





## Review

# Nutritional Contributions and Health Associations of Traditional Fermented Foods

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**Abstract:** The growing interest in the consumption and study of traditionally fermented food worldwide has led to the development of numerous scientific investigations that have focused on analyzing the microbial and nutritional composition and the health effects derived from the consumption of these foods. Traditionally fermented foods and beverages are a significant source of nutrients, including proteins, essential fatty acids, soluble fiber, minerals, vitamins, and some essential amino acids. Additionally, fermented foods have been considered functional due to their prebiotic content, and the presence of specific lactic acid bacterial strains (LAB), which have shown positive effects on the balance of the intestinal microbiota, providing a beneficial impact in the treatment of diseases. This review presents a bibliographic compilation of scientific studies assessing the effect of the nutritional content and LAB profile of traditional fermented foods on different conditions such as obesity, diabetes, and gastrointestinal disorders.

**Keywords:** traditional fermented foods; diabetes; obesity; irritable bowel syndrome; lactic acid bacteria



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## 1. Introduction

Fermentation is the oldest and most affordable preservation process used by humans around the world [1]. It results from the biochemical transformation of some of the food compounds by the action of specific microorganisms, conferring nutritional properties and modified attributes of taste, aroma, and texture to the transformed product [2]. According to Wang et al. [3], the earliest reports on the use of fermentation are registered in the province of Henan, China, around 7000 B.C., where the local people consumed a fermented beverage prepared by mixing rice, honey, and fruit.

Similarly, historical data describe the manufacture of other fermented beverages such as *kombucha* in 220 B.C. and *kefir*, which through a recent proteomic analysis, revealed to have been made for 3500 years in Asia [4]. In Mesoamerica, the most distinctive fermented products were those derived from corn, such as *tesgüino* and *pozol*, from honey, and other fruits, mainly mead extracted from different species of *Agave* that was used for the production of alcoholic beverages, which had a significant cultural and social impact [5–7].

Recently, there has been an increasing interest in consuming traditional fermented foods prepared using different raw materials, microorganisms, and techniques for their preparation [8]. Most traditional fermented foods are made in Asia, Africa, and Middle Eastern countries, in homes, villages, or small-scale industries [9,10]. Similarly, over the past 15 years, there has been a growing number of studies involving traditional fermented foods and beverages, which have primarily focused on analyzing their microbial and

nutritional composition and their health and probiotic effects [11]. However, information on the relationship between specific fermented products such as non-dairy beverages and their impact on human health is limited. Hypothetically, any such beverage may provide a health benefit, yet this affirmation requires scientific evidence in the form of randomized, controlled, and repeatable human interventions [12].

Alternatively, the health benefits provided by fermented foods have been demonstrated in several in vitro and in vivo studies, displaying antihypertensive, hypoglycemic, antidiarrheal, and antithrombotic effects, among others [13–18]. In India, for instance, 60% of the milk production is transformed into traditional fermented dairy products such as *dahi*, *mishti doi*, *shrikhand*, *lassi*, *chach*, or *mohi*, among others. Features including the reduction of gastrointestinal infections and serum cholesterol levels and their antimutagenic activity have made these products largely consumed by the Indian population [19]. In this context, it has been demonstrated that food products made from fermented milk confer modulatory effects on the human brain and anticarcinogenic activities [20]. Among these products, research on the consumption of *kefir*, a worldwide known fermented beverage, has reported a positive impact on the gastrointestinal tract, stimulations of the immune system, anti-inflammatory, and anticancer effects [1,20].

Meanwhile, in Japan, the most traditional fermented foods are *miso*, *natto*, and *tempeh*, which use traditional methods to mix cultures of beneficial microorganisms (*Lactobacillus* species, *A. oryzae*, *S. cerevisiae*, *B. subtilis*, etc.); these products have attracted worldwide attention for promoting longevity and be considered as functional foods [21].

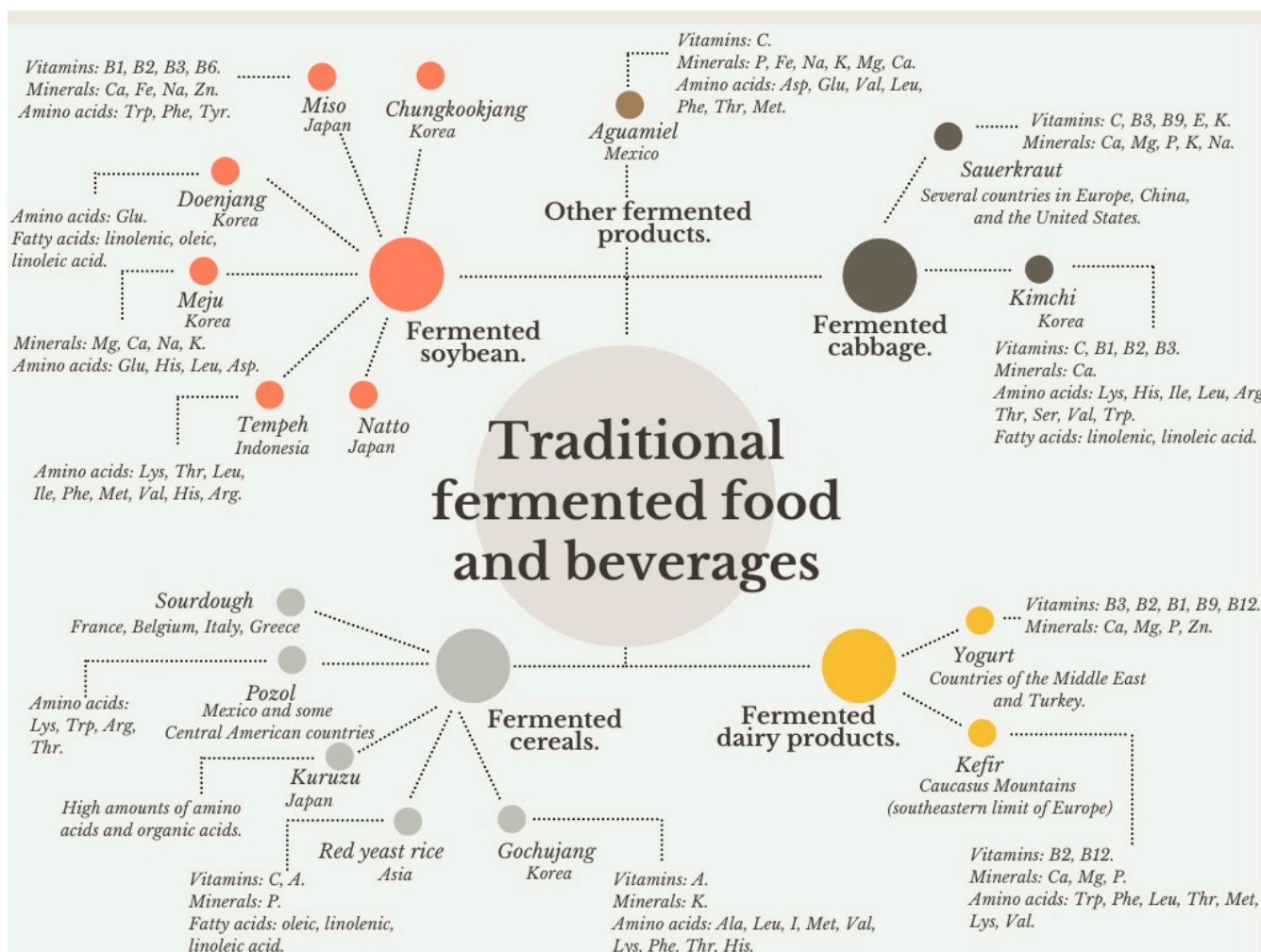
As a result, fermented foods could be categorized as functional foods, since besides providing nutrients, they also confer health benefits to the host, as they typically contain probiotics, prebiotics, proteins, and peptides that might display specific biological activities [22,23]. Microorganisms have played an essential role in the production of food for human consumption [24]. Generally, LAB of different genera, mainly, *Lactobacillus*, *Streptococcus*, and *Leuconostoc*, predominate in fermented foods, although other bacteria, fungi, and yeasts also contribute to the fermentation process [25]. Thus, some bacteria, yeasts, and fungi can also be considered probiotics, which are living microorganisms that, when administered in adequate amounts, confer health benefits to the host; these probiotics serve as a supplement to the host's microbiota [26,27]. The amount varies from country to country depending on its legislation; however, generally, a probiotic product should contain more than  $10^6$ – $10^8$  CFU/g or more than  $10^8$ – $10^{10}$  CFU/day [28,29].

Moreover, during meat fermentation, an ancient preservation technique [30], one of the most important processes undergone is proteolytic degradation, leading to the release of ACE-I inhibitors and antioxidant peptides [31]. In this regard, a few studies have described some peptides and free amino acids from fermented meats that have antioxidant and antihypertensive effects [32]. However, to the best of our knowledge, no studies analyzed the effect of the administration of traditional fermented meat products on obesity, type 2 Diabetes Mellitus (T2DM), and irritable bowel syndrome; as a result, this review does not include information concerning this. Therefore, the objective of this review is to carry out a bibliographic compilation of different traditional fermented foods and beverages in the world, emphasizing those in which their effect on specific diseases affecting human health has been evaluated.

## 2. Traditional Fermented Foods and Beverages in the World, and Their Association with Health

Recently, interest in consuming traditional fermented foods made from a wide variety of raw materials, microorganisms, and manufacturing techniques has increased worldwide. It is estimated that around 3500 different fermented foods and drinks based on milk, vegetables, or fruits are produced globally. Traditional fermented foods and beverages provide a significant source of nutrients depending on the substrate used for their production. Fermented foods based on soybean and cabbage (*chungkookjang*, *doenjang*, *meju*, *gochujang*, *natto*, *sauerkraut*, *tempeh*) are a source of protein, essential fatty acids (linoleic and linolenic), soluble fiber, minerals such as iron and zinc, as well as vitamin K, vitamin B9,

B1, and B6. Similarly, certain fermented foods made from milk (*yogurt, kefir, dahi*) contain mainly high-biological value proteins, calcium, and vitamins B2, B12, and B9. In contrast, fermented foods made from cereals (*pozol, red yeast rice*) possess essential amino acids (threonine, valine, isoleucine, leucine) and insoluble fiber (Table 1 and Figure 1).



**Figure 1.** Classification of traditional fermented foods and beverages based on their substrate and their nutritional content.

**Table 1.** Traditional fermented foods and beverages around the world.

Food	Identified Microorganisms	Description	Health Benefits	Physicochemical Properties	References
Aguamiel	<i>Z. mobilis</i> <i>L. acidophilus</i> <i>L. acetotolerans</i> <i>L. kimchii</i> <i>L. dextranicum</i> <i>L. mesenteroides</i> <i>P. lindneri</i> <i>S. carbajal</i>	<i>Aguamiel</i> is a sap produced by the agave plant. It is a translucent liquid that becomes amber with time. The production of sap reaches 4 to 6 L per day. It is obtained by cutting the central leaves of the mature plant; then, it is scrapped to create a 20–30 cm deep cavity that functions as sap storage.	<i>Aguamiel</i> produced a lower increase in blood glucose and serum insulin in C57BL6 mice despite the elevated glucose content. Moreover, <i>aguamiel</i> improved the diabetic condition, especially in glycemic control.	pH: 6–7 °Brix: 11–12 Acidity: 1–2%	[33–37]
Chungkookjang	<i>B. subtilis</i>	<i>Chungkookjang</i> is prepared by fermenting steamed soybeans in a closed and humid container at about 40 °C for 2 to 3 days; the fermentation is performed by airborne microbes or endogenous soybean microflora. <i>B. subtilis</i> is the dominant microorganism and provides its characteristic texture and flavor.	<i>Chungkookjang</i> enhanced antidiabetic function because it improved the suppression of hepatic glucose by enhancing the IRS2-Akt signaling pathway in diabetic rats.	pH: 8.4	[38,39]
Doenjang	<i>B. aryabhattai</i> <i>B. licheniformis</i> <i>B. methylotrophicus</i> <i>B. siamensis</i> <i>E. faecalis</i> <i>E. faecium</i> <i>T. halophilus</i> <i>S. equorum</i> <i>S. nepalensis</i> <i>S. saprophyticus</i>	<i>Doenjang</i> is a fermented soybean paste that is essential in Korean cuisine for its flavor and nutritional properties. For its preparation, soybean is mixed with brine (18%), and reposed in a porcelain vessel. The liquid portion is separated and boiled; the remaining solid portion is crushed and fermented for 30 to 180 days in the porcelain vessel.	<i>Doenjang</i> induced adiponectin production which suppresses the expression of nuclear factor -κB, a transcription factor associated with obesity. Moreover, <i>doenjang</i> extracts improved insulin secretory capacity.	pH: 5.0–6.0	[40–44]
Gochujang	<i>B. amyloliquefaciens</i> <i>B. licheniformis</i> <i>B. subtilis</i> <i>B. velezensis</i> <i>Oceanobacillus</i> sp. Yeasts <i>C. lactis</i> <i>Z. rouxii</i>	Traditional Korean food prepared from glutinous rice that is soaked in water for 24 h, strained, and milled. In a separated container, malt is steeped in water for 6 h, filtered, and heated. Rice and malt are mixed and cooked for 30 min to 50 °C and let cooled; finally, red pepper powder and salt are added, and the product is fermented for 1 to 2 years.	<i>Gochujang</i> is reported to have great antiobesity effects, weight loss, and improvements in serum lipid metabolism. Moreover, it has antiobesity properties that inhibit body weight gain, without affecting food intake, and that improve lipid profiles in the serum, liver, and adipose tissue.	pH: 4.52–4.68	[45–50]

Table 1. Cont.

Food	Identified Microorganisms	Description	Health Benefits	Physicochemical Properties	References
Kefir	<i>L. delbrueckii</i> subsp. <i>Bulgaricus</i> <i>L. helveticus</i> <i>L. brevis</i> <i>L. plantarum</i> <i>L. kefiranofaciens</i> <i>L. lactis</i> subsp. <i>lactis</i> <i>S. thermophilus</i> . Yeasts: <i>K. marxianus</i> <i>C. inconspicua</i> <i>C. maris</i> <i>S. cerevisiae</i>	Beverage obtained from the fermentation of cow, goat, sheep, camel, or buffalo milk. The fermentation is performed by a microorganism consortium grouped into a matrix named <i>kefir</i> grains. The yellowish grains have a gelatinous consistency measuring 0.3–3.5 cm. For its production, the milk is homogenized and pasteurized; later on, it is cooled to 20–25 °C and inoculated with 3–5% of <i>kefir</i> grains. The product is then fermented for 18 to 24 h at 20–25 °C, and the <i>kefir</i> grains are strained and placed aside to be washed for later use. Finally, <i>kefir</i> is stored at 4 °C until consumption.	<i>Kefir</i> has shown antidiabetic effects; it lowers plasma glucose, and decreases the fasting blood glucose and HbA1C levels, and can be useful as adjuvant therapy for diabetes.	Acidity: 5–9%. Sugar: 3.51–3.41% pH: 4.4–4.6	[1,20,51–60]
Kimchi	<i>L. mesenteroides</i> <i>L. sakei</i> <i>L. plantarum</i> <i>L. citreum</i> <i>L. gasicomitatum</i> <i>L. gelidum</i> <i>L. brevis</i> <i>W. koreensis</i> <i>W. confusa</i> <i>L. curvatus</i>	<i>Kimchi</i> refers to a group of fermented and salted vegetables, mainly cabbage, whose flavor depends on the fermentation conditions. For its production, cabbage is cut, washed, and brined (10%) overnight; then, it is drained and mixed with garlic, radish, ginger, anchovy juice, sugar, and green onion. This blend is fermented in a closed vessel for 1 to 3 weeks at room temperature.	<i>Kimchi</i> reduced body weight, leptin, total cholesterol levels, hepatic triglycerides concentration, serum insulin levels, and increased HDL in mice. Moreover, it reduced triglyceride levels and decreased expression of anabolic lipid genes in fat tissue cells. In obese patients, <i>kimchi</i> decreased the waist-hip index, body fat, blood pressure, insulin levels, total cholesterol, leptin, and fasting glucose.	Acidity: >0.9% pH: 4.27–5.64	[61–65]
Kurozu	<i>A. pasterianus</i> <i>A. aceti</i> <i>K. xylinus</i> <i>A. oryzae</i> <i>Saccharomyces</i>	This food is also known as black rice vinegar. Its production involves the utilization of large pottery jars in which the following ingredients are layered: steamed rice containing <i>koji</i> ( <i>A. oryzae</i> ), steamed rice, spring water, and a final lid-type layer of <i>koji</i> . The fermentation process is performed outdoors and ranges between 6 months to 3 years.	<i>Kurozu</i> improved human liver lipid profile, decrease body weight and visceral fat in women with obesity. Moreover, it decreased serum cholesterol levels in mice fed with high-fat diet.	pH: 4.0	[15,21,66–68]



Table 1. Cont.

Food	Identified Microorganisms	Description	Health Benefits	Physicochemical Properties	References
Meju	<i>Bacillus</i> sp. <i>B. subtilis</i> <i>B. licheniformis</i> <i>B. cereus</i> <i>C. filamentosum</i> <i>B. megaterium</i> <i>Monascus</i> sp. <i>P. expansum</i> <i>P. roqueforti</i> <i>Fusarium</i> cf. <i>incarnatum</i> <i>F. fujikuroi</i> <i>A. cibarius</i> <i>A. fumigatus</i> <i>A. oryzae</i>	Traditional Korean <i>meju</i> is a dried fermented soybean brick, which serves as the basis for many Korean condiments. The natural fermentation of <i>meju</i> takes 60 to 90 days. During the first 40 to 80 days, the <i>meju</i> is dried at low temperatures (below 15 °C), usually during winter (November to February), promoting the active growth of some moulds. During the last stage (10 to 30 days), the <i>meju</i> is stacked in layers and covered with thick cloths to be stored at temperatures above 45 °C, allowing other species of moulds to grow.	<i>Meju</i> decreased glucose levels in diabetic rats and reduced body weight gain, decreased serum triglyceride and leptin levels in obese mice.	pH: 6.7 Acidity: 1.31%	[16,69–73]
Miso	<i>A. oryzae</i> <i>S. cerevisiae</i>	<i>Miso</i> is the product of the fermentation of soybeans, rice, or barley with the fungus <i>koji</i> . The most common recipe is made from soybeans. The fermentation time ranges from 1 week to 20 months; similarly, the salt content varies between 5–13%.	<i>Miso</i> decreased bodyweight, serum aspartate transaminase level, and lipid peroxidation in the liver in mice fed with a high-fat diet. Moreover, it suppressed visceral fat accumulation in mice fed with a high-fat diet by increasing the expression of Hsl (lipase, hormone-sensitive) involved in lipolysis and the expression of <i>PPAR-γ</i> .	pH: 4.8–5.5	[21,74–77]
Natto	<i>B. subtilis</i>	<i>Natto</i> is the product obtained from the fermentation of soybeans with spores of <i>B. subtilis</i> . For its preparation, soybeans are soaked, boiled until soft, drained, and cooled at 40 °C. Then, the spores of <i>B. subtilis</i> are added to the soybeans and placed in a wooden container, or a polyethylene bag to ferment for 12–20 h.	<i>Natto</i> improved insulin and postprandial glucose profiles, enhanced insulin sensitivity and cholesterol levels, and oxidative stress were reduced, decreasing malondialdehyde-modified low-density lipoprotein and N-carboxyl methyl kinase in overweight patients.	Acidity: 1.7% pH: 6.9	[21,78,79]

Table 1. Cont.

Food	Identified Microorganisms	Description	Health Benefits	Physicochemical Properties	References
Pozol	<i>Lactobacillus</i> <i>A. pozolis</i> <i>A. azotophilum</i>	<i>Pozol</i> is a beverage made from nixtamalized corn that is ground and kneaded with water to form a dough. The dough is shaped into small balls which are wrapped into banana leaves before the fermentation step. Afterwards, the fermented dough balls are dissolved in water and let cool. <i>Pozol</i> can be consumed alone or combined. Different flavoring ingredients can be added, such as cacao, corozo, rice, sweet potato, coconut, milk, and aromatic essences.	<i>Pozol</i> modifies the intestinal microbiota and the metabolism, due to the presence of lactic acid bacteria. In addition, during fermentation, the concentration of some components such as amino acids increases.	Humidity: 30% pH: 4.5	[80–84]
Red yeast rice (Hon-chi)	<i>M. purpureus</i>	Fermented red rice is produced traditionally by fermenting washed and cooked rice with red wine mash, knotgrass juice, and alum water. The commercially prepared <i>red yeast rice</i> extract is fermented for nine days with a specific red yeast called <i>M. purpureus</i> Went, at 25 °C	<i>Red yeast rice</i> reduced the concentration of total cholesterol in serum and the relationship between total cholesterol and high-density cholesterol, and also reduced triglyceride levels thanks to the presence of polyketides, fatty acids, and trace elements.	pH: 5–6	[72,85–87]
Sauerkraut	<i>L. mesenteroides</i> <i>L. fallax</i> <i>Leuconostoc</i> sp. <i>L. plantarum</i> <i>L. brevis</i>	Also called <i>choucroute</i> , it is mainly made by fermentation of cabbage (cut into strips 0.7–2 mm thick) that is submerged in salt at 0.7–2.5%, in covered glass containers at room temperature. Fermentation time ranges between one week to several months. To improve its flavor, spices, carrot, or wine can be added before the fermentation process.	<i>Sauerkraut</i> reduced the symptom severity of patients who suffer from IBS. Furthermore, it produced significant alterations in the bacterial diversity of IBS patients.	Acidity: 1–2%. pH: 3.4–3.7	[88–90]

Table 1. Cont.

Food	Identified Microorganisms	Description	Health Benefits	Physicochemical Properties	References
Sourdough	<i>F. sanfranciscensis</i> <i>L. reuteri</i> <i>L. panis</i> <i>L. pontis</i> <i>L. frumenti</i> <i>Leuconostoc</i> <i>Weissella</i> <i>S. cerevisiae</i>	The use of <i>sourdough</i> in bread production improves its quality and flavor, increasing its volume and shelf life. Its ingredients are wheat or rye flour and yeast. In its production, the initial lactic fermentation is achieved by mixing and fermenting the ingredients for three days at 30 °C. Then, more flour is added to the fermented dough, and the blend is reposed at the same temperature to reactivate the fermentation. Finally, the dough can be baked for bread obtention, or stored to be used as inoculum for further production of bread.	<i>Sourdough</i> has been used successfully to improve the quality of gluten-free bread, thus being useful for the production of better foods for people with gluten intolerance.	pH: 4.31	[91–94]
Tempeh	<i>L. plantarum</i> <i>R. oligosporus</i> <i>L. fermentum</i> <i>L. reuteri</i> <i>L.s lactis</i>	<i>Tempeh</i> is a traditional Indonesian food made mainly from soybean. For its production, soybeans are lightly cooked, inoculated with <i>R. oligosporus</i> spores, and packaged in perforated banana leaves before being incubated at 30 °C for 24 h or until soybeans are bound by the fungus mycelium.	<i>Tempeh</i> prevents cancer, cardiovascular diseases, type 2 diabetes mellitus and the regulation of glucose in the blood, due to its components such as genistein, daidzein, and $\beta$ -sitosterol.	pH: 4.0–5.0 Acidity: 4.0–6.0	[95–100]
Yogurt	<i>S.thermophilus</i> <i>L. delbrueckii</i> subsp. <i>bulgaricus</i>	Yogurt is a widely known commercial beverage obtained through the lactic fermentation of <i>S. thermophilus</i> and <i>L. delbrueckii</i> subsp. <i>bulgaricus</i> , which are added as inoculum to cow milk. The incubation is performed at 42–45 °C for 3 to 6 h or until the milk has reached a pH of 4.4.	Yogurt is a source of probiotic bacteria; therefore, it improves the intestinal microbiota, and this plays an important role in appetite control.	Acidity: 1.31%. pH: 4.1–4.4. °Brix: 7.30–20.4.	[1,101–104]



Among the nutrients mentioned above, several studies have also confirmed the participation of fiber in carbohydrate metabolism by delaying glucose absorption in the gut, increasing insulin sensitivity in people with obesity, and decreasing preprandial and postprandial glucose levels in patients with T2DM [105,106]. Meanwhile, essential fatty acids have been demonstrated to decrease symptoms of irritable bowel syndrome by reducing inflammation in the intestine. Likewise, polyunsaturated fatty acids have been shown to reduce cardiovascular risk by lowering triglyceride levels and possessing atheroprotective properties (reduction of inflammation markers, cholesterol crystal formation, and endothelial dysfunction) [107–109]. Accordingly, Vitamin B9 promotes the decrease of homocysteine, a protein involved in increasing the risk of cardiovascular disease, obesity, hypertension, and T2DM [110,111]. Homocysteine has also been related to the inhibition of the phosphorylation of substrate 2 of the insulin receptor (IRS2) and serine-threonine protein kinase (Akt), leading to insulin resistance and an increase in glucose levels [112,113]. Furthermore, it has been reported that the fermentation process developed by probiotic bacteria increases the number of nutrients and bioactive compounds in the food [114,115]. For instance, according to Jung et al. [116], the probiotic bacteria contained in *kimchi* (*L. mesenteroides* and *Lactobacillus sakei*) contribute to the increase of vitamin B9 and B2; in *tempeh*, the presence of *R. oligosporus* aids in the increase of vitamins B9, B3, B2, and B6 [117].

It is widely recognized that traditional fermented dairy foods are the primary source of probiotic strains of the *Lactobacillus* genus [118,119]; however, these bacteria have also been isolated from other fermented foods. In this regard, Lee et al. [120] reported the presence of *Lactiplantibacillus plantarum* in *kimchi*, reporting that these probiotic bacteria prevented the growth of *H. pylori*, a bacterium causing stomach infection. Besides, some LAB produce antimicrobial compounds such as bacteriocins, which have exhibited antagonistic activity against *L. monocytogenes*, *S. aureus*, *E. coli*, and *S. typhimurium* [121]. Similarly, Ibarra-Sánchez et al. [122] informed that *L. lactis*, a probiotic strain isolated from *dahi*, produced nisin Z, an effective bacteriocin that inhibited the growth of *L. monocytogenes* and *S. aureus*. Moreover, it has been reported that Japanese foods such as *natto*, *chungkookjang*, and *tempeh*, possess antioxidant activity due to the hydrolytic activity of LAB [123,124]. A brief description of traditional fermented foods worldwide, the microorganisms that have been identified, their physical-chemical features, and their nutritional content are presented in Table 1 and Figure 1.

Several studies have demonstrated that fermented foods provide health benefits to the host, showing positive effects in treating diseases such as obesity, diabetes, and gastrointestinal disorders. The following section will address the effects of administering traditional fermented food and beverages for the treatment of the conditions mentioned above.

### 3. Use of Fermented Foods and Beverages as an Adjuvant in the Treatment of Obesity

According to the World Health Organization, over the last 40 years, overweight rates and obesity have tripled in both developed and undeveloped countries for adult and child populations, with approximately 1.9 billion overweight adults, 650 million obese, and 340 million overweight and obese children in the world [125]. Obesity is a pathological condition determined by an accumulation of visceral and abdominal fat accompanied by chronic low-grade inflammation, which contributes to the appearance of the metabolic syndrome characterized by insulin resistance, dyslipidemia, hepatic steatosis, and cardiovascular disease according to Jung and Choi [126]. The etiology of this disease is multifactorial, with dietary (imbalance between energy intake and expenditure), environmental (sedentary lifestyle), genetic, and metabolic factors being involved. However, other influencing factors have been described, such as psychological and microbiota dysbiosis [127,128].

Moreover, the development of this disease is followed by the production of inflammatory cytokines, such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), interleukin-6 (IL-6), and IL- $\beta$  [129,130]. These cytokines lead to systemic inflammation contributing to the de-

velopment of obesity-related complications [13]. Given their elevated hospitalization costs, these complications are of great concern in terms of global public health, thus the increased interest in looking for treatment alternatives focused on the prevention of obesity. Among these, the use of traditional fermented foods and beverages arises as a practical and low-cost alternative [131–133]. Different studies *in vitro* and *in vivo* have shown that traditional fermented foods such as *kimchi*, *doenjang*, *meju*, *cheonggukjang*, *gochujang*, *chungkookjang*, *kefir*, and *kurozu* can aid in reducing body weight, fat tissue, serum, liver triglycerides, cholesterol, inflammatory cytokines, and oxidative stress markers [13–15,64,73,134].

In a murine model study, Nam et al. [13] found that mice fed with a high-fat diet and *doenjang* (14.4%) for 11 weeks showed a decrease in body weight, fat tissue weight, levels of oxidative stress markers (p40phox involved in superoxide production), and a reduction in specific inflammatory adipokines (TNF- $\alpha$  and MCP-1) compared to mice fed with unfermented soybean (11%). These results are in agreement with those observed by Kwak et al. [135], who fed rats (Sprague-Dawley) with a high-fat/*doenjang* diet for eight weeks, reporting a decrease in visceral fat content, adipocyte size, and fat deposits compared with rats fed with a high-fat and cooked soybean diet. Meanwhile, in an intervention study of 51 overweight adults (men and women) supplemented with *doenjang* (9.9 g/day) for 12 weeks, a significant decrease in body weight, fat mass, and visceral fat was observed as compared to the placebo group; however, no changes in subcutaneous fat and lipid profile were detected [136]. In contrast, in another study, 60 overweight patients were treated with *doenjang* (9.8 g/day) for 12 weeks, and their amounts of visceral and subcutaneous fat were assessed; only the former exhibited a significant decrease in those patients with PPAR- $\gamma$  on the T allele compared to the placebo group [137].

Additional studies using *meju*, *gochujang*, *cheonggukjang*, *chungkookjang* have reported similar effects to the ones described above. According to Shin et al. [49], rats fed with a high-fat diet and 10% of *gochujang* for five weeks showed reduced weight gain, decreased adipose tissue weight, serum LDL cholesterol, serum leptin levels, triglyceride levels, and total cholesterol in the liver compared to rats fed with a high-fat diet. Similar results were obtained by Ahn et al. [14], who performed an *in vitro* test treating adipocyte cells (3T3-L1) with 1 mg/mL of *gochujang* for three days, obtaining a decrease in leptin, glycerol secretion, and adipocyte size compared to the untreated group. Likewise, Bae et al. [73] detected a reduction in weight gain and serum triglyceride levels, an increase in HDL cholesterol levels, and a decrease in the expression of lipid metabolism genes (*SREBP-1c*, PPAR- $\gamma$ , and *ACC*) when mice (C7BL/6J) were fed with a high-fat diet with 30% traditionally fermented *meju* (60–90 days of fermentation) for 16 weeks, compared with mice fed with a high-fat diet and standardized fermented *meju* (6 days of fermentation).

However, in the study conducted by Cha et al. [138] in which 53 overweight patients were treated with 30 g/day of *gochujang* for 12 weeks, no decrease in triglyceride, LDL, HDL, nor a weight reduction was observed, only reporting a reduction in visceral fat compared to the untreated group. Interesting results were obtained by Byun et al. [134] after treating 83 overweight and obese patients with *chungkookjang* for 12 weeks, reporting that only female patients had a decreased body fat percentage, waist circumference, waist-hip index, and C-reactive protein levels compared to the placebo group. Conversely, Back et al. [139] reported significant decreases in blood triglyceride, LDL levels, and Apo B levels in 55 patients, men and women included, after being treated with *chungkookjang* (26 g three times a day) for 12 weeks compared to the placebo group.

On the other hand, several investigations have compared the effect of spontaneous- and inoculated-fermented foods on specific obesity markers. Some of these studies reveal that inoculated fermented products might yield better results than spontaneously fermented ones. For instance, Park et al. [63] reported better effects on the reduction of body weight, leptin, total cholesterol levels, hepatic triglycerides concentration, serum insulin levels, and increased HDL concentration when mice (C57BL/6J) were fed with a high-fat diet complemented with *kimchi* at 3% inoculated with *W. koreensis* OK1–6 for 12 weeks. In the case of Lee et al. [64], a reduction in triglyceride levels and a decreased

expression of anabolic lipid genes (*PPAR- $\gamma$* , *C/EBP- $\alpha$*  and *FAS*) were observed when fat tissue cells (3T3-L1) were supplemented with 100  $\mu$ g/mL of *kimchi* inoculated with *L. mesenteroides* and *L. plantarum* for 24 h. Conversely, Kim et al. [65] demonstrated that not only had the fermented nature of the food products a significant role in obesity markers, but also the fermentation time. In this study, 22 overweight and obese patients were treated with 1-day-old or 10-day-old *kimchi* and found that those treated with 10-day-old *kimchi* (300 g/day) for four weeks had significant decreases in their waist-hip index, body fat, blood pressure, insulin levels, total cholesterol, leptin, and fasting glucose compared to those patients treated with the same dose of fresh *kimchi*.

Studies on diverse traditional fermented foods such as *kefir* that use milk as the substrate have shown an improved liver lipid profile in mice. Regarding this, Bourrie et al. [140] reported that mice (C57BL/6) fed with a high-fat diet and 100  $\mu$ L of traditionally fermented *kefir* showed a reduction in plasma total cholesterol levels, *PPAR- $\gamma$*  gene expression, and in IL-1 $\beta$  compared to those mice treated with commercial *kefir*. The authors associated these effects with the presence of LAB, which effectively inhibits weight in obese animals by preventing the accumulation of intracellular lipids in the adipocyte [141,142].

On the other hand, the traditional fermented food *kurozu*, which uses vinegar as a substrate, has improved human liver lipid profile. For example, Hamadate et al. [15] supplemented 48 obese adults with 879 mg/day of this fermented product for 12 weeks. Although no significant reduction in waist circumference was detected, the treated patients showed a significant decrease in body weight compared to the placebo group. Complementary parameters that included total, subcutaneous, and visceral fat were detected to increase in both groups; however, a significantly lower increase was detected in the females treated with *kurozu*. There is also evidence that *L. plantarum* reduces adipogenesis and lipogenesis by inhibiting the activation of *PPAR- $\gamma$* , *C/EBP- $\alpha$* , and *FAS* [143]. In addition, the researchers hypothesized that the fermentation process of soybean favors the increase of isoflavone-aglycones, mainly genistein and daidzein. Genistein has been found to play an essential role in regulating lipid metabolism and preventing the production of cytokines and reactive oxygen species (ROS) [144,145]. Furthermore, genistein may increase the activity of the liver enzyme carnitine palmitoyltransferase I (CPT-1), which regulates another enzyme involved in the oxidation of fatty acids. Increased fatty acid oxidation results in increased energy expenditure, decreasing both body fat and weight [146].

According to the results reported in this section, it is observed that traditionally fermented foods might be an alternative for both the treatment and prevention of obesity, since the fermentation process favors the presence of LAB, which can participate in the regulation of lipid metabolism and the expression of specific genes involved in adipogenesis. Moreover, these foods have been shown to increase the bioavailability of isoflavone-aglycones such as genistein, which participate in reducing ROS and inflammatory cytokines. Nonetheless, further interventions are needed to ensure these effects, since although most of the reviewed studies showed promising results in key obesity parameters (weight, percentage of body and visceral fat, waist circumference, and waist-hip index), not all of them offered an evident decrease in the lipid profile of patients.

#### 4. Use of Fermented Foods and Beverages as an Adjuvant in the Treatment of Type 2 Diabetes Mellitus (T2DM)

According to the World Health Organization, in the last 34 years, the prevalence of diabetes has doubled from 4.7% to 8.5% in the world adult population, mainly affecting undeveloped countries where more than 80% of deaths occur due to the disease alone [147]. Diabetes is a severe chronic disease that ensues when  $\beta$  cells in the pancreas do not secrete enough insulin or the tissues cannot use it [148,149]. Three types of diabetes exist, type 1 diabetes mellitus (insulin-dependent), type 2 diabetes, and gestational diabetes. According to the American Diabetes Association [150], there are different tests for the diagnosis of diabetes; one of the most important is the glycosylated hemoglobin (HbA1C) test that measures the blood glucose average for the past two to three months and if it has a value of 6.5% or more indicates that the person has diabetes.

To prevent this disease, it is essential to modify lifestyle choices, like reducing energy intake, choosing better fats, trying to avoid refined carbohydrates, and choosing a diet rich in fiber and low glycemic foods [151]. There is evidence that low glycemic foods can reduce glucose and insulin responses, protect against weight gain, and reduce the risk of developing T2DM [152,153].

In this respect, fermented foods have shown hypoglycemic effects in model animals and humans. The mechanism implicated is that the process of fermentation can reduce the concentration of soluble carbohydrates, increase dietary fiber levels, and increase levels of resistant starch [154]. For instance, during sourdough fermentation, acetic and lactic acids are produced; both participate in the decrease of the glycemic index by delaying gastric emptying and reducing the availability of starch, respectively [155,156].

In search of a potential alternative treatment to overcome this global health issue, numerous researchers have performed in vivo tests to determine the effect of traditionally fermented foods (*kefir*, *kimchi*, *meju*, *chungkookjang*, *natto*, *sourdough*, and *hon-chi*) on diabetes markers. To date, results obtained comprise decreased serum glucose and insulin levels, increased liver insulin sensitivity, improved oxidative stress levels, reduced cholesterol and triglyceride levels, and regulated glucose homeostasis, among others [157–160].

In the first instance, tests employing traditionally fermented foods using soybean as the substrate have shown hypoglycemic effects in rats with T2DM by favoring liver insulin signaling cascades. Yang et al. [16] observed that rats fed with a high-fat diet supplemented with 10% traditionally or standardized fermented *meju* for 60 and 6 days, respectively, during eight weeks, exhibited lower glucose levels than the control group (no treatment). The results were attributed to an increase in liver insulin sensitivity and insulin secretion due to the phosphorylation of Akt and a decrease in the expression of phosphoenolpyruvate carboxykinase (PEPCK). Moreover, after performing a glucose tolerance test (GTT), the researchers found that blood glucose decreased in rats treated with both types of *meju* due to an increase in insulin levels in the first phase; furthermore, the glucose binding technique also displayed an increase in insulin levels in the first and second phases. These effects agree with those reported by Kwon et al. [17], who treated diabetic rats with 5% of standardized or traditionally fermented *gochujang* for 6 and 60 days, respectively, for eight weeks; in both treatments, rats showed a decrease in blood glucose levels, an increase in liver insulin sensitivity, and a reduction of glucose levels during a GTT, compared to the untreated rats; however, an increase in insulin secretion levels was not observed in rats. As a complement, the glucose binding technique revealed an increase in insulin levels only during the first phase due to phosphorylation of signal transducer and transcription activator 3 (STAT 3), AMP-activated protein kinase (AMPK), and the decrease in the expression of PEPCK.

Similarly, Kwon et al. [161] reported an increased insulin production during a GTT that improved glucose homeostasis on diabetic rats fed with a high-fat diet and *chungkookjang* for eight weeks. Results on the glucose binding technique displayed a decrease in glucose levels attributed to an enhanced insulin sensitivity related to phosphorylation of IRS2 and Akt and decreased expression of PEPCK compared to those fed with casein. The effect of the administration of *natto* in 11 overweight patients with hyperinsulinemia and glucose intolerance was studied by Taniguchi-Fukatsu et al. [79]; the treatment was complemented with viscous vegetables and white rice, while the control group was treated with white rice and cooked soybeans. After eight weeks of treatment, improved insulin and postprandial glucose profiles were observed. Interestingly, when the treatment was administered during breakfast, insulin sensitivity was enhanced, and cholesterol level and oxidative stress were reduced, thus decreasing malondialdehyde-modified low-density lipoprotein and N-carboxyl methyl kinase. The authors concluded that the high fiber content of viscous vegetables modified the carbohydrate metabolism, and the consumption of *natto* and rice improved insulin sensitivity in patients.

Results obtained in assessing the relationship between the administration of soybean-based fermented food and diabetes markers have been associated with several potential



factors. Particularly, Hyun Jung Yang et al. [48] pointed out that the effects are related to the fermentation process of soybeans and the involved LAB, which increase the presence of small peptides, esters, organic acids, and aglycone isoflavones (genistein, daidzein, and glycitein). Moreover, Sanjukta and Rai [162] dismiss that these effects are due to the presence of phytochemicals as capsaicin, present in *gochujang*, which decreases significantly in the fermentation process.

Regarding the effect of milk-based fermented food products on the treatment of diabetes, Ostadrahimi et al. [52] treated 60 adult patients with T2DM with 600 mL of *kefir* containing *S. thermophilus*, *L. casei*, *L. acidophilus*, and *B. lactis* for eight weeks. Significant reductions in serum glucose levels and HbA1C compared to the control group (treated with conventional fermented milk containing *S. thermophilus* and *L. bulgaricus*) were observed at the end of the treatment. However, no significant reduction in cholesterol and triglyceride levels was detected, attributed to the differences in probiotic strains and patients' genetics. The authors associated these effects with the presence of LAB, which have a hypoglycemic effect by producing insulinotropic polypeptides and glucagon-like peptides that induce glucose absorption into the muscle and stimulate the liver to store glucose. Additionally, these LAB are related to antioxidant activity by their interaction with various metabolic pathways, which triggers the reduction of blood glucose and fasting Hb1AC [163].

In contrast, Alihosseini et al. [51] reported no decrease in insulin levels when 60 patients with type 2 diabetes were treated with 600 mL of *kefir* or conventional fermented milk per day. Nevertheless, a reduction in the insulin resistance index in the group treated with *kefir* was recorded. Moreover, both treatments reduced homocysteine levels at the end of the study, with no significant difference between them. In this sense, Alihosseini [51] mentions that probiotic bacteria in food improve blood glucose levels by inhibiting the production of reactive oxygen species and cytokines that participate in the destruction of pancreatic cells  $\beta$ . Similarly, according to Zulfania et al. [164], the reduction of homocysteine is owed to the presence of probiotic bacteria, which contribute to the synthesis of folates, which in turn participate in the conversion of homocysteine into methionine by yielding a methyl group, thus reducing cardiovascular disease risk in patients with T2DM.

Meanwhile, in the study of Punaro et al. [165], where rats with type 1 diabetes were treated with 1.8 mL of *kefir* per day for eight weeks, a decrease in ROS production was observed compared to the control group (no treatment). According to the authors, oxidative stress is associated with an immunological modulation and the anti-inflammatory properties exerted by probiotics, which modify the intestinal microbiota and maintain the integrity of the intestine. Still, the precise mechanism of the diabetes–probiotic relationship remains unknown; Miraghajani et al. [166] investigated the mechanisms related to the diabetes–probiotic relationship and proposed four main mechanisms (1) the local effects of probiotics, (2) the effects of probiotics on inflammatory and immune response, (3) the effects on probiotics in oxidative stress and (4) the effects of probiotics on gene expression.

Additionally, studies using different substrates such as fermented cabbage (*kimchi*), *sourdough*, and *fermented rice (hon-chi)*, have also exhibited antidiabetic properties. For instance, Islam and Choi [167] treated rats with a high-fat diet complemented with 0.5 or 2% of *kimchi*, finding that  $\beta$  cells function increased, and HbA1C decreased in rats compared to the control group (no treatment); they also detected a significant difference in the reduction of serum insulin in the 2% *kimchi*-treated group. The results were attributed to the fermentation of the ingredients in *kimchi* (Chinese cabbage, onion, ginger, garlic, and red chili), which have demonstrated hypoglycemic, insulinotropic, and antidiabetic effects. In the study of Maioli et al. [168], a comparison between two formulations of *sourdough* on diabetes markers of 16 glucose intolerance patients was performed. Results indicated that 100 g of *sourdough* fermented with *S. cerevisiae*, *Levilactobacillus brevis*, and *L. plantarum* exhibited a significant reduction in insulin and plasma glucose levels compared to *sourdough* fermented with *S. cerevisiae*. These effects were associated with the presence of LAB, which transformed simple sugars into lactic acid, favoring the delay of glucose intolerance in diabetes. While in the study carried out by Cheng et al. [169], who fed diabetic male

Wistar rats with *hon-chi* at different doses (50, 100 y 350 mg/kg), it was observed that the treatment was able to reduce the plasma glucose, being concentration-dependent. It was also found that *hon-chi* exerted a beneficial effect on glucose metabolism in diabetic rats with a lack of insulin; this mechanism was attributed to a change produced in the hepatic protein PEPCK, which contributes to the suppression of gluconeogenesis.

In brief, the information cited in this section confirms that the consumption of specific fermented foods might provide several benefits in the treatment of diabetes, including reductions in serum glucose, insulin levels, postprandial glucose, and oxidative stress, as well as increasing insulin sensitivity in liver and muscle, both in rats and humans. In this regard, researchers attribute such effects mainly to the presence of LAB that produce metabolites involved in glucose homeostasis and regulate molecular mechanisms that lead to the decreased expression of PEPCK protein and Akt phosphorylation.

### 5. Use of Fermented Foods and Beverages as an Adjuvant in the Treatment of Irritable Bowel Syndrome (IBS)

IBS is among the most common gastrointestinal diseases treated by gastroenterologists, affecting approximately 7–21% of the world population, with a higher prevalence in women [170,171]. IBS's etiology is still unknown; however, several factors have been associated with this disease, such as poor eating habits, stress, and alterations in intestinal microbiota [172,173]. IBS is characterized by abdominal pain and abnormal bowel habits, such as diarrhea, constipation, or both, in addition to having other symptoms such as abdominal distention, bloating, flatulence, and urge to defecate, which can significantly affect people's life quality [174,175]. These symptoms have also been associated with the consumption of oligosaccharides, disaccharides, monosaccharides, and fermentable polyols (FODMAPs), which exist in fruits (melon, pear, apple), dairy products, rye, wheat, artichoke, garlic, onions, broccoli, mushrooms, cauliflower, and artificial sweeteners [176,177].

On the other hand, recent studies have shown that dysbiosis in the microbiota is linked with an increase in the severity of IBS symptoms as it can cause abdominal hypersensitivity, epithelial barrier dysfunction, and loss of intestinal motility [178,179]. Therefore, treatments are focused on improving gut health either by intervention with probiotics, prebiotics, or low FODMAP diets [180,181]. Thus, traditional fermented foods might aid in treating IBS due to the presence of LAB and their prebiotic content.

In this context, Costabile et al. [182] conducted an in vitro trial isolating bacteria from feces of patients with and without IBS; feces were cultured with predigested *sourdough* and fermented for eight hours. In both cases, increased *Bifidobacterium* counts were observed after the fermentation process, while this effect was not observed when the groups were treated with bread containing *S. cerevisiae* as fermenting microorganism; thus, the authors suggested that *sourdough* might be beneficial to IBS patients by promoting a change in the composition and metabolism of the intestinal microbiota. Equally, Muir et al. [183] associated the beneficial effects of *sourdough* in IBS patients with the reduction of FODMAPs in bread due to the presence of LAB [184,185]. During the fermentation process, LAB can degrade carbohydrates such as fructose and fructans; to do so, the control of processing factors such as fermentation time and the microorganisms involved is essential [186]. Such processing leads to a lower load of undigested carbohydrates in the large intestine, reducing gastrointestinal symptoms [187].

In an intervention with patients with IBS ( $n = 26$ ), Laatikainen et al. [188] reported no improvement in gastrointestinal symptoms or inflammation markers after consuming six *sourdough* pieces (fermented for 12 h) per day for seven days, compared to patients who consumed traditional bread. Nevertheless, *sourdough* displayed a significant reduction of FODMAPs and amylase and trypsin inhibitors (ATIs) due to the fermentative activity of LAB. The authors associate these results with the intervention time, which was truly short, and the placebo effect, which had a determinant role in IBS patients; then, a crossover study might yield better results.

Further traditional fermented foods such as *sauerkraut* and *yogurt* have shown promising results in alleviating IBS symptoms. In the study of Nielsen et al. [90], fifteen patients



were treated with pasteurized or unpasteurized *sauerkraut* (75 g/day in both cases) for six weeks, with both groups showing a decrease in the total IBS symptom severity score. Besides, patients treated with unpasteurized *sauerkraut* manifested reduced days of pain, improved bowel habits, and enhanced presence of *L. plantarum* and *L. brevis* in the stool, compared to those treated with pasteurized *sauerkraut*. These findings were attributed to the fermentation process of LAB, which as aforementioned, promote the metabolism of glucose, fructose, sorbitol, galactooligosaccharides, and fructooligosaccharides present in the cabbage by using them as substrate. Meanwhile, in the research performed by Noorbakhsh et al. [189], it was observed that patients treated with 100 g of *yogurt* added with lactic acid bacteria (*L. bulgaricus*, *S. thermophilus*, *L. plantarum*, and *Limosilactobacillus fermentum*) and a prebiotic (xylooligosaccharides) for four weeks exhibited a significant reduction in abdominal distention and improvement in their quality of life, compared with the untreated group. Furthermore, an increased presence of *Lactobacillus* was found in the treated group's feces, along with a reduction in homocysteine levels. The authors remarked that the alleviation of IBS symptoms in the treated patients is due to the presence of high numbers of *Lactobacillus*. The presence of *Lactobacillus* suppresses the production of inflammatory cytokines and reduces the homocysteine levels, leading to a dysfunction of the intestinal barrier, producing inflammation [190,191].

In short, traditionally fermented foods can also assist in IBS treatments due to the presence of LAB, which given their metabolic process, allow for the reduction of FODMAPs and ATIs, which are entirely associated with the development of the symptoms of this disease; in addition, these bacteria can also improve the recovery of the intestinal microbiota in patients. Notwithstanding, it is imperative to consider the type of studies to perform, the interventions' length, the treated patients, and uncontrolled factors such as the nocebo effect, which has significantly impacted the treatment of this disease.

## 6. Conclusions

Traditionally fermented food and beverages, mainly those made from soybeans (*doenjang*, *meju*, *gochujang*, *chungkookjang*), milk (*kefir* and *yogurt*), and cabbage (*kimchi* and *sauerkraut*), have effects on lipid and glucose metabolism, regulate genes involved in adipogenesis, decrease ROS production and improve insulin sensitivity. Such effects have been attributed to LAB, which might be involved in the regulation of genes related to lipid and glucose metabolism; moreover, the LAB fermentation process aids in the increase of nutrients (B vitamins and fiber) and bioactive compounds such as the aglycone isoflavones that are implicated in the reduction of inflammatory cytokines and ROS. Therefore, these food products can potentially be used as adjuvant treatment and prevent chronic non-communicable diseases, such as diabetes and obesity. Correspondingly, *yogurt*, *sourdough*, and *sauerkraut* can be used as adjuvants in the treatment of IBS since LAB allow the reduction of symptoms, aid to restore dysbiosis of the microbiota and promote the removal of compounds such as FODMAPs and ATIs involved in the development of IBS symptoms. Most of the interventions performed in humans are of short duration and with small samples, so these factors must be considered for future research.

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