Chapter 11

Food Metabolomics: A New Frontier in Food Analysis and its Application to Understanding Fermented Foods

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Additional information is available at the end of the chapter

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Abstract

The emergence of food metabolomics, otherwise known as foodomics, has opened new frontiers and possibilities for scientists to characterize and simultaneously determine and obtain the comprehensive profile of the food metabolome. Qualitative and quantitative determinations of this metabolome offer insights into the underlying processes involved and details about the content of the food analytes. This had seemed technically challenging and impossible over time, but can now be done due to the advent of sophisticated analytical equipment and chemometric tools. The application of this technique offers enormous opportunities to obtain detailed information that can be correlated to various properties, functionalities and potentials in fermented foods. This chapter thus evaluated and documented studies presented in the literature on the food metabolomics study of fermented foods, with a view of appraising its prospects, applications and subsequent utilization in the study of fermented foods.

Keywords: foodomics, food metabolomics, fermentation, fermented foods, chemometrics

1. Introduction

Fermentation continues to be a viable food processing technique all over the world. This might be attributed to the ease and simplicity of the process and its numerous other benefits, including providing variety in foods, improving palatability and aesthetic value, detoxification and imparting desirable sensorial properties [1–3]. Furthermore, it plays significant role in conferring health promotion and functional benefits to fermented foods. In line with this are different

studies on fermented foods reporting their ability to reduce diarrhea, malnutrition, encourage child growth and development, exhibit nutraceutical and functional effects including being antidiabetic, antihypertensive, chemoprotective, reducing oxidative stress, cardiovascular diseases and possessing probiotic properties [1–8]. Sequel to these benefits and the ever growing market for functional foods, fermented food products are positioned as food sources that can improve consumer well-being and reduce the risk of diseases.

Although fermentation like other food processing techniques is needed for the transformation of food prior to consumption, it results in structural changes, formation, modification and/or degradation of compounds and an increase or decrease in these constituents could occur. Characterization and comprehensive monitoring of the metabolic, physicochemical, biochemical and structural changes occurring during the fermentation process have thus been relatively difficult. The advent of food metabolomics, also known as "foodomics" enables scientists to obtain detailed and comprehensive molecular profile of thousands of metabolites in foods, all in a single run [9, 10]. Food metabolomics thus presents a holistic approach of providing insight, resolving and identifying the complexities and multifunctionality of fermentation and its subsequent food products.

According to Cifuentes [9] and Garcia-Canas [11], food metabolomics is a valuable and promising tool for food processors and scientists to understand the metabolome of food, including its biochemistry and composition. Being one of the "omics" technology, it offers enormous opportunities to obtain detailed information that can be correlated to the functional and nutraceutical composition of foods. This chapter thus provides an overview of food metabolomics studies that have applied this to fermented foods in the literature and its prospects for further use.

2. Fundamentals of food metabolomics

Metabolomics itself is designated to mean a comprehensive analysis, study, identification and quantification of "as many small metabolites" as possible in a system at a specific time and condition through the use of omics technologies [12–18]. Related to this and taking a cue from earlier authors [9, 11, 19, 20], food metabolomics or foodomics can thus be defined as the study of "as many small metabolites" in food under a specific condition and time through the application of omics technologies. It is a discipline involving the combination of food, nutrition, advanced analytical and data processing techniques and bioinformatics. According to Wishart [21], metabolomics permits the simultaneous characterization of a variety of compounds and metabolites and thus offer food and nutrition scientists the privilege to acquire comprehensive and detailed molecular composition of food. This feature makes metabolomics applicable to different aspects of food science including food safety, food quality, functional foods, food microbiology, food processing and nutrition (**Figure 1**). Sequel to the potential embedded in food metabolomics, scientists are gradually utilizing advanced analytical strategies as opposed to the traditional and classical existing methodologies, which does not provide the much-needed information to understand the complexities in food. Such complexities are however compounded in fermented foods, containing a variety of nutrients, compounds and

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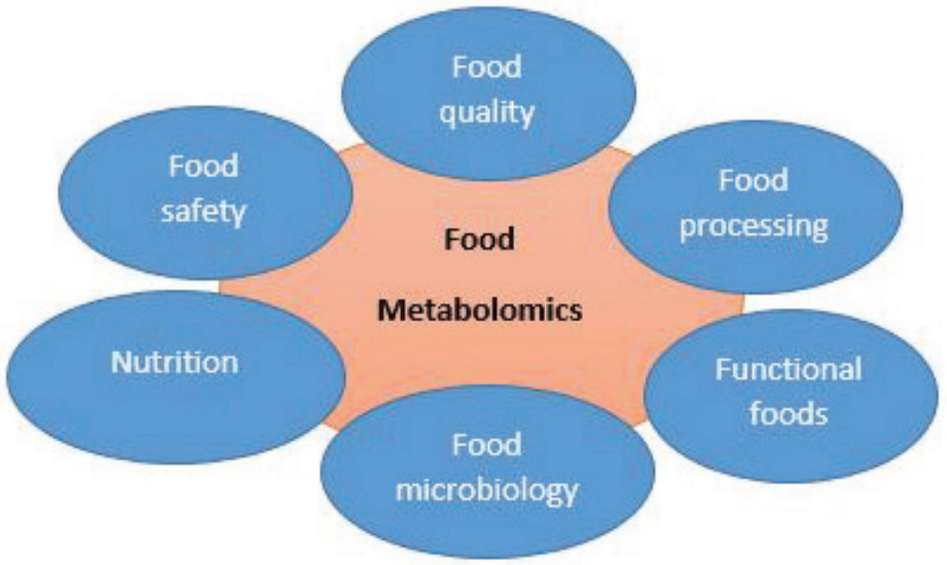

Figure 1. Different aspects of food metabolomics.

volatiles with diverse concentrations, chemical structures, affinity and polarities. Food metabolomics thus provides the opportunity for understanding this multifaceted analyte.

As with another metabolomics study, food metabolomics analyses can generally be classified into either targeted or untargeted. The targeted analysis focuses on a specific group of intended metabolites with such requiring subsequent quantification and identification [18, 22]. They are thus more detailed and require greater levels of extraction and purification prior to analysis. In contrast to targeted analysis, untargeted metabolomics analysis is broader and focused on the detection of a variety of metabolites to obtain fingerprints or patterns without essentially quantifying or identifying specific metabolites [16, 23, 24].

3. The process of food metabolomics analysis

Every metabolomics analysis consists of a sequence of steps prior to obtaining the data [16, 19, 24]. Not all the steps, depicted in **Figure 2** are not, however, necessary for food metabolomics or any other metabolomics studies. Major factors that determine the selection of steps include the type of study (targeted or untargeted), sample form (solid, liquid) and the available instrumentation and detection technique [gas chromatography-mass spectrometry (GC-MS), liquid chromatography-mass spectrometry (LC-MS), nuclear magnetic resonance (NMR), etc.] [16]. A description of these steps is nevertheless summarized in the ensuing sections of this chapter.

3.1. Sample preparation

Sample preparation is essential and vital in any analysis. This is needed to prepare the sample into a "ready state" form, release the analyte (metabolites) available, reduce experimental error

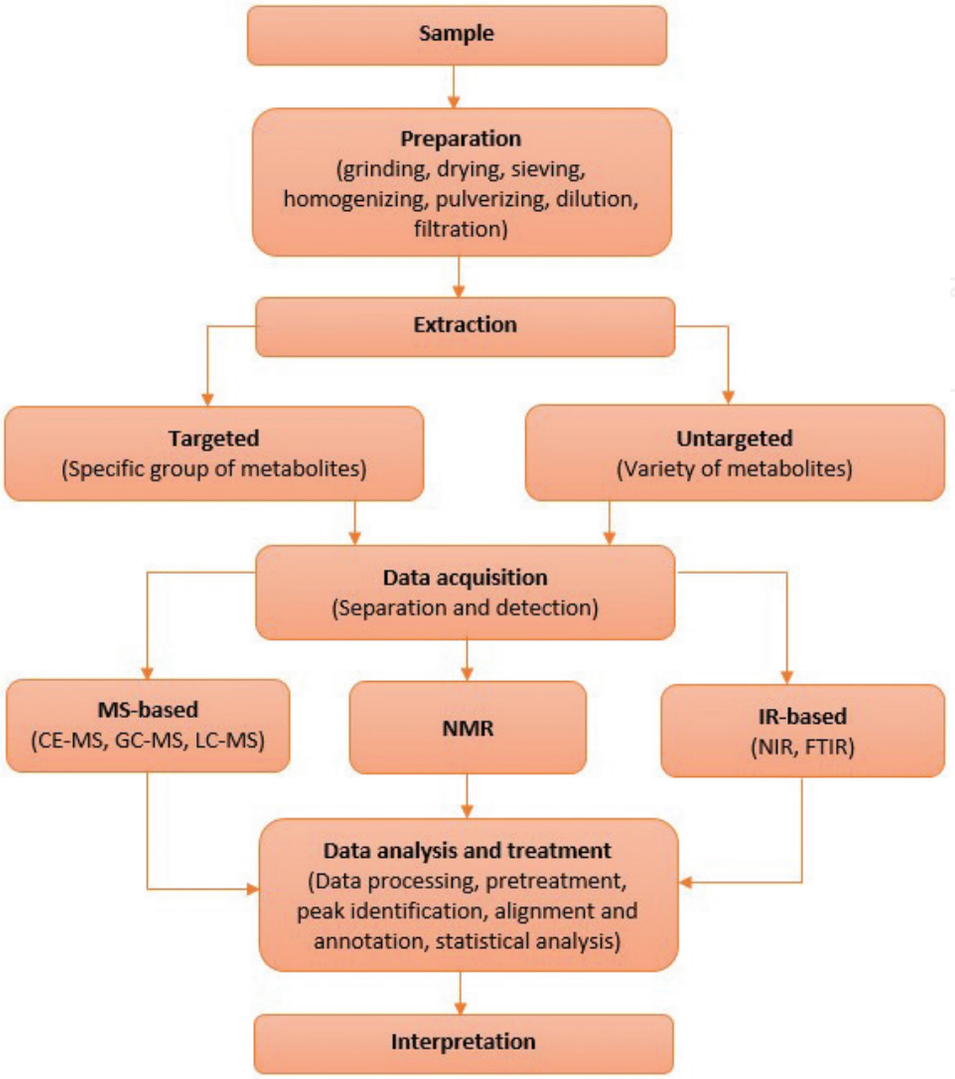

Figure 2. Schematic presentation of the food metabolomics process.

and ensure the analytical procedure is reproducible. Grinding, size reduction and homogenization are some of the needed steps prior to analysis to ensure proper mixing and present a sample that is a true representative. The concentration of samples is also important with freeze-drying and use of liquid nitrogen commonly used in food metabolomics studies of fermented foods. This not only concentrates the metabolites but also reduces the possibility of losing heat labile components during conventional oven drying techniques. Both freeze drying and liquid nitrogen have been applied in the preparation of fermented foods in food metabolomics studies for *cheonggukjang* [25, 26], *meju* [27], *doenjang* [28] and cocoa beans [29]. Nevertheless, care must be taken to avoid the introduction of any form of unwanted variability throughout this step, which might result in significant experimental discrepancy, that would surpass biological variance. Sampling conditions and time should also be controlled to limit inconsistency in results.

3.2. Extraction

Among the many steps for food metabolomics studies, extraction is a vital and important one. Considering the varying and diverse constituents and composition of fermented foods,

including but not limited to amino acids, organic acids, phytochemicals, sugars, minerals, nucleic acids, vitamins and other volatile compounds, extraction may be somewhat tricky. Hence, extraction techniques to be utilized would be largely dependent on the form of study (targeted or untargeted), characteristics, number and quantity of metabolites of interest [15, 30, 31]. Extraction protocol would not thus be an express decision but rather influenced by the focus of analysis (study).

For targeted analysis, a suitable purification scheme and the use of appropriate internal standards is important [15]. This might not be the case for untargeted analysis due to the need to target as many metabolites as possible. Extraction techniques commonly used for fermented foods are solvents (methanol, chloroform, ethanol, acetonitrile) [27, 28, 32], similar to those used in other metabolomics studies [15, 17, 24, 31]. When the focus of the study is on specific non-volatile metabolites, derivatization may be required prior to analysis on GC-MS. This is necessary to make sure the samples are thermostable, increase volatility and improve the detectability of the analyte [16, 18].

3.3. Data acquisition

Data acquisition in form of separation and detection of metabolites is a key step in metabolomics studies. It essentially requires advanced analytical techniques, considering the complexity, diversity and number of metabolites to characterize in food [16, 18]. Separation techniques commonly used for food and fermented foods include high-performance liquid chromatography (HPLC), ultra-performance liquid chromatography (UPLC), gas chromatography (GC), capillary electrophoresis (CE) and ion mobility spectrometry (IMS) [16, 18, 21, 33]. Detection techniques include mass spectrometry (MS), NMR, high-resolution magic angle spinning (HRMAS) NMR, Fourier transform (FT) NMR, near infrared spectroscopy (NIR) and Fourier transform infrared spectroscopy (FTIR) [15, 16, 18, 21]. A detailed review and working principle of these separation and detection techniques have been presented in the literature and can be consulted for further reading [15, 18, 21, 24, 30, 31, 34, 35].

In the studies of fermented foods using metabolomics, most separation are either done by GC or LC (for polar compounds), while detection is done majorly by MS with few other studies reporting the use of NMR and FTIR. A major consideration and factor in the use of GC and LC is their higher sensitivity and separation. While GC–MS is usually utilized for the determination of primary metabolites i.e., carbohydrates, amino acids, organic acids, fatty acids and phytochemicals, LC–MS are frequently employed for secondary metabolites including alkaloids, flavonoids, phenolic acids, peptides, polyamines and saponins [31, 36]. As indicated by Tugizimana et al. [24], developments towards the enhancement of chromatographic include the use of multidimensional separation systems such as two-dimensional liquid chromatography (LC × LC) and two-dimensional gas chromatography (GC × GC). Furthermore, the use of better MS platforms including time of flight (TOF), Orbitrap, MS × MS/MS^n provides better resolution, higher scan speeds, detailed fragmentation information, higher resolution, selectivity and better molecular specificity as seen with the Pegasus HRT GC. For separation, MS is most preferred and coupled with either GC or LC, it allows for the comprehensive evaluation and discrimination of compounds [18]. It should, however, be noted that due to the varying behaviors, polarity, volatility, structure, configuration, solubility and molecular weight of different metabolites in fermented

foods, a single data acquisition technique for the detecting and separating all these components is quite impossible. A combination of different techniques would rather provide a better analytical potential for a full metabolomics study.

3.4. Data analysis and treatment

Metabolomic studies are quite synonymous with the generation of a large amount of data, that may be somewhat confusing at first. Subsequent analysis of such high-throughput data can be roughly divided into two: pretreatment and analysis [37]. Handling these huge data would require an automated software for quantification and identification [24]. Pretreatment basically involves alignment, normalization, compound identification, centering, transformation, scaling, removing baseline artefacts and peak picking [16, 24, 38, 39], in order to convert the raw data set into a form that can be utilized for subsequent analysis. Succeeding analysis of the cleaned data in food metabolomics studies are majorly done using different chemometric tools, to provide a description and understanding of the variations and/or similarities in the metabolites. Wold [40] has defined chemometrics as a branch of science concerned with the data analysis (extracting information from data), ensuring that the data set contains maximum information using several mathematical multivariate data analysis (MVDA) tools.

Depending on the purpose of the food metabolomics study, there are three major categories of MVDA. These are exploratory/informative, classification/discrimination and regression/prediction [16, 38, 41]. While informative analyses are focused on identification and quantification to obtain sample intrinsic information (such as the development of metabolite databases and the discovery of biomarkers), discriminative analyses are majorly aimed at finding differences between samples/treatments [16, 42]. In contrast, predictive models are focused on quantification and prediction of a variable that may be difficult to quantify [16, 38]. MVDA tools commonly used in food metabolomics studies include artificial neural networks (ANN), principal component analysis (PCA), orthogonal projection to latent structures-discriminant analysis (OPLS-DA), partial least square discriminant analysis (PLS-DA), principal component regression (PCR), hierarchical cluster analysis (HCA), canonical correlation analysis (CCA) and others [16, 38, 43]. Detailed strategies, algorithms and explanation on these MVDA techniques have been described in detail elsewhere [24, 39, 43–46].

4. Food metabolomics of fermented foods

Food metabolomics has been applied and adopted in the study of different foods in the literature [11, 16–18, 21, 33, 47, 48]. Specifically, for fermented foods, which is the focus of this chapter, it is conventionally used to observe, monitor metabolite changes occurring during fermentation and to investigate the composition of such fermented food. Such knowledge has assisted in providing a comprehensive understanding of the fermentation process and probably predict sensory, nutritional, functionality and nutraceutical quality of the final fermented product. Few studies presented in the literature on food metabolomics studies of fermented foods are summarized in **Table 1**. This section of this chapter would thus focus on the

documented changes in metabolite groups and the use of metabolomics in understanding the modifications occurring during the fermentation process of these foods.

Metabolites produced during the fermentation of a Korean cuisine called *cheonggukang*, have been investigated by several authors [25, 26, 49–51] (**Table 1**). Using ^{1}H NMR, Choi et al. [25] observed a decrease in sugars and citric acid with fermentation time. Acetic acid, phenylalanine and tyrosine however increased with time. Baek et al. [49], reported a total of 5 sugar alcohols, 10 sugars, 7 organic acids and 20 amino acids in the same product after obtaining it using different *Bacillus* sp. with subsequent analysis on gas chromatography-time of flight mass spectrometry (GC-TOF-MS). Most of the amino acids showed increasing amounts with time, sugars and sugar alcohols (arabitol, ribitol, sorbitol, myoinositol and lactitol) showed decreases, whereas there were variations in organic acids. Similar occurrences and variations in amino acids, organic acids and also fatty acids, carbohydrates, soyasaponins, isoflavonoids and nucleosides were observed using different metabolomics techniques [26, 50, 51].

Chen et al. [52] reported the occurrence of 28 metabolites including 13 amino acids, six organic acids, three organic bases and sucrose in fermented crab paste as analyzed on NMR. Using PCA and OPLS-DA the authors were able to observe a decline in taurine, betaine, trigonelline, trimethylamine-N-oxide and inosine with an accumulation of sugars and hypoxanthine. 53 compounds including organic acids, alcohols, sugars, amino acids were identified from the metabolomic profiling of *daju* fermented with *Bacillus licheniformis* [53]. Using NMR and PCA, the authors observed a decomposition of polymers such as protein, starch and cellulose to smaller monomers and accumulation of saccharides. *Doejang*, a Korean delicacy has been studied using food metabolomics techniques (**Table 1**). Characterization and profiling on ^{1}H NMR, GC-MS, GC-TOF-MS and data analysis on PCA, PLS-DA revealed the presence of amino acids, sugars and sugar derivatives and organic acids in *doenjang* [28, 54]. Using PCA, Yang et al. [54] was able to discriminate *doenjang* samples fermented for different days and reported increasing levels of amino acids, with no significant change in sugars and variation in the levels of fatty acids. Likewise, Lee et al. [28] observed an increase in monosaccharides, sugar alcohols and most amino acids during fermentation of *doenjang*. Variations were also observed in the levels of organic acids, fatty acids isoflavones and soyasaponins [28]. Kang et al. [27], reported a decrease in the concentration of citric acid during fermentation, with variations in the quantities of peptides, amino acids, nucleosides, organic acids and urea cycle intermediates were reportedly altered throughout the fermentation process.

Using both GC-MS, high-performance liquid chromatography coupled to a diode array detector (HPLC-DAD) in combination with hierarchical cluster analysis (HCA), a strong correlation was observed between volatiles, flavonoids and polyphenolic compounds of two types of wheat dough [55]. The authors observed a general increase in polyphenol content of the wheat doughs, but a diverse metabolite profile in the two wheat substrates used. Likewise, Mayorga-Gross et al. [29] investigated the metabolites changes occurring during cocoa fermentation on an ultra-high performance liquid chromatography with electrospray ionization quadrupole time of flight mass spectrometry (UPLC-ESI^{+}-Q-TOF-MS) system and adopted a PLS-DA model for data processing. The clustering of ions according to retention times and mass spectrum on the PLS-DA model yielded a total of 37 discriminating metabolites. Sugars,

Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
Cheonggukjang	Soybean	Al[a]↑↓	1, 2, 3, 4-tetrakis[(trimethylsilyl)oxy]-butane, 2, 3-bis (trimethylsilyl)-butane, δ-tocopherol, γ-tocopherol, D-ribitol, tyramine, glycerol, hydroxylamine, phytol	^{1}HNMR*,CE-TOF-MS*, GC-FID[δ],GC-TOF-MS*,LC-MS/MS*	PCA, PLS-DA	[25, 26, 49–51]
		Am[b]	1,3-diamino-propane, phenethylamine, putrescine, tryptamine, serotonin, spermidine			
		AA[c]	α-aminobutyric, β-alanine, γ-aminobutyric (GABA), *g*-aminobutyric, 2, 6-diaminopimelate, alanine, aminoadipate, arginine, asparagine, aspartic, betanine, choline+, citrulline, DL-2-aminobutyric, DL-asparagine, DL-cysteine, DL-glutamine, DL-homoserine, DL-leucine, DL-methionine, DL-*N*-acetyl-serine, DL-ornithine, DL-phenylalanine, DL-threonine, DL-tryptophan, DL-valine, glutamic, glutamate, glycine, histidine, homotyrosine, homovaline, hydroxyproline, isoleucine, leucine, lysine, L-arginine, L-aspartic, L-cysteine, L-histidine, L-isoleucine, L-lysine, L-serine, L-tyrosine, methionine, *N*-*a*-acetylornithine, *N*-acetyl-glutamic acid, ornithine, phenylalanine, proline, pyroglutamate, pyroglutamic, serine, threonine, tryptophan, tyrosine, valine			
		SUG, SUGDs[d]	δ-trehalose, arabinose, arabitol, D-fructose, D-galactosamine, D-glucosamine, D-lactose, D-maltose, D-pintol, D-ribose, D-xylobiose, D-xylose, fructose, fructose-6-phosphate, galactose, galactinol, glucose, glucose-6-phosphate, inositol, isomaltose, lactate, lactitol maltose, mannose, mannotriose, melibiose, myo- ribitol, *N*-acetyl-raffinose, ribose, sorbitol, sucrose, xylose			
		FA[e]	Arachidic, behenic, linoleic, linolenic, myristic, oleic, palmitic, palmitoleic, stearic			
		IFVN[f]	6″-*O*-acetyldaidzin, 6″-*O*-acetylgenistin, 6″-*O*-malonylglycitin, daidzin, glycitin, genistin, quercetin-tri-*O*-β-glucopyranoside			
		NTs[g]	Adenine, adenosine, cytidine, cytosine, dihydrouracil, guanine, guanosine, hypoxanthine, thymine, uracil, xanthine			

Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		OA[h]	2-hrdoxyisobutyric, 2-hydroxy-glutaric, 3-methyl-2-[(trimethylsilyl)oxy]-pentanoic acid, acetic, benzenepropanoic, calcium pantothenate, *cis*-aconitate, citric, citrilamic, D-galacturonic, DL-isocitric, DL-lactic, Dl-malic, formic, fumaric, galactaric, gluconic, glutamic, glutaric, glycerate, glycolic, itaconic, lactic, malic, malinic, malonic, *n*-octadecanoic, oxalic, palmitic, phenylpyruvate, quinate, saccharic, shikimic, succinic, succinate, tartaric, *trans*-aconitic acid, *trans*-caffeic, *trans*-sinapic, trimethylsilyl, 3, 5-bis(trimethylsilyl)-3-methylvalerate			
		SSAPN[i]	A3, Bg, I, II, IV, V			
		V[j]	1, 3-diamino-propane, phenethylamine, putrescine, tryptamine, serotonin, spermidine			
			Choline, nicotinic acid			
		O[k]	3-amino-2-one-piperidin, allantonate, glycero-3-phosphate, mevalonolactone, phosphoric acid, R-(−)-1-amino-2-propanol, trigonelline, urea			
Crab paste	Crab	AA[c]	Alanine, arginine, glutamate, glycine, histidine, isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine, valine	^{1}HNMR[*]	PCA, OPLS-DA	[52]
		OA[h]	Acetate, formate, fuarate, lactate, succinate, taurine			
		OB[l]	Betaine, trimethylamine (TMA), trimethylamine-*N*-oxide			
		PUR, PYR[m]	2-pyridinemethanol, adenosine diphosphate (ADP), hypoxanthine, inosine, trigonelline			
		SUG[d]	Sucrose			
Daqu	Barley and peas	Al[a]	Ethanol, glycerol, isopropanol	^{1}HNMR[δ]	PCA	[53]
		AA[c]	2-Aminobutyrate, cysteine, glutamate, glycine, glycylproline, homoserine, isoleucine, proline, serine, threonine			

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Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		SUG, SUGDs[d]	Arabinitol, fructose, galactitol, galactose, glucose, gluticol, lactose, maltose, mannitol, myo-inositol, ribose, sucrose			
		OA[h]	2-hydroxyisobutyrate, 2-phosphoglycerate, acetate, glycerate, glycolate, isobutyrate, lactate, pyruvate, succinate, taurine			
		OB[l]	Betaine, *cis*-aconitate			
		O[k]	Acetone, allantoin, ascorbate, choline, ethylene glycol, galactonate, maltate, malonate, *N*-nitrosodimethylamine, *O*-phosphocholine, *O*-phosphoserine, oxypurinol, propionate, propylene glycol, *S*-sulfocysteine, urea			
Doenjang	Soybean	AA[c]	γ-aminobutyric, alanine, aminoaldiphic, aminobutyric, asparagine, aspartic, glutamine, glutamic, glycine, histidine, isoleucine, leucine, lysine, methionine, ornithine, phenylalanine, proline, pyroglutamic, sarcosine, serine, thioproline, threonine, tryptophan, tyrosine, valine	^{1}HNMR[δ]	PCA, PLS-DA	[28, 54]
		SUG, SUGDs[d]	α-glucose, β-glucose, arabinose, arabitol, erythrose, fructose, galactonic, galactose, glucitol, glucose, glycerol, glucosamine, inositol, mannitol, mannose, maltose, melibiose, *myo*-inositol, raffinose, ribitol, ribonic acid, sucrose, xylitol	GC-TOF-MS[*], UPLC–Q-TOF-MS[*]		
		FA[e]	Arachidic, behenic, caproc, eicosanic, eicosadienoic, lauric, linoleic, linolenic, magaric, myristic, oleic, palmitic, palmitoleic, pentadecyclic, stearic, tricosanoic			
		IFVN[f]	Acetyldaidzin, acetylgenistin, acetylglycitin, daidzin, daidzein, genistin, glycitin, glycitein, malonyldaidzin, malonyglycitin, malonygenistin			
		OA[h]	2-ketoglutaric, acetic, carbonic, citric, formic, fumaric, glucaric, glycolic, lactate, lactic, maleic, malic, malomic, malonic, manelic, oxalic, pipecolic, propionic, pyroglutamic, succinic, vanilic			
		SSAPN[i]	γg, γa, Bd, Be, I, II, III, IV, V			

Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		O[k]	Choline, phosphocholine			
Fermented cereal	Wheat	Al[a]	1-decanol, 1-dodecanol, 1-octanol, 1, 2-dodecanediol, 7-methyl-4-octanol, dimethyl-1-octanol, ethylalcohol, hexanol, isoamylalcohol, methyl-2-buten-1-ol, methyl-3-heptanol, octadien-2-ol, octen-3-ol, pentanol, phenethylalcohol	SPME-GC-MS[*]	HCA	[55]
		C[n]	1, 1, 3-trimethyl-3-cyclohexene-5-one, 6-methyl-5-hepten-2-one, acetoin, decadienal, dodecanal heptanal, hexanal, methylpentanal, nonadienal, nonanone, octanone, octenal, pentanal	HPLC-DAD[δ]		
		H[o]	1, 2-dimethyl-benzene, 1, 3-hexadiene, 2-ethyl-furan, 2-penthyl-furan, 2-methyldecane, 3-methyl-dodecane, 4-methyl-dodecane, 5-methyldodecane, 10-methylnonadecane, 10-methyl-eicosane, furanone			
		OA[h]	2-methylbutanoic, 3-methylbutanoic, acetic, dodecanoic, pentanoic, hexanoic, heptanoic			
		O[k]	Ester			
Fermented cocoa beans	Cocoa beans	CTH, CTHd[p]	Epicatechin, *O*-hexoside-proanthocyanidin A5′, *O*-pentoside-proanthocyanidin A5, procyanidin	UPLC-ESI-QTOF-MS[*]	PCA, PLS-DA,	[29]
		O[k]	Tripeptide, sucrose			
Fermented tea	Green tea, black tea	AA[c]	Glutamine, glutamic acid, glucoside, histamine, leucine, phenylalanine, proline, theanine, theanine-glucoside, tyrosine, tryptophan, valine	^{1}HNMR[*], UHPLC-QTOF-MS[*]	PCA	[56, 57]
		Ak[q]	Caffeine, choline, glycerophosphocholine, theobromine			
		CTH, CTHd[p]	3-galloylprocyanidin B1, Cathechin, epiafzelechin, epicatechin-3-gallate, epicatechin, epicatechin gallate, epigallocatechin, epigallocatechin gallate, epigallocatechin methylgallate, theaflavin-3-gallate, theaflavin 3, 3′-digallate, theaflavin-3′-gallate, theasinensin A, theasinensin F, pigallocatechin-3-gallate, procyanidin B1, procyanin B2			

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Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		FVNG, VOG[r]	Apigenin-6, 8-C-diglucoside, apigenin 6-C-glucoside 8-C-arabinoside, apigenin-6-C-arabinoside-8-C-glucoside, isoquercitrin, isovitexin, kaempferol 3-O-galactosylrutinoside, kaempferol 3-O-glucosylrutinoside, kaempferol-3-O-galactoside, kaempferol-3-O-glucoside, kaempferol-3-O-rutinoside myricetin 3-galactoside, quercetin-3-O-galactoside, quercetin 3-O-glucosylrutinoside, rutin			
		L[s]	LysoPC, MG			
		NTs[g]	(S)-5′-deoxy-5′(methylthio)adenosine, 5′-deoxy-5′(methylthio)adenosine, adenine, guanosine, inosine			
		OA[h]	3-O-*p*-coumaroylquinic, 4-O-*p*-coumaroylquinic, *p*-coumaric, caffeoylshikimic, theogallin			
		SUG[d]	α-glucose, β-glucose, sucrose			
		O[k]	Caffeine, gallic acid, *N*-(1-deoxy-1-fructosyl)leucine, *N*-(1-deoxy-1-fructosyl)tyrosine, *N*-vinyl-2-pyrrolidone, *O*-demethylfonsecin, theanine, unknown compounds			
Fermented milk	Milk	AA[c]↑↓	3-aminobutyric, alanine, arginine, asparagine, aspartic, GABA, glutamine, glycine, isoleucine, methionine, threonine	CE-TOF-MS*		[58]
		Am[b]↓	Cyclohexylamine			
		OA[h]↓↑	2-oxoglutaric, citric, isocitric			
		PUR↑↓	Adenine, guanine, hypoxanthine			
		P[t]↑	Ala-Pro, Leu-Pro, Pro-Pro, Val-Leu, Val-Pro, Val-Pro-Pro			
		SUG[d]↓	Fructose 1, 6-diphosphate			
		V[j]↓	Pyridoxamine			
Fermented soymilk	Soymilk	AA[c]↓	Phenylalanine, tyrosine	^{1}HNMR*	PCA	[59]

Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		OA[h]↑↓	Acetic, citric, fumaric, lactate, lactic, malic, oxalacetic, succinic,			
		SUG[d]↓	Raffinose, stachyose, sucrose			
		O[k]	Choline			
Fermented soybean	Soybean	AA[c]↑↓	Aspartic, GABA, glutamic, glycine, pyroglutamic, serine, threonine	GC-TOF-MS[δ], LC-ESI-MS[δ]	PCA, PLS-DA	[60]
		SUG, SUGDs[d]↑↓	Arabitol, fructose, galactose, maltose, mannitol, myo-inositol, ribose, sorbitol, tagatose			
		FA[e]↑	Palmitic, pentadecanoic, stearic			
		IFVN[f]↑↓	8-hydroxydaidzein, acetyldaidzin, acetylglycitin, acetylgenistin, daidzein, aidzin, genistin, glycitein, glycitin, hydroxygenistein, hydroxyglycitein			
		NT[g]↑	Uracil			
		OA[h]↓	Cinnamic, citric, malomic			
		SSAPN[i]	I			
Gochujang	Wheat/rice	AA[c]	Alanine, GABA, glycine, glutamic, isoleucine, leucine, phenylalanine, proline, pyroglutamic, serine, threonine, tyrosine, valine	UPLC-Q-TOF-MS[*], GC-TOF-MS[*]	PCA, PLS-DA	[61]
		Ak[q], DPH[u]	Alnustone, dihydrocapsaicin, capsaicin			
		IFVN[f], FLVD[v]	Apigenin-diglucoside, daidzein, glycitein, genistein, hydroxydaidzen, kaempferol, luteolin-diglucoside			
		L[w]	Lyso (PC16:0, PC18:1, PC18:2)			
		SUG[d]	Adonitol, arabinose, erythritol, fructose, fumaric, gentibiose, glucitol, gluconic, glucose, glycerol, glyceryl-glucoside, lactose, inositol, myo-inositol, xylose, xylitol			
		OA[h]	Citric, malic, malonic, phosphoric, propanoic, succinic			
		SSAPN[i]	I, III, V			

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Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		O[k]	glyceryl-glucoside, unknown compounds			
Kimchi	Vegetables	AA[c]↑↓	δ-aminobutyric, alanine, asparagine, aspartic, glycine, glutamic, glutamine, leucine, ornithine, proline, threonine, valine	GC-MS*	PCA, PLS-DA	[62]
		SUG, SUGDs[d]↑↓	D-fructose, galactose, glucose, glycerol, mannitol, myo-inositol, sucrose, xylose			
		OA[h]↑↓	1-Propene-1, 2, 3-tricarboxylic acid, 2-keto-L-gluconic acid, 2, 3, 4-trihydroxybutyric acid, citric, fumaric, gluconic, isocitric, lactic, malic, octadecanoic, palmitic, pentanedioic, propanoic, pyrotartaric, ribonic, succinic			
		O[k]↑↓	Adenine, Urea			
Koji	Rice	AA[c]↑↓	Alanine, aspartic, GABA, glutamic, glycine, isoleucine, leucine, lysine, methionine, ornithine, phenylalanine, proline, pyroglutamic, serine, threonine, tryptophan, tyrosine, valine	GC-TOF-MS*, UHPLC-LTQ-IT-MS/MS*	PCA, PLS-DA	[63]
		FA[e]↑↓	Hydroxy-oxo-octadecenoic, linoleic, linolenic, oleic, palmitic, pinellic, stearic			
		FLVN[v]↑↓	Apigenin-C-glucosyl-C-arabinoside, chrysoeriol-hexoside, chrysoeriol-rutinoside, isovitexin-O-glucoside, tricin, tricin-7-O-rutinoside, tricin-O-glucoside			
		LPL[x]↑↓	Lyso (PE14:0, PC14:0, PC18:3, PC16:1, PE18:2, PC18:2, PE16:0, PC16:0, PC18:1)			
		OA[h]↑↓	Citric, fumaric, gluconic, glyceric, kojic, lactic, malic, malonic, shikimic, succinic, oxalic,			
		PA[y]↑↓	4-hydroxybenzoic acid, ferulic acid			
		SUG, SUGDs[d]↑↓	Erythritol, fructose, glucose, glycerol, maltose, *myo*-inositol, pentitol, sorbitol, xylose, xylitol,			

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Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
V[j]↑↓	Nicotinic acid					
O[k]↑↓	Bacillibactin, unknowns					
Makgeolli	Rice	AA[c]	Alanine, asparagine, glutamic, glutamine, glycine, leucine, lysine, ornithine, proline, pyroglutamic, tryptophan, tyrosine	GC-MS[*]	OPLS-DA	[64]
		Al[a]↑	4-hydroxyphenylethanol			
		OA[h]↑	2-hydroxyglutaric, citric, lactic, malic, succinic			
		SUG,↑↓ SUGDs[d]	Erythritol, fructose, glucose, glycerol, *myo*-inositol, ribose			
		O[k]↑↓	1, 2-propanediol, phosphoric			
Meju	Soybean	AA[c]↑↓	γ-aminobutyric, acetylornithine, alanine, arginine, citrulline, glutamic, glutamine, histidine, isoleucine, leucine, lysine, methionine, ornithine, phenylalanine, proline, pyroglutamic, threonine, tryptophane, tyrosine valine	UPLC-Q-TOF MS[*]	PLS-DA	[27]
		NTs↑↓	Adenine, hypoxanthine, uracil, xanthine	OPLS-DA		
		OA[h]↑↓	Citric, pipecolic			
		P[t]↑↓	Glu-Gln, Glu-Tyr, Leu-Gln, Leu-Glu, Glu-Phe, Leu-Pro, Ser-Pro, Val-Glu, Val-Thr, Val-Leu, Leu-Val-Pro-Pro			
Miso	Soybean	AA[c]↑↓	Arginine, aspartate, glutamate, glutamine, lysine, phenylalanine, pyroglutamic,	LC-MS[δ]	PCA	[65]
		OA[h]↑	Citric			
		O[k]	Fructosyl-leucine, fructosyl-phenylalanine			
Myeolchi-aekjeot	Fish	AA[c]↑↓	Alanine, arginine, aspartate, glutamate, glutamic, glutamine, glycine, isoleucine, leucine, serine, threonine	[1]HNMR[*]		[66]
			Betanine, choline, creatine, inosine, methyl amines			

Produce	Raw material	Metabolite group	Metabolite forms	Data acquisition method	Data processing technique	Reference
		Am[b], NTs[g]↑↓				
		OA[h]↑↓	Acetate, lactate,			
		SUG,↑↓ SUGDs[d]	Glucose, glycerol			
Saeu-jeot	Shrimp	AA[c]↑	Alanine, arginine, asparagine, aspartate, glutamate, glutamine, glycine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, pyroglutamate, serine, threonine, tryptophan, tyrosine, valine	^{1}HNMR*	CCA	[67]
		Am[b]↑↓	Dimethylamine, trimethylamine			
		OA[h]↑	Acetate, butyrate, lactate			
		SUG,↑↓ SUGDs[d]	Glucose, glycerol			

a—alcohols, b—amines, c–amino acids, d–carbohydrates, sugars and sugar derivatives, e–fatty acids, f–isoflavonoids, g–nucleotides, h–organic acids, i–soyasaponins, j–vitamins, k–others (not classified), l–organic bases, m–purines and pyrimidines, n–carbonils, o–hydrocarbons, p–catechin and catechin derivatives, q–alkaloids, r–flavonol glycosides and flavone glycosides, s–lipids, t–peptides, u–diphenylheptanoid, v–flavonoids, w–lipids, x–lysophospholipids, y–phenolic acids, ↑–increase in metabolites, ↓–decrease in metabolites, ↑↓–both increase and decrease in metabolites, *–non-targeted/profiling metabolomics, $^{\delta}$–targeted metabolomics, CE-TOF-MS–capillary electrophoresis time of flight mass spectrometry, CCA–canonical correspondence analysis, FTIR–Fourier transform infrared spectroscopy, GC-FID–gas chromatography-flame ionization detector, GC-MS–gas chromatography-mass spectrometry, GC-TOF-MS–gas chromatography-time of flight mass spectrometry, ^{1}HNMR–proton nuclear magnetic resonance, HPLC-DAD–high performance liquid chromatography-diode array detector, LC-MS/MS–liquid chromatography tandem-mass spectrometry, OPLS-DA–orthogonal partial least square discriminant analysis, PCA–principal component analysis, PLS-DA–partial least square discriminant analysis, SPME-GC-MS–solid phase microextraction-gas chromatography-mass spectrometry, UPLC-ESI-QTOF-MS–ultra high performance liquid chromatography with electrospray ionization quadrupole time of flight mass spectrometry, UHPLC-LTQ-IT-MS/MS –ultra high pressure liquid chromatography linear ion trap-high resolution Orbitrap mass spectrometry, UPLC-Q-TOF MS–ultra performance liquid chromatography quadrupole time of flight mass spectrometry.

Table 1. Summary of food metabolomics studies of fermented foods reported in literature.

flavanols, anthocyanins were observed to decreased with fermentation time, while most oligopeptides initially increased, with a later decrease during fermentation [29].

Lee et al. [56] and Tan et al. [57] studied metabolic changes during tea fermentation. Using ^{1}H NMR, UPLC-Q-TOF-MS and PCA, these authors were able to differentiate partially and fully fermented tea according to their fermentation patterns. The authors observed a decrease in caffeine epicatechin, epigallocatechin, caffeine, quinate, theanine and sucrose, whereas gallic acid and glucose levels increased [56]. Alanine levels remained constant with caffeine being a major discriminator. A similar decrease in catechin, epigallocatechin in fermented tea was observed in another study, though levels of flavanols rapidly increased but later decreased [57]. Varying increases and decreases in the levels of flavonol and flavone glycosides, phenolic acids, alkaloids and amino acids were also recorded by these authors [57].

Other similar studies on the food metabolomics studies of fermented foods that have been reported in the literature include foods from milk [58, 59] soybean [27, 28, 65] and cereals [61, 63, 64] (**Table 1**). Others include *kimchi* [62], *myeolchi-aekjeot* [66] and *saeu-jeot* [67]. These fermented food products, their corresponding metabolites and trend in terms of increases or decreases in reported metabolites are summarized in **Table 1**.

5. Role of food metabolomics in the development of functional foods

Sequel to the relevance and importance of consuming functional foods for improved health, concerted efforts by relevant stakeholders in academia and food industry have been geared towards the development and delivery of functional foods to the populace. In this regard, food metabolomics as a technique is vital in the efficient and proper evaluation of such products and subsequent elucidation of the metabolite profile. Through the selection of appropriate techniques in combination with adequate MVDAs, a thorough understanding of the effects of processing parameters and different optimization steps during the development of such functional foods is possible. Successive data generated, could thus be interpreted in terms of the functionality and other health benefits such product would confer to intending consumers.

6. Future prospects

Fermented foods have distinct ecological niches that present an opportunity to use new approaches that take advantage of advances in 'omics' to understand and characterized them. Considering the wide range of these fermented foods in the world and the number of yet to be characterized and identified components, subsequent analysis of these components needs to be explored to further advance and contribute to existing knowledge. While the future of food metabolomics will involve the development of better analytical techniques, efforts should also be made at developing standardized databases of data from fermented foods.

Currently, metabolomics studies on fermented foods are still limited compared to plants. If harnessed well, the application of food metabolomics would play an invaluable role in the

development of strategies for improving the safety, quality, shelf life and overall composition of fermented foods. In the nearest future with concerted efforts, food metabolomics could be used as an effective alternative and/or complement traditional sensory evaluation for fermented foods. Since metabolites impact sensory qualities, food metabolomics can clarify the influence of fermentation on biomarkers responsible for sensorial qualities.

7. Conclusion

There is a steady growing interest in food metabolomics, due to its application and capability in providing high throughput data and a platform for detailed understanding on the fermentation process. The feasibility of food metabolomics approach also suggests its viability for future progress in food science, nutrition and other related fields. This also coincides with the recent sensitization and encouragement of the consumption of functional and nutraceutical foods that can reduce the risks of degenerative diseases and ensure healthy nutrition. Although considerable progress has been made in the field of food metabolomics and its application in understanding fermented foods as demonstrated in this chapter, challenges of fully interpreting the complex data generated from the sophisticated equipment used still needs to be addressed and simplified. Nonetheless, food metabolomics has provided a medium that will greatly improve our understanding of the diversity of fermented foods and even more potential to explore their functionality. Since the delivery of most functional foods to the populace is through the industry, subsequent adoption of this technology would translate to a better understanding of processes and its influence on product quality. This could thus save costs, time and labor that might have been expended in conventional analytical techniques, that would provide less information.

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