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Fermentation-enabled wellness foods: A fresh perspective

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ABSTRACT

Fermented foods represent an important segment of current food markets, especially traditional or ethnic food markets. The demand for efficient utilization of agrowastes, together with advancements in fermentation technologies (microbial- and enzyme-based processing), are stimulating rapid growth and innovation in the fermented food sector. In addition, the health-promoting benefits of fermented foods are attracting increasingly attention. The microorganisms contained in many common fermented foods can serve as “microfactories” to generate nutrients and bioactives with specific nutritional and health functionalities. Herein, recent research relating to the manufacture of fermented foods are critically reviewed, placing emphasis on the potential health benefits of fermentation-enabled wellness foods. The importance of the correct selection of microorganisms and raw materials and the need for precise control of fermentation processes are explored. Major knowledge gaps and obstacles to fermented food production and market penetration are discussed. The importance of integrating multidisciplinary knowledge, communicating with consumers, establishing regulatory frameworks specifically for fermentation-enabled wellness foods and functional fermented foods, are highlighted.

1. Introduction

Fermentation has a long history in human food production and consumption. Fermented foods have been an integral component of the human diet since 8000 BC and account for nearly a third of the world’s food consumption (up to 40% for some populations). The term “fermentation” comes from the Latin word “fermentum”, and is defined as a natural decomposition process which involves chemical transformation of complex organic substances into simpler compounds by the action of intrinsic organic catalysts generated by microorganisms of plant or animal origin (“microbial factories”, either naturally occurring or added) [1]. Fermentation is a traditional method for food preservation (alongside drying and salting), and for food quality modification and culinary enjoyment (owing to the distinct flavors, aromas and textures of fermented foods). The microorganisms used in the production of fermented foods and beverages include bacteria (e.g. lactic acid bacteria (LAB) such as *Lactobacillus*, *Streptococcus*, *Enterococcus*, *Lactococcus* and *Bifidobacterium*) and molds (e.g. *Aspergillus oryzae*, *Aspergillus sojae*, *Penicillium roqueforti* and *Penicillium chrysogenum*), and yeasts (e.g. *Saccharomyces cerevisiae*, *Andida krusei* and *Candida humilis*).

Considerable effort has been devoted to developing better fermentation processes, fermentation equipment, fermented food products and an associated scientific basis since the 19th century. The diversity of microbiota and raw materials, as well as the different types of production processes, lead to a wide range of fermented foods and beverages being available in today’s global food markets (i.e. more than 3500 fermented dairy-, cereal-/pulse-, vegetable-, tea-, fish- and meat-based products, with some representative examples given in Table 1). Many of these fermented foods are produced from local food sources and cultural preference, thus possessing distinct organoleptic properties such as doenjang, douchi, kimchi, kombucha, lambanog, leppetso, miang, narezushi and tempeh from East and Southeast Asia; Surströmming, mead, rakfisk, sauerkraut, salami, kefir, filmjölk, prosciutto, quark, smetana and crème fraîche from Europe; Boza, kushuk, mekhalel, torshi and lam-

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Table 1
Examples of global fermented food products.

Food source	Fermented products
Grain based	Amazake, beer, bread choujiu, gamju, injera, kvass, makgeolli, murri, ogi, sake, sikhye, sourdough, sowans, rice wine, malt whisky hisky, grainwhisky, idli, dosa, vodka, burukutu, pitoKaffir beer, busaa (maize beer), malawa beer, zambian opaquemaize beer, merissa, seketeh, bouza, kishk, vinegar
Vegetable based	Kimchi, mixed pickle, Indian pickle, sauerkraut, gundruk, Asinan, Burong mangga, Dalok, Jeruk, Kiam-chai, Kiam-cheyi, Kong-chai, Naw-mai- dong, Pak-siam-dong, Paw-tsay, Phak-dong, Phonlami-dong, Sajur asin, Sambal tempo- jak, Santol, Si-sek-chai, Sunki, Tang-chai, Tempoyak, Vanilla, Szechwan cabbage, Mootsanji, Oigee, Oiji, Oiso baegi, mushrooms, potato beer,
Fruit based	Wine (including pomace wine), vinegar, cider, perry, brandy, atchara, nata de coco, burong, mangga, asinan, pickling (*Lemon pickle, Lime pickle, Mango pickle*), vişinată, nata de coco, Nata de pina,
Honey based	Mead, metheglin, venigar
Dairy based	Cheese, kefir, kumis, dahi, shuba, cultured milk products like: quark, filmjölk, crèmefraîche, smetana, skyr, yogurt, whey vinegar
Fish based	Bagoong, faseekh, fish sauce, Garum, Hákarl, jeotgal, rakfisk, shrimp paste, surströmming, shidal, soy sauce, shiokara,
Meat based	Chin som mok, sausages, salami, Spanish salchichon and chorizo, Icelandic Slátur (blood sausage), Irish pig-blood derived black pudding (blood sausage), beef sticks, pepperoni, Bosnian sudžuk,
Rice, maize, barley based	Jamón ibérico, Chorizo, Salami, Pepperoni, Nem chua, Som moo, vinegar, kurosu, sorghum beer, vinegar, Kvass, Ogi, Amazake, sake, Pozol,
Tea based	Pu-erh tea, Kombucha, Bai-ming, Leppet-so, Miang
Soy based	Soy sauce soybean sauce, tempeh, tofu, miso, *natto*, *cheonggukjang*, *chunjang*, *doenjang*, *doubanjiang*, *gochujang*, tamari, *tauchu*, and yellow soybean paste, *amriti*, *dhokla*, *dosa*, *idli*, *papad*, and *wadi*

oun makbouss from Middle East; Garri hibiscus seed, hot pepper sauce, iru ogiri, laxoox, injera and mauoloh from Africa; Kaanga pirau, poi and sago bean-based fermented foods from Oceania.

Improving the safety of fermented foods is an ongoing global effort, with the health-promoting benefits of these foods recently attracting growing scientific interest because of consumer awareness of diet-disease relationships. Raw material(s) can be transformed through fermentation into new products with increased nutritional value (due to the generation or enrichment of certain bioavailable nutrients during fermentation), enhanced gut health properties (due to the involvement of probiotics in fermentation), as well as specific biological functionalities (due to the high diversity and amount of bioactive substances created during fermentation) [2,3]. Most recently, fermentation has been considered a sustainable approach for maximizing the utilization of the bioresources to address the recent global food crisis [4]. Fermented foods containing different numbers and species of live microorganisms are listed as one of the top 10 superfoods in 2017. Fermented foods of traditional or innovative nature are produced to possess nutritional and quality advantages, offering not only better nutrition to the general population, but also health functionalities to specific groups of consumers (including vegans, or those on lactose-intolerant or cholesterol restricted diets) [5]. The microorganisms used to initiate fermentation, along with the probiotic microbes supplemented in fermented foods, can function as "microbial factories" for the production of desired nutrients and bioactives while consuming undesired substances. For example, bacteria containing β-galactosidase in fermented milk enable the production of lactose-free/lactose-reduced products, since this strain breaks down lactose during fermentation. Different types of hydrolysis reactions may be induced by the inherent enzymes of microorganisms, which can release nutrients and bioactives with desirable molecular sizes and bioavailability (e.g. peptides and amino acids) from the raw materials [6]. Compared to the non-fermented counterparts, fermented foods can confer multi-level benefits to humans, such as improvements in digestibility, increase of glucose tolerance [7], inhibition of pathogenic bacteria growth and bacterial toxin formation, reduction of gastrointestinal disorders, degradation of plant toxins (e.g. cyanogenic glycosides), as well as decrease the risks of various illnesses and diseases including cardiovascular disease [8], arthritic disease [9], type 2 diabetes [10], periodontitis [11], respiratory problems [12], bladder disorders [13], bone problems [14], liver problems [15], and skin problems [16].

There exist a variety of books and review papers covering specific fermentation-related topics in great detail. This review will focus on fermentation-enabled foods with nutritional advantages, rather than traditional fermented foods and their physicochemical characteristics. Only a modicum of information on fermentation-induced sensory and quality attributes is provided, sufficient to allow the demonstration of multiple beneficial properties of a fermented product.

2. Classification of fermented foods

2.1. Fermented dairy products

Fermented dairy products represent one category of high-end fermented foods. They gain high popularity owing to their high contents of lactic acid, galactose, free amino acids, fatty acids and vitamins (especially B complex), and their favorable properties such as anti-inflammatory effects [17], anti-stress [18], memory-improving [19,20], neuroprotective and cognition-enhancing effects [21–23], improvement of lactose tolerance, enhanced absorption of nutrients (including minerals) and gut-associated immune response, decrease of cholesterol levels, shortened duration of diarrheal bouts, and incidence of arrhythmias, ischemia and cancer [24–26]. Fermented dairy products (such as yogurt, *dahi*, *shrikhand*, Bulgarian butter milk, acidophilus milk, kefir, koumiss, and cheese) are commonly manufactured throughout the world, especially using LAB [27]. Cheeses and yoghurts are well known vehicles for health-promoting microorganisms including probiotics, offering advantages in nutritional value and health benefits over non-fermented milks [28], An example includes Iranian ultrafiltered Feta cheese containing *Lactobacillus casei* with NaCl partially replaced by KCl [29]. Cheese is a rich source of essential nutrients including proteins, lipids, vitamins and minerals that have beneficial effects on human health e.g. calcium for osteoporosis [30] or dental caries [31], conjugated linoleic acid (CLA) with anticarcinogenic and antiatherogenic properties [32,33], and peptides with various biological activities. Yogurt, as a nutrient-dense fermented food, contains bacterial cultures and various macro-/micro-nutrients and bioactive metabolites derived from fermentation, thus, exerts health benefits beyond its initial raw material against health problems such as type 2 diabetes and cardiovascular disease [34]. Kefir is a self-carbonated slightly foamy alcoholic beverage made with milk from animals (e.g. goat, cow and camel) or plants (e.g. soya, rice and coconut), offering unique sensory and nutritional properties [35].

2.2. Fermented staple crop products

Fermented staple crop foods represent a large category of solid and liquid products, and these foods are welcome alternatives for certain populations, especially vegans, vegetarians or individuals with lactose intolerance. Cereals such as barley, maize, millet, oats, rice, rye, sorghum and wheat have been used as the substrates for fermentation. Compared to unfermented cereals, fermented cereal foods tend to be more palatable and have lower anti-nutritional effects, and higher bioavailability of minerals [36]. The health benefits of fermented cereals can be doubled, if probiotic microorganisms (e.g. *Lactobacilli* and *Bifidobacteria*) and raw materials containing prebiotic carbohydrates (e.g. beta-glucan, arabinoxylan, galacto-/fructo-oligosaccharides and resistant starch) are used. Rice and rice bran fermented with microorganisms like *Saccharomyces bouldardii* and *Monascus purpureus* were found to contain elevated contents of sterols, unsaturated fatty acids and phytochemicals (e.g. vitamins and phenolics), and possess health-promoting properties such as those against type 2 diabetes, cardiovascular disease, Alzheimer's disease, cancer, and human B lymphomas [37]. Vinegar and beer are two common fermented cereal products. Vinegars such as Shanxi aged vinegar, Zhenjiang aromatic vinegar, and Kurosu vinegar are fermented from sugar and alcohol [38], and exhibit a range of functionalities such as antioxidant, antibacterial, anti-infection, blood glucose-lowering, lipid metabolism-regulating, appetite-improving, fatigue-reducing and osteoporosis-fighting effects [39]. Other popular fermented cereal products include Amazake (a sweet fermented rice beverage consumed in Japan), Ogi (a fermented cereal porridge consumed in Nigeria), Pozol (a traditional beverage of fermented maize dough originated from Pre-Columbian Mexico), and Kvass (is a lacto-fermented alcoholic beverage from rye grain originated in Ukraine, Russia and Belarus) [40]. Beer is a low alcohol drink containing nutrients and bioactive substances such as nitrogen compounds, melanoidins, organic acids, vitamins, phenolic compounds and mineral salts [41]. Fermented sourdough products have been used as alternatives to gluten-free products, as these foods possess desirable textural, flavor and nutritional characteristics induced by proteolytic lactic acid bacteria and wheat flour endogenous enzymes [42].

2.3. Fermented soy products

Soybean is a popular food that can be easily grown, being rich in protein (40% on a dry basis). The FDA's approval of a health claim for soy in 1999 ("Diets low in saturated fat and cholesterol that include 25 g of soy protein a day may reduce the risk of heart disease") has encouraged the development and improvement of soybean products. Fermented soy products have unique flavor and high nutritional value associated with their significant amounts of amino acids and fatty acids [43]. Various soybean materials are subjected to fermentation with a yeast, bacteria, mold, or their combinations to yield fermented soy products such as soy or tamari sauce, miso, tempeh and natto. For example, tempeh is a traditional fermented food produced via fermenting soaked and cooked soybeans and/or cereal grains with a mold (usually the genus *Rhizopus*). The enzymes in the mold catalyze the hydrolysis process (by which soybean constituents are broken down to create distinct and desirable food texture and flavour while reducing or even eliminating antinutritional substances) [21]. Some fermented soy products have been used as seasonings to provide salty and umami flavors such as *Ganjang*/soy sauce (brown-colored liquid), *Doenjang* (brown-colored paste made by Meju), *Gochujang* (red pepper paste, a fermented spicy condiment), and *Cheonggukjang* (soybean paste fermented by *Bacillus* at 40–43 °C). In recent years, a focus has been placed on improving the health properties of fermented soy foods e.g. the increase of vitamin K2 (menaquinone), which is important to bone and cardiovascular health and present only in the fermented soybean and animal products [44]. Certain fermented soy products have demonstrated abilities to reduce the risks of age-/hormone-related diseases, inflammatory diseases, infection, asthma and cancer [45].

2.4. Fermented vegetable products

Fermented vegetable products can positively influence human health, because they are rich in substances beneficial to humans (e.g. dietary fiber, minerals, antioxidants and vitamins). Fermented vegetables such as kimchi, sauerkraut, carrots, cauliflowers, tomatoes, olives, green peas and peppers are traditional foods made at home or produced industrially. Sauerkraut, a popular fermented vegetable is made via lactic acid fermentation of salted **white** cabbage (*Brassica oleracea* var. *capitata*) [46]. Fermented cucumbers are produced *via* fermentation in brine (ususally 5%–8% NaCl) in open-faced tanks to convert saccharides into acids and other products [47]. Korean kimchi products include *ordinary* (without added water) and *mul-kimchi* (with water), *beachu* kimchi (diced Chinese cabbage), *tongbaechu* kimchi (whole Chinese cabbage), *yeolmoo* kimchi (young oriental radish), *kakdugi* (cubed radish kimchi), as well as *baik* kimchi (beachu kimchi with water), *dongchimi* (whole radish kimchi with water) and *nabak* kimchi (cut radish and Chinese cabbage). These kimchi products are produced via LAB fermentation of baechu cabbage along with other vegetables, thus contain significant amounts of LAB (10^7–10^9 CFU/g), dietary fibers, vitamins and minerals. Kimchi products have probiotic, antioxidant, anti-aging, anti-inflammatory, anti-bacterial, anti-obesity and anti-cancer effects [48].

2.5. Fermented fruit products

Fermented fruits can be produced using whole fruits (e.g. apples, lemons, mangoes, palms, papaya and pears) or fruit pulps/juices (e.g. banana and grape), via "spontaneous" fermentation by natural lactic bacterial surface microflora (such as *Lactobacillus* spp. and *Pediococcus* spp.), or "controlled fermentation" by starter culture(s) (such as L. *plantarum*, L. *rhamnosus* and L. *acidophilus*) [49]. Wine, cider and vinegar are fermented fruit drinks made *via* fermentation of grape, apple and/or pineapple with a combination of microorganisms involving yeasts and bacteria. A new generation of fermented fruit products are being developed to possess specific biological properties, in addition to distinct organoleptic characteristics. For example, red wine is developed to contain higher amounts of antioxidants especially certain polyphenols with specific health peoperties [50]. Fermented papaya preparation has been produced to possess antioxidant potency including free radical scavenging capacity [51]. Apple cider vinegar has the ability to lower the levels of cholesterol and triglycerides and protect LDL cholesterol particles from oxidation [52].

2.6. Fermented seafoods

Fermented seafoods are made through different processes involving fermentation of whole fish or derived by-products. Lactic-acid fermented fish is normally produced via fermentation with gram-positive cocci including LAB such as *Lactobacilli*, *Pediococci* and *Streptococci*. For example, *Nare-zushi* in Japan is a fermented sushi made from raw fish (e.g. mackerel, salmon, crucian carp or sandfish) along with rice or other carbohydrate-based materials [53]. Fish sauces and seasonings are produced, *via* long-term fermention, from fish mashes of anchovy, small shrimp, icefish and sand lance together with the by-products of tuna, sardine and squid. In Korea, *Jeot-gal* is served as a side dish or appetizer, and used as an essential seasoning of Kimchi. *Jeot-gal* is produced through fermentation at temperatures > 25 °C using marinated raw fish and microorganisms with proteolytic, lipolytic, and amylolytic activities. Through the optimization of processing conditions, *Jeot-gal* can be tailored to contain high contents of minerals (e.g. calcium, iron and phosphorus) and protein-based compounds (e.g. amino nitrogen, soluble nitrogen and volatile basic nitrogens) and possess antioxidative, angiotensin-1 converting enzyme (ACE)-inhibitory, gamma-aminobutyric acid (GABA)-producing, cholesterol-reducing and antitumor effects [53].

2.7. Fermented meat products

There are a wide range of fermented meat products worldwide, because fermentation has long been used to preserve meat. Fermented meat products (e.g. sausage and ham) are produced by utilizing naturally occurring microflora, or by using one or more species of commercial preparations of bacteria, yeasts and molds (such as LAB, *Micrococci* and *Staphylococci*). Meat fermentation is a low-energy acidulation process involving complex physical, chemical and microbiological events, resulting in products with unique color, flavor, texture and nutritional value [54]. Acids play important roles in monitoring microbial activities and consumption of sugars in the production of fermented meat. Oxidation of meat components such as lipids and proteins (including protein carbonylation), as well as the interactions between meat components (e.g. protein-lipid or protein-protein interactions), all take place during meat fermentation [55]. Traditional fermented meat products include Italian salami, Spanish salchichon and chorizo, Icelandic Slátur (blood sausage), Irish pig-blood derived **black** pudding (blood sausage), beef sticks and pepperoni. Fermented sausages produced through prolonged ripening and drying processes likely have a low moisture content, more concentrated flavor, firmer texture and higher amounts of nutrients.

2.8. Other fermented products

Besides the above-mentioned fermented foods, a broad spectrum of other fermented products can be found worldwide. Among which, fermented tea has gained wide popularity, due to the feasibility of modifying the contents of organic acids, vitamins, caffeine and polyphenols in teas for taste and helalth purposes using different strains of bacteria, yeasts and/or fungi [56]. These contents can be tailored *via* the fermentation step and associated processes, in order to enhance the tea's properties against undesirable microorganisms such as *Salmonella* and *Staphylococcus* [57] and contribution to the prevention and treatment of gastrointestinal infection, diabetes, cardiovascular diseases and cancer [58]. Fermented ginseng has been developed to improve behavioral memory function through reversing memory impairment and reducing β-amyloid accumulation in Alzheimer's disease mice [59]. Fermented olives are marketed as probiotic foods, as they can provide many vital nutrients and bioactive substances such as phenolic compounds that promote the performance of the human body while enhancing the protection on humans against a number of diseases [60].

3. Advantages of fermented foods

3.1. Changes in food composition and properties induced by fermentation

Fermentation doesn't require sophisticated equipment for the fermentation process or the subsequent handling and storage of fermented products, though advanced devices including on-line sensors and *in situ* computer visualization and simulation programmes have recently been installed into bioreactors to facilitate real-time measurements for precise control of the production of fermented foods. The initiation and progress of fermentation depend on its nature (spontaneous or evoked intentionally) and the applied and natural occurring microflorae. The fermentative changes directly influence the physical, chemical, biological and sensory properties of final fermented products.

During fermentation, food components in edible and sometimes inedible raw materials are enzymatically and chemically broken down and then modified via biotransformation reactions (e.g. the removal of glycol residues). As a result, the sensory quality, nutritional vaue and health-promoting properties of the fermented products are improved in a safe and effective manner: 1) Fermentation enables unique flavors, aromas and textures (by generating small molecule flavor compounds and texture-modifying substances like exopolysaccharides (EPSs)); 2) Fermentation can increase digestibility and accessibility, whilst reducing cooking times (allowing the nutrients, including initially nondigestible carbohydrates, to be digested and absorbed easier); 3) Fermentation facilitates the enrichment of nutrients (including macro- and micro-nutrients like essential amino acids, fatty acids, vitamins and minerals); 4) Fermentation can make foods with specific health benefits (through releasing target bioactives or transforming parent substances into into these bioactives (e.g. probiotics, prebiotics, and non-nutrient bioactives like phenolic antioxidants); 5) Fermentation can help improve food safety through suppressing the growth of pathogenic microorganisms (e.g. Gram-positive and Gram-negative bacteria), and promoting the degradation of toxins (e.g. mycotoxins), *via* producing natural preservatives, antimicrobial compounds and bacteriocins such as butyrate, promoting mucosal cell differentiation and immune barrier function of the epithelium, and removing/reducing anti-nutritional factors in raw materials (e.g. metabolic detoxification of mycotoxins and other endotoxins by *Rhizopus oryzae*) [61–66]. The impacts of fermentation on foods are microorganism-specific and raw material-dependent, and can be further modified by external environmental conditions, and influenced by other processes coupled with fermentation e.g. pre-roasting buckwheat groats prior to solid-state fermentation with *Rhizopus oligosporus* [64,67]. It is worth noting that physical properties including rheological attributes of foods (e.g. thermal dynamics, viscosity, consistency, hardness and adhesiveness) may change after fermentation, and these changes, in turn, influence the chemical, biological and sensory properties of final fermented foods.

Anti-nutritional factors may occur naturally (e.g. enzyme inhibitors, flatulence factors, glucosinolates, lectins, tannins, polyphenols, phytic acid and saponins found in mustard, rapeseed protein products, grains and legumes), and can harm humans by impairing intake, digestion, absorption or utilization of other foods and feed components e.g. formation of complexes with essential nutrients or inhibition of enzymes [68]. A number of technological processes have been established and used singly or in combination to reduce the anti-nutritional factors, such as mechanical, thermal, chemical, and biological processes involving germination, fermentation, enzymatic treatment, soaking, cooking, canning, irradiation, selective extraction, fractionation and isolation. Fermentation can enrich nutrients and bioactives (e.g.

amino acids and GABA), increase food digestibility and nutritional value, and remove unwanted substances (e.g. antinutrients), without deteriorating food quality (as compared to thermal, chemical and mechanical processes) [69]. Fermentation can also minimize or remove certain intrinsic substances that are undesired (such as protease, amylase and other enzyme inhibitors) and which might affect the rate and extent of important bioconversions [70]. In some occasions, fermentation and germination are combined to generate synergistic benefits. For example, the fermentation of germinated rice with probiotic organisms would enrich natural fibers, GABA and inositol hexaphosphate [71].

3.2. Fermentation and production of the "biotics"

The emerging 'biotics' including probiotics, prebiotics, synbiotics, postbiotics, oncobiotics, paraprobiotics, pharmabiotics and psychobiotics have gained much attention in the recent years. Fermentation is increasingly being used for the production of probiotics, prebiotics and synbiotics with high viability and functionality. Most recently, fermented foods and ingredients have attracted growing interest because they can facilitate healthy gut microbiota and promote human well-being.

Probiotics were defined in 2006 as "live microorganisms that should be alive by the end of the shelf-life of the product, and when administered in adequate amounts, confer a measurable health benefit on the host at a defined dose" [72]. Most of the currently commercialized probiotics for human consumption are LAB and *Bifidobacteria*, with LAB mainly composed of *Lactobacillus* spp. and *Streptococcus thermophilus* encompassing $\tilde{2}00$ different species. Probiotics should be maintained in foods at levels above 10^7 viable cells per gram or milliliter until consumption. For fermented foods, probiotic functionalities can be introduced through either the addition of probiotic cultures to fermented foods, or enhancement of the probiotic potential of the microorganisms present in fermented foods. The latter approach may have advantages in terms of the resistance to acidity and bile salts, adherence to colonocytes, generation of antimicrobials and/or lactase activity (since microbes have already adapted to the food environment) [73,74].

The food safety of probiotic fermented foods is enhanced, owing to the inhibitory effects on pathogenic bacteria of the antimicrobial bacteriocins produced by probiotic strains like *Lactobacillus* species. Further, the nutritional and health benefits of probiotic fermented foods can also be enhanced, because of the generated beneficial enzymes (e.g. β-galactosidase, which facilitates lactose hydrolysis and compensates for the reduction of human lactase activity over time), and nutrients or bioactives (e.g. enzyme cofactors, GABA, ACE peptide inhibitor, antihypertensive peptides, poly-unsaturated fatty acids, isoflavone aglycones and vitamins). The probiotic fermented foods have demonstrated positive roles in relief of lactose maldigestion symptoms, shortening of rotavirus diarrhea, immune modulation, regulation of serum cholesterol levels, treatment of irritable bowel syndrome, urinary tract infections, bladder cancer, and allergies associated with skin, gut and respiratory tract (including food allergies in infants) [75–77]. Although a large number of publications report the health benefits of probiotics or probiotics-containing fermented milk, only one health claim in relation to live yogurt cultures and their ability to improve lactose digestion has been approved under the current EU regulation of health claims on food. The limited number of efficacy claims is largely due to the complexity of the gut microbiota and effector strains affecting human health [77]. The health claims of probiotic fermented foods result from the interactions of ingested live microorganisms, bacteria or yeast with the host (probiotic effect), and/or the actions of ingested microbial metabolites formed during fermentation (biogenic effect) [78].

Another category of fermented foods in microflora management are fermented products with synbiotics (in which probiotics and prebiotics are used in combination to improve the viability of probiotic bacteria while conferring the benefits of both the live microorganism and prebiotics) [79]. Prebiotics, as substances linking gut health and probiotics, are defined as non-digestible food ingredients that affect the host beneficially through stimulating selectively the growth or activity of one or a limited number of bacterial species residing in the colon [80]. Prebiotics, such as fructo-oligosaccharides, lactulose and lactitol, inulin, β-glucan and galacto-oligosaccharides, must neither be hydrolyzed nor absorbed in the upper part of the gastrointestinal tract, instead, serve as a selective substrate for one or a limited number of potentially beneficial commensal bacteria in the colon. The health effect of a prebiotic resembles that of a probiotic i.e. improve the host health through modulating the gut microbiota (via increasing the number of specific microbial strains, or altering greatly the composition of the gut microflora). Moreover, prebiotics may be added together with other bioactives such as organic acids (e.g. butyrate), active fatty acids (e.g. CLA), B-group vitamins bioactive peptides (e.g. ACE inhibitory peptides), as such combinations can enhance the survival of probiotic strains and generation of desired bioactive substances e.g. the increased production of ACE inhibitors upon the addition of *Aloe vera* succulent plant powder [81].

4. Bioactive substances in fermented products

Fermentation has been used for "manufacturing" simple compounds (e.g. ethanol) and highly complex macromolecules (e.g. polysaccharides, proteins and enzymes), including bioactive metabolites (e.g. lactoferrin and flavonoids), from raw materials containing their precursors (Table 2). The newly generated substances can not only extend food shelf life and ensure safety, but also improve the sensory properties, nutritional value, and biological activities of foods against chronic diseases (e.g. *via* signal-regulating, lipid-modulating, immunity-boosting, anti-microbial, anti-parasitics or anti-cancer effects) [82,83].

During properly controlled fermentation, physico-chemical events (including the enzymatic and non-enzymatic reactions involved in microbial metabolism) can lead to desired hydrolysis and solubilisation of macromolecules present in raw food materials (such as proteins and cell wall polysaccharides). As a result, the macro- and micro-structure of substrate materials is beneficially altered, which further influence the retention, release and absorption of the nutrients and non-nutrients in the substrate material. The final fermented foods are therefore endowed with target health-promoting properties derived from the released nutrients and bioactive substances as both reaction intermediates and end products. Cereal foods are good examples. Cereals are rich in bioactive phytochemicals such as vitamins (e.g. thiamine, vitamin E and folate), phenolics (e.g. lignans and phenolic acids) and phytosterols (e.g. sterols and stanols). However, the development of cereal foods using raw material(s) high in fibre and whole grains frequently encounter challenges associated with sensory acceptability, nutrient digestibility (e.g. starch) and bioaccessibility (e.g. minerals), and anti-nutritional factors. Fermentation technologies are particularly useful to resolve these issues while increasing the content of nutrients and bioactive substances in the final product. Under tailored conditions, fermentation can soften plant tissues, loosen and break down cell walls; induce enzymatic degradation of macromolecules and anti-nutritional factors (like phytate); and solubilize minerals and decomposed carbohydrates/proteins [84–86]. Fermentation of wheat and rye flour matrix with LAB was found to decrease glycemic index (GI) and insulin index (II) of the obtained breads [87,88], probably through decreasing the degree of starch

Table 2
Bioactive products generated or transformed during fermentation.

Bioactives	Source	Fermentation conditions	Functionality and IC_{50} value	Sequence	Analysis	Reference
Peptides	Cured ham	Spontaneous fermentation	Antioxidative	SAGNPN, GLAGA	nano-LC–MS/MS	[291]
	Black pudding	*Aspergillus Niger strain* 60 h to 80 h, 30 °C	Antioxidative, 0.84 μg/mL	<10kDa	Ultrafiltration technique	[292]
	Fermented marine blue mussel (Mytilus edulis)	25% NaCl for 6 months	DPPH (96 μmol/L), Superoxide (21 μmol/L), Hydroxyl (34 μmol/L), carbon-centered radicals (52 μmol/L)	HFGNPFH MW 962 kDa	on-line HPLC	[293]
	Fermented **blue-**mussel sauce	25% NaCl at 20 °C for 12 months	Scavenged 89.5% of hydroxyl radical at 64.8 μmol/L	FGHPY, MW620 Da	RP-HPLC	[294]
	Blue mussels Mytilus edulis	25% NaCl (*m*/*m*) at 20 °C for 6 months	IC_{50} value of purified ACE inhibitory peptide was 19.34 μg/mL	EVMAGNLYPG	RP-HPLC	[295]
	Fermented shrimp pastes (*kapi*)	30 °C for 6 months	ACE inhibitory activity DPPH scavenging ability	Ser-Val (60.68 ± 1.06 μmol/L) Ile-Phe (70.03 ± 1.45 μmol/L) Trp-Pro (EC_{50} 17.52 ± 0.46 μmol/L).	RP-HPLC	[296]
	Oyster sauce	25% NaCl (*m*/*m*) at 20 20 °C for 6 months	IC_{50} value of 0.0874 mg/mL ACE-I inhibitors	Peptide fraction	RP-HPLC	[297]
	Calpis	SSF, *L. animalis* DPC6134 (1%, *m*/*V*) and incubated at 37 °C for 24 h	ACE-I inhibitors	IPP (5), VPP (9), NIPPLTQTPV (173.3), NIPPLTQTPVVVPPFIQ (450) (μmol/L)	HPLC–MS/MS	[298]
	GOUDA CHEESE	SSF	Antihypertensive	NH2-Arg-Pro-Lys-His-Pro-Ile-Lys-His-Gln-COOH (13.4 μmol/L), Tyr-Pro-Phe-Pro-Gly-Pro-Ile-Pro-Asn (14.8 μmol/L)	HPLC	[299]
	Manchego cheese	Bacterial starters	ACE-I inhibitors	VRGPFP, 99% with a protein content of 18.2 μg/ mL	ESI-MS/MS	[300]
	Milk β-cn	L.*rhamnosus*+digestion	ACEinhibitory	Asp-Lys-Ile-His-Pro-Phe, Tyr-Gln-Glu-Pro-Val-Leu	HPLC-MS-MS	[301]
	Milk β-cn, as1-cn	*Lactobacillus GG* enzymes + pepsin	Opioid, ACE-inhibitory,	Tyr-Pro-Phe-Pro, Ala-Val-Pro-Tyr-Pro-GlnArg,	HPLC-MS-MS	[301]
	Milk β-cn	*Lactobacillus delbrueckiis ubsp.,*	Antioxidative	Ala-Arg-His-Pro-His-Pro-His-Leu-Ser-Phe-met	HPLC-MS-MS	[301]
	Milk	*Lactobacillus helveticus* CP90	ACE-inhibitory	Lys-Val-Leu-Pro-Val-Pro-(Glu)	HPLC-MS-MS	[301]
	Fermented milk	30 °C, 48 h, 3% *V*/*V* of inoculum, *Enterococcus faecalis*	Antihypertensive	LVYPFPGPIPNSLPQNIPP, LHLPLP, LHLPLPL, VLGPVRGPFP, VRGPFPIIV	LC–MS/MS	[302]
	Fermented milk	30 °C, 48 h, 3% *V*/*V* of inoculum *Lactococcus lactis* NRRL-B-50571	ACE inhibitory	DDQNPH, LDDDLTDDI, YPSYGL, HPHPHLSFMAIPP, YDTQAIVQ, DDDLTDDIMCV, YPSYG	LC–MS/MS	[303]
	Fermented milk	30 °C, 48 h, 3% *V*/*V* of inoculum, *lactis* NRRL-B-50572	ACE inhibitory	DVENLHLPLPLL, YPSYGL, ENGEC	LC–MS/MS	[304]
	Fermented milk	37 °C, anaerobiosis, 24 h, 3% *V*/*V* of inoculum *Bb. bifidum* MF 20/5	ACE inhibitory	LVYPFP	LC–MS/MS	[305]
	Fermented milk	Not specified *Lb. helveticus* and *S. cerevisiae*	Antihypertensive, antiinflammatory, antiadipogenic, antiatherosclerotic	VPP, IPP	LC–MS/MS	[306]
	Koumiss	SSF	ACE inhibitory peptides	YQDPRLGPTGELDPATQPIVAVHNPVIV, 14.53 μmol/L, MPKDLREN, 9.82 μmol/L, LLLAHLL, 5.19 μmol/L, NHRNRMMDHVH13.42 μmol/L	HPLC-MS/MS	[307]
	Fermented milk	37 °C, 27 h, 107 CFU/mL *L. casei Shirota* and *S. thermophilus*	ACE inhibitory, antithrombotic	YQEPVLGPVRGPFPIIV	SE-HPLC	[308]
	Fermented milk	37 °C, Anaerobiosis, 26 h, 1% *V*/*V* of inoculum *L. helveticusLH2*	Immunomodulating	WMHQPHQPLPPTVMFPPQ, LYQQPVLGPVR, SCDKFLDD	HPLC-MSMS	[309]
	Fermented skip jack tuna	Notspecified *Aspergillus glaucus*	ACE inhibitory	LKPNM	LC-MS	[310]
	Fermented shrimp paste	30 °C, 6 months Natural fermentation	ACE inhibitory	SV60.68 μmol/L IF 70.03 μmol/L Trp-Pro 17.52 μmol/L	SPE	[296]

Table 2 (*Continued*)

Bioactives	Source	Fermentation conditions	Functionality and IC_{50} value	Sequence	Analysis	Reference
	Chorizo sausages	11 °C, 78% relative humidity, 1 month	Antioxidant	FGG, DM, RT, KPK	LC-MS/MS HILIC-MS/MS	[311]
	Chunghookjang (fermented soy bean)	40 °C, 72 h, 1% *V*/*m Bacillus licheniformis* B1	Antidiabetic	LE, EW, SP, VE, VL, VT, EF	LC-MS/MS	[312]
	Douchi (fermented soy bean)	*Aspergillus aegypticus*	ACE inhibitory	Peptide containing Phe, Ile, and Glyintheratio1:2:5	GFC	[313]
	Tofuyo fermented soybean	Not specified	ACEinhibitory	WL 29.9 μmol/L, IFL 44.8 μmol/L	HPLC	[314]
	Korean soybean paste	Not specified	ACE inhibitory	HHL	HPLC-MS	[315]
	Fermented soysauce	45 °C, 5 days, *Aspergillussojae*	Antihypertensive	Ala-Trp (10), Gly-Trp (30), Ala-Tyr (48), Ser-Tyr (67), Gly-Tyr (97), Ala-Phe (190), Val-Pro (480), Ala-Ile (690), Val-Gly (1100) μg/mL	LC-MS-MS	[316]
	Ryemalt	34 °C, 24 h hammesii DSM16381, *L. rossiae 34 J Lb. plantarum FUA3002*	ACE inhibitory	LQP, IPP, LLP, VPP	LC-MS-MS	[317]
	Whole wheat	30 °C, 5 h *L. sanfranciscensis* and *Candi dahumilis*	ACE inhibitory	VPFGVG 336 μmol/L	LC-MS-MS	[318]
	Bread (ryemalt and whole wheat,1:1)	30 °C, 2 h, 85% humidity *L. reuteri TMW1.106, yeast*	ACE inhibitory	IQP, LQP, IIP, LIP, LLP, IPP, LPP, VPP	LC-MS	[319]
	Rice wine (HuangJiu)	25–33 °C Natural fermentation	ACE inhibitory, antioxidant, hypocholesterolemic	FP, VY, LSP, WL, FR, LVQ, YW, LHV, VYP, LTF, HLL, LVR, LQQ, LHQ, LDR, YPR, LLPH	UPLC-ESI-MS/MS	[320]
	Fermentedbuckwheatsprouts	Room temperature, 2 weeks, 25 mL/kg of inoculum *L. plantarum* KT	Vaso relaxation and ACE inhibitory	DVWY (0.69) FDART (1.9) FQ (7.4) VAE (55.9) VVG (39.6) WTFR (6.7) (mmol/L)	LC-MS	[321]
	Fermented marine blue mussel (*Mytilus edulis*)	25% NaCl, 6 months	Antioxidant IC_{50} 96 μmol/L of DPPH	HFGBPFH (MW 962 kDa)	HPLC	[293]
	Kapi Ta Dam and Kapi Ta Deang	30 °C for 6 months	ACE inhibitory	Ser-Val IC_{50} values of 60.68 ± 1.06, Ile-Phe 70.03 ± 1.45 μmol/L	GPC–HPLC RP-HPLC	[296]
	Blue mussels	25% NaCl (*m*/*m*) at 20 °C for 6 months	ACE inhibitory activity	EVMAGNLYPG IC_{50} 19.34 μg/mL	GPC–HPLC RP-HPLC	[322]
	Fermented Oyster	25% NaCl (*m*/*m*) at 20 °C for 6 months.	ACE inhibitory activity	IC_{50} value of 0.0874 mg/mL	HPLC	[297]
	Anchovy sauce	Spountanous fermentation without starer culture	Anti-cancer	Peptide fraction 31 μg/mL	MALDI-MS and HPLC	[323]
	Manchego cheese	SSF	ACE-I inhibitor	KHPIKHQ (13.4), KHPIKHQG (13.4), KAVPQ (1000), RPKHPIKHQG (13.4), DKIHP (577.9), RPKHPI (>1000), EIVPK (1275.4), KKYNVPQ (716.9), VPSERY (706.1), ERYL(24.1), VRYL(24.1), VPQL(77.1), DKIHPF (256.8), VRGPFP (592) (mmol/L)	HPLC-MS-MS	[324]
	Burgos-type cheese	Chymosin, bovine pepsin, *C. carduncul*us*, Mucor miehei, 8h*	Antioxidant	SDIPNPIGSENSEKTTMPLW, YQQPVLGPVRGPFPIIV, LLYQQPVLGPVRGPFPIIV	HPLC-MS-MS	[325]
	Ovine and Caprine Cheese like	Each batch of milk was then divided in 2 equal portions: one portion was heated at 110 °C for 10 min, whereas the other received no thermal treatment. Milk sterility (for the first batch) was checked as the absence of microor-ganisms on plate count agar incubated at 30 °C for 48 h.	ACE-inhibitor Antioxidant	Tyr-Gln-Glu-Pro (689.40 μg/mL), Val-Pro-Lys-Val-Lys (2.45 μg/mL), Tyr-Gln-Glu-Pro-Val-Leu-Gly-Pro (653.98 μg/mL) from β-casein; Arg-Pro-Lys (36.68 μg/mL) Arg-Pro-Lys-His-Pro-Ile-Lys-His (892.83 μ g/mL) from αs1-casein Leu-Tyr (either in ovine or caprine β-casein), and corresponding to the β-casein sequence Tyr-Gln-Glu-Pro-*	HPLC	[326]
	Burgos-type cheese	Batch 1, 0.06% (*V*/*V*) of animal rennet (95% *chymosin* and 5% bovine pepsin) (*Abiasa, S.L.*,), batch 2, 0.03% (*V*/*V*) of rennet of plant origin (*C. cardunculus*) (*Abiasa, S.L.*,) and batch 3, 0.034% (*V*/*V*) of microbial rennet (*Mucor miehei*) (*Lactocyex, S.L.*,).	Radical scavenging peptides	SDIPNPIGSENSEKTTMPLW, YQQPVLGPVRGPFPIIV, LLYQQPVLGPVRGPFPIIV	HPLC-MS/MS	[325]
	Ripening mould cheeses (Brie and Rokpol)	Mold fermentation	Analgesic	Agonistic BCM7 and BCM5, casoxin-6 and casoxin-C (derived from bovine κ-casein), and lactoferroxin A (derived from lactoferrin) opioid peptides	SPE extraction	[327]

Table 2 (*Continued*)

Bioactives	Source	Fermentation conditions	Functionality and IC_{50} value	Sequence	Analysis	Reference
	Water buffalo cheese whey	SSF	Antiproliferative for H-CaCo2 cells	Peptides fraction	MALDI-TOF/MS	[328]
	Alpine cheeses	SSF	Antibacterial activity against *L. monocytogenes* strain 162 of Emmental de Savoie		HPLC	[329]
	Kefir	*Kefir grain* 25 °C. 24 h	immunomodulatory effects	Peptide fraction	nano-ESI-LTQ-Orbitrap MS	[330]
Phosphopeptides	Milk protein (αs1-, αs2-, β- and κ-caseins)	*L. helveticus*	Enhancement of calcium bioavailability	Peptide fraction	HPLC	[331]
CPP	Beaufort cheese	SSF	Enhancement of calcium bioavailability	48 peptides fractions	LC-ESI-MS/MS	[332]
	Parmigiano-Reggiano cheese	SSF	Enhancement of calcium bioavailability	ESLSPSPSPEESITRINK, LSPSPSPEES, LSPSPSPEESITR, LSPSPSPEESITRINK	HPLC	[333]
Immol/Lunomo-dulatory peptides	Milk: β-Casein (145-160;145-154; 143-154;192-220),α-Lactalbumin(115-122)	*Lactobacillus helveticus*; 37 °C; 50 h; SMF	Mediate the immune response	Peptide fraction	HPLC	[334]
	Milk protein	*L. rhamnosus GG*; 37 °C for 20 to 24 h; SMF	Cytomodulatory activity	Peptide fraction	HPLC	[335]
	soybean meal	*Bacillus subtilis*; SSF; 37 °C; 24 h	Antihypertensive effect/ACE-inhibitory activity IC_{50} = 0.022 mg/mL	Peptide fraction	HPLC	[336]
	Caprine Kefir	Kefir was prepared using pasteurized milk cultured with *kefir grains*	ACE-inhibitory activity	PYVRYL and LVYPFTGPIPN	HPLC-MS	[337]
	Milk protein	*Bifidobacterium longum* KACC91563/ *Lb. helveticus* CP790; 37 °C; 24 h; SMF	Antihypertensive effect, Within an IC_{50} range of 100–500 μmol/L	Peptide fraction	HPLC	[338,339]
Opioid peptides	Caseins and whey proteins	*L. rhamnosus* GG; 37 °C, 12 days; SMF		Peptide fraction	HPLC	[340]
Antioxidant peptides	Acanthogobius hasta processing by-product	Aspergillus oryzae; SSF;5 days; 30 °C	DPPH scavenging activity was 78.6% at 6 mg/mL	Peptide fraction	HPLC	[341]
	Milk protein	*L. delbrueckii* subsp. bulgaricus IFO13953	5 times stronger antioxidative activity than BHT in the β-carotene decolorization system.	Peptide fraction	HPLC	[342]
Antitumor peptide	Bicyclic depsipeptide	*Chromobacterium violaceum* No. 968.I. Taxonomy	Antitumor	Peptide fraction	HPLC	[343]
	Fermented meat	Sarcoplasmic and myofibrillar porcine proteins by the action of *L. sakei* CRL1862 and *L. curvatus* CRL705 at 30 °C for 36 h.	ACE inhibitory peptides	FISNHAY	RF-HPLC-MS/MS	[344]
	Fermented “chorizo” sausages	Natural fermentation	Antioxidant (DPPH-radical scavenging activity)	Phe-Gly-Gly	HILIC-ESI-MS/MS	[311]
	Anchovy sauce	SSF	antiproliferative effect against human lymphoma cell (U937) IC50 = 31 μg/mL	This peptide fraction presented a molecular weight of 440.9 Da and only comprised Ala and Phe residues at the ratio of approximately 4:1	HPLC	[323]

Polysaccharides	Source	Fermentation conditions	Functionality/IC_{50} and dose	Linkage	Analysis	Reference
EPS	Dextran	*Weissella cibaria Leuconostoc mesenteroides*	Improve moisture retention and viscosity; Inhibit sugar crystallization; Used to make resins for separation technology as microcarrier in tissue/cell cultures.	*α- D*-glucan linked by *α*-(1,6)-glycosidic bonds; 1,2-, 1,3-, or 1,4-bonds are also present in some dextrans	GC-MS	[345]

Table 2 (*Continued*)

Polysaccharides	Source	Fermentation conditions	Functionality/IC_{50} and dose	Linkage	Analysis	Reference
	Cellulose	*Acetobacter xylinum Gluconacetobacter xylinus*	Nondigestible fiber; Temporary artificial skin to heal burns or surgical wounds.	β-(1,4)-*D*-glucan	NMR	[346]
	Alginate	*Azotobacter vinelandii Azotobacter chroococcum*	Immobilization matrix for viable cells and enzymes; a microencapsulation matrix for fertilizers; a hypoallergic wound-healing tissue; an antiatherosclerotic; an antiangiogenic; and as an antimetastatic agent.	α-(1,6) and α-(1,3) glycosidic Linkages, with some α-(1,3) branching	NMR	[347]
	Gellan	*Sphingomonas paucimobilis*	Regeneration of living tissues in cellular tests before and/ or after implantation in animals and/or humans	Partially *O*-acetylated polymer of *D*-glucose-(1,4)-β-*D*-glucuronic acid-(1,4)-β-*d*-glucose-(1,4)-β-*L*-rhamnose tetrasaccharide units connected by α-(1,3)-glycosidic bonds	NMR	[348]
	Curdlan	*Alcaligenes faecalis*	As a gelling agent and immobilization matrix; Curdlan along with zidovudine shows antiretroviral activity (anti-AIDS drug).	β-(1,3)-*D*-glucan	NMR	[349]
	Levan	*Saccharomyces cerevisiae Bacillus subtilis*	Used for the production of confectionary and ice cream, as a viscosifier and stabilizer.	β-(2, 6) glycosidic bonds β-(2,1)-linked side chains	NMR	[350]
	Xanthan	*Xanthomonas campestris*	A stabilizer, emulsifier, viscosifier and suspending agent in foods; Used in pharmaceuticals, cosmetics, paints, pesticide, detergent formulations, secondary and tertiary crude-oil recovery.	β-(1,4)-linked glucan main chain with alternating residues substituted on the 3-position with a trisaccharide chain containing two mannose and one glucuronic acid residue	NMR	[351]
	Pullulan	*Aureobasidium pullulans*	Pullulan membranes/films are being used as coating and packaging materials for foods such as instant food seasonings, powdered tea and coffee.	α-(1,6)-linked α-(1,4)-*D*-triglucoside maltotriose	NMR	[352]
	Ganoderma lucidum	*G. lucidum*; SMF; 28 °C, 7 days	Antitumor, inhibition of histamine release, inhibition cholesterol synthesis and absorption	Not detected	Not detected	[353,354]
	Mycelia	Phellinus nigricans; SMF; 28 °C, 7 days	Inhibited the growth of tumor of mice-transplanted Sarcoma 180 (at a dose of 400 mg/kg)	Not detected	Not detected	[355]
Kefiran	Kefir	Rice hydrolyzate (RH) medium *L. kefiranofaciens*	Can significantly lower blood glucose in KKAy mice	Not detected	Not detected	[356]
Oligosaccharides	plant cell wall	*Bacteroides spp.*	Nondigestible	Not detected	HPLC	[357]

Amino acids	Source	Fermentation conditions	Functionality	Content	Analysis	Reference
	Yu-lu, a Chinese traditional fermented fish sauce	Incubating mixtures of small anchovies and 30% salt (salt/fish, *m*/*m*) at 30 ± 5 °C for 180 days	Enhance the flavor	Glutamic acid 472.61, Lysine 569.50, Leucine 530.48, Valine 422.94 (mg/100 g)	HPLC	[358]
	Fermented **blue** mussel	25% NaCl (*m*/*m*) at 20 °C for 12 months	Enhance the flavor	Glycine 14.39, Alanine 6.71, Proline 4.85, Aspartic acid 11.72, Glutamic acid 14.75 (g/100 g)	HPLC	[359]
	Fermented sardine (Sardina pilchardus)	Sodium chloride and glucose at 37 °C for 57 days.	Enhance the absorption of calcium and other bioactives	Lysine 1171.5 mg/100 g	HPLC	[360]
GABA	Wholemeal wheat sourdough	*LAB* fermentation	Not detected	258.7 mg/100 g	HPLC	[361]
	Whole wheat and soya sourdough	*L. plantarum* C48	Not detected	22.62 mg/100 g	HPLC	[362]
	Bread	SSF, Yersinia GAD supplementation	Not detected	115 mg/100 g	HPLC	[363]
	Bread	SSF, Yersinia GAD supplementation	Inhibitory neurotransmitter of the nervous system	66 mg/100 g	HPLC	[364]

Table 2 (*Continued*)

Amino acids	Source	Fermentation conditions	Functionality	Content	Analysis	Reference
	Cheese	SSF *L. Lactis spp. Lactis* as starter	Decrease the blood pressure	320 mg/100 g	HPLC	[365]
	Cheddar cheese	SSF, *Lactobacillus casei* Zhang, 6 months	Probiotic substance	6773.5 mg/100 g	HPLC	[366]
	Fermented milk	SMF *L. paracasei subsp. paracasei* NTU 101 or *L. plantarum* NTU 102 (*m*/*m* = 5%) for 3 or 6 days at 37 or 34 °C	Antihypertensive Effects	970 mg/100 g	RP-HPLC	[367]
	Fermented goat's milk	*S. thermophilus* CR12, *L. casei LC01*, *L. helveticus PR4, L. plantarum 1288*	Antihypertensive Effects	28 mg/100 g	HPLC	[368]
	Fermented milk by strains isolated on old-style cheese	ULAAC-A and ULAAC-H	Not detected	5000 mg/100 g	HPLC	[369]
	Fermented skimmol/Led milk by L. helveticus	*Lactobacillus* seed culture 37 °C for 18 h	Antihypertensive Effects	113.35 mg/100 g	HPLC	[370]
	Fermented milk	*L. casei strain Shirota and Lc. lactis YIT 2027*	Antihypertensive Effects	120 mg/100 g	HPLC	[371]
	Fermented milk by L. plantarum	*L. plantarum PU*11. 8 h, 30 °C	Antihypertensive Effects	77.4 mg/100 g	HPLC	[371]
	Fermented pork sausages	Fig proteases	Antihypertensive activity and improve brain function.	0.124 mg/100 g	HPLC	[372]
	Japanese lactic-acid fermented fish	*LAB, L. plantarum* for 1 year		1300 mg/100 g	HPLC	[373]
	Cheese	*L. brevis PM17, L. plantarum C48, L. paracasei PF6, L. delbrueckii subsp. bulgaricus PR1, and L. lactis PU1*	Not detected	15-63 mg/kg	HPLC	[374]
	kimchi	*L. brevis OPY-1, L. brevis OPK-3*		0.825 g/L and 2.023 g/L	HPLC	[375]
	Poacai	*L. brevis NCL912 and GABA057*		35.66 g /L and 23.40 g /L	HPLC	[376]
	sea tangle	*L. brevis BJ20*		2.465 mg/L	HPLC	[377]
	wholemeal wheat sourdough	LAB		258.7 mg/kg	HPLC	[378]
	Oat fermented	Fungi strain (*Aspergillus oryzae*)		435.2 μg/g	HPLC	[379]
	Cheese	*L. lactis ssp. lactis strain*		320 mg/kg	HPLC	[365]
	Fermented goat's milk	A mixed LAB starter		28 mg/kg	HPLC	[368]
	Fermented skimmol/Led milk	*Lactobacillus helveticus*		113.35 mg/L	HPLC	[380]
	Cheddar cheese	Probiotic strain		6773.5 mg/kg	HPLC	[366]
	Fermented milk	Strains isolated on old-style cheese		5000 mg/kg	HPLC	[369]
	Fermented milk	*L. plantarum*/ LAB combination		77.4/ 144.5 mg/kg	HPLC	[381]
	Fermented skimmol/Led milk	*L. plantarum*		970 mg/kg	HPLC	[382]
	Low fat fermented milk	LAB combination and protease		806 mg/kg	HPLC	[383]
	Japanese fermented fish	*Lactic-acid bacteria*		1300 mg/kg	HPLC	[384]
	Black raspberry juice	*L. brevis* GABA 100, 37 °C for 20 h		27600 mg/kg	HPLC	[385]

Table 2 (*Continued*)

Amino acids	Source	Fermentation conditions	Functionality	Content	Analysis	Reference
	Fermented pepper (Capsiccum annuum L.) leaves-based beverage	*L. homohiochii* JBCC 25 and *L. homohiochii* JBCC 46	Antioxidant and antidiabetic capacities	263000 mg/kg	HPLC	[385]
	Salchichon	*Pediococcus pentosaceus, Micrococcus varians (phh®),* (0.1 g/Kg batter), 3 days (25 °C, 90% RH)	Enhance the flavor, Antioxidant ability of taurine	Asp 22.97, glu 586.85, ser 45.41, asn 66.80, gly 69.59, Taurine 81.92, Threonine 34.11, Alanine 216.36, Carnosine 206.26, Tryptophan 43.59, Ornitine 11.99, Lysine 28.37(mg/100 g)	HPLC	[386]
	Fermented shrimp pastes	Spountanous fermentation for 180d	Enhance the flavor, Antioxidant ability of taurine	Taurine 919 ± 45, Aspartic acid 493 ± 13, Citrulline 528 ± 35, Methionine 183 ± 3, Tyrosine, 173 ± 15 (mg/100 g)	HPLC	[387]
Asp	Fermented cocoa	Spountanous fermentation	Enhance the flavor,	13.0 mg/100 g	HPLC	[388]
Glu				11.7 mg/100 g		
Leu				14.8 mg/100 g		
Ala				18.1 mg/100 g		
Phe				11.7 mg/100 g		
Tyr				1.8 mg/100 g		
Val				11.0 mg/100 g		
Ile				9.0 mg/100 g		
Lys				49.4 mg/100 g		
Arg				23.5 mg/100 g		
Thr				11.8 mg/100 g		
Ser				27.8 mg/100 g		
Gly				8.6 mg/100 g		
Met				7.2 mg/100 g		
Pro				14.0 mg/100 g		
Cys				2.7 mg/100 g		
His				4.9 mg/100 g		
Free amino acids	Mung bean and soy bean	*Rhizopus sp. 5351*; SSF; 48 h; 30 °C	Antioxidant and immunostimulant	Not dected	HPLC	[389]
L-Lysine	Complete media BY and BYG	*Corynebacterium glutamicum*; 40 °C, 28 h; SMF	Enhance the absorption of calcium and other bioactives	Not dected	Not detected	[390]
Minerals	Source	Fermentation condition	Functionality	Content	Detected method	
	Italian salami	SSF	Reduction the content of NaCl in the salami	Na 1881, K 440, Ga 37, Mg 16, P 304, Fe 1.4, Zn 4.1. (mg/100 g)	ICP-AES	[391]
	Camembert	SSF	Not dected	Calcium 116, Magnesium6.0, Phosphorus 104, Sodium 253, Potassium 56, Iron 0.10 (mg/100 g)	ICP-AES	[392]
	Sauerkraut	Spountanous fermented	Not detected	Ca 30, Fe 1.47, Mg 13, P 20, K 170, Na 661, Zn 0.19, Cu 0.096, Mn 0.15, Se 0.6, F 0.7 (mg/100 g)	ICP-AES	[393]
Vitimin	Source	Fermentation condition	Functionality	Content	Detected method	
Folate (Vitamin B9)	Yogurt	CRL871 + CRL803 + CRL415 and incubated at 42 °C	Not detected	180 ± 10 µg/L	microbiological assay	[394]
	Sauerkraut	Spontaneous fermentation of naturally present LAB, probably a mixture of several nonspecified LAB species.	Not detected	50–210 µg/kg	HPLC	[395]
	Tempeh	SSF with bacterium that accompanies the mold	Not detected	416.4 µg/100 mg	HPLC	[396]

Table 2 (*Continued*)

Amino acids	Source	Fermentation conditions	Functionality	Content	Analysis	Reference
Vitamin E	Salami Salchichón Chorizo Cervelat	Spontaneous fermentation	Not detected	0.23 mg/100 g 0.28 mg/100 g 0.28 mg/100 g 0.12 mg/100 g	HPLC	[392]
Vitamin K	Salami Pepperoni Sauerkraut			1.11 mg/100 g 5.8 mg/100 g 13 mg/100 g		
Thiamine VB1	Salami Salchichón Pepperoni Chorizo Cervelat			0.60 mg/100 g 0.2 mg/100 g 0.36 mg/100 g 0.3 mg/100 g 0.14 mg/100 g		
Vitamin B2	Salami Salchichón Pepperoni Chorizo Cervelat		Not detected	0.23 mg/100 g 0.21 mg/100 g 0.32 mg/100 g 0.13 mg/100 g 0.16 mg/100 g	HPLC	
	Tempeh	SSF with bacterium that accompanies the mold	Not detected	3.9 μg/100 g	HPLC	[396]
Niacin	Salchichón Pepperoni Chorizo	Solid state fermentation	Antioxidant ability, enhance Fermented meat color and Increase the shelf life	10 mg/100 g 4.6 mg/100 g 7.1 mg/100 g	HPLC	[397]
Vitamin B6	Salami Salchichón Pepperoni Chorizo Cervelat		Not detected	0.36 mg/100 g 0.15 mg/100 g 0.35 mg/100 g 0.15 mg/100 g 0.14 mg/100 g		
Vitamin B12	Salami Salchichón Pepperoni Chorizo Cervelat	SSF	Not detected	2.0 mg/100 g 1 mg/100 g 1.7 mg/100 g 1 mg/100 g 3 mg/100 g		
Pantothenic	Salami Pepperoni Cervelat		Not detected	1.66 mg/100 g 1.48 mg/100 g 0.4 mg/100 g		
Folic acid (VB)	Fermented sausage	Natural fermentation	Folic acid is associated with the prevention of several diseases, such as neural tube defects in birth and some cancers and CVDs.	0.88–3.37 mg/100 g		[398]
Vitamin C	Pepperoni Sauerkraut	SSF SSF	Antioxidant ability Antioxidant ability	0.7 mg/100 g 14.7 mg/100 g		[55]
	Fermented Cactus pear (Opuntia ficus-indica L.)	*L. plantarum*1MR20	Antioxidant to Caco-2/TC7 cells	7.2 ± 0.1 mg/100 g		[399]
Folate	Wheat and rye	Yeast fermentation	Not detected	Not detected	HPLC	[400,401]
Vitamin K 2	Soybean	*B. subtilis* strain MH-1;Shaking at 37 °C for 1 day and statically cultured at 45 °C for 5 days	Cofactor for posttranslational modification of glutamic acidresidues to g-carboxyglutamic acid residues	Not detected	HPLC	[402]
Antioxidant vitamins (Vitamin C and Vitamin E)	Seed of Lupinus albus L. var. Multolupa	Natural fermentation; 37°C, 48 h; Dark; SMF	Antioxidant capacity	Not detected	HPLC	[403]

Lipid	Source	Fermentation condition	Functionality	Content	Analysis	Reference
CLA	Yogurt	LAB fermentation	Antioxidant ability	6.9 mg/g	GC	[404]
	Cheese	SSF	Antioxidant ability	4.0 mg/g	GC	[405]
	Processed cheeses	SSF	Antioxidant ability	1.9 mg/g	GC	[406]
	Cheese (sheep milk)	SSF 180 days	Reductions of inflammatory cytokines, rheological parameters and platelet aggregation	Not detected	GC	[407]

Table 2 (*Continued*)

Lipid	Source	Fermentation condition	Functionality	Content	Analysis	Reference
	Cheeses	Natural fermentation	Not detected	Asiago 5.91 ± 1.95 mg/g Belpaese 5.22 ± 1.97 mg/g Caciotta 5.98 ± 1.18 mg/g Caciocavallao 5.35 ± 2.77 mg/g Cheddar 5.86 ± 0.89 mg/g Crescenza4.76 $\pm$ 0.79 mg/g Gouda 4.32 ± 1.43 mg/g	GC	[408]
EPA DHA	Shrimp (Acetes spp.)	Ferment for 360 days at ambient temperature (28–35 °C).	Antioxidant ability	Not dected	HPLC	[387]
DHA EPA	Fish sauce	SMF Without starter culture	Not detected	28.54% 6.82%	GC	[360]
FFA	Roquefort Blue Gamonedo Camembert Brie Parmesan Cheddar Swiss Provolone PortSalut Munster	SSF	Not detected	32453 mg/kg 32320 mg/kg 75,685 mg/kg 5066 mg/kg 2678 mg/kg 13697 mg/kg 997 mg/kg 4277 mg/kg 2671 mg/kg 700 mg/kg 6260 mg/kg	GC	[409]
Short-chain fatty acids	resistant starches dietary fiber	Probiotics Ferment in the colon	reduce the risk of developing gastrointestinal disorders, cancer, and cardiovascular disease	Not detected	GC	[410]
γ -linolenic acid	Pear pomace	*M. isabelline*; SSF	Enhance the content of GLA	2.9 mg/g	GC	[411]
Polyphenols	Source	Fermentation condition	Functionality	Content	Detected method	Referrence
	Red wine vinegar	Acetic acid bacteria	Antioxidant, enhance the falvor	Malvidin-3-glucoside (53.04), Malvidin-3-(6-acetyl)-glucoside (26.3), Malvidin-3-glucoside-4-vinyl (Vitisin B) (14.25),Acetyl vitisin B (11.77), Carboxy-pyranomalvidin-3-glucoside (vitisin A) (9.03), Malvidin3-(6-p-coumaroyl)-glucoside (8.2), Malvidin-3- glucoside-ethyl (epi) catechin (7.76), Catechyl-Pyranocyanidin-3-glucoside (5.63) (μg/mL)	LC-MS	[412]
	Apple vinegar	SMF	Antioxidant	Chlorogenic acid (347.7), Catechuic acid (68.2), Gallic acid (61.2), Caffeic acid (17.2) (μg/mL)	LC-PDA	[413]
	Pomegranate vinegar	SMF	Antioxidant	Gallic acid (67.8), Caffeic acid (47), Caffeic acid (13.4) (μg/mL)	LC-PDA	[414]
	Kiwi vinegar	SMF	Antioxidant	Gallic acid (9.67), Chlorogenic acid (3.12), Vanillic acid (1.78), Catechin (1.47), Phlorizin (0.49), P-coumaric acid (0.34), Caffeic acid (0.04), Ferulic acid (0.01), (μg/mL)	LC-PDA	[415]
	Sugarcane vinegar	Acetic acid fermentation	Antioxidant	Benzoic acid (3.6), Catechin (2.1), Gallic acid (0.3), Ferulic acid (0.1) (μg/mL)	LC-PDA	[416]
	Coconut vinegar	Acetic acid fermentation	Antioxidant	Catechin (4.3), Benzoic acid (3.6), Salicylic acid (2.1), Gallic acid (0.3), Caffeic acid (0.1), Ferulic acid (0.1) (μg/mL)	LC-PDA	
	Palm vinegar	Acetic acid fermentation	Antioxidant	Salicylic acid (85.0), Coumarin (2.9), Gallic acid (0.2), Ferulic acid (0.2), Caffeic acid (0.1) (μg/mL)	LC-PDA	
Gallic acid	Tannic acid	*Aspergillus awamori*; SMF; 37°C; 60 h.	Antioxidant capacity	Not detected	LC-PDA	[417]
	Creosote bush	*Aspergillus niger*; 30°C; 5 days	Antioxidant capacity			[418]
Ferulic acid	Eugenol	*Penicillium simplicissimum*; SMF; 48 h, 30°C.	Antioxidant capacity			[419]

Table 2 (*Continued*)

Lipid	Source	Fermentation condition	Functionality	Content	Analysis	Reference
	Rice bran	*LAB*; SMF; 30°C, 7 days.	Antioxidant capacity			[420]
Ellagic acid	Cranberry pomace	Lentinusedodes; SSF; 37 ± 1 °C; 14 days.	Antioxidant capacity			[421]

Enzymes	Source	Fermentation condition	Functionality	Content	Dected method	Referrence
Endo- and exopeptidases	Meat products	*D. hansenii CECT* 12487, 27 °C for 48 h	Enhance the content of free amino acids and peptides	Not detected	SDS-PAGE	[422]
Glutaminase	fermented sausages	*Debaryomyces spp. CECT 11* 815 40 °C for 48h	Neutralize the acid pH, generate L-glutamate that can act as a flavor enhancer	Not detected	Gel filtration chromatogra-phy	[266]
Fibrinolytic enzymes	Fermented Shrimp Paste	Natural fermentation	Anticoagulant activity	Sequence DPYEEPGPCENLQVA	SDS-PAGE	[423]
CoQ	*Doenjang*	*Meju* (soybean starter), rice, barley, *Aspergillusoryzae*, *Bacillus* sp., *Mucor* sp., *Penicilliumsp.*, *Bacillus licheniformis*	Antioxidantive	308.5 ± 18.9 μg/g	LC-MS	[424]
	Kochujang	*Saccharomyces cerevisiae*, *Saccharomyces delbrueckii*, *Sacch.rouxii*, *Sacch.bisporus* *Pichia membranefaciens* *Debaryomyces kloeckeri*	Antioxidantive	47.8 ± 5.8 μg/g	LC-MS	[424]
	Chonggukjang	*Bacillus subtilis*, *Bacillussubtilis* var. *natto*	Antioxidantive	241.5 ± 22.9 μg/g	LC-MS	[424]
	Soy sauce	*Meju Bacillussubtilis*, *Lactobacilus plantarum*, *Leuconostoc mesenteroids*, *Lactobacillus casei*, *Pediococcu shalophilus*, *Saccharomyces rouxii*, *Saccharomyces acidifaciens*, *Torulopsis dattila*, Liquid seasoning	Antioxidantive	5.5 ± 0.6 μg/g	LC-MS	[424]
	Kimchi	*Lactobacillus plantarum*, *Lactobacillus brevis*, *Leuconostoc mesenteroids*, *Streptococcus liquefaciens*, *Streptococcus faecalis*, *Pseudomonas* sp. Side dish	Antioxidantive	148.2 ± 12.3 μg/g	LC-MS	[424]
	Jeotgal	Raw fish (shrimp, anchovy, alaskan pollack egg, oyster, clam) *Bacillus subtilis*, *Leuconostoc mesenteroids*, *Pediococcus halophilus*, *Torulopsis* sp., *Sarcina* sp., *Saccharomyces*sp. Side dish, ingredients in Kimchi	Antioxidantive	296.8 ± 11.9 μg/g	LC-MS	[424]
	Jeotgal, a fermented fish	Not detected	Antioxidantive	315.9 ± 12.6 μg/g	LC-MS	
Fibrinolytic Enzyme	fermented shrimp paste	Natural fermented	Anticoagulant Activity	18 kDa, DPYEEPGPCENLQVA	SDS-PAGE	[423]
Fructosyl transferase	Agricultural by-products (cereal bran/ rice bran/ wheat bran)	*Aspergillus foetidus* and *A. oryzae*; SSF;28°C; 6 to 7days.	Hydrolyze Polysaccharides to Functional fructo oligosaccharides	Not detected		[425]

Alkaloids	Source	Fermentation condition	Functionality	Content	Detected method	Referrence
ascorbigen (ABG)	sauerkraut	Spontaneous fermentation	Anticarcinogenic properties	3 and 18 μmol/100 g fresh weight	HPLC	[426]
I3C	sauerkraut	Spontaneous fermentation	Antiinflammatory and protective properties against reactive oxygen species (ROS)	0.13–0.94 μmol/100 g fresh weight	HPLC	[426]

Table 2 (*Continued*)

indol-3-acetonitrile (I3A)	sauerkraut	Spontaneous fermentation	Cancer-protective properties	0.07–0.25 µmol/100 g fresh weight	HPLC	[426]
Alkaloids	Source	Fermentation condition	Functionality	Content	Detected method	Referrence
Sulforaphane (SFN)	sauerkraut	Spontaneous fermentation	Antioxidant	28–32 µmol/100 g dry weight	HPLC	[427]
allyl isoth-iocyanate (AITC)	sauerkraut	Spontaneous fermentation		16–125 µmol/100 g dry weight		[427]
daidzein	cheonggukjang	*Bacillus subtilis* CS90, 60 h		330.09 mg/kg dry weight	HPLC	[428]
genistein	cheonggukjang	*Bacillus subtilis* CS90, 60 h		25.62 mg/kg dry weight	HPLC	[428]
Carotenoids	Source	Fermentation condition	Functionality	Content	Analysis	Referrence
β-carotenoid	Whey/ Potato medium	*R.glutinis*/ *R.mucilaginosa*; SMF; Photo fementation; 28°C;48h	Membrane-protective antioxidants	Not detected	HPLC	[429]
	Crude glycero	*R. glutinis*; SMF; 30°C, 72 h				[430]
	Chicken feathers	*R. glutinis*; SMF; 30°C, 48 h				[431]
	Fermented radish brine	*R. glutinis*; 30°C, 72 h; SMF				[432]

Melatonin	Source		Fermentation	Functionality	Content	Analysis	Referrence
	Groppello		Not reported	Antioxidant	0.35	HPLC-MS-MS	[433]
	Melas				0.62		
	Nebbiolo				0.14		
	TerrediRubinoro				0.17		
	SyrahIGT				0.23		
	PlacidoRizzotto				0.05		
	LaSegreta				0.31 (ng/mL)		
	Cabernet Sauvignon		Not reported	Antioxidant	0.27	HPLC-MS-MS	[434]
	JaenTinto				0.16		
	Merlot				0.21		
	PalominoNegro				0.25		
	Petit Verdot				0.2		
	PrietoPicudo				0.2		
	Syrah				0.2		
	Tempranillo				0.14		
	Merlot				5.2		
	TintilladeRota				18.0 (ng/mL)		
	Sangiovese		Not reported	Not detected	0.5 (ng/mL)	HPLC-F	[435]
	Albana		Not reported	Antioxidant	0.6 (ng/mL)	MEPS-HPLC-F	[436]
	Pomegranate Wines	Wonderful	Yeast, *Saccharomyces cerevisiae* var. *bayanus* (Awri R2; Mauri Yeast Australia, Toowoomba, Queensland, Australia)	Not reported	5.5 (ng/mL)	LC–ESI-MS/MS	[437]
		MollardeElche			0.54 (ng/mL)		
		Coupage			2.91 (ng/mL)		
	Beer	Volt-Damm	Yeast fermentation	Antioxidant to human serum	0.17 (ng/mL)	HPLC	[438]
		Murphy's			0.14 (ng/mL)		
		MahouNegra			0.14 (ng/mL)		
		Amstel			0.13 (ng/mL)		
		Coronita			0.13 (ng/mL)		
		Budweisser			0.12 (ng/mL)		
		Guiness			0.12 (ng/mL)		
		Cruzcampo			0.11 (ng/mL)		
		Carlsberg			0.10 (ng/mL)		
		Mahou5estrellas			0.10 (ng/mL)		
		Heineken			0.09 (ng/mL)		
		SanMiguel			0.09 (ng/mL)		
		Mahou Clásica			0.08 (ng/mL)		
		LaikerSin			0.07 (ng/mL)		
		SanMiguel0.0			0.06 (ng/mL)		
		BucklerSin			0.05 (ng/mL)		
		KaliberSin			0.05 (ng/mL)		
		Buckler0.0			0.05 (ng/mL)		
Serotonin	Wine		SMF fermented by *L. plantarum*	Antoxidant ability	23 mg/L	HPLC	[439]

Bacteriocins	Source	Fermentation condition	Functionality	Content	Analysis	Referrence
	Italian type salami	SSF	Anti-Listeria activity	Lactobacillus curvatus	RAPD-PCR	[440]

Table 2 (*Continued*)

Bacteriocins	Source	Fermentation condition	Functionality	Content	Analysis	Referrence
	suan-yu (a Chinese traditional low-salt fermented whole fish)	SSF	Antimicrobial Activity Anti-L. monocyto genes, Staphylococcus aureus, and *Escherichia coli*	L. plantarum	RAPD-PCR	[441]
	budu	SSF	Inhibit the growth of indicator microorganisms (*Bacillus cereus, Lactococcus lactis, S. aureus, Salmonella enterica, L. monocytogenes, and E. coli*).	*Lactobacillus paracasei LA07*	RAPD-PCR	[442]
	Hukuti maas		Bacteriocin active against foodborne pathogens and with specificity toward *Aeromonas spp.*	HKBT-9 strain	RAPD-PCR	[443]

Volatile compounds	Source	Fermentation condition	Functionality and dose	Content	Analysis	Referrence
2-Furfuraldehyde	Fermented paste fish (squid miso)	Squid mantle flesh with *Aspergillus oryzae-inoculated koji*	DPPH radical-scavenging activity 11.95 mg/mL	2.1 μg/mL	GC	[444]
Furfuryl alcohol			DPPH radical-scavenging activity 6.96 mg/mL	3.5 μg/mL		
2-Acetylpyrrole			DPPH radical-scavenging activity 7.32 mg/mL	9.2 μg/mL		
4-Ethylguaiacol			DPPH radical-scavenging activity 19.53 mg/mL	49.0 μg/mL		

gelatinisation and generating bioactive peptides, amino acids and free phenolic compounds [89,90].

During fermentation, unwanted substances such as sugars, antinutritional factors or even toxins may be reduced or eliminated simultaneously and efficiently. **Black** tea dust, a waste material with the same composition as its corresponding commercial tea, can be utilized through fermentation with the yeast *S. cerevisiae*. Fermentation for 6 h could convert over 80% of sugars (including sucrose), without decreasing the contents of total phenolics and the beneficial amino acid, *L*-theanine [91]. The alcohol-soluble proteins (prolamins) in barley and rye and the gliadins in wheat gluten have been associated closely with the damage of the small intestinal mucosa and the incidence of chronic inflammatory disorder (e.g. the Celiac disease) [92]. Fermentation produces foods with a lower risk of causing gluten intolerance, because fermentation facilitates desirable proteolysis reactions needed to break down the proteins (e.g. in sourdough breads) [89].

4.1. Bioactive peptides

Bioactive peptides are inactive sequence fragments within the precursor protein, and may exhibit potent bioactivities once being released from the precursor *via* proteolysis during aging and fermentation. During fermentation, large proteins are broken down via enzymatic hydrolysis into active peptides e.g. the milk-derived peptides with anti-oxidant, anti-hypertensive, antimicrobial, immunemodulatory and mineral-binding effects [93], and the soybean-derived taste-active peptides (e.g. umami and bitter peptides, with/without anti-hypertension and hypocholesterolemic activities) [94]. Antihypertensive and ACE-inhibiting and antiproliferative peptides as well as opioid peptides have been found in cheese [95] and other fermented products such as soy sauce and fish sauce [96,97]. Peptides of marine origin have demonstrated bioactivities such as cardio protective effects, antioxidant activity, and abilities to promote general well-being and mental health [98]. Proline-containing peptides, Lys–Pro and Ala–Pro, from anchovy sauce, as well as Ser–Val and Ile–Phe dipeptides in *kapi*, were found to possess significant ACE-inhibitory capacities [99]. The peptides obtained through fermentation of goat placental proteins by *Aspergillus Niger* exhibited strong antioxidant activity and immunoactivity (especially those with a molecular weight <10 KDa) [100]. In fermented meat products such as fermented sausages, bioactive peptides with high ACE inhibitory activities were also found [101].

4.2. Amino acids

Amino acids are well known for their central roles in human metabolism, performance and health. Amino acids contain carboxyl (-COOH) and amine (-NH_2) functional groups, and exhibit different tastes (sweet, sour, umami or bitter). The building blocks of natural proteins are exclusively *L*-amino acids. Thus, L-amino acids are of importance in nutrition. The amounts of amino acids required by the human body vary with the age and health status of the individual. Nine amino acids (His, Ile, Leu, Lys, Met, Phe, Thr, Trp and Val) are essential for humans (as the human body cannot synthesize them), while Arg, Cys, Tyr and Tau (though taurine is not technically an amino acid) are semi-essential for children [102,103].

In addition to normal chemical synthesis and biosynthesis, fermentation is another approach to produce amino acids. The profiles of amino acids in fermentaed foods are greatly affected by factors such as the nature of raw material(s), type and quantity of starters used for fermentation, and conditions of the fermentation process. Sulfur amino acids, methionine and cysteine were found in fermented soybean products [104]. In salt-fermented shrimp paste or **blue-**mussel fermented sauce, biologically active taurine can be found (which can fight against oxidative stress) [105]. Taste-active amino acids are abundant in fermented foods especially fermented seafoods, such as sweet amino acids (e.g. lysine, alanine, glycine, serine and threonine), bitter amino acids (e.g. phenylalanine, arginine, tyrosine, leucine, valine, histidine, methionine and isoleucine), as well as umami- and sour -tasting glutamic acid and aspartic acid [106]. The amino acid profile of kefir was found to change with the fermentation process and storage time, with higher contents of lysine, proline, cysteine, isoleucine, phenylalanine and arginine were found after fermentation [107]. Fermented anchovy and shrimp tend to have higher contents of free amino acids compared to their unfermented samples [108].

Microbial strains have been used to produce amino acids *via* fermentation e.g. *E. coli* strains for the production of amino acids like phenylalanine [109]. Strategies have been set to transform natural microbial fermentation towards metabolic engineering to achieve more precise and efficient production of amino acids [110]. Branched-chain amino acids are good examples. These amino acids are among the nine essential amino acids for humans and contain an aliphatic side-chain with a branch (*L*-valine, *L*-leucine and *L*-isoleucine). The branched-chain amino acids can be manufactured *via* fermentation with microorganisms such as *C. glutamicum*, *E. coli* and *S. thermophilus*, with those produced using *S. thermophilus* exhibiting positive functions in protein synthesis, muscle performance and maintenance of lean body mass [111]. GABA (a major inhibitory neurotransmitter) deserves extra attention here. GABA is abundant in fermented foods like kimchi, cheese and fermented seafood products, but is low in unfermented foods including fruits (grapes and apples), cereals (maize and barley), and vegetables (asparagus, broccoli, cabbage, potatoes, spinach and tomatoes) [112]. Some LAB strains such as *Lactobacillus buchneri, Lactobacillus brevis*, and *Streptococcus salivarius* are especially capable of catalyzing the decarboxylation of glutamate and converting glutamic acid to GABA [113,114]. It is worth noting that *D*-amino acids (DAA) may occur in significant amounts in fermented foods. *L*-amino acids are the dominant natural amino acids and more utilized by the body than *D*-amino acids with the same peptide chain sequence. However, food processing may allow racemization of *L*-amino acids to their *D*-isomers. Certain microorganisms enable enantiospecific modulation of amino acids during fermentation and subsequent storage of the obtained fermented foods (e.g. wine, yoghurt and cheese) [115,116]. The utilization of any DAA may be affected by the presence of other DAA in the diet. There is a need to investigate the roles of *D*-amino acids in human nutrition and their different effects on food properties as compared with their *L*-forms.

4.3. Enzymes

Fermentation and enzymes are closely related. Fermentation breaks down food molecules and produces new substances throught the action of enzymes contained within microorganism(s). Futher, fermentation is a technology used to produce enzymes and their cofactors from microorganisms, such as yeast and bacteria, in industrial settings. Two fermentation methods are mainly used: Submerged fermentation (SMF, which involves a liquid nutrient medium) and solid-state fermentation (SSF, which is performed on a solid substrate). Amylase is a commercial enzyme widely used in the industry and can be produced *via* SSF of agro-industrial wastes such as mustard oil seed cake as the substrate using *Bacillus* sp. The amylase obtained after a 72-h fermentation at 50 °C and pH 6 exhibited an activity of 5400 units/g and thermostability at 70 °C for about 2 h in the absence of salt [117]. Coenzyme Q or ubiquinones as endogenous lipophilic enzyme cofactors can be generated in *Jeotgal*, and its concentration in final fermented foods can reach 297–316 mg/kg [118]. Purified phytase can be produced *via* fermemtation with *Aspergillus oryzae* NRRL 1988, before purification by fractionation with acetone, gel filtration, and chromatographic separation [119]. Glycosidases can be obtained through malolactic fermentation with *Oenococcus oeni* strain Lalvin EQ54 in a wine medium [120].

4.4. Lipids

Natural resources or industrial waste products have been utilized to produce biofuels and biochemicals including lipids and desirable fatty acids. Carbohydrate- and lignin-rich materials have been used as substrates for this purpose. Bioconversion *via* fermentation has been proven efficient, when natural or engineered *Rhodococcus* strains (e.g. *R. opacus* PD630, *R. jostii* RHA1, and *R. jostii* RHA1 VanA−), especially in the form of their co-culture, were used for lipid production (by which glucose, lignins and their derivatives in the raw material were simultaneously converted into lipids) [121]. CLA is well known for its abilities to decrease blood LDL cholesterol level, promote immune function and bone formation, and prevent hyperinsulinemia, atherosclerosis, gastrointestinal and colon cancers. Certain *Bifidobacteria* and *Lactobacilli* strains can produce CLA isomers in fermented milk and derived dairy products, thus imparting the final fermented products with enhanced health properties [122]. Value-added functional lipid products can be produced *via* fermentation from industrial processing wastes such as seafood waste streams (such utilization of waste materials also helps resolve environmental pollution problems). Omega-3 polyunsaturated fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) (both are beneficial for fighting against neuropsychiatric disorders and cardiovascular diseases), can be produced through fermentation of the wastes from fish processing industries using a LAB culture such as *Pediococcus acidilactici* NCIM5368 [123].

4.5. Carbohydrates including polysaccharides and oligosaccharides

Raw materials contain more or less carbohydrates including monosaccharides, disaccharides, oligosaccharides and polysaccharides, with most monosaccharides and disaccharides being fermentable. The profile of carbohydrates undergoes dynamic changes during fermentation. The pattern and rate of such changes depend on the type and proportion of carbohydrate constituents in the substrate(s) for fermentation. EPSs with different structures and viscosity, such as glucan, fructans and gluco-/fructo-oligosaccharides, are produced as extracellular polysaccharides of microorganisms during fermentation. These EPSs either bind to the surface of cells or enter into the extracellular environment [124]. The EPSs produced by LAB exhibit prebiotic effects including the promotion of gut health [125,126] and enhancement of immune response [127]. Beer is rich in fibers that contain monosaccharides (e.g. arabinose, fructose, galactose, glucose and xylose), disaccharides (e.g. isomaltose and maltose) and trisaccharides (e.g. isopanose, maltotriose and panose), and exhibits high colonic fermentability (up to 98%) [128]. The content of total dietary fiber and the proportion of insoluble and soluble fibers in fermented legumes (such as **black** beans, cowpeas, lentils, bengal or green grams) depend greatly on the type of plant material, the type and activity of microorganism, as well as fermentation conditions. For example, the lignin content may be doubled in fermented lentils, whereas the contents of cellulose and hemicellulose decrease [129]. Rare sugars such as *L*-ribose [142] and low-calorie sugar substitutes such as sugar alcohols (e.g. xylitol) can be produced from hemicellulose hydrolysate *via* fermentation with an *E. coli* strain [130].

4.6. Polyphenols

Phenolic compounds are well known for their antioxidant properties and contributions to the prevention and treatment of various health problems. Fermentation has been proven feasible for releasing phenolic compounds from a wide range of natural food resources, and facilitating biotransformation of these compounds (which may increase their bioactivities and bioavailability). As a result, fermented foods and beverages contain different concentrations of simple phenols (e.g. phenolic acids), more complex phenolics (e.g. flavonoids, including monomeric (catechins) and oligomeric flavonols (proanthocyanidins)), chalcones (e.g. xanthohumol), lignans and ellagitannins [131]. Fermentation of Aronia (*Aronia melanocarpa*, a phenolic-rich native berry of the North America) was found to produce phenolic metabolites with higher antioxidant capacity, bioavailability and α-glucosidase inhibitory activity [132]. Fermentation improves the utilization of milling by-products such as wheat bran. The use of starter cultures L. *brevis* E-95612 and *Candida humilis* E-96250, together with the addition of cell-wall-degrading enzymes, was found to release free amino acids and phenols (e.g. hydroxycinnamic acids) and improve protein digestibility [133]. Fermentation of rice bran with *Rhizopus oligosporus* and *Monascus purpureus*, singly or in combination, increased the phenolic acid content and antioxidant activity (e.g. ferric reducing ability of plasma and DPPH radical-scavenging activity), with the combined use of the two strains resulting in the greatest release of ferulic acid [134].

Yeasts such as *Saccharomyces* strains may significantly affect the polyphenol composition of the obtained fermented product, because the metabolites generated during fermentation such as pyruvic acid and acetaldehyde can react further with the phenolic compounds [135]. Both alcoholic and malolactic fermentation can affect phenolic compounds, with their influence depending on the type of microorganism and fermentation conditions. Malolactic fermentation is often carried out after alcoholic fermentation to convert malic acid into lactic acid, causing the production of novel compounds e.g. *trans*-ferulic acid and some flavanols (which do not exist initially in wines before fermentation) and increasing the levels of certain bioactives (which already occur after alcoholic fermentation e.g. *trans*-resveratrol, epicatechin, catechin, caffeic acid, coumaric acid, myricetin and quercetin) [136,137]. The β-glucosidase occurring in microorganisms can contribute in different ways to malolactic fermentation, depending on the type of microorganism and activity of β-glucosidase [138]. The absence or presence of grape skin during fermentation also influences the impact of fermentation on the phenolic profile of wine [139].

4.7. Alkaloids

Alkaloids, a group of natural compounds with basic nitrogen atoms and bitter taste, exhibit significant biological activities including analgesic (e.g. morphine), antiarrhythmic (e.g. quinidine), antibacterial (e.g. chelerythrine), antimalarial (e.g. quinine), anticancer (e.g. homoharringtonine), antiasthma (e.g. ephedrine), antihyperglycemic (e.g. piperine), cholinomimetic (e.g. galantamine), and vasodilatory (e.g. vincamine) effects. Alkaloids can be produced by a wide range of organisms including plants, animals and microbes like bacteria and fungi. Alkaloids have been extracted from the leaves (e.g. **black** henbane), fruits or seeds (e.g. sour passion), root (e.g. *Rauwolfia serpentina*) or bark (e.g. *Cinchona*). Fermentation technologies allow the low-cost production of various alkaloids, such as those from the fungus *Trichoderma harzianum via* SSF [140]. An *Escherichia coli* fermentation system with a growth medium containing simple carbon sources but no additional substrate has been created to produce alkaloids (e.g. (*S*)-reticuline, with a yield of 46.0 mg/L culture medium) [141]. *De novo* production of the anti-cancer alkaloid, noscapine, was proven feasible *via* microbial fermentation with a single engineered yeast strain [142]. Producing ergot alkaloids *via* SSF with *Claviceps fusiformis* (an ascomycetous fungus) appeared to be advantageous (3.9 times higher contents of ergot alkaloids) over SMF [143].

4.8. Organic acids

Organic acids have pKa values in the range from 3 (carboxylic acid) to 9 (phenolic acid), and can be used as an acid, substrate, solvent, source of protons, and/or ligands for complexing metal cations such as aluminium and iron ions. Organic acids can preserve foods through penetrating the cell walls and disrupting normal physiology of pH-sensitive strains such as *Salmonella* spp., *Clostridia* spp, *E. coli*, *Listeria monocytogenes*, *C. perfringens*, and *Campylobacter* species [144]. The organic acids in fermented foods vary enormously, depending on the type of strain, nature of raw material, and fermentation method and conditions. The organic acids generated in fermented foods can inhibit the growth of spoilage and pathogenic microorganisms [39]. Fermentation with *E. coli* strain can produce organic acids and their derivatives from substrates such as cellobiose, cellulose glycerol and glucose [144,145]. In *chungkukjang*, the concentrations of volatile organic acids increase during fermentation, and branched-chain organic acids (2-methypropionic acid and 3-methylbutanoic acid) tend to have much higher contents than straight-chain organic acids [146]. Among the organic acids in fermented fish sauces, lactic acid has the highest content as it accumulates during fermentation [147]. In addition to suppressing undesirable microorganisms, the organic acids generated during fermentation also exhibit health benefits. For example, lactic acid generated helps regulate the glycemic response through lowering the rate of starch digestion [148], whilst acetic acid and propionic acid can slow gastric emptying [149].

4.9. Minerals

Minerals exist in the body as nutrients that are essential for human body's metabolic processes and sustaining life. Essential minerals (including calcium, chloride, copper, chromium, fluoride, iodine, iron, magnesium, manganese, molybdenum, phosphorus, potassium, selenium, sodium, sulfur and zinc) must be incorporated through the diet. Meat and meat products are a good source of iron (Fe), with fermented sausages having a Fe content in the range of 1–2.5 mg/100 g [150]. Fermented dairy products are rich in highly bioavailable minerals e.g. ripened cheeses have abundant minerals especially calcium, chloride, sodium, phosphorus, potassium and zinc, while yogurt is enriched with calcium, potassium, phosphorus and zinc [151]. The profile and bioavailability of minerals are modified during fermentation. The availability of calcium, phosphorus and magnesium was found to increase when cheese was produced using probiotic cultures, mainly due to the proteolysis and lipolysis processes involved [152]. The bioavailability of Zn and Fe minerals in fermented pulses can be increased by 50%–70% and 127%–277%, respectively [153]. A higher absorption of iron was reported for individuals who often consumed lactic fermented vegetables compared to those who tend to eat unfermented vegetables, probably due to the conversion of iron into the more absorbable ferric (Fe^{3+}) form during fermentation [154].

4.10. Vitamins

Fermented foods generally contain significantly higher vitamin contents than their raw counterparts [155]. Kefir is rich in vitamin B12 while yogurt has high concentrations of vitamins A, B and D [156]. Tempeh (a fermented soybean cake) has greater amounts of B group vitamins than unfermented soybean products. Natto (fermented soybean) produced with *Bacillus subtilis* is high in vitamin K (especially vitamin K2) [157]. The different contents of vitamins in fermented products result from the differences in raw materials, microbial strains and fermention conditions. Fermentation can improve the bioavailability of vitamins such as biotin, folate, riboflavin, pantothenic acid, pyridoxamine, pyridoxine, pyridoxal and thiamin, because of the actions of microorganisms [158]. Fermentation with *Lactobacilli* can decrease the content of vitamin B1 in fermented foods, whilst fermentation with yeast raises its level [159,160]. However, a reduction of vitamin content after fermentation is also possible. For example, a significant decrease of vitamin B1 content was found after the fermentation of chickpeas and cowpeas using *L. casei*, *L. leichmannii*, *L. plantarum*, *P. acidilactici* and *P. pentosaceus* [161].

4.11. Flavor or aroma-active compounds

Fermented foods are well known for their unique flavors. Fermentation leads to the production and accumulation of volatile and non-volatile aroma or aroma-active compounds including those related to bitter, umami, sweet, sour and salty tastes. The flavor or aroma-active compounds are mainly alcohols, aldehydes, amines, esters, fatty acids (especially those volatile species), ketones, organic acids, phenols, thiophene, sulfur compounds and other nitrogen-containing compounds (Table 3) [162]. The microbial strains used greatly affect the profile of flavor compounds in the final fermented foods. Yeasts mostly produce alcohols, aldehydes, esters, ketones, lactones, organic acids, terpenes and sulfur compounds, whereas, molds can generate a wide variety of flavor compounds such as alcohols, esters, ketones and pyrazines [163]. The macromolecules (i.e., proteins, carbohydrates and lipids) in raw food materials can contribute directly to the flavor of fermented foods, and may also serve as or deliver precursors of the flavor or aroma-active compounds e.g. sweet, sour, umami and bitter amino acids, bitter oligopeptides and organic acids [164]. For example, methyl methanethiosulfinate, methyl methanethiosulfonate, acetaldehyde, ethanol, ethyl acetate, methanol, *n*-propanol and 2-propanol are responsible for the characteristic aroma and flavor of sauerkraut [165,166]. Free amino acids, alcohols (mainly ethanol), aldehydes, esters, ketones, hydrocarbons, hydrocarbons, as well as sulfur compounds (such as α-copaene, α-farnesene, germacrene B or D, β-myrcene, α- or β-phellandrene, and β-sesquiphellandrene), are all important contributors to the flavor of kimchi [167].

5. Consumer perception, cultural impact and safety concerns

The success of new food development is highly dependent on consumer behaviors and attitudes associated with foods including food perception, acceptance, preference and choice [168]. Many factors affecting consumer food choice include 1) biological factors (e.g. hunger, satiety and palatability); 2) economic factors (e.g. cost, accessibility, income, education and knowledge); 3) physical factors (e.g. such as time and skills); 4) social determinants (e.g. culture, family, peers and family norms or setting); 5) psychological determinants (e.g. mood, stress, guilt, family and history influences); 6) meal attributes (e.g. patterns, convenience and familiarity); 7) other factors (e.g. belief, optimistic bias, and previous experience and knowledge about foods, dietary preference and restriction) [169–172]. Among these influencing factors, sensory properties are one of the most important determinants. Recognition of the interplays among individual preferences and cultural/social influences will promote the innovation associated with fermentation processes and fermented foods.

5.1. Tradition and consumer beliefs

Given the long history of fermented foods and their widespread distribution across the globe, high famililarity, popularity and diversity are key characteristics of traditionally-consumed fermented products. Familiarity strongly influences the liking and perception of a cross-cultural ethnic food [173]. This is probably one major reason why the global fermented food segment continues to grow and spread all around the world. During the development of fermented foods, cross-cultural differences in the appreciation of fermented foods, motivational differences between trying and regularly eating, along with the differences between the pre-existing consumer perception/expectation and the actual consumer acceptability, all deserve attention [174,175]. Certain western consumers like Americans do not appreciate or even dislike the fermented flavor of kimchi [176]. A cross-cultural study involving American and Korean consumers using kimchi revealed that the difference in food preference between the two groups of consumers was associated with the consumption frequency and fermentation degree of kimchi [177]. Moreover, consumers may have negative or neophobic reactions to unfamiliar foods (e.g. fear and doubts), which is likely due to insufficient background information about the foods [178]. This may also apply to fermented foods. Some individuals tend to associate the fermented flavor with signs of microbial spoilage (a negative response). Therefore, alleviating consumer concerns about microbial safety (through education and resources) and the stepwise introduction of new fermented foods would increase the likeability and acceptance of these foods [179].

Consumer perception on the typical sensory characteristics of certain fermented foods, (such as the perceived "*gu-soo* flavor", "well-aged flavor", "well-fermented flavor", and "high in bean-to-paste ratio" of traditional *Doenjang*), do not necessarily agree with the sensory attributes that drive the liking for commercial products (e.g. the preference for strong sweetness with umami taste of commercial *Doenjang*) [174]. Besides product characteristics, consumers' liking of fermented foods (e.g. commercial rice wines [180] and lager beer [181]) also depends on external factors such as brand, price, and nutritional label. Consumers around the world share almost the same definition of "traditional foods", but tend to perceive and respond differently to the concept of "innovation" [182]. Thus, it remains challenging to combine the two concepts, "tradition" and "innovation", in one single food product (as for fermented foods).

Modern consumers tend to enjoy new taste experiences and prefer convenient foods (due to their fast-paced lifestyles and

Table 3
Characteristic flavours generated during fermentation.

	Characteristic flavour	Key flavour compounds	Threshold	Source	Fermentation conditions	Reference
Volatile compounds	Fishy and sweaty nots	2-Ethylpyridine and dimethyl trisulfide	Not detected	Fish sauce	Submerged fermentation	[445]
	Balsamic, burnt, malt	3-Methyl-1-butanol	4×10^{-6}			
	Nutty, buttery, oily	2-Methylbutanal	1×10^{-6}			
	Almond, nutty, buttery	3-Methylbutanal	1.1×10^{-6}			
	Meaty, potato	3-(methylthio)-Propanal	0.45×10^{-6}			
	Rancid, sweaty odor, cheesy	3-Methylbutanoic acid	0.12×10^{-6}			
	Bitter almond, burnt sugar	Benzaldehye	750.89×10^{-6}			
	Alcoholic	Ethanol	$950{,}000 \times 10^{-6}$			
	Green, plastic	(E)-2-Penten-1-ol	89.2×10^{-6}			
	Solvent like, malty, pungent	2-Methyl-1-propanol	6505.2×10^{-6}			
	Burnt, meaty, pungent	1-Penten-3-ol	358.1×10^{-6}			
	Fusel oil, butter	2-Methyl-1-butanol	15.9×10^{-6}			
	Balsamic, burnt, malt	3-Methyl-1-butanol	4×10^{-6}			
	Green, wax	1-Pentanol	150.2×10^{-6}	Budu	Solid state fermentation	[446]
	Pungent	Propanal	15.1×10^{-6}			
	Nutty	2-Methylpropanal	1.5×10^{-6}			
	Nutty, buttery, oily	2-Methylbutanal	1×10^{-6}			
	Almond, nutty, buttery	3-Methylbutanal	1.1×10^{-6}			
	Almond, malt, pungent	Pentanal	0.012×10^{-6}			
	Fishy, Grassy	Hexanal	5×10^{-6}			
	Fishy, oily, fatty, sweet, nutty	Heptanal	2.8×10^{-6}			
	Light ethereal, nauseating	Acetone	100×10^{-6}			
	Chemical, burnt	2-Butanone	$35{,}400.2 \times 10^{-6}$			
	Rubber, pungent, burnt	2-Ethylfuran	2.3×10^{-6}			
	Beany, grassy, licorice	2-Pentylfuran	5.8×10^{-6}			
	Oily, burnt sugar	2-Furanmethanol	4500.5×10^{-6}			
	Cooked cabbage, vegetable, onion, putrid	Dimethyl disulfide	1.1×10^{-6}			
	Meaty, potato	3-(Methylthio)-propanal	0.45×10^{-6}			
	Fishy	Trimethylamine	0.000037×10^{-6}			
	Roasted, coffee, peanut	2,6-Dimethylpyrazine,	$0.2\text{-}9 \times 10^{-6}$			
	Bitter almond, burnt sugar	Benzaldehyde	750.89×10^{-6}			
	Pungent, vinegar like	Acetic acid	24×10^{-6}			
	Rancid, buttery, acidic, sour, cheesy	Butanoic acid	0.24×10^{-6}			
	Cheesy, butter	2-Methyl-propionic acid	6550.5×10^{-6}			
	Rancid, sweaty odor, cheesy	3-Methyl-butanoic acid	$0.12\text{-}0.7 \times 10^{-6}$			
Carbonyl compounds	Ethereal, fresh, green, pungent	Acetaldehyde	Not detected	yogurt	Submerged fermentation; anaerobic condition; Streptococcusspp. (thermophilus; salivarius)/L. delbrueckii	[447]
	Sweet, fruity, ethereal, wood pulp, hay	Acetone	Not detected	Cheese	Solid state fermentation	[447]
	Sweet, fruity Varnish-like, sweet, fruity	2-Propanone 2-Butanone	Not detected	yogurt	Submerged fermentation; anaerobic condition; Streptococcusspp. (thermophilus; salivarius)/L. delbrueckii	[447]
	Mushroom-like Buttery, creamy, vanilla	1-Octan-3-one Diacetyl	Not detected	cheese	Solid state fermentation	[448]

Table 3 (*Continued*)

	Characteristic flavour	Key flavour compounds	Threshold	Source	Fermentation conditions	Reference
	Buttery	acetoin				
	Metallic, aldehydic, herbaceous	3-Methyl-2-butenal	Not detected	yogurt	Submerged fermentation; anaerobic condition; Streptococcusspp. (thermophilus; salivarius)/L. delbrueckii	[447]
	Fruity, acetone	2-Pentanone	Not detected	cheese	Solid fermentation	[449]
	Green, malty, unripe, cocoa	3-Methylbutenal	Not detected	yogurt	Submerged fermentation; anaerobic condition; Streptococcusspp. (thermophilus; salivarius)/L. delbrueckii	[447]
	Butter, vanilla, mild	2,3-Pentanedione				
	Green, cut-grass	Hexanal				
	Floral, fruity	2-Hexanone				
	Green, sweet	Heptanal				
	Sweet, floral, citrus, grass-like	Nonanal				
	Fruity, musty	2-Nonanone	Not detected	Yogurt	Submerged fermentation; anaerobic condition; Streptococcusspp. (*thermophilus;salivarius)/L. delbrueckii*	[450]
	Sweet, fruity, cheesy	2-Pentanone				
	Fruity, spicy, cinnamon	Heptanone				
	Mushroom, fruity	3-Octanone				
	Mushroom-like, earthy, fruity	1-Octen-3-one				
	Grassy-herbal, **green-**fruity, floral	Nonanone				
	Floral, rose-like, herbaceous	2-Undecanone				
	Flowery, honey-like, rosey, **violet-**like, styrene	2-Phenylacetaldehyde	Not detected	Cheese	Solid state fermentation	[451]
	Malty	3-Methylbutanal	Not detected	Bread	SSF starter cultures: L. plantarum or L. delbrueckii or L. sanfrancisco or L. brevis and then added Baker's yeast (*S. cerevisiae*) /30 °C/20 h--------Bread lactic acid bacteria 24 h/28 °C	[452]
	Malty	2-Methylbutanal				
	Green, grassy	Hexanal				
	Fatty	(Z)-2-Nonenal				
	Fatty	(E)-3-Nonenal				
	Cooked-potato-like	3-(methylthio)Propanal				
	Cucumber-like	(E, Z)-2,6-Nonadienal				
	Deep fat fried	(E, E)-2,4-Nonadienal				
	Fatty	(E, Z)-2,4-Decadienal				
	Deep fat fried	(E, E)-2,4-Decadienal				
	Biscuit-like, putrid	(Z)-4-Heptenal				
	Heney-like	Phenylacetaldehyde				
	Cucumber-like	(E, Z)-2,6-nonadienol				
Alcohols	Alcoholic, iodoform-like	1-Pentanol	Not detected	Cheese Bread	Solid state fermentation for cheese Solid state fermentation for bread	[451] [453]
	Banana like, wine-like, fusel oil	1-Butanol				
	Sweet, fruity, fusel oil, wine-like	2-Butanol				
	Sweet, wine-like	1-Propanol				
	Fruity, ethereal, wine-like	2-Propanol				
	Green, alcoholic, fruity, fresh	2-Pentanol				
	Earthy, oily, fruity, green, sweetish, dry, dusty carpet	2-Heptanol				
	Fatty green	2-Honanol				
	Rose, **violet-**like, honey, floral	Phenylethanol				
	Malty, wine, onion	2-Methylbutanol				
	Alcoholic, fruity, grainy	3-Methylbutanol				
	Mushroom-like	1-Octen-3-ol				
	Mushroom	Oct-1-en-3-ol				
	Bacon, phenolic, smoked, spicy	Guaiacol				
Esters	Solvent-like, fruity, pineapple	Ethyl acetate	Not detected	Cheese Bread Soy sauce	Solid state fermentation for cheese Solid state fermentation for bread Solid state fermentation for soy sauce	[454,455]

Table 3 (*Continued*)

	Characteristic flavour	Key flavour compounds	Threshold	Source	Fermentation conditions	Reference
	Fruity, sweet, banana	Ethyl butanoate	Not detected	Fermented on sugarcane bagasse	Trichoderma viride EMCC-107 in solid state fermentation	[456]
	Fruity, apple, banana	Ethyl hexanoate				
	Fruity, banana, apple	Ethyl octanoate				
	Pineapple	Butyl acetate				
	Pineapple, sweet, fruity, banana	Ethyl caproate				
	Floral, rose, lily-jasmine, honey	Ethyl phenylacetate				
	Fruity, green, apple, banana	Ethyl butyrate				
	Fruity	Hexanoic acid ethyl ester				
	Coconut	δ-Octalactone				
	Peach	γ-Nonlactone				
	Coconut	δ-Lactone				
		6-Pentyl-α-pyrone (6-PP)				
	Peach	γ-Undecalactone				
	Slight coconut/fruity	γ-Dodecalactone				
	Sweet/fruity	δ-Dodecalactone				
Acids	Vinegar, sour, sharp, fresh cottage cheese	Ethanoic acid (acetic acid)	Not detected	Cheese Vinegar	Solid state fermentation for cheese Solid state fermentation for vinegar	[457]
	Vinegar, pungent, sour milk, pungent, cheese, gas, burnt, cloves, fruity	Propionic acid				
	Sharp, cheesy, rancid, sweaty, sour, putrid	Butyric acid				
	Sweet, mild, rotten apple	Isobutyric acid				
	Rotten fruit, mild, sweaty, rancid, fecal, putrid, flowery	Isovaleric acid				
	Pungent, rancid, flowery	Hexanoic acid				
	Wax, soap, goat, musty, rancid, fruity	Octanoic acid				
	Sour	Lactic acid				
	Sour	Formic acid				
	Sour	Propanoic acid				
	Sour	Butanoic acid				
	Sour	3-methyl butanoic acid				
	Sweaty, buffer, cheese, strong, acid, facel, rancid, dirty, sock	Butyric (n-butyric acid)				
	Stale, butter, sour, fruit, grassy, fatty, cheese, aged cheddar	Capric acid				
	Sweaty, cheesey, charp, goaty, bad breath	Caproic acid				
	Cheesey, rancid, pungent, sweaty	Caprylic acid				
	Cheesey, rancid, sweaty, rotten, sweaty	Isovaleric acid				
	Sweaty	2-and 3-Methylbutanoic acid				
	Sweaty	Pentanoic acid				
	Rancid	Decanoic acid				
Sulfur compounds	Intense, lactone-like, sulfurous, cabbage	Dimethyl sulfide	Not detected	Cheddar cheese	Solid state fermentation	[458]
	Boiled cabbage, cauliflower, garlic	Dimethyl disulfide				
	Sulfurous, fecal	Dimethyl trisulfide				
	Sulfur, cabbage-like, pomegranate	Di-methyl sulphide				
	Rotting cabbage, cheese, vegetative, sulphur	Methanethiol				
	Cooked cabbage, boiled potato, sulfury	Methional				
	Cooked cauliflower	s-Methyl thioacetate				

Table 3 (*Continued*)

	Characteristic flavour	Key flavour compounds	Threshold	Source	Fermentation conditions	Reference
Lactones	Coconut-like, peachy, creamy, milk fat	δ-Decalactone	Not detected	cheese	Solid state fermentation	[459]
	Cheesey, coconut, sweet, soapy, buttery, peach, milk fat	δ-Dodecalactone				
	Peach, almonds, herbs, lilacs, fruit, toffee	γ-Decalactone				
Amino acids	Umami	Glutamic acid	0.3 mg/mL	Jiangluobo	Air-drying in an oven at 60 °C for ~2–3 d to constant weight (Jiangluobo, 195.20 ± 0.05 g; salted radish, 324.40 ± 0.05 g)	[460]
	Umami	Aspartic acid	1mg/mL			
	Sweet/bitter	Proline	3 mg/mL			
	Sweet	Alanine	0.6 mg/mL			
	Bitter	Leucine	1.9 mg/mL			
	Sweet/bitter	Valine	0.4 mg/mL			
	Bitter/sweet	Arginine	0.5 mg/mL			
	Sweet	Glycine	1.3 mg/mL			
	Sweet	Threonine	2.6 mg/mL			
	Sweet/bitter	Lysine	0.5 mg/mL			
	Bitter	Isoleucine	0.9 mg/mL			
	Bitter	Phenylalanine	0.9 mg/mL			
	Bitter	Tryptophan	Not detected			
	Bitter	Tyrosine	Not detected			
	Bitter/sweet/sulfurous	Methionine	0.3 mg/mL			
	Bitter	Histidine	0.2 mg/mL			
	Sweet	Serine	1.5 mg/mL			
	Umami, sour,	Glutamic acid	Not detected	Vietnamese fish sauce	Submerged fermentation without starter culture	[461]
Peptides	Umami	Asp-Phe-Lys-Arg-Glu-Pro	Not detected	**White** Sufu (Fermented Tofu)	Actinomucor elegans AS 3.227, 28°C for 48 h.	[462]
	Umami and sour	Asp-Glu-Asp-Phe-Lys-Arg-Glu-Pro	Not detected			
	Caffeine-like	YPFPGPIHN YPFPGPIPNS LVYPFPGPIHN VYPFPGPIPN YPFPGPIPN YQQPVLGPVRGPFPIIV	Not detected	cheese	Solid state fermentation for cheese	[463]
Fatty acids	Orthonasal aroma	*n*-Hexanoic	9.2 mg/kg	Bouton de culotte® goat cheese	Ripening period was 3 wk	[464]
	Retronasal aroma	*n*-Octanoic	Not detected			
	Orthonasal aroma	*n*-Nonanoic	2.4 mg/kg			
	Orthonasal aroma	4-Methyl-octanoic	0.02 to 0.6 mg/kg			
	Orthonasal aroma	4-Ethyl-octanoic	0.0018 to 0.006 mg/kg			
	Orthonasal aroma	*n*-Decanoic	1.7 to 16 mg/kg			

abundant food options), while also demanding foods that promote their wellbeing naturally (owing to their increasing awareness of close relationship between diet and health). The wellbeing-driven demands of consumers motivate food industries to develop foods enriched with multiple nutrients and bioactives. Food fermentation enables *in-situ* enrichment of a range of health-beneficial substances, thus fermented foods and carry various essential nutrients and bioactive substances (e.g. probiotic microorganisms, prebiotics, enzyme(s), proteins, polysaccharides, bioactive lipids, antioxidants, minerals and vitamins). Further, consumers tend to equate fermented foods to probiotic foods and believe that the living microorganisms and their metabolic products in fermented foods have "positive effects on human health". Interestingly, in pursuit of fermented foods with health-promoting properties, there is no large difference between the Western and Eastern countries, and also between the rural and urban societies.

5.2. Safety concerns related to fermentation and resulting fermented foods

Fermented foods can be produced from all types of raw food materials including those of plant and animal origins. For most fermented foods, the processes involved in their production are inhibitory to many microorganisms, especially as fermentation can decrease the pH to below 4.0 through the conversion of carbohydrates into lactic acid. However, in some instances, pathogens may survive in the optimal environment for fermentation cultures and present significant food safety hazards. The pathogenic cultures potentially existing in fermented foods include *Listeria monocytogenes* (which can proliferate at refrigeration temperatures and grow at relatively high NaCl concentrations), *Escherichia coli* (which may occur in unpasteurized fermented foods and can be eliminated through heating ≥ 60 °C and by reducing water activity), *Clostridium* spp. (which have an optimum growth temperature at 60–75 °C and produces spores resistant to heating and hydrolases), *Salmonella* spp. (which can reside in the human intestinal tract, though are mostly killed under normal cooking conditions), and *Staphylococcus* spp. (which occurs on the skin and mucous membranes of humans. The failure of the starter culture during cheese making may allow *S. aureus* to grow) [183,184].

Contamination of mycotoxins represents a major food safety issue for fermented foods. In particular, indigenous fermentation (which involves old-fashioned processes and improper working conditions), or uncontrolled fermentation in the tropical and subtropical regions (where offer ideal conditions for the growth of fungal pathogens or molds), introduce increased risk of contamination by food borne pathogens and associated mycotoxins (including aflatoxins) [185]. For example, aflatoxins, a group of toxic fungal metabolites produced by some species of the genus *Aspergillus* (e.g. *Aspergillus flavus*, *Aspergillus parasiticus* and *Aspergillus nomius*), can cause severe harm to humans. Therefore, the main challenges with fermentation process are associated with the predictability of contamination caused by undesirable or even toxic microbes in fermented foods. The large scale and high diversity of commercial fermentation processes make the challenges more severe, due to the difficulty to monitor precisely the complex and interdependent/interactive metabolic pathways as well as the balance between synthesis of target substance(s) and innate cell physiology [186,187]. For the age-old practice of "spontaneous fermentation", uncontrolled fermentation caused by the developed epiphytic microflora is possible (which causes undesirable organoleptic properties or even detrimental microbiological/toxicological consequences) [188]. Accordingly, it is crucial to examine the physiological and metabolic properties of the intended microorganisms prior to their use [189].

The potential presence of nematodes and other species of worms (e.g. *Anisakis L3 larvae* and *trematodes*) in the raw seafood materials for fermentation, deserves extra attention, because fermented seafoods are mostly produced without thermal processing. Therefore, these parasites are food-safety hazards of these fermented products. Salting ($\geq$ 15% NaCl for 7 d) alone, or in combination with freezing (e.g. $-20\,^{\circ}$C for 48 h or $-40\,^{\circ}$C for 24 h) or irradiation can inactivate parasites effectively [190]. Standardizing the fermentation protocols and proper control over the fermentation process (especially the microorganisms involved) have been the important approaches for ensuring and improving the safety of fermented foods. Like other types of foods, fermented foods must meet all the international standards and requirements, including good manufacturing practices (GMP) and good hygienic practices (GHP) as the basic principles, hazard analysis & critical control points (HACCP) as the practical guidelines outlined by the Codex Alimentarius Commission (Alinorm 97/13A) and the European Parliament (Regulation EC no. 852/2004), and optional certifications like the ISO 22000 developed by the Codex Alimentarius Commission, and the food safety scheme British Retail Consortium Global Standard for International Food developed by food industry experts from retailers, manufacturers and food service organisations. Upgrading indigenous fermentation process is necessary to resolve manufacturing hygiene issues and uncontrolled reactions caused by unspecific microflora (individual or combined action of bacteria, yeast and fungi). Efficient and accurate methods for analyzing mycotoxins in various fermented foods are important for food safety. Chromatographic techniques such as gas chromatography (GC), high-performance liquid chromatography (HPLC) and thin-layer chromatography (TLC), as well as fluorescence-based detection methods, have been used for this purpose [191].

As for the safety assessment, it is important to consider the food matrx effect. Raw food materials used for the production of fermented foods naturally contain various species of microorganisms (which may be desired or undesired e.g. LAB, *Bacillus cereus* and *Vibrio parahaemolyticus*) [192]. Inhibition and elimination of food pathogens and other undesired microbes are critical to improving the hygiene of final fermented foods. Fermentation may degrade aflatoxins [193] due to the action of certain microorganisms e.g. LAB and *Saccharomyces cerevisiae* (which bind to aflatoxins) [194,195]. Moreover, during the risk assessment regarding food safety, the host function and barrier effect of a specific fermented food matrix on the bioactivation and biological effects of both the existing toxic or carcinogenic substances, and the newly generated (unstudied) substances must be carefully considered. In 2013, the U.S. Food and Drug Administration (FDA) released the final rule to address the uncertainty encountered during interpreting the results of conventional gluten test methods for fermented or hydrolyzed foods in terms of intact gluten and gluten cross-contact for gluten-free labeling. Communication on both the benefits and risks of fermentation food intake is imperative, to provide consumers with full story about the positive and potentially negative impacts of fermentated food consumption.

5.3. Microorganisms, raw materials and the safety of fermented foods

There are different types of microorganisms involved in fermentation processes, and these microorganisms may decrease or improve the safety of fermented foods. The safe use of microbial food cultures concerns not only microbial culture preparation, but also about their characteristics in different applications (strain levels, processing conditions and fermented food matrices). For the newly discovered or developed strains, safety assessments should be performed to examine metabolism, carcinogenicity/mutagenicity, and toxicity (including short-term, long-term, developmental and reproductive toxicity, immunotoxicity and neurotoxicity along with toxicokinetics/toxicodynamics). These assessments should also be applied to the new strains derived from the organisms that may already have a long history of safe use in food fermentation (e.g. LAB). As foods for human consumption, fermented foods should be subjected to routine microbiological assessment e.g. the control of *E. coli* O157:H7, *Bacillus cereus*, *Salmonella enteritidis*, *Staphylococcus aureus,* and *Listeria monocytogenes* in fermented vegetable products like kimchi [196,197].

Various chemical, physical, and biological methods have been used to prevent, reduce and eliminate aflatoxin contamination of fermented foods. Effective approaches include improvements in production, packaging and storage conditions, the application of thermal and nonthermal treatments (e.g. heating, drying, roasting, microwaving or high pressure processing (HPP)), and the use of organic solvents, ozone, charcoal, vitamin C, fungicides, or antimicrobial-containing plant-based extracts/oils) [60]. Amongst these, biological control has attracted special attention, owing to its perceived "naturalness" and effectiveness (especially when certain aflatoxins exhibit high temperature resistance). Biological control approaches suppress the growth of pathogenic or toxigenic microorganisms, *via* introducing bioprotective microbes with potent antagonistic properties to the fermented food system (such as fungi and bacteria e.g. *Lactobacillus*, *Bacillu*s, *Pseudomonas*, *Ralstonia* and *Burkholderia*) [198,199]. Probiotic strains such as *Lactobacillus*, *Leuconostoc*, *Lactococcus*, *Pediococcus*, and *Bifidobacterium* can assist the breakdown of some toxic chemicals that have been ingested together with food [200]. LAB strains are inhibitory to many other microorganisms including the spoilage organisms. Thus, the use of LAB as part of the co-culture can improve microbiological safety and the shelf life of fermented foods [201].

5.4. Biogenic amines and other harmful or toxic compounds

Toxic compounds such as biogenic amines (BAs) and carcinogenic molecules (e.g. ethyl carbamate) may be formed during food fermention by microorganisms. BAs are a class of compounds generated through microbial decarboxylation of amino acids, or amination and transamination of aldehydes or ketones during fermentation. BAs vary greatly in their chemical structures (e.g. number of amine groups), biosynthesis pathway and physiological functions. BAs are often grouped in aliphatic amines (e.g. putrescine (Put), cadaverine (Cad), agmatine (Agm), spermine (Spm), and spermidine (Spd)), aromatic amines (e.g. tyramine (Tym), and phenylethylamine (Phem)), and heterocylic amines (e.g.

Table 4
The biogenic amines in the fermented products.

Fermented products	Biogenic amine/(mg/kg)									
	Agmatine	Tryptamine	B-phenylethylamine	Putrescine	Cadaverine	Histamine	Serotonin	Tyramine	Dopamine	Reference
Anchovy sauce	15.2	152.1	10.6	140.3	74.9	810.5	41.8	202.5	6.2	
Sand lance sauce	12.5	201.7	2.2	163.4	41.4	538.2	117.4	212.8		
Squid paste		3.7	5.3	1.7	3.9	2.9	3.4			[465]
Clam paste	10.6		8.2	11.8	14.9	2.7	4.9			
Shrimp paste	13.3	8.1	9.2	7.6	30.1	4.6	22.7			
Fermented herring	2.28	3.69	3.24	2.34	2.77		2.91	2.75	3.74	
Anchovy paste	1.16	1.85	0.85	0.63	0.77		1.02	2.45	2.58	[466]
Smoked salmon	0.31	1.81	0.94	1.31	2.4		1.55	2.58	1.69	
Marinated anchovy	2.04	2.68	2.64	3.33	1.6		2.46	1.44	2.63	
Yulu in guangdong	22.1		120.7	348.1	230.5		142.7	7.8	9.9	[467]
Hard cheeses raw milk			0–40.7	176.32	328.45	510.2		453.77		
Hard cheeses pasteurized milk				175.39		65.45		301.06		[468]
Blue cheeses raw milk			0.27.42	875.8	756.78	1041.81		1051.98		
Blue cheeses pasteurized milk				0–237.56	40–89.4	127.02		526.63		
Dry sausage			ND2 -6.1	3.1–39.6	5.6	55.0		150.6		
Sauerkraut				0.1–4.0	3.0	20.0		2.0		
Fish paste		ND-16.3	ND-60.0		3.5	64.0		0.84		
Shrimp sauce								24.5		
Soy sauce		ND-93.0				274.0		466.0		
Sufu					47.0			49.0		
Miso								42.6		[469]
American red wine				0.6–5.5	4.0–47.0	0.2–15.5		0.2		
American white wine				0.7–11.7	3.2–108.3	0.2–11.4		0.5		
European red wine						ND-30		25.4		
European white wine						ND-20		6.5		
Nigerian palmwine								11.27		
American beer				3.7–7.1				7.1		

histamine (Him) and tryptamine (Trm)). BAs can be found in fermented meat (e.g. sausages), seafood (e.g. fish), dairy products (e.g. cheese), fruit and vegetables (e.g. sauerkraut), soybean products (e.g. temph), and alcoholic beverages (e.g. wine and beer) (Table 4). Factors favoring the formation and accumulation of BAs include the presence of decarboxylase-positive microorganisms such as those naturally occurring in raw materials (e.g. in spontaneous fermentation), starter cultures used for controlled fermentation (especially strains of *Lactobacillus* species), availability of free amino acids, raw material composition, substrate formulation (e.g. presence of salts, sugars or nitrites), and processing and handling conditions (pH, water activity, fermentation time and temperature) [202–204]. Higher amounts of BAs are normally found in the fermented foods produced, handled and stored under poorly hygiene conditions, even though initial raw materials are low in BAs.

BAs at low concentrations may be required for certain physiological functions and normally do not cause harm to humans (e.g. the self-detoxifying ability of amine oxidases like mono- and di-amine oxidases inside the human intestine). However, intake of BAs at high concentrations can be toxic for humans. The toxic dose of a BA depends greatly on the efficiency of an individual's detoxification. In addition to routine raw material quality control and assurance of sanitary conditions for handling and processing [205], other approaches are used to minimize BAs in fermented foods: 1) The use of nonamine forming (amine-negative) or amine oxidizing starter cultures and probiotic bacterial strains alone or in combination for fermentation; 2) The use of enzymes (di-amine oxidase), or bacteria containing this enzyme like *Arthrobacter crystallopoietes* KAIT-B-007 to oxidize the formed BAs [206–208]; 3) The application of non-thermal treatments e.g. high-pressure processing (HPP) [209], or low-dose irradiation [210,211] to reduce the BAs formed during fermentation. It was found that some strains could degrade BAs by up to 60%, with/without producing bacteriocin-like substances, such as L. *plantarum*, *S. xylosus* N°.0538, *B. amyloliquefaciens* FS-05 and *S. carnosus* FS-19, *S. intermedius* FS-20, *B. subtilis* FS-12, *Natrinema gari*, yeast strain Omer Kodak M8 [212–215]. The amounts of BAs indicate the degree of freshness/spoilage of a fermented product. The European Food Safety Authority (EFSA) regulates the safety of starters *via* a premarket safety assessment based on the "Qualified Presumption of Safety" (QPS) status. The EFSA pointed out that Him and Tym are likely the most toxic amines, and set a maximum Him amount of 200 mg/kg for products associated with *Clupeidae*, *Coryphaenidae*, *Pomatomidae*, *Scombreresocidae* and *Scombridae* families [216]. The European Union (EU) regulations allows a maximum Him amount of 100 mg/kg in fresh or canned fish, whilst 200 mg/kg in fermented fish or other enzymatically ripened foods [217]. The U.S. FDA defines a food as spoiled if the Him level is 50×10^{-6}, and set 50 mg/kg as the upper Him limit for most fish products [218,219]. Canada, Switzerland and Brazil set the maximum legal Him limit of 100 mg/kg for fish and fishery products. The Australian and New Zealand Food Standards Code does not allow the Him level of fish or fish products to be above 200 mg/kg [220]. For wine products, the European countries set different upper Him limits on wine: 2 mg/L in Germany, 3.5 mg/L in the Netherlands, 5–6 mg/L in Belgium, 8 mg/L in France, 10 mg/L in Austria, Hungary and Switzerland [206]. Due to the low volatility of BAs, lack of chromophores for most BAs and the low BA concentrations in complex food matrices, ultraviolet and visible spectrometric or fluorimetric techniques are not suitable for the detection and analysis of Bas. Instead, enzymatic methods along with TLC are used for qualitative or semiquantitative evaluations of BAs, with quantitation of BAs requiring capillary electrophoresis (CE), GC, HPLC, Ultra-HPLC (UHPLC) and/or ion-exchange chromatography (IEC) [221,222]. Some rapid analysis methods have recently been established including commercial test kits based on selective antibody and immunoassay methods [223] and enzymatic sensors [224].

Other harmful or toxic substances may also occur in fermented foods. Besides Him [225], fermented fish products may also contain *N*-nitroso compounds and genotoxins (which contribute to the incidence of cancer) [226]. Soy sauce made under improper conditions may contain ethyl carbamate (a Group 2A carcinogen) [227], or 3-MCPD (3-monochloropropane- 1,2-diol) and 1,3-DCP (1,3-dichloropropan-2-ol) (Group 2B carcinogens) [228]. The level of carcinogenic 3-MCPD (3-monochloropropane-1,2-diol) is deemed safe at 0.02 mg/kg by the EU and at 1.0 part per million by the Health Canada [228,229]. Furthermore, the removal of contaminated heavy metals is particularly important for fermented products such as fermented seafoods, as heavy metals such as arsenic, cadmium, lead and/or mercury are often found at high levels in certain seafoods. The uses of halotolerant bacteria (genus *Staphylococcus* and *Halobacillus*), tannins and/or cation-chelating resins may reduce or efficiently remove heavy metals in fermented foods, without changing the profile of nutrients and associated biological activities [230,231].

6. Strategies for creating fermented food products beneficial to human well-being

Successful food products in the modern marketplace often possess multiple desirable features related to sensory attributes (e.g. taste and texture), quality attributes (e.g. freshness, naturalness, safety and traceability), health attributes (e.g. nutritional value, biological value, clear health claims, or claims of toxin/allergen elimination), emotional attributes (e.g. happiness, enjoyment, communication and food experience), processing (e.g. spontaneous or controlled fermentation), and handling (e.g. ease of access, transport and disposal; visibility; resealability; labeling). Like other foods, consumers expect all these features to be included into a fermented product.

The development of fermented foods for human well-being "fermentation-enabled wellness foods" begins with the inclusion of cerain microorganisms (e.g. probiotic strains) in appropriate amounts. Then, food formulation and processing methods should be optimized to improve consumer acceptance of fermented foods [172]. Traditional fermentation methods based on empirical knowledge are progressively being replaced with science-based fermentation processes, advanced fermentation technologies and equipment, and modern industry safety practices. Science-based fermentation involves tailored microbial metabolism and enzymatic actions [232].

6.1. Fermented foods for human well-being

Scientific evidence has demonstrated that diet has an essential role in the prevention and management of chronic problems such as diabetes, obesity and cardiovascular diseases [233]. Popular fermented foods can make a huge contribution. For example, fermented papayas exhibits relatively high antioxidant activity [234]. The importance of fermented foods in human health can be enhanced and tailored, through increasing the amounts and bioactivities of nutrients and bioactive compounds, whilst removing undesired substances. Microbial fermentation provides an attractive alternative to chemical synthesis of nutrients and bioactives, and represents an efficient, convenient and safe synthesis process that can utilize different types of food materials to produce various macro-/micro-nutrients and bioactive substances such as flavonoids, isoflavones, terpenoids, alkaloids, polyketides and non-ribosomal peptides (Fig. 1) [235,236]. Unlike primary metabolites (which are essential for the growth of living organisms), secondary metabolites vary widely in chemical structures. The biofunctionalities of a fermented food are the sum of the independent effects of each co-existing active substances in the fermented food, evidenced for example in the anti-diarrhoea effects of fermented soya bean which realte to the multiple components in the product [237,238]. More details about "microbial chemical factories" will be presented in next section.

The consumer demand for healthier foods has lead to widespread efforts to reduce salt intake. To produce fermentation-enabled wellness foods or functional fermented foods, reducing the content of salt (especially sodium salts) in fermented foods is an essential pre-requisite. High salt intake can cause health problems such as heart disease, high blood pressure and stroke. The sodium salt content of many traditional fermented products (e.g. some condiment pastes, fish sauces and fermented sausages) remains very high. For some fermented foods (e.g. raw milk, specialty and artisanal cheeses), lowering the quantity of sodium salt is challenging, because the salt is involved in the physical and chemical interactions among food components, and influences the microorganisms and enzymes involved, food structure and flavor [239]. Three major approaches are adopted to decrease the salt content in final fermented foods: (1) Reduce the quantity of salts through the thorough washing of raw materials (like washed seafood muscle), partial replacement of NaCl with KCl or flavor enhancers, and addition of fish juice, koji or other umami microbial extract, and/or enzyme(s) (e.g. flavourzyme), accompanied by a fast fermentation process [240–243]; (2) Use certain starter cultures e.g. a high proteolytic starter culture for hard cheese [244], or probiotic strain L. *plantarum L4* in combination with *Leuconostoc mesenteroides* LMG 7954 for sauerkraut [245]; (3) Remove or reduce the salts through post-fermentation steps such as various extraction and separation processes (e.g. electrodialysis, reverse osmosis, nano-/ultra-filtration and chromatography) without changing the typical characteristics of target fermented products [246]. More research should be directed towards the reduction of salts in fermented foods, as the currently available approaches still have limitations. For example, fish sauces with a high potassium content made through replacing NaCl partially with KCl may not be suitable for patients with kidney disease; the use of $CaCl_2$ to replace sodium salts demands care that the residual $CaCl_2$ concentration in final fermented product is lower than the legal limit e.g. $\tilde{3}6$ mM for fermented vegetables (21 CFR 184.1193), and to avoid bitterness issues (i.e. which are detectable at 36 mmol/L $CaCl_2$).

6.2. Improve the performance of strains during fermentation

Many starter cultures (e.g. commercial organisms: *Aspergillus* spp. fungal culture, *Saccharomyces cervisae* yeast, and *Lactobacillus*, *Streptococcus* and *Bifidobacterium* bacteria) have been isolated from the nature. With the breakthroughs in cell biology, recombinant DNA technology, biomolecular engineering and metabolic modeling techniques, novel strains with enhanced productivity and tailored functional properties have also been developed. The strains used in the production of fermented food (Table 5) must be live, with GRAS (generally recognized as safe) safety status, and defined metabolic dynamics.

In many organisms, metabolic pathway components and pathway-specific regulators are tunable. The microbial production of desirable metabolites can be enhanced considering the balances in carbon flux and enzyme levels. Many aspects should be considered when one selects the pathway(s) for biosynthesis of nutrients and bioactives as metabolite products of fermentation. Accessibility is one major hurdle for such biosyntheses, because the substances are naturally generated in low yields in the native organisms and often exist in multiple forms. For example, the availability of a NADPH pathway is a factor that restricts a high production of (+)-catechins in *E. coli* [247]. It becomes more challenging when multiple strains are involved in fermentation. The co-existing strains produce their own products, which may be in competition for building blocks or interfere with the targeted pathway. In order to increase the efficiency of the fermentation system and obtain higher amounts of target metabolite products, it is important to remove (at least reduce) the competing pathway(s), delete the unwanted catabolism pathway(s) and selectively shift towards the

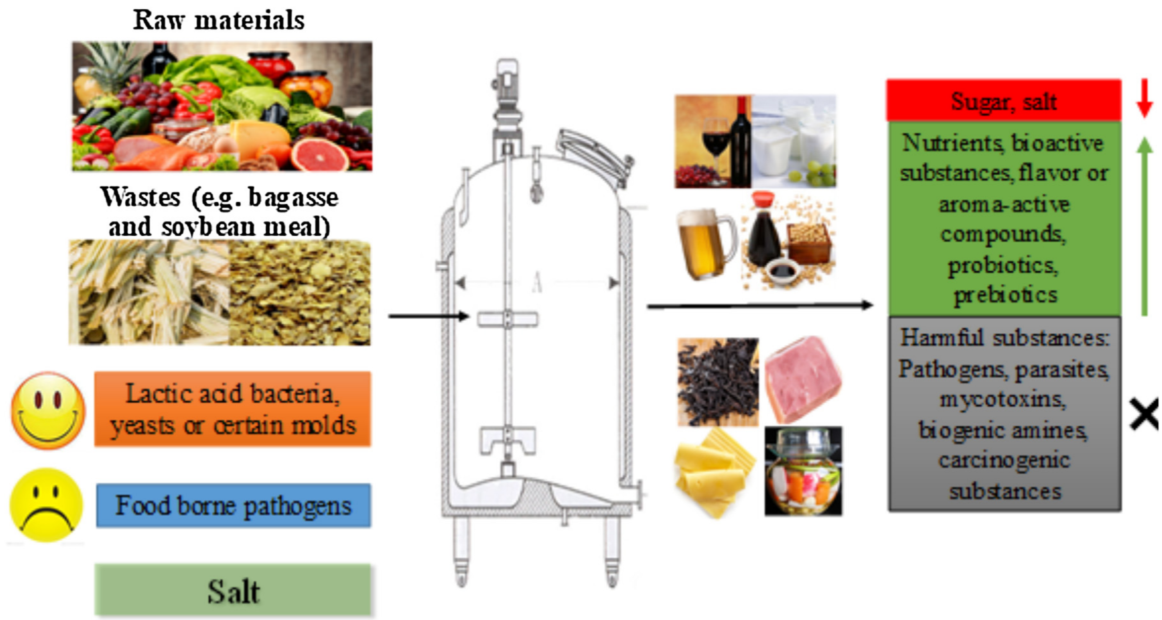

Fig. 1. The safe and sustainable production of beneficial microbes and fermentation-enabled wellness foods *via* precise control of microbial fermentation.

Table 5
The microorganisims used or detected in the fermentation process.

Microorganisim		Fermented products	Reference
Bateria	Lactic acid bacteria (LAB, *Lactobacillus spp.*) and coagulase-negative cocci (CNC, *Staphylococcus and Kocuria spp.*)	Fermented and ripening of sausages	[470]
	Staphylococcus xylosus and Staphylococcus carnosus	Fermented sausages of Vallo di Diano (Southern Italy)	[471]
	LAB including *Lactobacillus plantarum* and *Lactobacillus pentosus*	Fermented Thai fish product (som-fak (prepared with a mixture of fish, salt, rice, sucrose, and garlic)	[472]
	Lactobacillus sakei, Lactococcus, Vagococcus, Enterococcus, Macrococcuss, and *Staphylococcus*	*chouguiyu* (a traditional Chinese fermented-fish product)	[473]
	L. plantarum and *Pediococcus pentosaceus* ZY40 GY23	Grass carp sausages	[474]
	Lactobacillus and *Pediococcus*	Fermented narezushi (modern Japanese sushi)	[475]
	Virgibacillus sp. SK33, Virgibacillus sp. SK37, and *Staphylococcus sp.* SK1-1-5	Fermented anchovy sauce	[476]
	LAB (lactococci and lactobacilli)	**Blue** cheese	[252]
Bacterial	B. subtilis natto B. subtilis	Natto, Chungkookjang, kinema, hawaijar, tungrymbai, bekang	[477]
Molds	Molds	Fermented sausage	[478]
	koji molds (containing live *Aspergillus oryzae*) and douchi starter cultures	silver carp fish	[479]
	Commercial molds starters (eg, SP-01, NY, M1 and kome miso)	Fish pastes	[272]
Kefir grains	*Lactobacillus kefiri, Lactobacillus kefiranofaciens, Lactobacillus kefirgranum, Lactobacillus parakefiri, Lactobacillus delbrueckii, Lactobacillus acidophilus, Lactobacillus brevis, Lactobacillus helveticus, Lactobacillus casei, Lactobacillus paracasei, Lactobacillus fermentum, Lactobacillus plantarum, and Lactobacillus gasseri*	kefir	[480]
Yeast	*Candida, Kluyveromyces, Pichia, Saccharomyces, Yarrowia, Rhodotorula, Debaryomyces, Cryptococcus, and Trichosporon*	Fermented meat products	[481]
	Yeasts (21 strains from *Saccharomyces, Kluyveromyces, and Issatchenkia*)	Kefir	[482]
Fungi	*P. roqueforti, P. camemberti and Penicillium nalgiovense Penicillium species (eg, Penicillium brevicompactum, Penicillium commune, Penicillium verrucosum) Aspergillus species (eg, Aspergillus versicolor)*	Camembert and Brie cheeses mold-ripened cheeses	[477]

desired pathway(s) while upregulating the rate-limiting enzymes to enhance precursor supply.

The selection of microorganisms ("microbial factories") for producing probiotic fermented foods (i.e. products containing probiotics, or products with desired probiotic functionalities) should also consider carefully the nature and performance of the microbes (e.g. their productivity, viability, stability and metabolic characteristics). The different enzymes potentially produced by starter cultures (e.g. proteases and glycoside hydrolases) should also be considered, as these biocatalysts can modify both the ingested food components and the metabolite products yielded by the existing microorganisms. Such modifications may be beneficial or undesirable. The interactions between the starter cultures and other co-existing substances in food matrix, or between the microbes and digesta biomolecules in the gut, may become more intensive, when probiotics are used as a component of the starter culture. Among all the known metabolite products generated by microorganisms, bacteria account for approximately 70%. The most common heterologous hosts for bacteria-derived metabolite products are *Streptomyces* hosts and *E. coli*. Fungi are responsible for about 30% of the microbial metabolite products, and their share increases rapidly owing to low-cost carbon sources required for their growth and value-added metabolite products such as polyketides terpenoids, peptide-based compounds (e.g. nonribosomal peptides), and their combinations [248]. The heterologous production of beauvericin in *E. coli* [249] and the reconstruction of the four-gene pathway to produce tenellin in *A. oryzae* [250] represent two recent highlights in this field.

The strain selection for biosynthesis of nutrients and bioactives that exert health benefits to the humans must consider the presence of human gut microbiota as "micro manufactories and processors" (which can modify further the food components in the ingested fermented foods) [251]. LAB like L. *casei*, L. *acidophilus*, L. *paraplantarum*, L. *rhamnosus* and *Bifidobacterium* spp.) are commonly present in fermented foods such as kimchi, fermented olives, fermented cucumber, cheeses and salami. They may be used as primary starter cultures (e.g. the mesophilic and thermophilic LAB species for blue cheeses), or as part of the selected secondary microbiota (adjunct species) specifically for certain steps of the entire manufacturing process of fermented foods (e.g. flavor development, and acid or gas production) [252]. The studies on LAB have not been limited to the search for ideal starters, but also their uses as probiotics. LAB-containing fermented foods may possess health benefits associated directly with LAB (e.g. the well known protective effects of LAB as the probiotics on the host against detrimental microbes), and other properties such as antioxidant antiinflammatory and hemolytic activities, anticholesteremic and immunostimulatory effects, enhancement of the host's gut health and immune system, improvement of digestibility and bioavailability of essential nutrients, and suppression of antinutritional effect, allergy reactions, inflammatory symptoms, lactose intolerance and incidence of certain cancers [253–255]. Also, the health benefits of LAB-containing fermented foods may result from the released metabolites upon the action of LAB (e.g. polyohenols and alkaloids) [256].

Acetic acid bacteria have seen increasing interest in recent years, as more evidence becomes available on the health benefits associated with their fermented products such as vinegars and ciders. More than 40 acetic acid bacteria (including *Acetobacter*, *Gluconacetobacter* and *Komagataeibacter* species) can convert ethanol into acetic acid (a process known as "acetification", with strict requirements for oxygen) [257]. The oxygen level plays a critical role in the metabolism and performance of acetic acid bacteria: Aerobic respiratory metabolism is favored for most species when oxygen is the final electron acceptor, whereas, under nearly anaerobic conditions, survival and metabolism by some species is possible (other compounds act as final electron acceptors), causing wine fermentation [258]. In addition to the processing method and nature of strains, the origin of raw materials (e.g. apple, cherry, grape, oak, chestnut or strawberry) for vinegar fermentation determines both the sensory properties and the bioactive profiles of vinegar products, such as the type and amount of flavanols (e.g. catechin), hydroxybenzoic acids (e.g. gallic acid), hydroxycinnamic acids (e.g. caffeic acid), and tartaric esters of hydroxycinnamic acids (e.g. caffeoyl tartaric acid) [259,260].

Yeast has been used in various fermented foods and beverages (e.g. kimchi, bread, salami and cheese), especially as a key strain in bread making and alcoholic fermentation through metabolizing substrates like maltose and/or glucose. The species involved are mostly *Brettanomyces, Candida, Cryptococcus, Debaryomyces, Galactomyces, Geotrichum, Hansenula, Hanseniaspora*, *Kluyveromyces, Lodderomyces Metschnikowia, Pichia, Rhodotorula, Saccharomyces, Saccharomycodes, Saccharomycopsis, Torulopsis, Trichosporon, Yarrowia* and *Zygosaccharomyces.* These species can be grouped differently based on the strain nature, food application and product characteristics, for example, the bottom-fermenting *S. carlsbergensis* and top-fermenting *S. cervisae* for *Saccharomyces yeasts*. Fermentation with yeast(s) not only generate or modify food flavor through influencing volatile compounds, but also improve the nutritional quality and health properties of the food product *via* the production and/or bioconversion of nutrients and bioactives such as dietary fibers, proteins, purines and vitamins [261]. The nitrogen-containing substances greatly influence the performance and metabolism of yeasts, including metabolic pathways of yeast, redox status of yeast cells, rate of fermentation, production of biomass during fermentation (e.g. ethanol, acetic acid, glycerol and succinic acid) [262]. The use of yeast in fermented meat and dairy products such as salami and cheese is to improve product flavor through the actions of a number of enzymes from the yeast (e.g. endo-/exo-peptidases, amino-transferases, alcohol dehydrogenases, α-keto acid decarboxylases, aldehyde oxidases, NADP-glutamate dehydrogenase and/or glutaminase) [263–266]. Some yeast strains are of special interest, because of their distinct characteristics such as the ability to inhibit the growth of other microorganisms for the *Candida lusitaneae, Kluyveromyces marxianus* var. *bulgaricus*, and *Saccharomyces cerevisiae* strains isolated from aguamiel [267], and ability to produce inulinase of the *Kluyveromyces lactis* var. *lactis* strain from pulque [268]. In fermented foods like bread, symbiotic interactions are often observed between yeasts and *Lactobacillus* spp., e.g. as yeast induces dough leavening by generating carbon dioxide, *Lactobacilli* acidify the dough by the releasing lactic and acetic acids.

Molds can secrete hydrolytic enzymes that degrade natural materials including complex biopolymers such as starch, lignin and cellulose into simpler substances. While many molds are known for causing food spoilage, some play important roles in the production of fermented foods (e.g. mold-ripened cheeses, soy sauce and *Katsuobushi*). The koji molds, the *Aspergillus* species (especially *A. oryzae* and *A. sojae*), have been cultured in Eastern Asia for centuries to ferment a mixture of soybean and other raw materials (e.g. wheat) for the development of various soybean paste and soy sauce products. Koji molds can initiate a process called "saccharification" (by which the starch molecules in raw materials are broken down). Most recently, efforts have been undertaken to optimize the manufacture of soy sauce with *A. oryzae* e.g. the optimization of SSF and proteolytic hydrolysis to overcome the limitations related to defatted soybean meal [97], and the temperature for initial moromi fermentation [269]. Mold starter cultures have been incorporated into the production of fermented sausage products (e.g. salami) to improve sausage's flavour and color while reducing nitrites and bacterial spoilage [270,271]. Molds (e.g. SP-01, barley koji and kome miso) have been used to to prepare ferment fish

Table 6
A nonexhaustive list of recent studies on the development of fermentation-enabled wellness foods.

Strategy	Functional entities involved	Food type	Improvements in product properties	Reference
Addition of probiotic microbe(s)	LAB species	Fermented meat products	Inhibit spoilage and pathogen development	[483]
	LAB species	Paste-like fish products	Reduce the amount of salt while still inhibiting the growth of spoilage or pathogenic microorganisms and degrading biogenic amines	[484]
	LAB species	Cheese	Produce CLA	[485]
	Prebiotic substance (inulin) and probiotic strains (*B. animalis* and *L. acidophilus*)	Cream cheese	Increase the content conjugated linoleic acid (CLA)	[486]
	L. rhamnosus GG, ATCC 53,103 (LGG)	Cheese	Short-term consumption would diminish caries-associated salivary microbial counts in young adults.	[487]
	L. rhamnosus HN001, *L. paracasei* LPC-37, and *L. acidophilus* NCFM	Dutch-type cheese	Increased the availability of calcium ($\tilde{2}.5\%$), phosphorus ($\tilde{6}\%$), and magnesium ($\tilde{1}8\%$).	[488]
	L. casei 279, *L. casei* LAFTI® L26 and *L. acidophilus* LAFTI® L10	Cheddar cheeses	Probiotic Lb. casei 279, Lb. casei LAFTI® L26 and Lb. acidophilus LAFTI® L10 can be added successfully in Cheddar cheeses to improve the ACE-inhibitory activity.	[489]
	Streptococci, *lactobacilli* and *lactococci*	Yogurt	Produce EPS	[490]
Microbial generation of bioactive compounds	LAB species such as Lactococcus sp. or Lactobacillus sp.-containing starter cultures.	Blue cheese	Produceenzymes, peptides, amino acids	[491]
	LAB and fungi	Kefir	Produce kefiran (which can significantly reduce the serum cholesterol levels)	[356]
	LAB species	Cheese, yogurt, vinegar	Produce desired aroma compounds	[492]
Addition of nonmicrobial ingredients	Polyphosphates	Sausages	Reduce nitrite.	[493]
	Glucose	Mediterranean-style sausages	Improve fermentation and inhibit Himine accumulation.	[494]
	Inulin, cereal fiber (oat and wheat) and fruit (peach, orange), ι- and κ-carrageenan, short-chain fructo-oligosaccharides, and soy fiber	Fermented sausage	Produce of a low-fat fermented sausage rich dietary fiber but low in fat (decrease by 40%–50%), with improved sensory properties	[495]
	Oil of vegetable (olive, linseed, sunflower, soy, canola) or marine origin (fish, algae, etc.)	Fermented sausages	Adjust the fat content by increase the contents of health-beneficial fatty acids (*n*-3 fatty acids).	[496]
	Nitrate-rich vegetable powders	Fermented meat products	Reduce the content of nitrate and nitrite	[497]
	Glucono-δ-lactone and ascorbic acid	Turkish-type fermented sausage (Sucuk)	Reduce the content of nitrate and nitrite	[498]
	Extract from aerial parts (stems, leaves or flowers) of Kitaibelia vitifolia	Dry-fermented sausages	Produce nonnitrite-added dry-fermented sausages	[499]
	Olive oil; Pre-emulsified with ISP	Turkish dry fermented sausages (sucuk)	Fat and cholesterol reduction; Increase oleic and linoleic acid contents in fermented product	[500]
	Soy oil; Pre-emulsified with ISP	Dry fermented sausages (chorizo)	Cholesterol reduction; Decrease the SFA/UFA ratio, while increasing the PUFA content in fermented product	[501]

Table 6 (*Continued*)

Strategy	Functional entities involved	Food type	Improvements in product properties	Reference
	Flaxseed oil/encapsulated, flaxseed oil/pre-emulsified with ISP or SC, canola oil/pre-emulsified with ISP, fish oil/encapsulated	Dutch style fermented sausage	Increase MUFA and PUFA contents; Decrease the *n*-6/*n*-3 ratio	[502]
	Hazel nut oil/ pre-emulsified with whey protein powder (WPP)	Turkish dry fermented sausages (sucuk)	Cholesterol reduction; Increase the MUFA content, PUFA content, and (MUFA+PUFA) / SFA ratio	[503]
	Walnut paste	Turkish dry fermented sausages (sucuk)	Fat reduction; Improve the lipid profile of fermented product	[504]
	Linseed and algae oils (3:2, w/w)/ pre-emulsified with ISP	Dry fermented sausages (chorizo)	Increase PUFA content (α-linolenic, EPA and DHA). The reduction of *n*-6/*n*-3 ratio	[505]
	Pre-emulsified olive oil	Chorizo de Pamplona	Reduction of cholesterol content while increasing total MUFA and PUFA contents, without negative effects on sensory properties	[506]
	3.3% of linseed oil and 100 mg BHA (butylated hydroxyanisole) plus 100 mg BHT (butylated hydroxytoluene)	Dry fermented sausages	Increase the PUFA/SFA ratio with a decrease of *n*-6/*n*-3 ratio	[502]
	Fish oil	Dutch-style sausages	Sausages contained encapsulated fish oil with minor differences in PUFA/SFA and *n*-6/*n*-3 ratios	[496]
	Deodorized fish oil and addition of BHA + BHT	Chorizo de Pamplona	Lead to a high PUFA + MUFA/SFA ratio but low *n*-6/*n*-3 ratio, with minimal secondary oxidation	[507]
	Inulin	Dry fermented sausages	Lead to a low-fat fermented sausage enriched in fiber, low in fat and calories, and improved sensory properties	[495]
	Wheat, oat, peach, orange, or apple dietary fiber	Dry fermented sausages	Reduced-fat DFSs with acceptable sensory properties can be produced with 10% of fat fortified with no more than 1.5% wheat, oat, peach, orange, or apple dietary fiber	[508]
	Orange fiber	Salchichón (Spanish DFS)	A decrease in residual nitrite and enhanced micrococcus growth rate (to improve sausage safety and quality), while maintaining sensory attributes.	[509]
	Carrot dietary fiber	Mallorca DFS	Leads to sausages with additional nutritional benefits while maintaining physicochemical and sensory properties	[510]
	Dry tomato peel	salchichón	Leads to sausages with significant lycopene content, and good sensory and textural acceptability	[511]
	Green tea extract and Thymbraspicata oil	Turkish dry-fermented sausage	Reduce the formation of BAs (putrescine, histamine, and tyramine), while retaining L-theanine and polyphenols	[512]

Table 6 (*Continued*)

Strategy	Functional entities involved	Food type	Improvements in product properties	Reference
Removal of undesired compounds	Reduction of sugar	Black tea and goji berries	Reduction of sugar by S. cerevisiae fermentation to retain L-theanine and polyphenols	[513]
	Replacement of NaCl with KCl, and addition of 1% or 2% concentrations of yeast extract	Fermented sausage	Reduction of NaCl by 25%-50% of their NaCl replaced by KCl and supplemented with 1% or 2% concentrations of yeast extract	[514]
	Using a starter with low or no amino-acid decarboxylase activity	Fermented meat products	Reduction of BAs	[515]
	Partial replacement of NaCl with KCl and $CaCl_2$	Dry fermented sausages	Reduction of NaCl content without affecting the development of starter culture and hygienic quality of products	[516]
	The combined use of enterocins A and B with high pressure (400 MPa) after ripening	Fermented sausages	Reduce counts of Salmonella and L. monocytogenes below 1 log cfu/g	[517]
	Omer Kodak yeast	Fish sauce	BAs can be eliminated	[215]
	Gamma irradiation	Low salt-fermented soybean paste	Degrade undesired compounds such as Him	[518]
	The use of bentonite	Fish sauce	Him reduction via adsorption	[519]
	The use of *B. amyloliquefaciens* FS-05, *Staphylococcus carnosus* FS-19, *Staphylococcus intermedius* FS-20 and *B. subtilis* FS-12	Fish sauces	Degrade Him, putrescine and cadaverine	[520]
	The use of yeast strain Omer Kodak M8	Fish sauce	Degrade BAs (Him and Tym), improve smell and taste, and enhance umami taste, cheese- and meat-like aroma, while decreasing fishy, ammonia and rancid odors of final products	[215]
	The use of tannin and cation-chelating resin	Fish sauce	Reduce 30% of Cd content	[230]

products with improved sensory and nutritional qualities e.g. Chum salmon sauce mash and fish pastes [272,273]. Furthermore, molds can inhibit unwanted yeasts, molds and bacteria such as *Listeria monocytogenes* [274].

6.3. Fermentation process and its interplay with other processing technologies

Fermentation process is induced by the sole or joint effort of bacteria, yeasts and molds. The production of a fermented food may involve different fermentation techniques, and treatments before and after fermentation. Therefore, selecting an appropriate fermentation process and optimizing the interplay between fermentation and other associated processing treatments are both important for producing safe fermented foods with high nutritional value and specific health benefits (Table 6).

Using a short-term or long-term fermentation process depends on the specification of the target fermented product. The molecular weight and quantity of macronutrients and bioactives in the fermented foods may change with fermentation time. Fermented soy foods made after a short-term fermentation (< 72 h) with *Bacillus* and *Aspergilus* species contain higher quantities of large carbohydrate and isoflavone molecules, as compared to those produced *via* long-term fermentation (> 6 months) e.g. chungkukjang versus meju and doenjang [275,276]. A sausage product made within a short ripening period tends to contain more *Lactobacilli* in the early stages of fermentation, whilst a sausage product obtained after a longer maturation period would have more *Micrococcaceae* species [277].

Fermentation can be an aerobic or anaerobic process, or involves both. SMF and SSF represent two different approaches for fermentation. SMF is employed when microorganisms require a high moisture (e.g. bacteria) and allows the utilization of free flow liquid substrates to produce enzymes and bioactive compounds. During SMF, a microorganism with a high-water activity is basically cultivated in a liquid medium containing nutrients, and it consumes substrate(s) in a rapid manner to release metabolite products (e.g. decomposed nutrients and bioactive constituents). SMF requires constant supply of substrate(s) but allows efficient separation and purification of the metabolite products [140]. In comparison, SSF is a solid-liquid-gas three-phase process that utilizes solid substrates including nutrient-rich waste materials. SSF typically employs fermentation with bacteria before fungal fermentation. During SSF, the microbial growth and the formation of product take place in the absence of water, and substrates are converted slowly but steadily into more digestible and more bioavailable bioactive compounds. SSF requires less effluent generation and energy consumption, and leads to less waste water production [278,279].

After selecting microbioal strains and fermentation process, one still needs to choose appropriate treatments before and

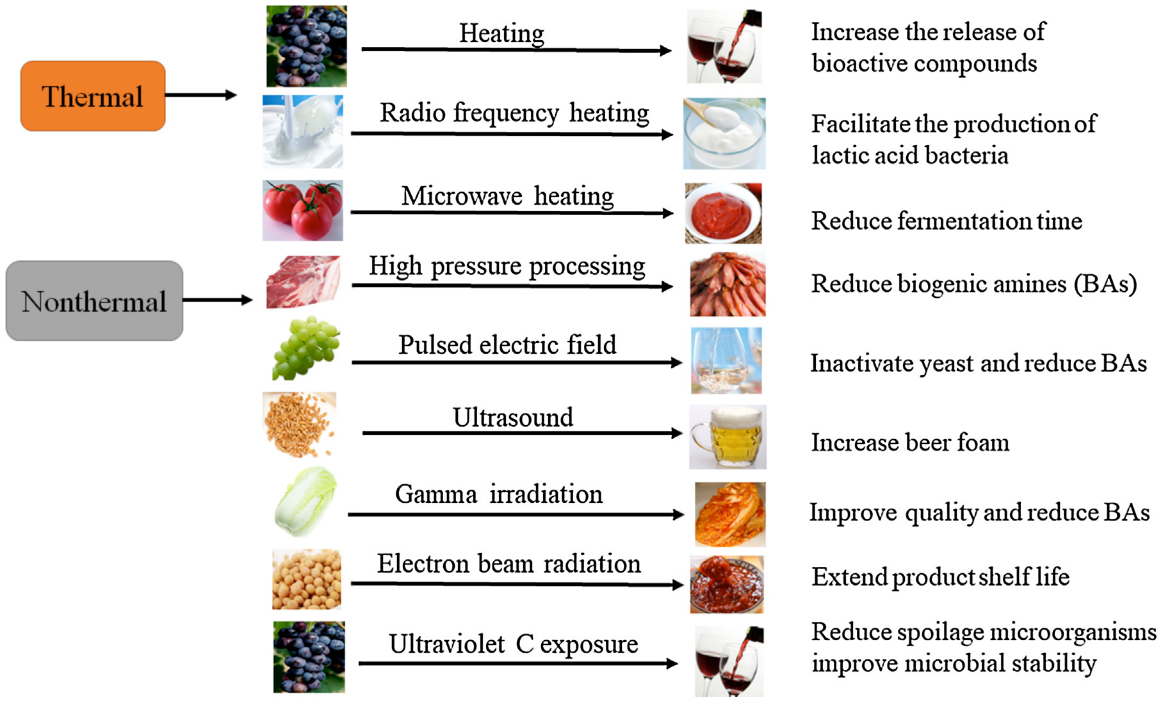

Fig. 2. The importance of optimizing the interplay between fermentation and other thermal or nonthermal processing technologies in the development of fermented products with desirable properties.

after the fermentation step in order to produce fermented foods and derived metabolite products i.e. pre-treatments (such as overnight soaking and heating), and post-treatments (such as filtration, sterilization and packaging). These pre- and post-treatments may involve thermal and non-thermal processes (e.g. HPP, high-pressure homogenization, ultrasonic processing, pulsed electric field, X-ray irradiation, microwave heating and ohmic heating). These processes can influence the microstructure of raw materials (which further affects the heat and/or mass transfer in subsequent processing steps), as well as the activation/inactivation, survival, growth, metabolism and performance of desired or undesired microorganisms [280,281]. These pre- or post- treatments may impart additional effects on the final fermented products (Fig. 2) e.g. A 30-s microwave pretreatment was found to increase the production of target metabolite products, *via* SSF of wheat by *A. oryzae* [282], and a HPP treatment of green table olives at 500 MPa for 30 min was effective in extending the shelf-life (5 months at 20 °C) of fermented olive products [283]. Furthermore, one may protect the selected strains, and control the growth and target activity of microorganisms as well as enzymatic conversions through encapsulation technologies [284]. Such an encapsulation pretreatment would exert additional effects on the fermentation process and the characteristics of fermented foods [285].

Modifications of fermentation processes and derived fermented foods should be carefully conducted, with considerations on the special legislative or cultural requirements of the country or region where fermented foods are intended to be sold. Altering a fermentation process (including the starting material(s), microorganism(s), fermentation conditions, processing steps, handling approaches and storage methods) may introduce new safey challenges in relation to legal barriers e.g. the legal limit of certain substances, and the newly generated substances as new hazards (e.g. the metabolites derived from the strains) [286]. Accordingly, efficient and effective detection and analysis techniques are required and should be advanced to keep up with the progress in fermented food development. Considerable progress has been made on the development and advancement of analysis methods for determining desired substances (e.g. nutrients and bioactives) and unwanted substances (e.g. BAs and mycotoxins) in various fermented food matrices, and examining the diversity and dynamics of microflora and enzymes, using restriction fragment length polymorphism (RFLP), random amplified polymorphic DNA (RAPD)-PCR, repetitive element sequenced-based (Rep)–PCR, single-strand conformation polymorphism–PCR (SSCP-PCR), multilocus sequence typing (MLST), pulsed field gel electrophoresis (PFGE), denaturing gradient gel electrophoresis (DGGE), immunological assays (radioimmunoassay and enzyme-linked immunosorbent assays), chromatographic techniques (e.g. HPLC and GC) coupled with mass spectrometry [287].

The nutritional guides on fermented foods vary by country. For example, probiotics are listed as particular health-promoting substances in Japapanese "Food for specified health uses" (FOSHU). Yogurt and kefir are listed as recommended items under the dairy products section with no appreciation of their nature as fermented foods or as a healthy category in the food guides of Canada and the USA. The food guide of the United Kingdom has emphasized the consumption of fruits and vegetables without specifying their derived fermented products as a category. In Asia fermented foods are generally not considered as a separate category in food guides, except for India (which classifies fermented foods as a product category) and China (which specifies yogurt as a regular food for the populations who do not tolerate milk). The Swedish healthy eating food guide recommends foods low in fat and high in fiber without indication to fermented foods. In the EU, restrictive legal boundaries have been set for probiotic foods [288]. As with any functional foods that targets specific health claims, functional fermented foods (including those for gut health) will need to comply with existing regulations for full official endorsement of their health claims [289,290].

7. Conclusion and future outlook

There exist many substances in fermented foods, including health promoting nutrients, bioactives and enzyme microorganisms, as well as some other undesired substances. These substances may exert positive or negative impacts on the well-being of specific populations and individuals, and their effectiveness and safety requires case-by-case examinations. Further, the microorganisms in the daily consumed fermented foods are considered as "micro-factories" to produce and enrich nutrients and bioactives with specific nutritional and health functionalities.

Advances in molecular microbial ecology and characterization techniques, together with detailed knowledge on the microbial interactions during food fermentation and interplays between fermentation and other processing technologies, are anticipated to take the fermented food segment to a higher level in the coming years. More effort should be directed towards the production of beneficial microbes and fermentation-enabled wellness foods to help address the escalating public health issues. To achieve this goal, fermentation-enabled wellness foods should be sustainable and specially designed for various populations and cultural groups. Precise control of the production of metabolite products *via* tailoring microbial fermentation, and monitoring the interplays between the fermentation process and other pre-/post-treatments (especially those involving emerging processing technologies), represent two major challenges. Any new fermented products including those with high nutritional value and specific biological functionalities (fermentation-enabled wellness foods and functional fermented foods) should be subjected to full and rigorous safety assessment as a novel food before any validation of their nutritional and health properties.

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