







## Review Article

# Bioactive Ingredients in Traditional Fermented Food Condiments: Emerging Products for Prevention and Treatment of Obesity and Type 2 Diabetes

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Obesity and type 2 diabetes (T2D) are severe metabolic diseases due to inappropriate lifestyle and genetic factors and their prevention/treatment cause serious problems. Therefore, searching for effective and safe approaches to control obesity and T2D is an essential challenge. This study presents the knowledge regarding the possible use of traditional fermented condiments (TFC), a known major source of bioactive compounds (BACs), as an adjuvant treatment for obesity and T2D. Data on antiobesity, antidiabetic, and different mechanisms of BACs action of TFC were collected using a methodical search in PubMed, Scopus databases, Web of Science, SciELO, and the Cochrane Library. We discuss the mechanisms by which BCs prevent or treat obesity and T2D. The effects of TFC on obesity and T2D have been found both in animal, human, and clinical studies. The findings demonstrated that BACs in TFC confer potential promising antiobesity and antidiabetic effects. Because of the potential therapeutic significance of bioactive ingredients, the consumption of TFC could be recommended as a functional condiment. Nevertheless, further investigation is required in more clinical studies of TFC to support the formulation of functional fermented condiments and nutraceutical and pharmaceutical applications.

## 1. Introduction

Fermentation is one of the oldest methods used by humans throughout the world, especially in Asian, Western, and African countries, to preserve, store, and produce foods with high-protein quality, other bioactive ingredients, the sensory quality of the final products, as well as probiotics. The probiotic bacteria can be defined as live microorganisms which are consumed adequately in order to confer a health benefit on the host consumer from the fermented food

microbiome [1]. The probiotic bacteria such as lactic acid bacteria (LAB) and some *Bacillus* are recognized as safe [2]. During the fermentation process, it involves many microorganisms such as bacteria, yeasts, fungi, or enzymes, which are responsible for the hydrolysis of ingredients such as proteins, peptides, lipids, carbohydrates, vitamins, and flavonoid glycosides during the process of fermentation [3].

Yang et al. [4] reported that flavor compounds and microbes in traditional Pixian Doubanjiang correlated with a significant difference and indicated that *Aspergillus*,

*Bacillus*, and *Lactobacillus* influenced positively on some flavor compounds, including aspartate, leucine,  $\beta$ -ionone, and 2-acetylpyrrole. The enzymes in both bacteria and fungi also impact the characteristics of free amino acids and volatile compounds [4], thus different fermented condiments may differ from one another with different biological health effects provided to consumers.

Generally, the LAB included in fermented products is predominantly *Lactobacillus*, *Streptococcus*, *Pediococcus*, and *Leuconostoc* [5], while yeast and fungi are represented by *Saccharomyces cerevisiae* and *Aspergillus* spp., respectively. The metabolites presented in fermented condiments are responsible for the food quality, as reported by Li et al. [6] in a famous condiment in Chinese cuisine, Pixian Doubanjiang. However, fermented products provide continuous health benefits for consumers compared to nonfermented products through biological enrichment and the reduction of toxic substances. The bioactive metabolites such as peptides, amino acids, vitamins, fatty acids, exopolysaccharides, phenolics, isoflavones, organic acids, volatile compounds, and probiotics may vary considerably; they can affect the biological health effects with a significant difference. Therefore, in this way, fermented foods have a wide range of biologically active peptides depending on the protein source [7].

In fact, fermented products are considered as functional foods because they offer health benefits by suppressing cancer cells of the proliferating, preventing diabetes, obesity, boosting the immune system, and reducing the risk of other diseases [8]. Foods are classified as fermented dairy foods and fermented food condiments (FFC). Fruits, legumes, cereals, oil seeds, or animals such as meat, milk, and fish are usually used as raw materials to ferment these foods with different characteristics. For example, fermented soybean products have been commonly consumed in different Asian countries, including Japan, Korea, China, India, Taiwan, Malaysia, and Indonesia, as well as in African countries. TFC is a liquid, solid, or semisolid state which has been used by humans for centuries as seasonings or flavoring ingredients for improving the appetite, desirable flavor, digestion, and health benefits. In various parts of Africa such as Central, East, and West Africa, TFC is considered as an important cheap source of dietary protein, flavoring, and seasoning ingredients used in soups, sauces, and other ready foods, as well as other nutrients.

Some fermented condiments have attracted more attention than others due to their unique and high-quality flavor [9]. In Asian countries, there are various TFFC, including doenjang, ganjang, kimchi, and meju (Korea), dajiang, douchi, kanjang, Yu jiangsuan and Pixian Doubanjiang/Pixian broad bean paste) (China), Thua nao and soybean kapi (Thailand), miso (Japan), tempoyak (Indonesia and Malaysia), as shown in Table 1. In African countries, including various varieties, Owoh, Ugba/Ukpaka, Okpehe/Okpiye, Iru, and Ogiri (Nigeria), Mbuja (Cameroon), Awaze, Datta, Siljo, and Azo (Ethiopia), Soumbara (Côte d'Ivoire), Afitin, Tayohounta, and Dikouanyouri (Benin), Maari, Bikalga, Mantchoua, and Soumbala (Burkina Faso), and Dawadawa (South Africa, Nigeria, Ghana) are presented

in Table 1. The nutritional and biological effects of some of them were investigated by many researchers using different sensitive analytical instruments, such as gas chromatography mass spectrometry (GC-MS) and liquid chromatography mass spectrometry (LC-MS) [41]. Their bioactive metabolites have been recognized as nutraceuticals and functional food condiments by many populations since ancient centuries.

According to the International Diabetes Federation (IDF), diabetes has increased in developed and developing countries as well during the last decades and this could increase to 643 million by 2030 from 783 million by 2045 [48]. While undiagnosed, there are estimated to be 240 million people who have diabetes. For the World Obesity Federation (WOF) 2022, more than one billion people globally will be living with obesity by 2030. These noncommunicable diseases are currently causing huge deaths around the world with a significant loss in the economy in different countries. The prevention and treatment of these diseases by drugs may have great side effects, and it has been recognized that all results are inconsistent. In order to prevent or to decrease the risk of these diseases, researchers are searching for foods with bioactive compounds, probiotics, and nutraceuticals without side effects to control them. In this line, Onikanni et al. [49] worked on bioactive compounds in plants and found that Kaempferol and ferulic compounds from *Clompanus pubescens* leaves can be used as a promising bioactive metabolite to treat type 2 diabetes and its complications. Other compounds can affect the genes expression of enzymes to regulate the glucose level and insulin efficacy. For example, Elnagar et al. [50] observed in their study the effects of oxytocin on Fibrillin-1 (FBN1) expression and phosphoenolpyruvate carboxykinase (PEPCK) enzyme activity in the obesity-induced diabetic rat model by decreasing PEPCK enzyme activity and glycogenolysis in the liver. It was also demonstrated that bioactive peptides with antioxidant, anti-inflammatory, antiviral, and anticancer properties have been used to control metabolic diseases such as diabetes and obesity [51].

Different results of various studies *in vitro*, *in vivo*, and clinical models demonstrated that TFC has anticancer, antiobesity, and antidiabetic properties. Bioactive peptides resulted from bacterial and fungal activities of different food matrices have been known to restore health against metabolic disorders such as hypertension, hyperglycemia, hyperlipidemia, and obesity [3, 52]. Besides, bioactive peptides inhibit both  $\alpha$ -amylase and  $\alpha$ -glucosidase enzymes [43, 51, 53]. The fermentation may also increase the bioaccessibility and bioavailability of phenolics as well as some of them may be biotransformed into new metabolites with high bioactivity against digestive enzymes such as  $\alpha$ -glucosidase and  $\alpha$ -amylase [54].

Therefore, this review aims to provide an update of data about the recent reports on the antiobesity and antidiabetic effects of bioactive compounds biosynthesized by microorganisms in traditional fermented food condiments (TFFC) for the first time (1), to analyze the fundamental mechanisms of different bioactive compounds of TFFC (2), and to discuss

TABLE 1: Different types of traditional fermented condiments and their characteristics.

Fermented condiments	Use	Features	Major raw materials	Main microorganisms	Country	References
Dajiang	Flavor	Alkaline, paste	Soybean	<i>Lactobacillus</i> and <i>Tetragenococcus</i> , <i>Aspergillus oryzae</i>	China	Chun et al. [10] An et al. [11]
Doenjang	Flavor/ seasonings	Alkaline, paste	Soybean	LAB: <i>Aspergillus oryzae</i> , <i>Bacillus</i> spp., <i>Lactobacillus</i> , and <i>Pediococcus</i> , <i>Weissella</i> spp. and yeast	Korea	Chun et al. [10] Jeong et al. [12] Lee et al. [13]
Miso	Flavor	Alkaline, paste	Soybean	<i>Bacillus</i> spp. and <i>Aspergillus</i> spp.	Japan	Chun et al. [10]
Thua nao	Flavor/ seasoning	Alkaline, paste	Soybean	<i>Bacillus</i> spp.	Thailand	Chun et al. [10]; Dajanta et al. [14]
Owoh	Flavor	Alkaline	Cotton seeds	<i>Bacillus</i> spp., <i>Staphylococcus</i> spp.	Nigeria	Ezekiel et al. [15]
Ugba/Ukpaka	Flavor	Alkaline, glossy	African oil bean seeds ( <i>Pentaclethra macrophylla</i> )	<i>Bacillus</i> spp., <i>Staphylococcus</i> , and <i>Leuconostoc</i>	Nigeria	Anyanwu et al. [16] Ogueke et al. [17]
Kimchi	Seasonings	Alkaline, paste	Napa cabbage, cabbage, green onion, hot pepper, and ginger	LAB: <i>Bacillus</i> spp., <i>Lactobacillus</i> spp., <i>Leuconostoc</i> spp., <i>Saccharomyces</i> spp., and <i>L. brevis</i> KU15153	Korea	Patra et al. [18]; Irorita Fugaban et al. [19]
Mbuja	Flavor	Alkaline	<i>H. sabdariffa</i> seeds	<i>LAB</i> and <i>Bacillus</i> spp.	Cameroon	Mohammadou et al. [20]
Okpehe/Okpiye	Flavor	Alkaline, sticky	<i>P. africana</i> seeds	<i>LAB</i> and yeasts	Nigeria	Balogun and Oyeiola [21]
Iru	Flavor	Alkaline, sticky	<i>Prosopis africana</i> seeds	<i>LAB</i> and yeasts	Nigeria	Adesulu-Dahunsi and Jeyaram [22]
Ogiri	Seasoning/ flavor	—	Groundnut, melon seeds, castor oil seeds, pumpkin bean, and sesame	<i>LAB</i> and yeasts	Nigeria	Chukwu et al. [23]; Adesulu-Dahunsi and Jeyaram [22]
Soumbala	Flavor	Alkaline, sticky	African locust bean seeds and <i>H. sabdariffa</i> seeds	<i>LAB</i> and <i>Bacillus</i> spp.	Burkina Faso	Esse et al. [24]; Yérobessor et al. [25]
Bikalga	Flavor	—	<i>H. sabdariffa</i> seeds	<i>Bacillus</i> spp.	Burkina Faso	Savadogo et al. [26]
Soybean kapi	Flavor	Alkaline, paste	Soybean	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , and <i>Bacillus</i> spp.	Thailand	Wittanalai et al. [27]
Awaze	Flavor	—	Red sweet pepper and spices	<i>LAB</i>	Ethiopia	Wedajo Lemi [28]
Datta	Aromas/flavor	—	Chili pepper, garlic, and ginger	<i>LAB</i>	Ethiopia	Wedajo Lemi [28]
Siljo	Flavor	—	Safflower and faba bean	<i>Lactococcus</i> spp., <i>Lactobacillus</i> spp., and yeasts	Ethiopia	Wedajo Lemi [28]
Azo	Taste enhancer/ seasonings	—	Cereal and leaves	<i>LAB</i>	Ethiopia	Wedajo Lemi [28]
Dawadawa	Flavor	Alkaline, sticky	African locust bean, Bambara groundnut ( <i>Vigna subterranea</i> ), and soybean	<i>LAB</i> and yeasts	South Africa, Nigeria, Ghana	Nwagu et al. [29] and Adebiyi et al. [30]

TABLE 1: Continued.

Fermented condiments	Use	Features	Major raw materials	Main microorganisms	Country	References
Maari	Flavor	Alkaline, sticky	Baobab seeds	LAB, <i>Bacillus</i> spp., and <i>Staphylococcus</i>	Burkina Faso	Parkouda et al. [31, 32]
Douchi	Flavor	Alkaline, paste	Soybean ( <i>Glycine max</i> )	<i>B. amyloliquefaciens</i> , <i>B. subtilis</i> , <i>Asp. Oryzae</i> , and <i>Lactobacillus</i> spp. <i>Staphylococcus</i> spp., <i>Pichia guilliermondii</i> , <i>Pichia farinose</i> , Yeasts, and fungi	China Taiwan	Hu et al. [33] Li et al. [34] Chen et al. [35]
Pixian Doubanjiang/ Pixian broad bean (paste)	Flavor	Alkaline, paste	Red pepper	<i>Saccharomyces cerevisiae</i> , <i>Weissella Aspergillus</i> spp., and <i>Bacillus</i> spp.	China	Li et al. [5] Zhang et al. [36]
Kanjang/soy sauce/ shoyu	Seasonings/ flavor	Alkaline, paste	Soybean	<i>Aspergillus</i> spp. and <i>Bacillus</i> spp.	China, Japan, Korea	Devanathi and Gkatzionis [37]
Mantchoua	Flavor	—	Kapok seeds	<i>Bacillus</i> spp.	Burkina Faso	Kere-Kando et al. [38]
Tayohounta; Dikouanyouri	Flavor	—	Baobab seeds	<i>Bacillus</i> spp.	Benin	Chadare et al. [39]
Aftin	Flavor	Alkaline, sticky	African locust bean (parkia biglobosa)	LAB and yeasts	Benin	Azokpota et al. [40]
Ganjang	Flavor/ seasonings	Alkaline, paste	Soybean	LAB, <i>Staphylococcus</i> , and yeast	Korea	Song et al. [41]
Soumbara	Flavor	Alkaline, sticky	African locust bean seeds	<i>Bacillus</i> spp. and <i>Staphylococcus</i>	Côte d'Ivoire	Kouamé et al. [42]
Meju	Flavor	Alkaline, paste	Soybean	LAB, <i>B. subtilis</i> , <i>B. cereus</i> , <i>C. filamentosum</i> , and <i>A. oryzae</i>	Korea	Yang et al. [43]
Tempoyak	Seasonings	Alkaline, paste	Fruit of durian ( <i>durio zibethinus</i> murr.)	<i>Enterococcus</i> spp., <i>Lactobacillus</i> spp., <i>L. plantarum</i> , and <i>Saccharomyces cerevisiae</i>	Indonesia and Malaysia	Pato and Surono [44]; Chuah et al. [45]; Ahmad et al. [46]
Yu jiangsuan	Flavor	Paste	Red pepper and ginger	<i>Weissella</i> , <i>Lactobacillus</i> , and <i>Fructobacillus</i>	China	Jiang et al. [47]

the use of functional fermented condiments for the effective prevention and treatment of obesity and type 2 diabetes (T2D).

## 2. Materials and Methods

**2.1. Data Collection.** We developed a methodical search in PubMed, EMBASE, SciELO, Scopus databases, Web of Science, and the Cochrane Library to identify potential studies addressing the traditional fermented condiments (TFC). We searched strategically by including the terms: “TFC,” or “fermented condiments,” or “food condiments,” or “TFC, diabetes and obesity,” or “fermented condiment to prevent T2D,” or “fermented and obesity risk,” or “fermented food condiment and metabolic diseases,” or “soy condiment,” or “fermented soy sauce condiment,” or “fermented soy condiments as seasonings,” or “seasonings fermented condiments,” or “flavor seasonings and fermented condiments,” or “soy fermented condiments,” or “LAB in fermented condiments,” or “diabetes and fermented condiments,” or “diabetes, obesity and TFC,” or “diabetes, obesity, and fermented condiments,” or “bioactive compounds in fermented condiments,” or “LAB, probiotics in fermented condiments.” The literature research was conducted from March 2022 up to November 2022 by reviewing all citations of the articles eligible for our review.

**2.2. Study Selection.** The criteria for exclusion of studies were as follows: noneligible publication types such as comments, minireviews, editorials, opinions, meta-analyses, guidelines, and letters. The criteria of inclusion were based on the date of the journal publication, language of publication (only English), and no restriction of countries. The titles (step 1), abstracts (step 2), and full texts (step 3) of different articles were screened, and then they were reviewed independently by two (2) reviewers and when there was disagreement, another reviewer was required for clarification, and the final list was chosen after consensus between reviewers.

**2.3. Data Extraction and Quality Assessment.** The data extraction was conducted by two (2) reviewers, and for any disagreements there were discussed and resolved with another reviewer independently. The final list was chosen by consensus.

**2.4. Types of Traditional Fermented Condiments.** Different traditional fermented condiments (TFC) are consumed in different forms around the world, including in Africa, Asia, North America, South America, and Europe. TFC can be classified as seasonings, flavoring, or taste enhancer used in soups, stews, and many other traditional dishes (Table 1). They are produced by using vegetables, seeds, legumes, fruit, and cereals in spontaneous, uncontrolled, or controlled fermentation. Among these TFC identified and commonly consumed, 18 originated from African countries and 12 in Asian countries (Table 1). These include doenjang, ganjang, and meju [11, 13, 41], dajiang, douchi, kanjang, and Pixian

Doubanjiang/Pixian broad bean paste [10, 12, 34], Thua nao, soybean kapi, and miso [10, 27] which are produced from soybean (*Glycine Max*) (Table 1). Tempoyak [46], Yu jiangsuan [47], and other TFC produced from fruit and red pepper and ginger in Indonesia, Malaysia, and in China, respectively (Table 1) [44–46]. Some of these TFC are in a liquid state, such as ganjang, kanjang, soybean sauce, and others are in a solid state (Figure 1). While TFC is produced in various African countries including Owoh, Ugba/Ukpaka, Okpehe/Okpiye, Iru, and Ogiri [22], Mbuja [20], Awaze, Datta, Siljo, and Azo (cereal) [28], Soumbara, Aftin, Tayohounta, and Dikouanyouri, Maari, Bikalga, Mantchoua, Soumbala, and Dawadawa [29, 32, 38] (Table 1). All these TFC are in a solid state except Okpehe/Okpiye which is in a liquid or semisolid state. The samples of some different types of TFC are presented in Figure 1.

## 3. Microorganisms and Probiotics in Traditional Fermented Condiments

**3.1. Microorganisms.** Microorganisms present in traditional fermented condiments (TFC) are different from the environment they come from, such as yeasts, fungi, and bacteria. These microorganisms metabolize the constituents of raw materials during the fermentation process, hence enhancing the nutritive and bioactive values and preserving the quality of the final product. The LAB presents common characteristics such as being nonspore-forming, Gram-positive, catalase-negative without cytochromes, nonaerobic or aerotolerant, fastidious, acid-tolerant, and strictly fermentative [55]. The LAB genera isolated from various TFC are *Lactobacillus*, *Pediococcus*, *Enterococcus*, *Lactococcus*, *Leuconostoc*, *Oenococcus*, *Streptococcus*, and *Weissella* (Table 1). Among LAB, *Lactobacillus* is the predominant in TFC, while their particularity is that produce organic acids, mostly lactic acid, which is the characteristic fermentative of the final product and can reduce the pH of the substrate to a level where the growth of pathogenic, putrefactive, and toxigenic bacteria are inhibited [13, 55–57]. In addition, *Bacillus* is reported as a Gram-positive, endospore-forming, rod-shaped, catalase positive, motile, and aerobic to semi-anaerobic bacterium.

The most common genera of yeasts are *Candida*, *Pichia*, *Saccharomyces*, and *Saccharomycopsis* [3, 58, 59] (Table 1). During any fermentation of the substrate, *Saccharomyces* can ferment sugar, produce secondary metabolites, and inhibit the growth of mycotoxin-producing molds. It has many enzymatic activities such as lipolytic, proteolytic, pectinolytic, glycosidic, and urease activities [58]. Among molds, there are common genera of filamentous fungi associated with fermented foods, such as *Actinomucor*, *Amylomyces*, *Aspergillus*, *Monascus*, *Mucor*, *Neurospora*, *Penicillium*, *Rhizopus*, and *Ustilago* [60]. In the present study, it is found that *Aspergillus* is predominant (Table 1). Fungi have some functional properties in fermented foods such as the production of enzymes (maltase, invertase, pectinase,  $\alpha$ -amylase,  $\beta$ -galactosidase, amyloglucosidase, cellulase, hemi-cellulase, acid/alkaline proteases, lipases), the degradation of antinutritive factors, or improving the

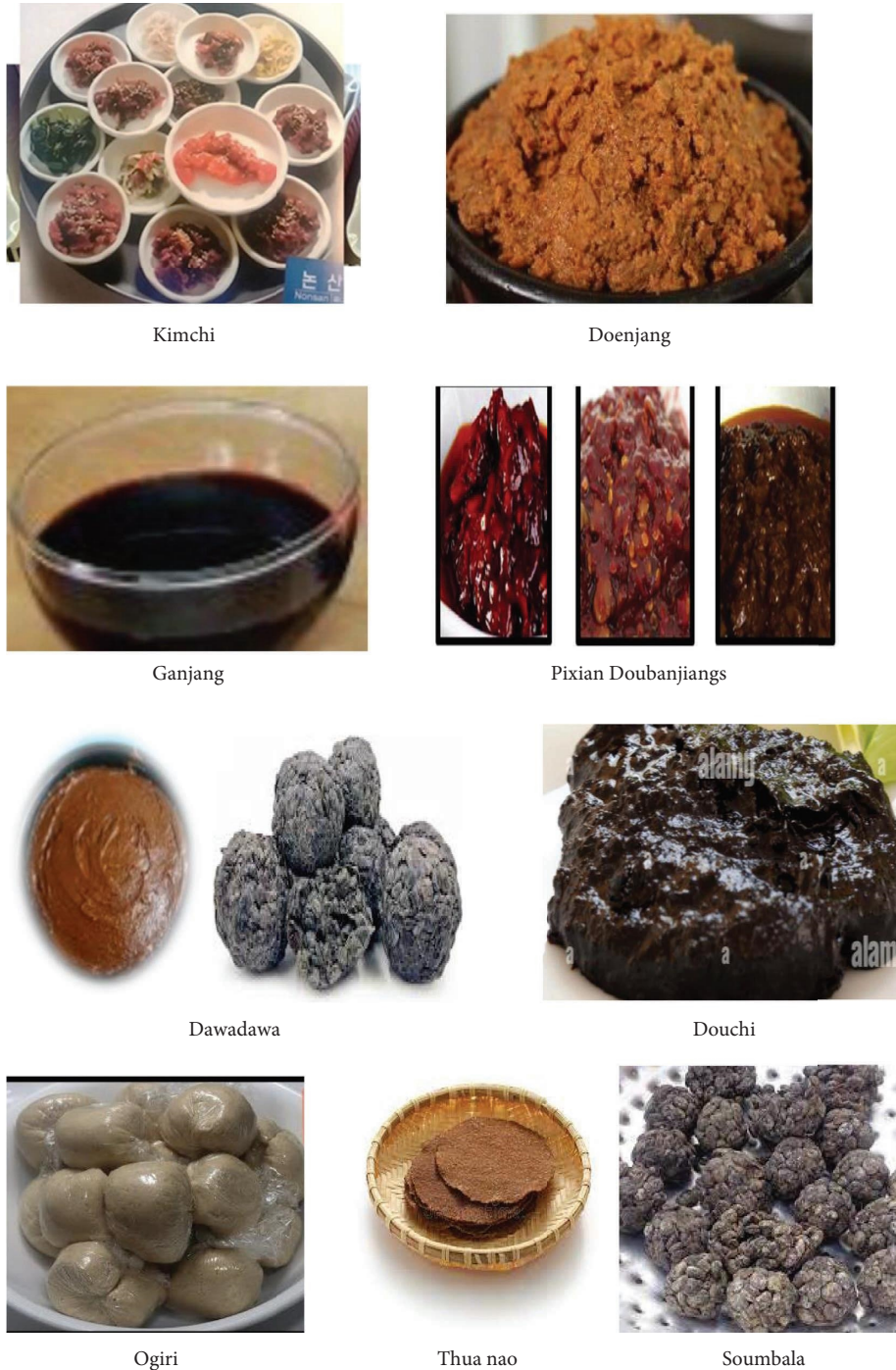


FIGURE 1: Different types of some traditional fermented condiments.

bioavailability of minerals [13, 60]. All these third groups of microorganisms are isolated in different TFC with the most predominant LAB (Table 1). The results may correlate to their important role played during the fermentation process of the production of the TFC.

**3.2. Probiotics.** Probiotics are defined as “live microorganisms” consumed in adequate quantities conferring health benefits to the host’ [61]. Probiotic organisms are generally

found in fermented foods and play an important role for consumers by providing health benefits. They have many functional roles, such as antioxidant, antidiabetic, antiobesity, anti-allergy, blood lipid reducing, anti-inflammatory, and anticancer properties and improve host health [57, 62, 63]. The LAB synthesizes cell factories for producing enzymes, antibodies, vitamins, exopolysaccharides, and various feedstocks [13]. Nowadays, the probiotic bacteria are of the genera *Lactobacillus* and *Bifidobacterium*. *Lactobacillus acidophilus*, *L. rhamnosus*, *L. helveticus*, *L. bulgaricus*,

*L. plantarum*, *L. salivarius*, *L. reuteri*, *L. casei*, *L. brevis*, *Bifidobacterium infantis*, *B. lactis*, *B. bifidum*, *Pediococcus acidophilus*, and *Streptococcus thermophilus* are representative LAB probiotics [63–65]. These probiotics microorganisms are shown in Table 1. However, this mentioned only the main microorganisms found in TFC.

The species of *Lactobacillus* that have been isolated include *L. acidophilus*, *L. johnsonii*, *L. casei*, *L. rhamnosus*, *L. gasseri*, and *L. reuteri* in some TFC (Table 1). While for *Bifidobacterium*, they include *Bifidobacterium bifidum*, *Bifidobacterium longum*, and *B. infantis*. Different yeast species of probiotics are also known, such as *S. cerevisiae*, *D. hansenii*, *Torulaspora delbrueckii*, *Kluyveromyces lactis*, *K. marxianus*, and *Kluyveromyces lodderae* [66]. *S. cerevisiae* is mostly reported in TFC (Table 1). LAB are the most commonly used health-related bacteria in food production due to their long history of safe use and they have been listed as Generally Regarded as Safe (GRAS) at the strain level by the United States Food and Drug Administration (FDA), or as Qualified Presumption of Safety (QPS) at the species level by the European Food Safety Authority (EFSA) [3, 13, 55, 65]. LAB fermentative ability is well-known for providing enrichment of nutrients, improving organoleptic properties, improving food safety, as well as providing health benefits to the host [67]. Furthermore, the ability of a functional food based on probiotics (LAB) can annihilate the toxic effect of cadmium on the kidneys and liver [68, 69].

*Bifidobacterium*, *Lactobacillus*, and some Bacteroidetes show antiobesity activities [63, 70]. For example, *Lactobacillus plantarum* LP104 isolated from kimchi improves hyperlipidemia, liver metabolic disorders, and liver oxidative stress response [71]. Probiotics LAB are involved in various TFC and they are isolated, such as *Bacillus* and *Lactobacillus* as the predominant (Table 1). All these may be attributed to diverse raw materials, types of fermentation, environments, and times of fermentation in different TFC populations, which significantly affect the population of microorganisms during the significantly affecting process, hence different health benefits for the consumers.

#### 4. Bioactive Compounds in Traditional Fermented Condiments

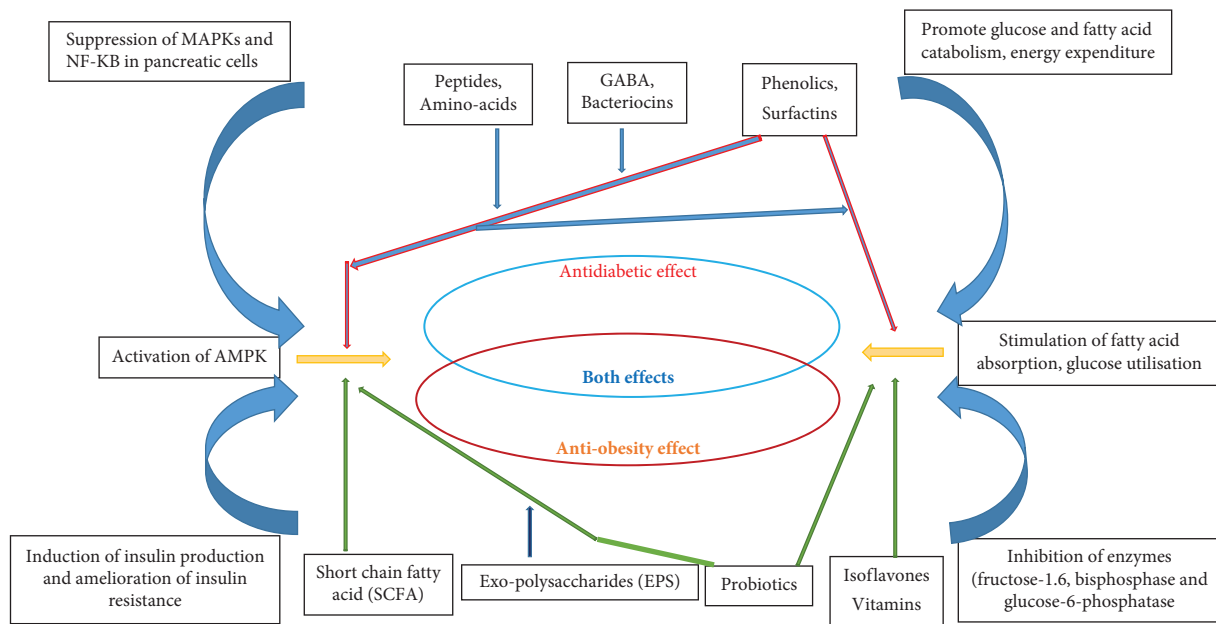
**4.1. Peptides/Amino Acids, Surfactins, and Bacteriocins.** Bioactive peptides are biological ingredients produced during proteolytic cleavage or maturation of food proteins with many beneficial and positive effects on human health [51, 72]. All TFC contain bioactive peptides which affect humans and positively affect the health of humans. In fact, the peptides have been reported to possess antioxidant, anticancer, anti-inflammatory, antimicrobial, antihypertensive activities, and immunomodulatory agents [51, 73]. Diverse bioactive peptides are synthesized during the fermentation process that can decrease blood glucose level, improve insulin uptake, and inhibit some key enzymes ( $\alpha$ -amylase and  $\alpha$ -glucosidase) involved in the development and progression of diabetes [72] (Figure 2). Many researchers also reported that the peptide fragments released from hydrolysed food proteins typically contain several

biologically active peptides that could positively alter physiological function and reduce disease risk such as obesity and diabetes [51, 72].

The results of the present study showed that some TFC contained branched-chain amino acids (BCAAs) (Table 2). BCAAs are known as essential amino acids which possess many physiological and metabolic benefits such as stimulation of pancreatic insulin secretion, adipogenesis, and enhanced immune function [94]. It is reported that impaired BCAA metabolism has been linked to a causal role in diabetes development [95]. Bishop et al. [96] also reported that using individual BCAAs supplementation of long-term high-fat leucine feeding could lead to protective effects with regards to diet induced adiposity and insulin sensitivity. The free amino acids (FAA) profiles increased significantly after fermentation as compared with raw, which may help to reduce blood cholesterol and improve the lipid profile. Xu et al. [97] reported that FAA increased significantly in douchi compared to nonfermented soybean. For instance, antiobesity has already been reported by many researchers [98, 99].

Surfactin is a natural lipopeptide produced by *Bacillus* spp. in TFC among other metabolites, which is gaining much attention for potentially biomedical and pharmaceutical applications [100]. It can be classified into six major types including hydroxylated and cross-linked fatty acids (mycolic acids), glycolipids, lipopolysaccharides, lipoproteins, lipopeptides, phospholipids, and complete cells [101]. Because of their amphiphilic properties, these compounds are used widely in industrial processes such as for emulsification, foaming, detergency, wetting, dispersing, and solubilization. Surfactin also has various physiological activities, such as an inhibitor of fibrin clotting, a cell lysate agent, antibacterial, antiviral, antifungal, antimycoplasma, anti-inflammatory, and hemolytic [102, 103]. For instance, surfactin has the potential properties to control diabetes incidence [100, 104]. It is there for oral or intrainestinal delivery of insulin in indiabetic patients by its role as an effective protease inhibitor and permeability enhancer [36, 100]. Besides, other researchers reported that surfactin *B. subtilis* KLP2015 can be an ideal molecule that can be developed as a candidate drug for the treatment of obesity [105].

Bacteriocins are peptides, known as antimicrobial peptides, synthesized during the fermentation process by microorganisms, mostly the LAB species, as primary metabolites which possess anticancer, anti-inflammatory, immune-modulatory antidiabetic, and antiobesity activities [106, 107]. They can be classified as class I (lanthipeptide, lasso peptide, head-to-tail cyclized peptides, thiopeptide, glycosylated bacteriocin, and sactipeptide), class II (heat-stable, small peptides below 10 kDa such as IIa/b/c/d) and class III (thermally unstable peptides larger than 10 kDa) [108]. Bacteriocins from LAB have gained high interest because of their potential as safe food preservatives or alternatives for medically important antibiotics for treating infectious diseases [109]. Additionally, bacteriocins produced by LAB are GRAS compounds to be incorporated into foods for many health benefits regarding metabolic diseases [13].



MAPK : Mitogen-activated protein kinase ; AMPK : AMP-activated protein kinase ; GABA : Gamma-Aminobutyric Acid

FIGURE 2: Summary of proposed mechanisms of the antidiabetic and antiobesity of traditional fermented condiments.

**4.2. Gamma-Aminobutyric Acid (GABA) and Exo-Polysaccharides (EPS).** Gamma-aminobutyric acid (GABA) is a bioactive nonprotein amino acid found in TFC (Table 2) mainly synthesized via the decarboxylation of L-glutamic acid, and the reaction is catalyzed by the cytosolic enzyme glutamate decarboxylase [110, 111]. GABA is isolated in some TFC as a bioactive compound for their many health benefits. It especially plays a major role as an inhibitory neurotransmitter in the central nervous system. Many researchers found in their studies that GABA protects against the development of diabetic complications resulting from impaired glucose metabolism and can improve insulin resistance via rising glucose transporter GLUT4 and by decreasing the gluconeogenesis pathway and glucagon receptor gene expression [6, 87, 112, 113]. In addition, some studies have been reported that GABA can prevent obesity [114, 115].

Exopolysaccharide (EPS) (such as levan, inulin, kefiran, oligosaccharides, glucan, alternant, and dextran) are extracellular macromolecules found in TFC and they are either soluble or insoluble generally formed in mucilage secretion during microorganisms growth in fermentation process such as yeast, bacteria, and fungi and they are known as GRAS. There are two groups of EPS include: homopolysaccharides which are polymers composed of one type of monosaccharide and heteropolysaccharides which are polymers of repeating units. EPS synthesized by LAB enhances the texture, mouthfeel, and stability of food products [116]. The most prominent EPS producing LAB are *Lactobacillus*, *Lactococcus*, *Bifidobacterium*, *Leuconostoc*, *Pediococcus*, *Streptococcus*, *Enterococcus*, and *Weissella* sp. [117]. These compounds possess antitumor, antidiabetic, anti-obesity, immunomodulatory, antioxidant, drug delivery, as well as cholesterol-lowering activities [22, 118–121].

**4.3. Organic Acids, Fatty Acids, Vitamins, and Minerals.** Free fatty acids (FFA), vitamins, and minerals are among the main compounds found in different TFCs. It was known that an intake of weak organic acid in foods improves insulin resistance of T2D [122]. For example, experimental studies have also indicated that citrate intake improved serum glucose levels in diabetes mellitus. However, it was associated with elevation of interstitial fluid pH [123]. For instance, short chain fatty acids (SCFAs) have been conferred antiobesity properties in both animal models and human subjects [124]. The branched short chain fatty acid (BSCFAs) and SCFAs reduce insulin-mediated phosphorylation of protein kinase B. BSCFAs have effects on adipocyte lipid and glucose metabolism that can contribute to improved insulin sensitivity in individuals with disturbed metabolism [124]. SCFAs production and glucose homeostasis with possible implications in terms of management and prevention of altered glucose metabolism and T2D as well as obesity are reported by Portincasa et al. [125]. It also reported that intake of omega-3 polyunsaturated fatty acids decreases high-fat diet-induced high blood glucose, glucose oxidation and glycogen synthesis. Hence, it enhances the insulin signals and improves high-fat diet-induced insulin resistance [126].

Some vitamins play a vital function for healthy glucose metabolism and insulin resistance. Vitamin A can protect beta-cells and improve beta-cell formation and the metabolism of glucose, thus increasing insulin sensitivity. Vitamins B7, B11, and B12 are produced in fermented dairy products by *Lactobacillaceae* (*Lactiplantibacillus plantarum*, *Lactobacillus delbrueckii*, and *Limosilactobacillus reuteri*), *Propionibacterium*, *Bifidobacterium*, and several species of *Streptococcus* [127]. B vitamins can also lower homocysteine levels in the human body, which can prevent



TABLE 2: Bioactive compounds in traditional fermented condiments.

Fermented condiments	References	Peptides/ AA	Bacteriocins/ surfactins	FA	GABA	Minerals/ vitamins	Polyphenolics	EPS	Probiotics
Dajiang	Liang et al. [74]; Kim et al. [75]; and Wu et al. [76]	AA	Bacteriocins	FA	—	Minerals	Total polyphenolics	—	<i>Staphylococcus</i> , <i>Lactobacillus</i> , <i>Leuconostoc</i> , <i>Bacillus</i> , <i>Lactobacillus plantarum</i> , <i>Leuconostoc mesenteroides</i> , <i>Leuconostoc gasicomitatum</i> , <i>Enterococcus faecium</i>
Doenjang	Jeong et al. [12]; Jeong et al. [12]; Ryu et al. [77]; and Shukla et al. [78]	Dipeptide, AA	Bacteriocins	Linoleic acid, oleic acid	GABA	Minerals	Isoflavones, soyasaponins, and phytoestrogens	EPS	<i>Staphylococcus</i>
Miso	Shirakoa et al. [79]	AA	Bacteriocins	FA	GABA	Minerals	Phenolics, isoflavones, and lecithin	—	<i>Bacillus</i> spp.
Thua nao	Dajanta et al. [14]	AA	—	FA	GABA	Vitamins	Total polyphenolics	—	<i>Bacillus subtilis</i> TN51, <i>Micrococcus halobius</i> , <i>Ped.halophilus</i> , <i>Streptococcus</i> sp., <i>Sacch.rouxii</i> , <i>Zygosaccharomycesrouxii</i> , <i>Asp.oryzae</i>
Owoh	Sanni and Ogbonna [80]	AA	—	—	—	Minerals	Total polyphenolics	—	<i>Bacillus subtilis</i>
Ugba	Anyanwu et al. [16] and Ogueke et al. [17]	AA	Bacteriocins	FA	—	Vitamins	Phenol	—	<i>Bacillus subtilis</i> , <i>Bacillus</i> , <i>Staphylococcus</i> , <i>Micrococcus</i> , <i>Leuconostoc</i> , <i>Lactobacillus plantarum</i> , <i>Proteus</i> , <i>Enterobacter</i>
Kimchi	Wang et al. [81]	AA	Bacteriocins (lactacin BH5 and pediocin K23-2)	FA	GABA	Vitamins B, C	Benzyl isothiocyanate, indole compounds, thiocyanate, and b-sitosterol are	EPS	<i>Lactobacillus brevis</i> , <i>Lactococcus lactis</i> BH5, <i>Lactobacillus brevis</i> KU15153, <i>Lactobacillus plantarum</i> (now, <i>Lactiplantibacillus plantarum</i> ) LRCC5310, LAB, <i>Leuconostoc mesenteroides</i> MKSR
Mbuja	Mohammadou et al. [20]	AA	—	—	—	Vitamins	Alkaloids, steroids, saponin, phenols, flavonoids, and tannins	—	<i>Bacillus amyloliquefaciens</i>
Okpehe	Balogun and Oyeiola [21] and Uzodinma et al. [82]	AA	Bacteriocins	—	—	Minerals Vitamins B, E	Alkaloids, steroids, saponins, phenols, and flavonoids	—	<i>Bacillus</i> spp., <i>Aspergillus niger</i> , <i>Mucor</i> sp. <i>Paecilomyces</i> sp.

TABLE 2: Continued.

Fermented condiments	References	Peptides/AA	Bacteriocins/surfactins	FA	GABA	Minerals/vitamins	Polyphenolics	EPS	Probiotics
Iru	Omodara and Aderibigbe (2018)	AA	Z1116, AU02, and PKT0003	—	—	Minerals	Phenolics	—	<i>Bacillus subtilis</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus aureus</i> , <i>Saccharomyces cerevisiae</i> , <i>Penicillium</i> spp., <i>Rhizopus stolonifer</i> , <i>Saccharomyces cerevisiae</i> var <i>ellipsoideus</i>
Ogiri	Jc et al. [83] and Chukwu et al. [84]	AA	Bacteriocins	$\Omega$ -linoleic acid, and $\alpha$ -linolenic acid	—	Vitamins	Tannin, saponin, phenols, and flavonoids	—	Yeast, LAB <i>Bacillus subtilis</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus aureus</i> , <i>Saccharomyces cerevisiae</i> , <i>Penicillium</i> spp., <i>Rhizopus stolonifer</i> and <i>Saccharomyces cerevisiae</i> var <i>ellipsoideus</i>
Sombala	Ouba et al. [85]; Yérobessor et al. [25]	AA	Bacteriocins	FA	—	Minerals	—	—	<i>Bacillus subtilis</i> <i>Lactobacillus</i>
Bikalga	Ouba et al. [85] and Parkouda et al. [31]	AA	Bacteriocins and surfactins	—	—	Minerals	—	—	<i>B. subtilis</i> , <i>B. licheniformis</i> , <i>B. megaterium</i> , <i>B. pumilus</i>
Soybean kapi	Wittanlai et al. [27]	AA	—	FA	—	Minerals	Phenolics	—	<i>Bacillus</i> , LAB
Awaze	Lemi et al. [28] and Koricha et al. (2020)	AA	—	—	—	—	—	—	<i>Bacillus</i> spp., LAB
Datta	Wedajo Lemi [28] and Koricha et al. (2020)	AA	—	—	—	—	—	—	<i>L. plantarum</i> and <i>L. acidophilus</i>
Siljo	Wedajo Lemi [28] and Koricha et al. (2020)	AA	—	—	—	—	—	—	<i>Lactobacillus acidophilus</i> , <i>L. plantarum</i> , and <i>L. delbrueckii</i> and the yeasts <i>Saccharomyces cerevisiae</i> , <i>Rhodotorula glutinis</i> , <i>Yarrowia lipolytica</i> , and <i>Saccharomyces rouxii</i>
Azo	Wedajo Lemi [28] and Koricha et al. (2020)	AA	—	—	—	—	—	—	LAB
Dawadawa	Adebiji et al. [30]	AA	Bacteriocins (Z1116, AU02, and PKT0003)	$\alpha$ -linolenic acid	—	Minerals Vitamins	Phenolics	EPSs	<i>Lactobacillus plantarum</i> Z1116, <i>Enterococcus faecium</i> AU02 and <i>Leuconostoc lactis</i> PKT0003
Maari	Parkouda et al. [32]	AA	Subtilis and sublancin	Oleic, linoleic, and linolenic	—	—	—	—	<i>Bacillus</i>
Douchi	Yang et al. [86]; Chen et al. [87]; Ding et al. [88]; and Wang et al. [89]	Peptide, AA	Bacteriocins	FA	GABA	—	Daidzein, genistein, phenolics, and isoflavones	EPS	<i>Aspergillus</i> ; <i>Lactobacillus</i> , <i>B. amyloliquefaciens</i> , <i>B. subtilis</i> , <i>Asp. Oryzae</i> , <i>Lactobacillus</i> spp., <i>Staphylococcus</i> spp. and few <i>Bacillus</i> spp

TABLE 2: Continued.

Fermented condiments	References	Peptides/ AA	Bacteriocins/ surfactins	FA	GABA	Minerals/ vitamins	Polyphenolics	EPS	Probiotics
Pixian Doubanjiang	Zhang et al. [36] and Yang et al. [4]	AA, small peptide	Bacteriocins	Linolenic acid, linoleic acid, and oleic acid	GABA	Vitamins	Phenolics	—	<i>Leuconostoc</i> , <i>Lactobacillus</i> spp, <i>Aspergillus</i> , <i>Bacillus</i> and <i>Lactobacillus</i> , <i>Saccharomyces</i>
Kanjang/soy sauce	Devanathi and Gkatzionis [37]	Dipeptide, AA	—	Linoleic acid, and oleic acid	—	Minerals	Isoflavones, soyasaponins, and polyphenols	EPS	<i>Staphylococcus</i> LAB
Mantchoua	—	AA	—	—	—	—	Phenolics	—	—
Tayohounta and dikouanyouri	Chadare et al. [39]	—	—	—	—	—	—	—	<i>Bacillus subtilis</i> and <i>Bacillus pumilus</i>
Afitin	—	AA	—	FA	—	—	—	—	—
Ganjang	Kim et al. [90] and Liu et al. [91]	AA, peptide	Bacteriocins and putrescine	FA	GABA	Minerals Vitamins	Isoflavone, polyphenols, and melanoidins	—	<i>Bacillus</i> and <i>Halomonas Bacillus subtilis</i> EMD4
Soumbara	Kambire et al. [92] and Kouamé et al. [42]	AA	Bacteriocins	—	—	—	—	—	Yeast, mold, LAB
Meju	Ryu et al. [77] and Yang et al. [43]	AA	Bacteriocins	FA	GABA	Minerals	Total polyphenolics	EPS	<i>Tetragenococcus halophilus</i> EFEL7002
Tempoyak	Leisner et al. [93]; Pato and Surono, [44]; Chuah et al. [45]; and Ahmad et al. [46]	AA	Bacteriocins	FA	GABA	Minerals	Total polyphenolics	EPS	<i>Enterococcus</i> sp., <i>Lactobacillus</i> sp <i>Weissella</i> , <i>Streptococcus</i> , <i>Leuconostoc</i> , <i>Lactococcus</i> ,
Yu jiangsuan	Jiang et al. [47]	AA	Bacteriocins	FA	—	—	Alkaloids, derivatives, isoflavone, and phenolic	—	<i>Weissella</i> , <i>Lactobacillus</i>

AA: amino acids; FA: free fatty acid; GABA: gamma-aminobutyric acid; EPS: exo-polysaccharides; —: not available.

oxidative stress due to free radicals, endothelial dysfunction,  $\beta$ -cell dysfunction, hence improving insulin resistance [128]. Vitamin C is a water soluble antioxidant that reduces free radicals by improving superoxide dismutase, glutathione, blood glucose circulation, and its utilization [128]. In addition, vitamin E reduces free radicals, can prevent lipid peroxidation, and improves insulin function [128].

Many research studies show a tight relationship between minerals (micronutrients and trace elements) and T2D because of their role as components or cofactors for enzyme systems involved in glucose metabolism. Some of these trace elements or micronutrients, including copper, chromium, magnesium, vanadium, zinc, iron, and selenium, increase the insulin action by the activation of the insulin receptor sites [129, 130]. In clinical studies, mineral supplementation in obese individuals could improve the serum lipid profiles. The calcium supplementation in obese Chinese women improved lipid profiles [131].

**4.4. Polyphenolics.** TFFC is rich in polyphenolics which exert many benefits for the consumers. However, their levels may vary with the origin of raw material, species of microorganisms involved during fermentation, times of fermentation, as well as the environment. While, the phenolic profiles increased significantly after fermentation as compared with raw as well as their bioavailability and bioactivity [54, 97]. An obvious trend of conversion of the glucoside form in raw soybeans into the aglycone-form isoflavones in fermented soybean products was reported by Xu et al. [97]. The isoflavones such as genistein, glycitein, daidzein, soyasaponins, and phytoestrogens are derived from soybean fermented food condiments. Polyphenolic have been documented as antioxidants thereby promoting the proliferation of gut microbiota [132] and anti-inflammatory activities, as well as their therapeutic effects such as anti-hypertensive, antidiabetic, and antiobesity. Furthermore, polyphenolics prevent diabetes by improving the insulin secretion, glucose utilization, and regulating the intestinal microbiota. Polyphenolics including catechins, anthocyanins, and proanthocyanidins are considered as important prebiotics by increasing the abundance of some microorganisms including, *Lactobacillus*, *Bifidobacterium*, *Akkermansia*, *Roseburia*, and *Faecalibacterium* [133]. Moreover, the prebiotic potential of the polyphenols has recently tested by Haş et al. [134] and the results showed significant growth index on *Lactobacillus plantarum*, *L. casei*, *L. rhamnosus*, *L. fermentum*, and *Saccharomyces boulardii*. Many other researchers demonstrated the prebiotic effects of polyphenolics [132, 135–137]. These microorganisms may increase the production of the SFACs, including acetate and butyrate [133, 138] and inhibit the harmful species such as *Bacteroides* spp. and *Clostridium/histolyticum* [132].

The mechanism of their action may vary with the types or classes of polyphenolics and the fractions of polyphenolics. During the fermentation process, phenolics of different classes are converted into compounds that are often more bioactive than the parent compounds [54]. For example, Laya et al. [139] reported in their *in vitro* study that

different forms of phenolics (bound and free) inhibited the digestive enzymes with a significant difference. Polyphenolics can also act as antioxidants by reducing free radicals and protecting cells from oxidation. In addition, polyphenolics may compete with the toxic substances which may induce the deterioration of cells. For instance, polyphenolics may inhibit the growth of harmful bacteria [6, 132, 138], thereby improving the health of the host since they may boost the secretion of antimicrobial peptides.

## 5. Antiobesity and Antidiabetic Activities of Traditional Fermented Food Condiments

**5.1. Antiobesity Activity.** Obesity is a metabolic disease characterized by high fat in the human body due to improper food habits, consumption of diet linked to inappropriate lifestyle, less or no physical exercise, as well as environmental factors. TFC can be an alternative to therapeutic properties attributed to bioactive compounds (Table 2) synthesized during fermentation processes and which may have various health benefits. Dajiang and doenjang are TFC which showed antiobesity activities attributed to bioactive components (dipeptides, linoleic acid, oleic acid, isoflavones, soyasaponins, phytoestrogens, GABA, AA, probiotics LAB, and so on), which exert the biological effects (Table 3). Figure 2 summarizes the mechanisms of some bioactive ingredients contained in TFC. For example, SCFAs have antiobesity effects which may act by binding to the free fatty acid receptors in the intestine and activating oxidation of fatty acids, leading to hindered adiposity [169].

Peptides also have the ability to control obesity by decreasing body weight and lipid levels, thus improving hyperglycemic conditions as well as treating diseases induced by hyperglycemia [78, 86, 141, 145]. Among these bioactive peptides, some others may inhibit genes implied in the metabolism, such as lupin peptides which can alter the transcription factors SREBP2 and HNF1 $\alpha$  of cholesterol metabolism [170]. Furthermore, especially lupin and lupin proteins may improve the uptake of LDL via hepatocytes and bind the bile acid or salt, thereby inhibiting cholesterol solubility.

On the other hand, Doenjang contains GABA that can prevent obesity [114, 115]. In addition, the antiobesity effects of free amino acids have been reported by many researchers [98, 99]. Miso, like other fermented foods, is a popular TFC from Japan which has been reported to suppress high fat diet-induced obesity due to its bioactive compounds such as isoflavones, lecithin, free fatty acids, bacteriocins, amino acids, and probiotics (Table 2). The genistein is an effective antiobesity which acts by activating the AMPK signal pathway and thus may result in inhibition of adipogenesis in 3T3-L1 cells [171] (Figures 2 and 3).

The probiotic LAB involved in this TFC (Table 2) may be another antiobesity as reported in the literature. For example, *Lactobacillus reuteri* 263 has demonstrated its antiobesity effects by improving the browning of white adipose tissue through upregulating the expression of browning-related genes Ppar- $\gamma$ , PR domain containing 16 (PrdSm16), Ppar- $\gamma$  coactivator-1 $\alpha$  (Pgc- $\alpha$ ), bone morphogenetic protein

TABLE 3: Antiobesity and antidiabetic effects of traditional fermented condiments.

Fermented condiments	Antidiabetic	Antiobesity	Type of study	References
Dajiang	(i) Lowers blood glucose and improves intestinal permeability	(i) Decreases cholesterol levels	<i>In vitro</i>	Kim et al. [75]
	(i) Ameliorates insulin resistance	(i) Improves cholesterol profile and prevents obesity	<i>In vivo, animal</i>	Choi et al. [140]
		(ii) Increases free fatty acid levels caused by elevated lipolysis	<i>In vivo, human</i>	Lee et al. [141]
		(iii) Decreases visceral fat accumulation and adipocyte size	<i>In vivo, animal</i>	Kwak et al. [142]
		(iv) Ameliorates systemic inflammation and oxidative stress in obesity <i>via</i> inhibition of inflammatory signals of adipose tissue	<i>In vivo, animal</i>	Nam et al. [143]
		(v) Decreases body weight and lipid levels	<i>In vitro</i>	Park et al. [144]
		(vi) High consumption of kimchi decreases the risk of hypertension	<i>In vivo, human</i>	Song et al. [145]
		(vii) Peptides have ability to control obesity by decreasing body weight and lipid levels	<i>In vivo, animal</i>	Shin et al. [109]
	(ii) Peptide to control insulin resistance	(viii) Improves hyperglycemic conditions as well as treating diseases induced by hyperglycemia	<i>In vivo, animal</i>	Shukla et al. [78]
	(iii) Reduces blood glucose responses to carbohydrate challenge, improves hyperglycemic conditions as well as treating diseases induced by hyperglycemia such as obesity and diabetes	(ix) Promotes gut health by regulating gut microbiota and its LPS concentrations and suppressing harmful enzyme production	<i>In vivo, animal</i>	Jang et al. [146]
(iv) Peptide and isoflavone may improve insulin sensitivity and decrease blood glucose	(x) Inhibits of $\alpha$ -glucosidase	<i>In vivo, animal</i>	Kwon et al. [147]	
(v) Inhibits adipogenesis	(xi) Reduces the body weight and body fat, in mice under high-fat diet condition and improves lipid profile	<i>In vivo, animal</i>	Yang et al. [86]	
(vi) Improves the glucose metabolism and enhance the antioxidant defense status in mice	(i) Suppresses high-fat diet-induced obesity	<i>In vivo, animal</i>	Chung et al. [148]	
Miso	(i) Peptide and isoflavone improve and regulate insulin secretion	(ii) Suppression of lipid accumulation in the adipose tissues by miso consumption	<i>In vivo, animal</i> <i>In vitro</i> A cross-sectional study	Shirako et al. [79] Cai et al. [149] Takahashi et al. [150]
	(ii) Isoflavones in miso may inhibit the accumulation of visceral fat and the loss of muscle mass and strength in women	(iii) Inhibition of $\alpha$ -glucosidase	<i>In vivo, animal</i>	Okouchi et al. (2019)
	(iii) Inhibition of $\alpha$ -glucosidase	(iii) Inhibition of lipase	<i>In vitro</i>	Jiang et al. [151]
	(iv) Decrease glycemic index	(i) Amino acids and fatty acids may induce the reduction of blood cholesterol	<i>In vivo, animal</i>	Kawamura et al. [152]
Thua nao	—	—	<i>In vitro</i>	Dajanta et al. [14]
Owoh	—	—	—	—
Ugba	—	—	—	—

TABLE 3: Continued.

Fermented condiments	Antidiabetic	Antiobesity	Type of study	References
Kimchi	Ameliorates insulin resistance  (i) Decreased insulin resistance, and increase insulin sensitivity  (ii) Improves and regulates blood glucose and insulin secretion (iii) Induces bile salt hydrolase activity and cholesterol assimilation (iv) Capsaicin and probiotics improve insulin secretion	(i) Reduces body weight gains and adipose tissue weights; modulates serum lipid profiles and hepatic lipogenesis; and reduces adipocyte size and inflammatory response in epididymal fat tissues	<i>In vivo</i> , animal	Cui et al. [153]
		(ii) Prevents obesity	<i>In vivo</i> , animal	Choi et al. [140]
		(iii) Enhances lipolysis and reduces adipogenesis/lipogenesis in 3T3-L1 adipocytes	<i>In vivo</i> , human <i>In vitro</i>	An et al. [154] Lee et al. [57]
		(iv) Reduces body weight and improves metabolic parameters in overweight and obese patients	<i>In vivo</i> , human	Kim et al. [155]
		(v) Suppression of lipid synthesis and inflammation and facilitation of fatty acid oxidation and cholesterol excretion	<i>In vivo</i> , animal	Woo et al. [156]
		(vi) Induces high $\alpha$ -glucosidase inhibitory activity	<i>In vivo</i> , animal	Islam and Choi [157]
		(vii) Reduces accumulation of visceral fat and control blood cholesterol	<i>In vitro</i> <i>In vivo</i> , animal	Lee et al. [158] Jung et al. [159]
Mbuja	—	—	—	—
Okpehe	—	—	—	—
Iru	—	(i) Reduces cholesterol level in the blood stream	<i>In vivo</i> , animal	Atere et al. [160]
Ogiri	—	—	—	—
Soumbala	(i) Regulates insulin secretion	—	<i>In vivo</i> , human	Yérobessor et al. [25]
Bikalga	—	—	—	—
Soybean kapi	—	—	—	—
Awaze	—	—	—	—
Datta	—	—	—	—
Siljo	—	—	—	—
Azo	—	—	—	—
Dawadawa	—	—	—	—
Maari	—	—	—	—
Douchi	(i) Peptides P5 and P7 promote glucose uptake <i>via</i> AMPK and MAPK signaling pathways	—	<i>In vitro</i>	Yu et al. [161]
	(ii) Inhibition of digestive enzymes	(i) Inhibitory effect on lipid peroxidation and may mitigate the degree of the lipidosis of hepatocytes to improve lipid metabolism in liver	<i>In vitro</i> <i>In vitro</i> , <i>In vivo</i> ; animal	Zhu et al. [162] Wang et al. [163]
Pixian Doubanjiang	—	—	—	—
Kanjang/soy sauce	(i) Peptide and isoflavone, control diabetes by improving insulin secretion	(i) Decreases systolic blood pressure	<i>In vivo</i> , animal	Mun et al. [164]
	(ii) Peptide reduce body weight gains; hepatic lipid anabolic	(ii) Peptide reduce body weight gains; hepatic lipid anabolic	<i>In vivo</i> , animal	Shin et al. [109]

TABLE 3: Continued.

Fermented condiments	Antidiabetic	Antiobesity	Type of study	References
Mantchoua	—	—	—	—
Tayohounta and dikouanyouri	—	—	—	—
Afitin	—	—	—	—
Soumbara	—	—	—	—
Ganjang	—	—	—	—
Fermented soybean condiments (FSC)	(i) Induce an increase in the blood glucose, $\alpha$ -amylase and intestinal $\alpha$ -glucosidase with corresponding decrease in pancreatic GPx and GSH contents	—	<i>In vivo</i> , animal	Adedayo et al. (2014)
	(ii) Inhibition of $\alpha$ -amylase and $\alpha$ -glucosidase	—	<i>In vitro</i>	—
	(iii) Reduces postprandial glucose and oxidative stress level, particularly 8-epi-PGF $2\alpha$ , in subjects with IFG, IGT, or newly diagnosed type 2 diabetes	—	<i>In vivo</i> , animal	Ahn et al. [165]
Fermented parkia biglobosa condiment (FPBC)	(i) Reduces significantly ( $p \leq 0.05$ ) the glucose, total triglycerides, total cholesterol, and LDL	—	<i>In vivo</i> , animal	Awoyinka et al. [166]
	(ii) Reduces body weight gains; hepatic lipid anabolic was significantly decreased	—	<i>In Vivo</i> , animal	Bae et al. [167]
Meju	(i) Enhances hepatic insulin sensitivity through activating insulin signaling in diabetic rats	(ii) Isoflavones suppress digestion of dietary lipids and ameliorate hyperlipidemia	<i>In Vivo</i> , animal	Yang et al. [43]
	(ii) Isoflavonoid aglycones and peptides improve glycemic control by potentiating insulinotropic actions and alleviating hepatic insulin resistance in diabetic rats	—	<i>In vitro</i> ; <i>In vivo</i> , animal	Kang et al. [168]
	(iii) Increases insulin secretion capacity	—	<i>In vivo</i> , animal	Yang et al. [43]
Tempoyak	—	—	<i>In vitro</i>	Kwon et al. [147]
Yu jiangsuan	—	—	—	—

—: not available.

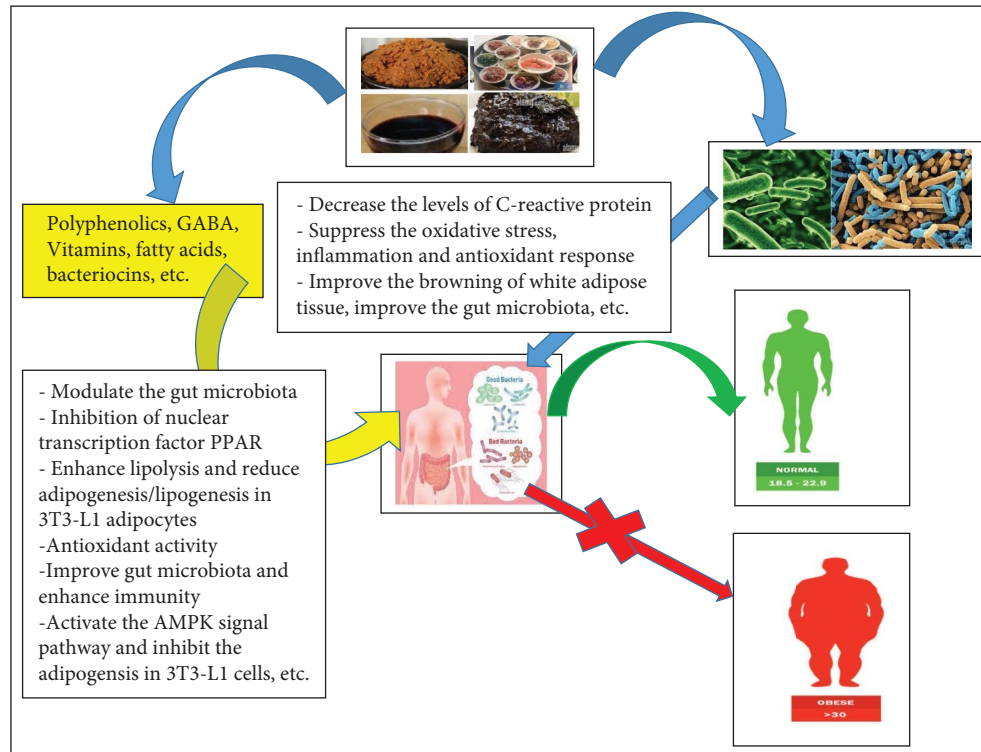


FIGURE 3: Mechanisms of antiobesity of polyphenolics, GABA, fatty acids, bacteriocins, and probiotics from traditional fermented condiments.

7 (Bmp7), and fibroblast growth factor 21 (Fgf21) [172]. In addition, probiotics may increase phagocytosis as well as the activity of natural killer cells thus preventing the inflammatory diseases due to harmful bacteria [137]. Probiotics can also improve digestion, enhance immunity and loss weight thus exerting the antiobesity [173] (Figure 3). Moreover, the *in vitro* study showed that Thua nao has antiobesity activity [14]. It may be due to amino acids and FFA, which can induce the reduction of blood cholesterol. Kimchi is another TFC rich in bioactive components including bacteriocins, ESP, GABA, amino acids, polyphenolics, fatty acids, and probiotics, which may cause antiobesity (Table 2). In fact, fermented foods rich in ESP are known to lower blood cholesterol [174]. The most important SCFAs, including acetate, propionate, and butyrate have been known to have antiobesity properties in both animal models and human subjects [3, 124]. In particular, acetate can affect host energy and substrate metabolism via secretion of the gut hormones like glucagon-like peptide-1 and peptide YY, thus affecting appetite via a reduction in whole-body lipolysis, systemic proinflammatory cytokine levels, and via an increase in energy expenditure and fat oxidation [175]. Besides, butyrate can affect insulin sensitivity by stimulating the secretion of GLP-1 [176]. However, propionate and butyrate can reduce total cholesterol and triglyceride levels [177] thereby improving obese patients.

FAA may reduce the accumulation of visceral fat and control blood cholesterol. Iru and douchi are other FFCs that possess antiobesity activities (Table 3). These TFC contain peptides, amino acids, isoflavones (daidzein and genistein),

GABA, and probiotics (Table 2) which are known to enhance lipolysis and reduce adipogenesis/lipogenesis in 3T3-L1 adipocytes or to suppress the lipid synthesis and inflammation, and facilitate fatty acid oxidation and cholesterol excretion, thereby leading to reduce body weight and improve metabolic parameters in overweight and obese patients. Kanjang/soy sauce also exhibited antiobesity [109, 164]. This TFC contains FFA, which may induce antiobesity activity. For example, 10-oxo-12(Z)-octadecenoic acid, a linoleic acid from lactic acid bacteria can induce energy expenditure by activating transient receptor potential vanilloid (TRPV) 1-mediated browning in white adipose tissue, which inhibited diet-induced obesity development [75, 178].

Furthermore, possibly peptides reduce body weight gains and hepatic lipid anabolic by inhibiting the expression of the nuclear transcription factor PPAR (Figure 3). The antiobesity of meju may be due to isoflavones, among other bioactive compounds (Table 2) which can suppress digestion of dietary lipids and ameliorate hyperlipidemia [43, 167]. Probiotics such as *Lactobacillus plantarum* can decrease the levels of C-reactive protein, insulin-like growth factor binding proteins-3, and monocyte chemoattractant protein (MCP)-1 in white adipose tissue and lower the total plasma triglyceride level [158]. Polyphenolics have the ability to modulate the gut microbiota [132], thereby exerting their antiobesity [179]. For example, Jiao et al. [180] demonstrated that blueberry polyphenolics extract can be used as a potential prebiotic with antiobesity effect on C57BL/6J mice by modulating the gut microbiota (Figure 3). On the basis of the



different results, it should be concluded that bioactive compounds in different TFCs have effective antiobesity effects both in animal and human models.

**5.2. Antidiabetic Activity.** T2D is one of the multiclustering metabolic diseases characterized by high blood glucose as the result of insulin deficiency, peripheral insulin resistance, or both. The inhibition of key enzymes such as  $\beta$ -glucosidase,  $\alpha$ -amylase, and pancreatic lipase by using bioactive compounds can be considered as one of the promising treatments of T2D [54]. The ingestion of these bioactive compounds can enhance immunity, reduce free radicals, and regulate homeostasis of the host. They are present in plant-based foods, especially fermented foods such as condiments. TFCs are consumed as GRAS due to their bioactive compounds which promote health benefits beyond their nutritional aspects (Table 3). The *in vitro* antidiabetic effect of TFC of dajiang was reported by Kim et al. [75]. This result may be due to bioactive compounds such as polyphenolics, peptides, fatty acids, and probiotics which lower blood glucose and improve intestinal permeability of glucose (Table 2). The results may correlate with the findings of Dong et al. [181], who demonstrated that the cereal polyphenolics can impede the formation of advanced glycation end products (AGEs), which can potentially cause the insulin resistance and diabetic complications. In this line, Li et al. [182] stated that it is important to impede the production of AGEs as the natural treatment of diabetes.

The summary mechanisms of different bioactive ingredients such as antidiabetic are presented in Figure 2. Choi et al. [140] found in an *in vivo* study that doenjang can improve insulin resistance by improving the sensitivity of insulin secretion. This effect may be due to dipeptide, linoleic acid, oleic acid, GABA, isoflavones, soyasaponins, and phytoestrogens known as antidiabetic compounds [113, 121, 125]. On the other hand, the acetate can improve insulin sensitivity and glucose homeostasis by decreasing lipid overflow to peripheral insulin-sensitive tissues [175]. Peptides and isoflavones may also control and increase insulin sensitivity by decreasing blood glucose [3, 146, 183]. Besides, FFA and isoflavones can improve glucose metabolism and enhance antioxidant defense, thus preventing DNA damage [134, 148].

In addition, consumption of omega-3 polyunsaturated fatty acids in TFC may decrease high-fat diet-induced high blood glucose and glycogen synthesis and improve insulin signals [126]. Other compounds act by reducing blood glucose responses to carbohydrate challenge, improving hyperglycemic conditions, as well as treating diseases induced by hyperglycemia such as obesity [147]. Polyphenolics can act as antioxidants by reducing free radicals, quenching the reactive oxygen species, and protecting cells from oxidation which may alter the function of original proteins and induce the disturbance of signaling pathways [181]. Polyphenolics can also regulate the anti-inflammatory markers thereby preventing the disease in the human by restoring the endothelial dysfunction. They can also inhibit the RAGEs which may activate an increased production of

proinflammatory markers including interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF- $\alpha$ ) which induce the T2D [181, 184]. Spagnuolo et al. [185] are already reported that polyphenolics protect the cells damage induced by AGEs by many mechanisms. Moreover, polyphenolics may inhibit dipeptidyl peptidase-4 (DPP-IV), thereby lowering the hepatic blood glucose quantity (Figure 4). The mechanism of these bioactive compounds is shown in Figures 2 and 4. Various other studies demonstrate the antidiabetic properties of miso condiment (Table 3). This TFC contains some bioactive compounds including bacteriocins, peptides, GABA, isoflavones, fatty acids, and probiotics LAB (Table 2) which may confer the antidiabetic activity. For example, peptides and isoflavones may increase and regulate insulin secretion, or isoflavones can inhibit the accumulation of visceral fat, leading to the loss of muscle mass [149, 150]. Peptides have also the ability to promote DPP-IV,  $\alpha$ -amylase, and  $\alpha$ -glucosidase inhibition (Figure 4). Thus, they decrease in blood glucose level. This can improve the diabetic status. On the other hand, isoflavones may induce inhibition of  $\alpha$ -glucosidase, thereby decreasing the glycemic index [151, 152].

Furthermore, probiotics could inhibit  $\alpha$ -glucosidase and  $\alpha$ -amylase and the absorption of monosaccharides is indirectly inhibited; hence, the maintenance of postprandial glycemia. For instance, the antioxidants, including glutathione, vitamin E, and C, produced by probiotics [186] may neutralize the reactive oxygen species, thereby preventing the damage of cells. On the other hand, vitamin E and C can prevent the formation of advanced glycation end products (AGEs) [187]. Besides, a plausible mechanism by which GABA acts may be to lower blood glucose, stimulate insulin release, and protect the pancreas from damage (Figure 4). Kimchi is a popular seasoning in Korea with the antidiabetic effects reported by many researchers (Table 3). This TFC contains amino acids, ESP, bacteriocins (*Lacticin BH5*), GABA, and polyphenolics, among others. These bioactive ingredients are known to decrease insulin resistance and increase insulin sensitivity, which may lead to improvement and regulation of blood glucose [153, 154, 157]. Isoflavones also act by inducing high  $\alpha$ -glucosidase inhibitory activity [158]. Kwon et al. [147] found in their study that genistein and peptides from kimchi had elevated glucose-stimulating insulin secretion capacity in mouse insulinoma cells, as genistein and daidzein stimulated glucagon-like peptide-1 (GLP-1) secretion in enteroendocrine NCI-H716 cells, generating insulinotropic actions [159].

Moreover, capsaicin and probiotics improve insulin secretion and regulate blood glucose [159]. Soumbala is reported to have antidiabetic effects [25] (Table 3). Douchi is another TFFC originating from China rich in peptides: GABA, bacteriocins, daidzein, genistein, and phenolics (Table 2). Its antidiabetic was reported in the literature, as shown in Table 3. This possible effect is due to peptides (P5 and P7) which promote glucose uptake via AMPK and MAPK signaling pathways [161] or by inhibiting digestive enzymes [162] (Figure 2). For instance, the GLP-1 hormone delays the evacuation of the gastrointestinal contents; hence, prolonging the feeling of stomach satisfaction, reducing the

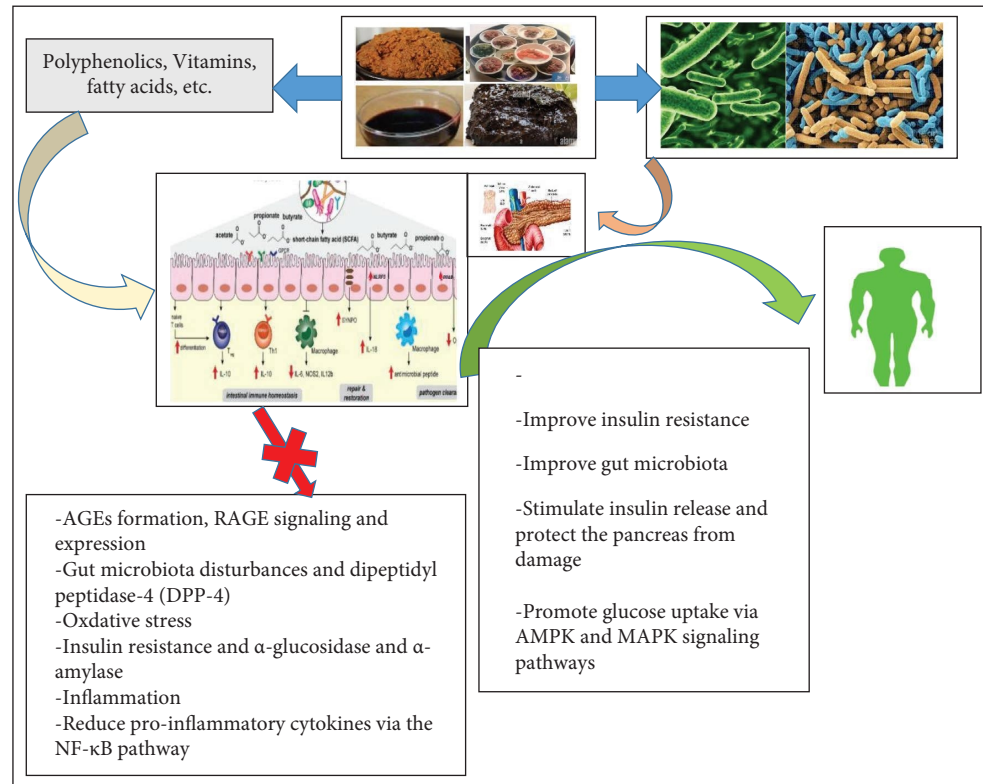


FIGURE 4: Mechanisms of antidiabetic of compounds from traditional fermented condiments.

desire for further food consumption and having an overall effect of body weight loss [173, 188]. Besides, GABA, another bioactive compound, can improve insulin resistance via the rising glucose transporter GLUT4 and by decreasing the gluconeogenesis pathway and glucagon receptor gene expression [112]. Kanjang/soy sauce was also documented for its high antidiabetic effects which may be attributed to amino acids, dipeptides, linoleic acid, oleic acid, isoflavones, soyasaponins, and LAB. For example, *L. acidophilus* La-5 and *B. lactis* BB-12 showed antidiabetic potential by decreasing TNF- $\alpha$ , resistin, and fructosamine levels in diabetic patients in randomized human clinical trials [189]. The short chain fatty acids (SCFAs) can activate the G-protein-coupled receptors on L-cells and promote the release of glucagon-like peptide-1 and peptide YY, such as the increase of insulin, decrease of glucagon secretion, and suppression of appetite [90]. SCFAs also have antilipolytic activities in adipocytes and improve insulin sensitivity via GLUT4 through the upregulation of 5'-AMP-activated protein kinase signaling in muscle and liver tissues [90]. Peptides and isoflavones can also control diabetes by improving insulin secretion [3, 109]. Besides, the antidiabetic effects of meju are reported by many researchers [43, 168].

The isoflavonoid aglycones and peptides may improve glycemic control by potentiating insulinotropic actions and alleviating hepatic insulin resistance in diabetic rats. In this line, daidzein in meju may improve insulin-stimulated glucose uptake by activating peroxisome proliferator-activated receptor-g (PPAR-g) in 3T3-L1 adipocytes [147]. The activators of PPAR- $\gamma$  may also enhance insulin

sensitivity through adipogenesis stimulation and post-prandial fatty acid and triacylglyceride storage within the adipocytes. In addition, polyphenolics are known to have high antioxidant activity, may reduce the harmful effects of advanced glycation end-products (AGEs) by inhibiting the reactive oxygen species, thereby promoting the health of the host by increasing antioxidant defenses, including glutathione reductase, superoxide dismutase, and intracellular glutathione [182, 190, 191] (Figure 4). Furthermore, polyphenolics may block either AGEs-RAGE interaction or cell signaling as well as some of them can inhibit AGEs formation by the mechanism of metal chelation thus preventing the T2D. They may induce autophagy thereby inhibiting the formation of AGEs via the activation of autophagy by the AMPK-mTOR signaling pathway [182]. In fact, polyphenolics are known as important antiglycation agents [190]. Probiotics can also improve the microbiota gut by inhibiting AGEs production and interaction with receptors for AGEs (RAGEs) axis, thereby preventing type 2 diabetes.

Other bioactive compounds such as GABA and polyphenolics may also act synergically and enhance hepatic insulin sensitivity through activating insulin signaling in diabetic subjects. In the same line, probiotics LAB are the best antidiabetic among bioactive compounds; thus probiotic treatment is considered as a new promising approach to reduce cholesterol levels in serum blood [192]. Other potential mechanisms of the antidiabetic effects of probiotics may be attributed with enhanced immunity, increased anti-inflammatory cytokine production, reduced intestinal permeability, and reduced oxidative stress [90]. Furthermore,

the antidiabetic properties of probiotics can be explained by reducing proinflammatory cytokines via the NF- $\kappa$ B pathway, reducing intestinal permeability, and lowering oxidative stress. The probiotics have the ability to improve the gut microbiota by preventing the AGEs production and accumulation which may induce oxidative stress and inflammation response, thereby preventing the disease. In fact, the abundance of LAB was associated with the production of SFAs [193], which act as antioxidant against AGEs, thereby preventing the T2D. For example, it was reported that AGEs have the ability to alter the composition in human gut microbiota which may increase the harmful bacteria and these can promote the inflammation in the human body, leading to T2D development [181, 194]. In addition, Nakashima et al. [195] reported that *Lactiplantibacillus* (Lb.) *plantarum* TOKAI 17 and *Lb. pentosus* TOKAI 35 isolated from soymilk yogurt inhibited  $\alpha$ -glucosidase, DPP-IV, and AGEs formation *in vitro*, thereby preventing the development of T2D. Furthermore, some probiotics such as probiotic strains of *E. coli* can metabolize the AGEs components into nontoxic products, including N<sup>''</sup>-carboxymethyllysine [196]. The results of this study demonstrated that TFC can be a promising alternative for the prevention and treatment of T2D.

## 6. Conclusions, Perspective, and Recommendations

Different types of traditional fermented condiments (TFC) contain probiotic microorganisms which exert many beneficial health benefits. TFC is well known to possess major bioactive compounds which confer various health benefits such as prevention and treatment of metabolic diseases including antiobesity and antidiabetic effects. The *in vitro* and *in vivo*, animal and human models studied both expressed antiobesity and antidiabetic effects. In particular, isoflavones, peptides, bacteriocins, GABA, SFACs, amino acids, vitamins, polyphenolics, and probiotics are generated during the fermentation which act by multiple mechanisms. However, clinical studies on the therapeutic or preventive effects of TFC in obesity and T2D are limited. Further research regarding clinical trials to evaluate TFC and its bioactive compounds may be beneficial in order to make specific dietary recommendations to patients with obesity and T2D.

## Abbreviations

BCAAs:	Branched-chain amino acids
DPP-IV:	Dipeptidyl peptidase-4
EFSA:	European food safety authority
FAA:	Free amino acids
FDA:	United States Food and Drug Administration
FFAs:	Free fatty acids
Fgf21:	Fibroblast growth factor 21
GABA:	Gamma-aminobutyric acid
GRAS:	Generally regarded as safe
LAB:	Lactic acid bacteria
MAPK:	Mitogen-activated protein kinase

NF- $\kappa$ B:	Nuclear factor- $\kappa$ B
PPAR-g:	Peroxisome proliferator-activated receptor-g
QPS:	Qualified presumption of safety
SCFA:	Short chain fatty acid
T2D:	Type 2 diabetes
TFFC:	Traditional fermented food condiments
TNF:	Tumor necrosis factor
TRPV:	Transient receptor potential vanilloid.

## Data Availability

The data used to support the findings of this study are available in PubMed, EMBASE, SciELO, Web of Science, and Google Scholar.

## Conflicts of Interest

The authors declare that there no conflicts of interest.

## Authors' Contributions

LA conceptualized the study. LA and EC performed the methodology. LA, IF, RD, and HW performed data curation. LA, IF, and JO wrote the original draft. LA, IF, and EC wrote, reviewed, and edited the article. All authors have read and agreed to the published version of the manuscript.

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