Journal of Trends in Life Sciences
ISSN: 2960-0200
DOI: 10.61784/jtls240127

THE ROLE OF METABOLOMICS IN FOOD SCIENCE AND ENGINEERING

Scott Wernegreen
University of Connecticut, Storr.

Abstract: Metabolomics is an emerging omics field after genomics, transcriptomics and proteomics, and has become an important part of systems biology. Metabolomics has the characteristics of high throughput, high sensitivity and robustness, and can effectively overcome the limitations of traditional methods. It has received widespread attention in many fields in recent years. This article outlines the analysis process of metabolomics and introduces the application and research progress of metabolomics in food safety, food quality control, food processing, food traceability and the impact of food on human health in recent years.
Keywords: Metabolomics; Food science; High-throughput

1 INTRODUCTION

Metabolomics was first proposed by Professor Jeremy Nicholsonrst in 1999. It is an important part of systems biology. The main research objects are mostly small molecule metabolites with a relative molecular mass of less than 1000, such as sugars, organic acids, amino acids, lipids, etc. [1]. These small molecules originate from cellular metabolism and can not only directly reflect the results of complex biochemical reaction networks, but also combine genomics, metabolomics, proteomics, lipidomics and transcriptomics to describe and analyze growth, genetic modification, and disease., environment and other factors, it plays an important role in human health and disease detection, food quality control and crop quality analysis, and environmental pollution assessment.
Metabolomic analysis can be classified into targeted metabolomics or untargeted metabolomics. Targeted profiling metabolomics focuses on identifying and quantifying specific expected metabolites. Targeted metabolomics often requires higher levels of purification and selective extraction of metabolites. Untargeted metabolomics focuses on detecting as many groups of metabolites as possible without necessarily identifying or quantifying specific compounds. In food science, metabolomics is used in plant, health, and other food research programs. Metabolomics has been considered an effective tool to address the future needs of agriculture and human nutrition [2]. The food metabolome mainly includes metabolites from animals, plants and microorganisms. Various factors such as food type, origin, temperature, and even farming methods will affect food metabolites [3]. At the same time, these metabolites are constantly changing due to microorganisms, processing, storage, and contamination. These changes continue until consumed by the consumer. These changes in food metabolites directly affect food quality and affect the human body in many ways. At present, metabolomics analysis in food has been widely used.

2 METABOLOMICS ANALYSIS PROCESS

There are many types of compounds in the metabolome, and there are currently no methods that can efficiently analyze all of them. Techniques for metabolomics research include traditional NMR, liquid chromatography-mass spectrometry (LC-MS) and gas chromatography-mass spectrometry (GC-MS) and In recent years, capillary electrophoresis-mass spectrometry (CE-MS) and ion mobility spectrometry-mass spectrometry (IM-MS) have emerged [4-9]. To better identify metabolites, these methods are often combined. This results in significant improvements in data sensitivity, resolution and mass measurement accuracy. However, this improvement has produced extremely complex data sets, making metabolomics data processing increasingly challenging [10]. Metabolomics analysis includes a series of steps such as sample preparation, metabolite extraction, derivatization, metabolite isolation, detection and data processing. These steps will have an impact on the results of food metabolomics. Great impact on students.

2.1 Sample Preparation

Food metabolomics samples may come from various sources such as solid food, liquid food, blood, urine, etc., each of which is suitable for different sample preparation methods [11]. Solid food samples are usually ground under liquid nitrogen or after freeze-drying. Proper grinding enhances the release of metabolites during extraction. Lyophilization is a concentration step that minimizes metabolite differences due to differences in moisture content between sample groups. Liquid food samples can be concentrated by lyophilization and solid-phase microextraction (SPME). Harborne et al. compared several drying methods and believed that using lower temperature Tray drying can quickly dry the sample without affecting the metabolites in the sample [12]. Sample preparation is necessary in most experiments, but

there are methods for direct extraction using raw materials. Moco et al. directly used fresh tomato samples for LC-MS analysis [13]. Seeger et al. proposed a new strategy to directly detect original samples in NMR [14]. These methods lay the foundation for rapid detection of metabolites.

2.2 Metabolite Extraction

The extraction step aims to maximize the quantity and concentration of target compounds. Currently, various extraction methods such as pressure extraction, ultrasonic extraction, and supercritical extraction have been applied to food [15-17]. In untargeted metabolomics, where the nature of the target compounds is mostly unknown, several solvents and extraction methods should be tested and compared between groups of samples. Mushtaq et al. compared three extraction technologies: microwave-assisted extraction, solid-phase extraction, and supercritical fluid extraction, and found that extraction technology has a great impact on the metabolites that can be analyzed [18]. Martineau et al. used a variety of solvents with different polarities to extract cellular metabolites and found that methanol or methanol/chloroform/water extracted more metabolites [19]. Ser et al. conducted a systematic evaluation of extraction conditions for metabolite analysis and found that cleaning samples can also have a significant impact on the measurement intensity of intracellular and extracellular metabolites [20]. There are many methods for extracting metabolites, but currently there is no method that can completely extract all metabolites. Many extraction methods also have an impact on metabolites and should be chosen appropriately based on the purpose.

2.3 Derivatization

In food metabolomics, derivatization is often used to increase the volatility of analytes prior to GC analysis. Derivatization is usually a two-step process, starting with oximation of the sample to reduce tautomerism, followed by silylation to reduce the hydrophilicity of the functional groups to increase volatility. The time and temperature of derivatization affect each metabolite independently at the beginning of the reaction. Therefore, preliminary experiments should be conducted to determine the optimal derivatization time and temperature to maximize the detection of target compounds [21-22]. Gao et al. developed a quantitative metabolomics method for human feces based on trimethylsilane derivatization and GC/MS analysis [23]. Lu et al. explored and optimized the derivatization reagent 2-hydrazinoquinoline, which can be used to simultaneously analyze carboxylic acids, aldehydes and ketones in LC-MS [24]. Mochizuki et al. newly synthesized L-pyroglutamic acid succinimide ester and its isotope variants, used it as a derivatization reagent for the separation of amino acid enantiomers, and conducted differential analysis of serum and yogurt respectively to verify This proves the effectiveness of this method [25]. Derivatization is an effective method to improve metabolite detection capabilities and has been applied in many experiments.

2.4 Separation and Detection

Separation and Detection Separation and detection of metabolites are key steps in metabolic profiling. Traditional separation technologies include liquid chromatography (LC), gas chromatography (GC), capillary electrophoresis (CE), etc. Detection techniques include mass spectrometry (MS), nuclear magnetic resonance (NMR) and Near infrared spectroscopy (NIR), etc. In food metabolomics, most separation analyzes have been performed by GC, CE and LC [26-27]. In recent years, ion mobility spectrometry (IMS) has been used for food metabolomic analysis. In this method, food metabolites are ionized in an inert gas flow and separated by gas flowing in the opposite direction [28-29]. Among detection methods, MS and NMR are most widely used in food metabolomics. MS is often used in combination with high-throughput separation techniques such as HPLC or UPLC to obtain large amounts of data. Although not as sensitive as other detection techniques, NIR Provides rapid non-destructive analysis in some metabolomic analyses. Rapid metabolite detection methods have become a trend in the field of food testing. Using FT-Raman, Márquez et al. The method of fusion with NIR data was used to detect samples of hazelnut paste adulterated with almonds, and achieved good results [30]. Direct infusion mass spectrometry (DIMS) does not require prior separation steps to achieve faster results and can be used for rapid detection of large-scale samples. McDougall et al. used direct infusion mass spectrometry technology to conduct high-throughput analysis of polyphenol components in berries [31]. Extraction electrospray ionization mass spectrometry (EESI-MS) is also a rapid detection method. Xue et al. used EESI-MS to analyze broccoli sprout extracts under different light quality treatments. EESI-MS can simultaneously detect 19 compounds within 1 minute [32].

2.5 Data Processing

Metabolomics data are typically processed through compound identification and statistical analysis. Compound identification is primarily achieved through database matching and comparison with pure standards run under the same conditions. Typically, metabolomics data have been corrected for instrumental bias in retention/migration times before comparison, and appropriate data preprocessing methods can greatly enhance the accuracy of statistical analysis. in obtaining generation After metabolite data, some statistical analysis methods still need to be used to transform the data

into meaningful conclusions, such as biomarkers, etc. Based on the applicability of statistical methods, corresponding statistical analysis methods are used for different metabolome data [33]. Commonly used methods include principal component analysis (PCA), partial least squares (PLS), linear discriminant analysis (LDA), least absolute shrinkage and selection operator (LASSO), random forest (RF), etc. PCA is a commonly used dimensionality reduction method in metabolomics to reduce the number of metabolites being analyzed. dimension. PCA creates new variables from linear combinations of detected metabolites while maximizing sample variation. PLS Samples can be distinguished by reducing the dimensionality while maximizing the correlation between variables. It is a supervised discriminant analysis statistical method and is often used to screen biomarkers in metabolomics research [34-35]. PLS has become a dominant technique in predictive metabolomic studies. LDA with a priori classification hypotheses can be used to differentiate samples based on source and find the metabolite variables that best separate the classification result classes. linear combination. LASSO aims to fit a model that reduces the spatial dimensionality of the variables while performing regression analysis for all metabolites. Furthermore, correlation techniques such as correlation network (CN) analysis have successfully identified connections between metabolites and identified possible responses in several formative metabolomics studies. Random Forest (RF) allows multivariate data comparisons without reducing dimensionality and is often used for missing data estimation and outcome analysis in metabolomics, if the relationship between metabolites and outcomes is complex and nonlinear. Often better results can be obtained than other methods [36]. Uarrota et al. used PCA, PLS and other methods to identify the metabolite detection data of different cassava samples and achieved good prediction of the samples [37]. Mazzilli et al. used LASSO regression to evaluate the correlation between dietary questionnaire data and serum metabolites, and found 102 food-related metabolites [38]. Beckmann et al. used random forest to model the relationship between the chemical composition of potato varieties and tuber quality traits, ranked the importance of the subset of metabolite signals that explain the composition differences between individual genotypes, and correctly predicted the relationship between the chemical composition and tuber quality traits in potato tubers. Metabolites related to flavor and pigment properties [39]. Data processing is essential in metabolomics research and is key to linking metabolites to actual traits. By using these statistical methods, people can better understand the relationship between food metabolites, food sources, human health and other aspects.

3 METABOLOMICS APPLICATIONS IN FOOD

3.1 Application of Metabolomics in Food Safety

The application of metabolomics in food safety mainly includes the detection of chemical contaminants and the detection of microbial contaminants. Chemical contaminants mainly detect veterinary drugs and pesticide residues that have strict regulations on the maximum acceptable amount in food [40]. The advantage of metabolomics is that multiple chemical components can be quantified simultaneously. Tengstrand et al. established a method that can detect ppm level contaminants in food by combining ultra-high pressure liquid chromatography and electrospray ionization time-of-flight mass spectrometry, which can be used to detect whether food is contaminated [41]. Inoue et al. used methods such as hydrophilic interaction chromatography, electrospray ionization, and multivariate statistical analysis to evaluate non-targeted compounds in infant formula and detect chemical contaminants in them, which can be used to improve the quality and safety of infant formula. Evaluation[42]. Dasenaki et al. successfully applied liquid chromatography combined with electrospray ionization and tandem mass spectrometry (LC-ESI-MS/MS) to establish a simple and sensitive method for the determination of different categories of drug residues in animal-derived foods [43]. Microbial contaminants can be divided into direct contamination of food by pathogenic microorganisms and indirect contamination by toxins produced by microorganisms. It may originate from any link in food production and may cause harm to the human body. have serious consequences [44]. Compared with the cost of traditional microbiological testing methods, Time-consuming and labor-intensive, metabolomics detection technology can conduct high-throughput detection of microbial contaminants in samples. It has been applied to a certain extent and shows great potential. Carraturo et al. invented a system for real-time monitoring of bacterial contamination of meat matrices, using headspace solid phase microextraction (HS-SPME) and gas chromatography-mass spectrometry (GC/ MS) method to detect volatile organic compounds (VOCs), which can It is fast and accurate enough to detect pathogens in raw meat. It saves time and requires smaller sample volume than traditional methods. It has the potential to be used in different detection methods. Potential for multiple pathogens in food matrices [45]. Bacteria on food can also affect the food itself and the human body. Jahangir used food metabolomics to study the metabolic changes caused by the response of plants such as rapeseed to different typical food-borne bacteria. It was found that different bacteria have different effects on metabolites, and metabolites such as amino acids, alcohols, carbohydrates and phenols can be identified, proving the potential of metabolomics to study the interaction between these food-borne bacteria and vegetables [46].

3.2 Application of Metabolomics in Food Quality Control

The development of novel metabolomic technologies, such as IMS, has allowed the monitoring of quality attributes during food processing, and the ability to identify food components using metabolic profiling can also be used to assess food adulteration and food contamination. Bueno et al. achieved the distinction between conventional tomatoes and

organic tomatoes through markers [47]. Surowiec et al. used OPLS-DA to model the metabolites of meat, achieving the distinction between machine-recycled meat (the product of mechanical processing of residues after manual deboning) and normal meat [48]. Metabolomic data can also be used to study the safety of controversial foods. Ricroch et al. conducted a summary analysis of metabolomics studies on 44 genetically modified crops and concluded that the currently approved genetically modified crops are essentially equivalent to ordinary crops, and there is not much difference in quality [49].

3.3 Application of Metabolomics in Food Traceability

Food metabolites vary depending on genotype and growth conditions (e.g. such as climate, soil composition, fertilization and irrigation). In the past, methods such as chemical chromatography were commonly used to determine certain major and minor components of food to achieve food certification. New methods such as food metabolomics can be a good complement to food certification methods. The main advantage of metabolomics in food certification is that it is non-specific, allowing it to New fraud detected [50]. Klockmann et al. selected and identified 20 major metabolites with significantly different abundances in hazelnuts and used them to identify the geographical origin of hazelnuts [51]. Mazzei used 1H-HRMAS-NMR to directly identify specific metabolites in intact mozzarella cheese samples and found that they came from Campa There are significant metabolic differences between mozzarella cheese samples from two different production locations in Nigeria [52]. Lee et al. found that the content of theanine and catechin derivatives in green tea and white tea has a strong relationship between countries and cities, which can be used to evaluate the quality of tea or the production of tea. Land[53]. Cajka et al. used the direct analysis in real time (DART) ion source combined with high-resolution time-of-flight mass spectrometry (TOFMS) and conducted metabolomic analysis by mass spectrometry (MS) and found its good effect in beer source identification [54]. Different origins Metabolite data for food varieties can provide reliable information about the origin and authenticity of the food.

3.4 Metabolomics Applications in Food Processing

Food processing involves a combination of physical and chemical events that can lead to significant changes in food composition. Traditional food composition analysis includes protein, fat, carbohydrates, fiber, vitamins, trace elements, etc. With the advent of food metabolomics, food and beverages are now analyzed in more detail, with hundreds or even thousands of different chemical components detected and/or identified in some foods [55]. Allows food scientists to understand the molecular details of unique taste, texture, aroma or color in food to improve food processing options. Gallego et al. performed a metabolomic analysis of flavonoids in cocoa cell suspensions under light and dark conditions and found that cells grown under light conditions had a higher degree of polymerization of glycosylated flavonoids and proanthocyanidins and lipids, Flavonoids and phytosterols are increased. demonstrated the potential of cocoa cell suspensions in food biotechnology and the impact of chocolate on human health [56]. Gu et al. detected the metabolites of soybeans after germination and found that germination is a useful processing step to improve the nutritional quality of soybeans. Metabolomic analysis can help understand nutritional changes during germination [57]. Xu et al. developed a prediction method for marked hybrid rice yield using metabolomic data and showed a substantial increase in yield through genomic hybrid breeding [58]. Metabolomic analysis can provide valuable information to the food development industry.

3.5 Applications of Metabolomics in Food and Health

Dietary intake has a strong impact on human health and is associated with a variety of diseases. Exploring food-health associations is challenging due to the diversity of essential nutrients and bioactive compounds in foods and their possible interactions in the body. Traditional methods such as questionnaires can produce subjective estimates of portion size, recall bias, and false positives, making research more difficult [59]. Metabolomics is one solution to this dilemma. Through the detection and research of food intake biomarkers, great progress has been made in the study of food metabolism in the human body. The link between habitual dietary patterns and metabolic profiles was explored by O'Sullivan et al. By measuring metabolites in plasma and urine, O-acetylcarnitine and phenylacetylglutamine were found to be positively correlated with the intake of red meat and vegetables, respectively. Potential biomarkers of red meat and vegetable intake were identified [60]. Langenau et al. identified associations between 44 foods and metabolites in serum, including coffee, fish, chocolate, alcohol, butter, poultry, and wine. And found gender differences in the association between food and serum metabolites [61]. Catalán et al. identified several biomarkers related to food consumption through untargeted metabolomic analysis of plasma and red blood cells, which can be used for nutritional assessment in humans [62]. O'Gorman et al. identified fish biomarkers that can be used to relate fish intake to disease risk in epidemiological studies [63]. Pallister et al. explored dietary regulation and its relationship with metabolic syndrome and found that hippuric acid can be used as a metabolomic marker of intestinal microbial diversity [64]. These studies illustrate the increasingly widespread application of metabolomics in exploring food and health, and these studies will provide important clues to elucidate the relationship between food and health.

4 CONCLUSION

Metabolomics has become a powerful tool in food research, playing an important role in food quality, traceability, contamination, processing, and the relationship between food and health. With the development of rapid detection technologies such as DIMS, IMS and EESI, food metabolomics has shown its potential for use in more and more environments. However, the number of metabolite species in foods is extremely large, and although metabolomics can already analyze hundreds to thousands of molecules in a single experiment, it is expected that there are tens of thousands of possible metabolites in food metabolomes. The chemical compositions, most of which have yet to be determined. At the same time, many The mechanism of the metabolites is also not yet clear. In addition, although metabolomics has been used in conjunction with other analysis methods such as genomics and transcriptomics, a large number of analyzes are still limited to a single technology, and joint analysis has not yet been widely used. The ability of metabolomics to perform discrimination, prediction and information analysis can provide important information to the food industry. In the future, there is potential for further development in breeding, testing, nutrition, medicine and other aspects.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

REFERENCES

[1] Yang Q, Zhang A H, Miao J H. Metabolomics biotechnology, applications, and future trends: A systematic review. RSC Advances, 2019, 9(64): 37245-37257.
[2] Cevallos-Cevallos J M, Reyes-De-corcuera J I, Etxeberria E. Metabolomic analysis in food science: A review. Trends in Food Science & Technology, 2009, 20(11-12): 557- 566.
[3] Johanningsmeier S D, Harris G K, Klevorn C M. Metabolomic technologies for improving the quality of food: Practice and promise. Annual Review of Food Science and Technology, 2016, 7: 413-438.
[4] Beale D J, Pinu F R, Kouremenos K A. Review of recent developments in GC-MS approaches to metabolomics-based research. Metabolomics, 2018, 14(11): 1-31.
[5] Cui L, Lu H T, Lee Y H. Challenges and emergent solutions for LC-MS/MS based untargeted metabolomics in diseases. Mass Spectrometry Reviews, 2018, 37(6): 772-792.
[6] Emwas AH, Roy R, McKay R T. NMR spectroscopy for metabolomics research. Metabolites, 2019, 9(7): 123.
[7] Zhang W, Ram aut ar R. CE -MS for meta bol om ics: Developments and applications in the period 2018-2020. ELECTROPHORESIS, 2021, 42(4): 381-401.
[8] Zhang W, Hankemeier T, Ramautar R. Next-generation capillary electrophoresis-mass spectrometry approaches in metabolomics. Current Opinion in Biotechnology, 2017, 43: 1-7.
[9] Zhang X, Quinn K, Cruickshank-Quinn C. The application of ion mobility mass spectrometry to metabolomics. Current Opinion in Chemical Biology, 2018, 42: 60-66.
[10] Segers K, Declerck S, Mangelings D. Analytical techniques for metabolomic studies: A review. Bioanalysis, 2019, 11(24): 2297-2318.
[11] Ulaszew ska M M, Weinert C H, Trimigno A. Nutrimetabolomics: an integrative action for metabolomic analyses in human nutritional studies. Molecular Nutrition & Food Research, 2019, 63(1): 1800384.
[12] Harbourne N, Marete E, Jacquier J C. Effect of drying methods on the phenolic constituents of meadowsweet (Filipendula ulmaria)and willow(Salix alba). LWT- Food Science and Technology, 2009, 42(9): 1468-1473.
[13] Moco S, Bino R J, Vorst O. A liquid chromatography- mass spectrometry-based metabolome database for tomato. Plant Physiology, 2006, 141(4): 1205-1218.
[14] Seeger K. Simple and rapid(extraction)protocol for NMR metabolomics-direct measurement of hydrophilic and hydrophobic metabolites using slice selection. Analytical Chemistry, 2021, 93(3): 1451-1457.
[15] Mustafa A, Turner C. Pressurized liquid extraction as a green approach in food and herbal plants extraction: A review. Analytica Chimica Acta, 2011, 703(1): 8-18.
[16] Vilkhu K, Mawson R, Simons L. Applications and opportunities for ultrasound assisted extraction in the food industry—A review. Innovative Food Science & Emerging Technologies, 2008, 9(2): 161-169.
[17] Herrero M, Cifuentes A, Ibañez E. Sub- and supercritical fluid extraction of functional ingredients from different natural sources: Plants, food-by-products, algae and microalgae: A review. Food Chemistry, 2006, 98(1): 136-148.
[18] Mushtaq M Y, Choi Y H, Verpoorte R. Extraction for metabolomics: Access to the metabolome. Phytochemical Analysis, 2014, 25(4): 291-306.
[19] Martineau E, Tea I, Loaëc G. Strategy for choosing extraction procedures for NMR-based metabolomic analysis of mammalian cells. Analytical and Bioanalytical Chemistry, 2011, 401(7): 2133-2142.
[20] Ser Z, Liu X J, Tang N N. Extraction parameters for metabolomics from cultured cells. Analytical Biochemistry, 2015, 475: 22-28.

[21] Halket J M, Waterman D, Przyborowska AM. Chemical derivatization and mass spectral libraries in metabolic profiling by GC/MS and LC/MS/MS. Journal of Experimental Botany, 2005, 56(410): 219-243.
[22] OrataF. Derivatization reactions and reagents for gas chromatography analysis. Advanced gas chromatography-progress in agricultural, biomedical and industrial applications, 2012: 83-108.
[23] Gao X F, Pujos-Guillot E, Sébédio J L. Development of a quantitative metabolomic approach to study clinical human fecal water metabolome based on trimethylsilylation derivatization and GC/MS analysis. Analytical Chemistry, 2010, 82(15): 6447-6456.
[24] Lu Y W, Yao D, Chen C. 2 -hydrazinoquinoline as a derivatization agent for LC-MS-based metabolomic investigation of diabetic ketoacidosis. Metabolites, 2013, 3(4): 993-1010.
[25] Mochizuki T, Todoroki K, Inoue K. Isotopic variants of light and heavy l-pyroglutamic acid succinimidyl esters as the derivatization reagents for dl-amino acid chiral metabolomics identification by liquid chromatography and electrospray ionization mass spectrometry. Analytica Chimica Acta, 2014, 811: 51-59.
[26] Zeki Ö C, Eylem C C, Reçber T. Integration of GC- MS and LC-MS for untargeted metabolomics profiling. Journal of Pharmaceutical and Biomedical Analysis, 2020, 190: 113509.
[27] Ortiz-Villanueva E, Benavente F, Piña B. Knowledge integration strategies for untargeted metabolomics based on MCR-ALS analysis of CE-MS and LC-MS data. Analytica Chimica Acta, 2017, 978: 10-23.
[28] Mairinger T, Causon T J, Hann S. The potential of ion mobility-mass spectrometry for non-targeted metabolomics. Current Opinion in Chemical Biology, 2018, 42: 9-15.
[29] Sinclair E, Hollywood K A, Yan C Y. Mobilising ion mobility mass spectrometry for metabolomics. The Analyst, 2018, 143(19): 4783-4788.
[30] Márquez C, López M I, Ruisánchez I. FT-Raman and NIR spectroscopy data fusion strategy for multivariate qualitative analysis of food fraud. Talanta, 2016, 161: 80-86.
[31] McDougall G, Martinussen I, Stewart D. Towards fruitful metabolomics: High throughput analyses of polyphenol composition in berries using direct infusion mass spectrometry. Journal of Chromatography B, 2008, 871(2): 362-369.
[32] Xue A, Liang W J, de Wen S. Metabolomic analysis based on EESI-MS indicate blue LED light promotes aliphatic - glucosinolates biosynthesis in broccoli sprouts. Journal of Food Composition and Analysis, 2021, 97: 103777.
[33] Antonelli J, Claggett B L, Henglin M. Statistical workflow for featureselection in human metabolomics data. Metabolites, 2019, 9(7): 143.
[34] Kalivodová A, Hron K, Filzmoser P. PLS-DA for compositional data with application to metabolomics. Journal of Chemometrics, 2015, 29(1): 21-28.
[35] Szymańska E, Saccenti E, Smilde A K. Double- check: Validation of diagnostic statistics for PLS-DA models in metabolomics studies. Metabolomics, 2012, 8(1): 3-16.
[36] Chen T L, Cao Y, Zhang Y N. Random forest in clinical metabolomics for phenotypic discrimination and biomarkerselection. Evidence-Based Complementary and Alternative Medicine, 2013, 2013: 298183.
[37] Uarrota V G, Moresco R, Coelho B. Metabolomics combined with chemometric tools(PCA, HCA, PLS-DA and SVM)for screening cassava(Manihot esculenta Crantz) roots during postharvest physiological deterioration. Food Chemistry, 2014, 161: 67-78.
[38] Mazzilli K M, McClain K M, Lipworth L. Identification of 102 correlations between serum metabolites and habitual diet in a metabolomics study of the prostate, lung, colorectal, and ovarian cancer trial. The Journal of Nutrition, 2020, 150(4): 694-703.
[39] Beckmann M, Enot D P, Overy D P. Representation, comparison, and interpretation of metabolome fingerprint data for total composition analysis and quality trait investigation in potato cultivars. Journal of Agricultural and Food Chemistry, 2007, 55(9): 3444-3451.
[40] Castro-PuyanaM, Pérez-Míguez R, Montero L. Reprint of: Application of mass spectrometry-based metabolomics approaches for food safety, quality and traceability. TrAC Trends in Analytical Chemistry, 2017, 96: 62-78.
[41] Tengstrand E, Rosén J, Hellenäs K E. A concept study on non-targeted screening for chemical contaminants in food using liquid chromatography-mass spectrometry in combination with a metabolomics approach. Analytical and Bioanalytical Chemistry, 2013, 405(4): 1237-1243.
[42] Inoue K, Tanada C, Sakamoto T. Metabolomics approach of infant formula for the evaluation of contamination and degradation using hydrophilic interaction liquid chromatography coupled with mass spectrometry. Food Chemistry, 2015, 181: 318-324.
[43] Dasenaki M E, Thomaidis N S. Multi-residue determination of 115 veterinary drugs and pharmaceutical residues in milk powder, butter, fish tissue and eggs using liquid chromatography-tandem mass spectrometry. Analytica Chimica Acta, 2015, 880: 103-121.
[44] Li S B, Tian Y F, Jiang P. Recent advances in the application of metabolomics for food safety control and food quality analyses. Critical Reviews in Food Science and Nutrition, 2021, 61(9): 1448-1469.
[45] Carraturo F, Libralato G, Esposito R. Metabolomic profiling of food matrices: Preliminary identification of potential markers of microbial contamination. Journal of Food Science, 2020, 85(10): 3467-3477.

[46] Jahangir M, Kim H K, Choi Y H. Metabolomic response of Brassica rapa submitted to pre-harvest bacterial contamination. Food Chemistry, 2008, 107(1): 362- 368.
[47] Martínez Bueno M J, Díaz-Galiano F J, Rajski. A non-targeted metabolomic approach to identify food markers to support discrimination between organic and conventional tomato crops. Journal of Chromatography A, 2018, 1546: 66-76.
[48] Surowiec I, Fraser P D, Patel R. Metabolomic approach for the detection of mechanically recovered meat in food products. Food Chemistry, 2011, 125(4): 1468-1475.
[49] Ricroch A E, Bergé J B, Kuntz M. Evaluation of genetically engineered crops using transcriptomic, proteomic, and metabolomic profiling techniques. Plant Physiology, 2011, 155(4): 1752-1761.
[50] Cubero -Leon E, Peñalver R, Maquet A. Review on metabolomics for food authentication. Food Research International, 2014, 60: 95-107.
[51] Klockmann S, Reiner E, Bachmann R. Food fingerprinting: Metabolomic approaches for geographical origin discrimination of hazelnuts (Corylus avellana) by UPLC-QTOF-MS. Journal of Agricultural and Food Chemistry, 2016, 64(48): 9253-9262.
[52] Mazzei P, Piccolo A. 1H HRMAS-NMR metabolomic to assess quality and traceability of mozzarella cheese from Campania buffalo milk. Food Chemistry, 2012, 132(3): 1620- 1627.
[53] Lee J E, Lee B J, Chung J O. Metabolomi c unveiling of a diverse range of green tea (Camellia sinensis) metabolites dependent on geography. Food Chemistry, 2015, 174: 452-459.
[54] Cajka T, Riddellova K, Tomaniova M. Ambient mass spectrometry employing a DART ion source for metabolomic fingerprinting/profiling: A powerful tool for beer origin recognition. Metabolomics, 2011, 7(4): 500-508.
[55] Wishart D S. Metabolomics: Applications to food science and nutrition research. Trends in Food Science & Technology, 2008, 19(9): 482-493.
[56] Gallego AM, Rojas LF, Rodriguez HA. Metabolomic profile of cacao cell suspensions growing in blue light/dark conditions with potential in food biotechnology. Plant Cell, Tissue and Organ Culture: PCTOC, 2019, 139(2): 275-294.
[57] Gu E J, Kim D W, Jang G J. Mass -based metabolomic analysis of soybean sprouts during germination. Food Chemistry, 2017, 217: 311-319.
[58] Xu S, Xu Y, Gong L. Metabolomic prediction of yield in hybrid rice. The Plant Journal, 2016, 88(2): 219- 227.
[59] McNamara A E, Collins C, Harsh a P S C S. Metabolomic-based approach to identify biomarkers of apple intake. Molecular Nutrition & Food Research, 2020, 64 (11): 1901158.
[60] O 'Sullivan A, Gibney M J, Brennan L. Dietary intake patterns are reflected in metabolomic profiles: Potential role in dietary assessment studies. The American Journal of Clinical Nutrition, 2011, 93(2): 314-321.
[61] Langenau J, Oluwagbemigun K, Brachem C. Blood metabolomic profiling confirms and identifies biomarkers of food intake. Metabolites, 2020, 10(11): 468.
[62] Catalán Ú, Rodríguez M Á, Ras M R. Biomarkers of food intake and metabolite differences between plasma and red blood cell matrices; a human metabolomic profile approach. Molecular BioSystems, 2013, 9(6): 1411-1422.
[63] O'Gorman A, Brennan L. Metabolomic applications in nutritional research: A perspective. Journal of the Science of Food and Agriculture, 2015, 95(13): 2567-2570.
[64] Pallister T, Jackson M A, Martin T C. Hippurate as a metabolomic marker of gut microbiome diversity: Modulation by diet and relationship to metabolic syndrome. Scientific Reports, 2017, 7: 13670.