performance liquid chromatography-tandem mass spectrometry. J Chromatogr A 1262:8–18

Laghi L, Picone G, Capozzi F (2014) Nuclear magnetic resonance for foodomics beyond food analysis. TrAC Trend Anal Chem 59:93–102

Lanucara F, Holman SW, Gray CJ, Eyers CE (2014) The power of ion mobility-mass spectrometry for structural characterization and the study of conformational dynamics. Nat Chem 6:281–294

Lara FJ, García-Campaña AM, Alés-Barrero F, Bosque-Sendra JM (2008) In-line solid-phase extraction preconcentration in capillary electrophoresis-tandem mass spectrometry for the multiresidue detection of quinolones in meat by pressurized liquid extraction. Electrophoresis 29:2117–2125

Laufer AS, Grass J, Holt K, Whichard JM, Griffin PM, Gould LH (2015) Outbreaks of *Salmonella* infections attributed to beef—United States, 1973–2011. Epidemiol Infect 143:2003–2013

Le Boucher C, Courant F, Royer AL, Jeanson S, Lortal S, Dervilly-Pinel G, Thierry A, Le Bizec B (2015) LC–HRMS fingerprinting as an efficient approach to highlight fine differences in cheese metabolome during ripening. Metabolomics 11:1117–1130

Lee JE, Hwang GS, Van Den Berg F, Lee CH, Hong YS (2009) Evidence of vintage effects on grape wines using 1H NMR-based metabolomic study. Anal Chim Acta 648:71–76

Le Gall G (2015) Sample collection and preparation of biofluids and extracts for NMR spectroscopy, vol 1277. Humana Press, New York, pp 15–28

Lewis IA, Shortreed MR, Hegeman AD, Markley JL (2012) Novel NMR and MS approaches to metabolomics. In: Fan T, Higashi RM, Lane AN (eds) The handbook of metabolomics, vol 17. pp 199–230

Li C, Schmidt NE, Gitaitis R (2011) Detection of onion postharvest diseases by analyses of headspace volatiles using a gas sensor array and GC-MS. LWT—Food Sci Technol 44:1019–1025

Li K, Pidatala VR, Shaik R, Datta R, Ramakrishna W (2014) Integrated metabolomic and proteomic approaches dissect the effect of metal-resistant bacteria on maize biomass and copper uptake. Environ Sci Technol 48:1184–1193

Lima MRM, Diaz SO, Lamego I, Grusak MA, Vasconcelos MW, Gil AM (2014) Nuclear magnetic resonance metabolomics of iron deficiency in soybean leaves. J Proteome Res 13:3075–3087

Liu Z, Zhao J, Li Y, Zhang W, Jian G, Peng Y, Qi F (2012) Non-uniform distribution pattern for differentially expressed genes of transgenic rice Huahui 1 at different developmental stages and environments. PLoS One 7:e37078

Maghari BM, Ardekani AM (2011) Genetically modified foods and social concerns. Avicenna J Med Biotechnol 3:109–117

McWhorter AR, Davos D, Chousalkar KK (2015) Pathogenicity of *Salmonella* strains isolated from egg shells and the layer farm environment in Australia. Appl Environ Microbiol 81:405–414

Marriott PJ, Chin ST, Maikhunthod B, Schmarr HG, Bieri S (2012) Multidimensional gas chromatography. TrAC Trends Anal Chem 34:1–20

Marušić A (2011) Food safety and security: what were favourite topics for research in the last decade? J Global Health 1:72–78

Mas S, Villas-Bôas SG, Hansen ME, Åkesson M, Nielsen J (2007) A comparison of direct infusion MS and GC-MS for metabolic footprinting of yeast mutants. Biotechnol Bioeng 96:1014–1022

Mastovska K, Wylie PL (2012) Evaluation of a new column backflushing set-up in the gas chromatographic-tandem mass spectrometric analysis of pesticide residues in dietary supplements. J Chromatogr A 1265:155–164

Melnik BC (2015) Linking diet to acne metabolomics, inflammation, and comedogenesis: an update. Clin Cosmet Investig Dermatol 8:371–388

Mondello L, Zoccali M, Purcaro G, Franchina FA, Sciarrone D, Moret S, Conte L, Tranchida PQ (2012) Determination of saturated-hydrocarbon contamination in baby foods by using on-line liquid-gas chromatography and off-line liquid chromatography-comprehensive gas chromatography combined with mass spectrometry. J Chromatogr A 1259:221–226

Motarjemi Y (2014) Hazard analysis and critical control point system (HACCP). Food safety management: a practical guide for the food industry. Elsevier, Amsterdam, pp 845–872

Motarjemi Y, Mortimore S (2014) Assessment of food safety management systems. In: Motarjemi Y, Lelieveld H (eds) Food safety management: a practical guide for the food industry. Elsevier, Amsterdam, pp 987–1004

Motarjemi Y, Lelieveld H (2014) Food safety management: a practical guide for the food industry. Elsevier, Amsterdam

Motarjemi Y, Vanschothorst M, Käferstein F (2001) Future challenges in global harmonization of food safety legislation. Food Control 12:339–346

Motarjemi Y, Stadler RH, Studer A, Damiano V (2008) Application of the Haccp approach for the management of processing contaminants. Process-induced food toxicants: occurrence, formation, mitigation, and health risks. Wiley, New York, pp 563–620

Mulas G, Galaffu MG, Pretti L, Nieddu G, Mercenaro L, Tonelli R, Anedda R (2011) NMR analysis of seven selections of Vermentino grape berry: metabolites composition and development. J Agric Food Chem 59:793–802

Nevedomskaya E, Ramautar R, Derks R, Westbroek I, Zondag G, Van Der Pluijm I, Deelder AM, Mayboroda OA (2010) CE-MS for metabolic profiling of volume-limited urine samples: application to accelerated aging TTD mice. J Proteome Res 9:4869–4874

Nguyen YTB, Kamoshita A, Dinh VTH, Matsuda H, Kurokura H (2016) Salinity intrusion and rice production in Red River Delta under changing climate conditions. Paddy Water Environ 1–12

Nokkoul R, Wichitparp T (2014) Effect of drought condition on growth, yield and grain quality of upland rice. Am J Agric Biol Sci 9:439–444

Ogrinc N, Košir IJ, Spangenberg JE, Kidrič J (2003) The application of NMR and MS methods for detection of adulteration of wine, fruit juices, and olive oil. A review Anal Bioanal Chem 376:424–430

Ojima-Kato T, Yamamoto N, Suzuki M, Fukunaga T, Tamura H (2014) Discrimination of *Escherichia coli* O157, O26 and O111 from other serovars by MALDI-TOF MS based on the S10-germs method. PLoS One 9:e113458

O'Leary D, McCabe EM, McCusker MP, Martins M, Fanning S, Duffy G (2015) Acid environments affect biofilm formation and gene expression in isolates of *Salmonella enterica Typhimurium* DT104. Int J Food Microbiol 206:7–16

Ordoudi SA, Cagliani LR, Lalou S, Naziri E, Tsimidou MZ, Consonni R (2015) 1H NMR-based metabolomics of saffron reveals markers for its quality deterioration. Food Res Int 70:1–6

Osselaere A, Devreese M, Goossens J, Vandenbroucke V, De Baere S, De Backer P, Croubels S (2013) Toxicokinetic study and absolute oral bioavailability of deoxynivalenol, T-2 toxin and zearalenone in broiler chickens. Food Chem Toxicol 51:350–355

OzFoodNet Working Group (2014) OzFoodNet quarterly report, 1 April to 30 June 2013. Commun Dis Intell Q Rep 38:E376–E382

Pacilli M, Cortese MM, Smith S et al (2015) Outbreak of gastroenteritis in adults due to Rotavirus genotype G12P[8]. Clin Infect Dis 61:e20–e25

Park SE, Yoo SA, Seo SH, Lee KI, Na CS, Son HS (2016) GC–MS based metabolomics approach of Kimchi for the understanding of *Lactobacillus plantarum* fermentation characteristics. LWT—Food Sci Technol 68:313–321

Parrott W, Chassy B, Ligon J, Meyer L, Petrick J, Zhou J, Herman R, Delaney B, Levine M (2010) Application of food and feed safety assessment principles to evaluate transgenic approaches to gene modulation in crops. Food Chem Toxicol 48:1773–1790

Pereira GE, Gaudillere JP, Pieri P, Hilbert G, Maucourt M, Deborde C, Moing A, Rolin D (2006) Microclimate influence on mineral and metabolic profiles of grape berries. J Agric Food Chem 54:6765–6775

Pérez-Ortega P, Gilbert-López B, García-Reyes JF, Ramos-Martos N, Molina-Díaz A (2012) Generic sample treatment method for simultaneous determination of multiclass pesticides and mycotoxins in wines by liquid chromatography-mass spectrometry. J Chromatogr A 1249:32–40

Pérez S, Rial D, Beiras R (2015) Acute toxicity of selected organic pollutants to saltwater (*mysid Siriella armata*) and freshwater (*cladoceran Daphnia magna*) ecotoxicological models. Ecotoxicology 24:1229–1238

Picariello G, Mamone G, Addeo F, Ferranti P (2012) Novel mass spectrometry-based applications of the 'omic': sciences in food technology and biotechnology. Food Technol Biotechnol 50:286–305

Piccinonna S, Ragone R, Stocchero M, del Coco L, de Pascali SA, Schena FP, Fanizzi FP (2016) Robustness of NMR-based metabolomics to generate comparable data sets for olive oil cultivar classification. An inter-laboratory study on Apulian olive oils. Food Chem 199:675–683

Pinu FR (2015) Metabolomics-The new frontier in food safety and quality research. Food Res Int 72:80–81

Pinu FR, Edwards PJB, Jouanneau S, Kilmartin PA, Gardner RC, Villas-Boas SG (2014) Sauvignon blanc metabolomics: grape juice metabolites affecting the development of varietal thiols and other aroma compounds in wines. Metabolomics 10:556–573

Pisano MB, Scano P, Murgia A, Cosentino S, Caboni P (2016) Metabolomics and microbiological profile of Italian mozzarella cheese produced with buffalo and cow milk. Food Chem 192:618–624

Pizarro C, Rodríguez-Tecedor S, Pérez-del-Notario N, González-Sáiz JM (2011) Recognition of volatile compounds as markers in geographical discrimination of Spanish extra virgin olive oils by chemometric analysis of non-specific chromatography volatile profiles. J Chromatogr A 1218:518–523

Pizzutti IR, De Kok A, Scholten J, Righi LW, Cardoso CD, Necchi Rohers G, Da Silva RC (2014) Development, optimization and validation of a multimethod for the determination of 36

mycotoxins in wines by liquid chromatography-tandem mass spectrometry. Talanta 129:352–363

Pluskal T, Castillo S, Villar-Briones A, Orešič M (2010) MZmine 2: modular framework for processing, visualizing, and analyzing mass spectrometry-based molecular profile data. BMC Bioinform 11:395

Pope GA, MacKenzie DA, Defernez M et al (2007) Metabolic footprinting as a tool for discriminating between brewing yeasts. Yeast 24:667–679

Qi X, Chen S, Sheng Y, Guo M, Liu Y, He X, Huang K, Xu W (2015) Safety assessment of genetically modified rice expressing human serum albumin from urine metabonomics and fecal bacterial profile. Food Chem Toxicol 76:1–10

Qin J, Chao K, Kim MS (2014) Authenticating powdered foods and ingredients using a high-throughput Raman chemical imaging method. Am Soc Agric Biol Eng 3:1912–1919

Radosavljevic V, Finke EJ, Belojevic G (2015) *Escherichia coli* O104:H4 outbreak in Germany—Clarification of the origin of the epidemic. Eur J Pub Health 25:125–129

Ragone R, Crupi P, Piccinonna S, Bergamini C, Mazzone F, Fanizzi FP, Schena FP, Antonacci D (2015) Classification and chemometric study of Southern Italy monovarietal wines based on NMR and HPLC-DAD-MS. Food Sci Biotechnol 24:817–826

Ramautar R, Mayboroda OA, Somsen GW, De Jong GJ (2011) CE-MS for metabolomics: developments and applications in the period 2008-2010. Electrophoresis 32:52–65

Raupp J (2014) Social agents and news media as risk amplifiers: a case study on the public debate about the *E. coli* outbreak in Germany 2011. Health Risk Soc 16:565–579

Rejczak T, Tuzimski T (2015) Recent trends in sample preparation and liquid chromatography/mass spectrometry for pesticide residue analysis in food and related matrixes. J AOAC Int 98:1143–1162

Reynolds TL, Nemeth MA, Glenn KC, Ridley WP, Astwood JD (2005) Natural variability of metabolites in maize grain: differences due to genetic background. J Agric Food Chem 53:10061–10067

Rischer H, Oksman-Caldentey KM (2006) Unintended effects in genetically modified crops: revealed by metabolomics? Trend Biotechnol 24:102–104

Robotti E, Marengo E (2016) Chemometric multivariate tools for candidate biomarker identification: LDA, PLS-DA, SIMCA, Ranking-PCA. Methods Mol Biol 1384:237–267

Rodrigues JA, Barros AS, Carvalho B (2011) Probing beer aging chemistry by nuclear magnetic resonance and multivariate analysis. Anal Chim Acta 702:178–187

Rodríguez-Carrasco Y, Fattore M, Albrizio S, Berrada H, Mañes J (2015) Occurrence of *Fusarium* mycotoxins and their dietary intake through beer consumption by the European population. Food Chem 178:149–155

Rul F, Monnet V (2015) How microbes communicate in food: a review of signaling molecules and their impact on food quality. Curr Opin Food Sci 2:100–105

Russo R, Severino V, Mendez A, Lliberia J, Parente A, Chambery A (2012) Detection of buffalo mozzarella adulteration by an ultra-high performance liquid chromatography tandem mass spectrometry methodology. J Mass Spectrom 47:1407–1414

Samelis J, Sofos JN, Kendall PA, Smith GC (2001) Fate of *Escherichia coli* O157:H7, *Salmonella Typhimurium* DT 104, and *Listeria* monocytogenes in fresh meat decontamination fluids at 4 and 10°C. J Food Prot 64:950–957

Sapozhnikova Y, Lehotay SJ (2013) Multi-class, multi-residue analysis of pesticides, polychlorinated biphenyls, polycyclic aromatic hydrocarbons, polybrominated diphenyl ethers and novel flame retardants in fish using fast, low-pressure gas chromatography-tandem mass spectrometry. Anal Chim Acta 758:80–92

Sato S, Yanagisawa S (2010) Capillary electrophoresis-electrospray ionization-mass spectrometry using fused-silica capillaries to profile anionic metabolites. Metabolomics 6:529–540

Scalbert A, Brennan L, Fiehn O, Hankemeier T, Kristal BS, van Ommen B, Pujos-Guillot E, Verheij E, Wishart D, Wopereis S (2009) Mass-spectrometry-based metabolomics: limitations and recommendations for future progress with particular focus on nutrition research. Metabolomics 5:435–458

Schipilliti L, Dugo P, Bonaccorsi I, Mondello L (2011) Headspace-solid phase microextraction coupled to gas chromatography-combustion-isotope ratio mass spectrometer and to enantioselective gas chromatography for strawberry flavoured food quality control. J Chromatogr A 1218:7481–7486

Schipilliti L, Tranchida PQ, Sciarrone D, Russo M, Dugo P, Dugo G, Mondello L (2010) Genuineness assessment of mandarin essential oils employing gas chromatography-combustion-isotope ratio MS (GC-C-IRMS). J Sep Sci 33:617–625

Schurek J, Vaclavik L, Hooijerink H, Lacina O, Poustka J, Sharman M, Caldow M, Nielen MWF, Hajslova J (2008) Control of strobilurin fungicides in wheat using direct analysis in real time accurate time-of-flight and desorption electrospray ionization linear ion trap mass spectrometry. Anal Chem 80:9567–9575

Self RL (2013) Direct analysis in real time-mass spectrometry (DART-MS) for rapid qualitative screening of toxic glycols in glycerin-containing products. J Pharm Biomed Anal 80:155–158

Self RL, Wu WH (2012) Rapid qualitative analysis of phthalates added to food and nutraceutical products by direct analysis in real time/orbitrap mass spectrometry. Food Control 25:13–16

Senyuva HZ, Gökmen V, Sarikaya EA (2015) Future perspectives in Orbitrap™-high-resolution mass spectrometry in food analysis: a review. Food Addit Contam Part A 32:1568–1606

Shen S, Fang FC (2012) Integrated stress responses in Salmonella. Int J Food Microbiol 152:75–81

Shen Y, van Beek TA, Claassen FW, Zuilhof H, Chen B, Nielen MWF (2012) Rapid control of Chinese star anise fruits and teas for neurotoxic anisatin by Direct Analysis in Real Time high resolution mass spectrometry. J Chromatogr A 1259:179–186

Sheng Y, Qi X, Liu Y, Guo M, Chen S, He X, Huang K, Xu W (2014) Subchronic toxicity study in vivo and allergenicity study in vitro for genetically modified rice that expresses pharmaceutical protein (human serum albumin). Food Chem Toxicol 72:242–246

Shulaev V (2006) Metabolomics technology and bioinformatics. Brief Bioinform 7:128–139

Signes-Pastor AJ, Carey M, Meharg AA (2016) Inorganic arsenic in rice-based products for infants and young children. Food Chem 191:128–134

Singhal N, Kumar M, Kanaujia PK, Virdi JS (2015) MALDI-TOF mass spectrometry: an emerging technology for microbial identification and diagnosis. Front Microbiol 6:791

Skov T, Honoré AH, Jensen HM, Næs T, Engelsen SB (2014) Chemometrics in foodomics: handling data structures from multiple analytical platforms. TrAC Trend Anal Chem 60:71–79

Smith CA, Want EJ, O'Maille G, Abagyan R, Siuzdak G (2006) XCMS: processing mass spectrometry data for metabolite profiling using nonlinear peak alignment, matching, and identification. Anal Chem 78:779–787

Soni KA, Nannapaneni R (2010) Removal of *Listeria* monocytogenes biofilms with bacteriophage P100. J Food Prot 73:1519–1524

Spraul M, Schütz B, Humpfer E, Mörtter M, Schäfer H, Koswig S, Rinke P (2009a) Mixture analysis by NMR as applied to fruit juice quality control. Magn Reson Chem 47:S130–S137

Spraul M, Schütz B, Rinke P, Koswig S, Humpfer E, Schäfer H, Mörtter M, Fang F, Marx UC, Minoja A (2009b) NMR-based multi parametric quality control of fruit juices: SGF profiling. Nutrition 1:148–155

Squadrone S, Ciccotelli V, Prearo M, Favaro L, Scanzio T, Foglini C, Abete MC (2015) Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA): emerging contaminants of increasing concern in fish from Lake Varese, Italy. Environ Monit Assess 80:155–158

Stackhouse RR, Faith NG, Kaspar CW, Czuprynski CJ, Wong ACL (2012) Survival and virulence of *Salmonella enterica serovar enteritidis* filaments induced by reduced water activity. Appl Environ Microbiol 78:2213–2220

Stewart I, McLeod C (2014) The laboratory mouse in routine food safety testing for marine algal biotoxins and harmful algal bloom toxin research: past, present and future. J AOAC Int 97:356–372

Storelli MM, Scarano C, Spanu C, De Santis EPL, Busco VP, Storelli A, Marcotrigiano GO (2012) Levels and congener profiles of polychlorinated dibenzo-p-dioxins (PCDDs), polychlorinated

dibenzofurans (PCDFs) and polychlorinated biphenyls (PCBs) in sheep milk from an industrialised area of Sardinia, Italy. Food Chem Toxicol 50:1413–1417

Sumner LW (2010) Recent advances in plant metabolomics and greener pastures. F1000 Biology Reports 2

Sun X, Zhang L, Li P, Xu B, Ma F, Zhang Q, Zhang W (2015) Fatty acid profiles based adulteration detection for flaxseed oil by gas chromatography mass spectrometry. LWT—Food Sci Technol 63:430–436

Teo CC, Chong WPK, Ho YS (2013) Development and application of microwave-assisted extraction technique in biological sample preparation for small molecule analysis. Metabolomics 9:1109–1128

Theodoridis G, Gika H, Franceschi P, Caputi L, Arapitsas P, Scholz M, Masuero D, Wehrens R, Vrhovsek U, Mattivi F (2012) LC-MS based global metabolite profiling of grapes: solvent extraction protocol optimisation. Metabolomics 8:175–185

Tiganitas A, Zeaki N, Gounadaki AS, Drosinos EH, Skandamis PN (2009) Study of the effect of lethal and sublethal pH and aw stresses on the inactivation or growth of *Listeria monocytogenes* and *Salmonella typhimurium*. Int J Food Microbiol 134:104–112

Tomita S, Nemoto T, Matsuo Y, Shoji T, Tanaka F, Nakagawa H, Ono H, Kikuchi J, Ohnishi-Kameyama M, Sekiyama Y (2015) A NMR-based, non-targeted multistep metabolic profiling revealed l-rhamnitol as a metabolite that characterised apples from different geographic origins. Food Chem 174:163–172

Trivedi TK, DeSalvo T, Lee L, Palumbo A, Moll M, Curns A, Hall AJ, Patel M, Parashar UD, Lopman BA (2012) Hospitalizations and mortality associated with norovirus outbreaks in nursing homes, 2009-2010. J Am Med Assoc 308:1668–1675

Trufelli H, Palma P, Famiglini G, Cappiello A (2011) An overview of matrix effects in liquid chromatography-mass spectrometry. Mass Spectrom Rev 30:491–509

Tsilia V, Devreese B, De IB, Mesuere B, Rajkovic A, Uyttendaele M, Van De Wiele T, Heyndrickx M (2012) Application of MALDI-TOF mass spectrometry for the detection of enterotoxins produced by pathogenic strains of the *Bacillus cereus* group. Anal Bioanal Chem 404:1691–1702

Unnevehr L (2015) Food safety in developing countries: moving beyond exports. Glob Food Secur 4:24–29

Van Houdt R, Michiels CW (2010) Biofilm formation and the food industry, a focus on the bacterial outer surface. J Appl Microbiol 109:1117–1131

Van Oort PAJ, de Vries ME, Yoshida H, Saito K (2015) Improved climate risk simulations for rice in arid environments. PLoS One 10:e0118114

Versari A, Parpinello GP, Scazzina F, Rio DD (2010) Prediction of total antioxidant capacity of red wine by Fourier transform infrared spectroscopy. Food Control 21:786–789

Vestal ML (2011) The future of biological mass spectrometry. J Am Soc Mass Spectrom 22:953–959

Vikram A, Prithiviraj B, Hamzehzarghani H, Kushalappa AC (2004) Volatile metabolite profiling to discriminate diseases of McIntosh apple inoculated with fungal pathogens. J Sci Food Agric 84:1333–1340

Villas-Bôas SG, Koulman A, Lane GA (2007) Analytical methods from the perspective of method standardization. In: Nielsen J, Jewett MC (eds) vol 18, pp 11–52

Villas-Bôas SG, Delicado DG, Åkesson M, Nielsen J (2003) Simultaneous analysis of amino and nonamino organic acids as methyl chloroformate derivatives using gas chromatography-mass spectrometry. Anal Biochem 322:134–138

Villas-Bôas SG, Mas S, Åkesson M, Smedsgaard J, Nielsen J (2005) Mass spectrometry in metabolome analysis. Mass Spectrom Rev 24:613–646

Walker CH (1990) Persistent pollutants in fish-eating sea birds—bioaccumulation, metabolism and effects. Aquat Toxicol 17:293–324

Walorczyk S, Kopeć I, Szpyrka E (2015) Pesticide residue determination by gas chromatography-tandem mass spectrometry as applied to food safety assessment on the example of some fruiting vegetables. Food Anal Methods 9:1155–1172

Wan Q, Wu G, He Q, Tang H, Wang Y (2015) The toxicity of acute exposure to T-2 toxin evaluated by the metabonomics technique. Mol Biosyst 11:882–891

World Health Organization (2006) WHO consultation to develop a strategy to estimate the global burden of foodborne diseases. World Health Organization, Geneva, p vii. Available from http://www.who.int/foodsafety/publications/foodborne_disease/fbd_2006.pdf

Xia J, Mandal R, Sinelnikov IV, Broadhurst D, Wishart DS (2012) MetaboAnalyst 2.0-a comprehensive server for metabolomic data analysis. Nucleic Acids Res 40:W127–W133

Xu Y, Cheung W, Winder CL, Goodacre R (2010) VOC-based metabolic profiling for food spoilage detection with the application to detecting *Salmonella typhimurium*-contaminated pork. Anal Bioanal Chem 397:2439–2449

Yang Y, Zheng N, Zhao X, Zhang Y, Han R, Yang J, Zhao S, Li S, Guo T, Zang C, Wang J (2016) Metabolomic biomarkers identify differences in milk produced by Holstein cows and other minor dairy animals. J Proteomics 136:174–182

Yogi K, Oshiro N, Inafuku Y, Hirama M, Yasumoto T (2011) Detailed LC-MS/MS analysis of ciguatoxins revealing distinct regional and species characteristics in fish and causative alga from the pacific. Anal Chem 83:8886–8891

Zeng W, Hazebroek J, Beatty M, Hayes K, Ponte C, Maxwell C, Zhong CX (2014) Analytical method evaluation and discovery of variation within maize varieties in the context of food safety: transcript profiling and metabolomics. J Agric Food Chem 62:2997–3009

Zhan J, Yu XJ, Zhong YY, Zhang ZT, Cui XM, Peng JF, Feng R, Liu XT, Zhu Y (2012) Generic and rapid determination of veterinary drug residues and other contaminants in raw milk by ultra performance liquid chromatography-tandem mass spectrometry. J Chromatogr B Anal Technol Biomed Life Sci 906:48–57

Zhang A, Sun H, Wang P, Han Y, Wang X (2012) Modern analytical techniques in metabolomics analysis. Analyst 137:293–300

Zhang D, Park JA, Kim DS, Kim SK, Shin SJ, Shim JH, Shin SC, Kim JS, Abd El-Aty AM, Shin HC (2015) A simple extraction method for the simultaneous detection of tetramisole and diethylcarbamazine in milk, eggs, and porcine muscle using gradient liquid chromatography-tandem mass spectrometry. Food Chem 192:299–305

Zhang XZ, Li CJ, Chen SS, Li XJ, Han H, Ma XD (2009) Direct determination of atrazine residue on Chinese cabbage leaf using desorption electrospray ionization-tandem mass spectrometry and its application for diagnosing atrazine drift phytotoxicity. J AOAC Int 92:1587–1592

Zhou B, Xiao JF, Tuli L, Ressom HW (2012) LC-MS-based metabolomics. Mol Bio Syst 8:470–481