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Bioactive compounds in fermented foods: Health benefits, safety, and future perspectives

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ABSTRACT

Fermentation is a vital biotechnological process that enhances food safety, nutrition, and bioactive compound production through microbial activity. Traditional fermentation relies on spontaneous microbial communities, generating diverse metabolites such as GABA and SCFAs, which support neuroprotection, gut health, and metabolic regulation. In contrast, modern fermentation employs controlled biotechnological processes to optimize bioactive compound yield and ensure product consistency and safety. While traditional methods involve complex microbial interactions that result in inconsistent bioactive profiles, industrial fermentation utilizes selected strains to maximize efficiency and standardize outcomes. However, traditional fermentation presents safety concerns, including hygiene risks and inconsistent microbial control. Standardized fermentation agents (starter cultures) mitigate these risks, improving reproducibility and safety in industrial applications. Fermented foods contain bioactive compounds that contribute to weight management, cardiovascular health, glucose and lipid regulation, and immune support. Strengthening fermentation through improved practices and starter cultures enhances its potential for producing functional foods and nutraceuticals, particularly benefiting underdeveloped regions.

1. Introduction

Globally practiced for millennia, fermentation is a microbial process transforming foods, beverages, and dairy (Ashenafi, 2006; Siddiqui et al., 2023). This biotransformation enhances preservation, creates diverse products, and improves nutritional value, organoleptic properties, and shelf life (Gopikrishna et al., 2021; Kaur et al., 2017; Ozturk & Young, 2017; Vilela & Cosme, 2020). Particularly crucial where resources are limited, fermentation improves nutrient bioavailability, reduces anti-nutrients, and creates beneficial compounds (Sharma et al., 2020; Voidarou et al., 2021). Traditional fermented foods, including dairy, cereals, and vegetables, offer nutritional and potential health benefits, such as disease prevention and improved digestion (Anal, 2019; Das et al., 2020; Dimidi et al., 2019). Increased consumer awareness highlights the digestive and immune benefits of these fermented products (Pessione & Cirrincione, 2016).

Fermentation, vital for food production, benefits from modern molecular microbiology and bioinformatics, revealing complex microbial interactions and enhancing product quality (Mataragas & Bosnea, 2022; Senanayake et al., 2023). Future genomics will improve monitoring. Furthermore, fermentation repurposes food byproducts into bioactive compounds and biopolymers, yielding valuable substances like peptides, antioxidants, and polysaccharides for health and sustainability (Paula, 2024; Verni et al., 2019). Fermented foods with high acidity, salt, or alcohol content have a strong safety record (Jeon et al., 2015). Lactic acid bacteria (LAB) enhance safety by inhibiting pathogens. Fermentation improves food safety and nutrition by removing toxins and anti-nutrients, crucial for foods like cassava, cereals, and legumes. Sourdough fermentation, for example, increases mineral bioavailability and may improve tolerance to wheat (Frontela et al., 2011; Garrido et al., 2015; Gibson et al., 2018; Lopez et al., 2001; Marco et al., 2021; Sharma et al., 2020).

Fermented foods, with cereals as key substrates, constitute a significant portion of global diets (Xi et al., 2023). Fermentation enhances food safety and nutritional value by improving digestibility and removing toxins, transforming inedible materials. Lactic acid-fermented foods, particularly porridges, are crucial weaning foods in developing countries, boosting energy density and digestibility (Sajjad et al., 2020).

Both traditional and modern fermentation technology are utilized to transform food, but with basically different attitudes and potential.

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Traditional fermentation is dependent on the spontaneous activity of natural populations of microorganisms in raw materials and results in culturally specific foods like sauerkraut and bread from a sourdough starter (Table 1). The technology was inexpensive and provided nutrient-rich alternatives in most regions (Abbaspour, 2024; Hotessa & Robe, 2020; Siddiqui et al., 2023; Sionek et al., 2023). As opposed to this, modern fermentation, driven by the precision of science and biotech advancements, is the deliberate development of selected microbial strains under carefully controlled conditions to maximize yields. Advances such as strain improvement, process development, and feedstock optimization enhance efficiency (Faria et al., 2025; Pal et al., 2024). Modern fermentation also promotes ecological sustainability by recycling food waste into useful by-products like enzymes and biofuels, resulting in a circular economy. It also helps in avoiding non-communicable diseases as it supports health-nourished diets and aids in cost-effective production of specialist food ingredients and high-value bioproducts from renewable raw material (Faria et al., 2025; Pal et al., 2024).

2. The roles of predominant microbes in food fermentation

Fermented foods contain living organisms that can modulate gut microbiota, physiology, and cellular redox homeostasis, and also enrich the host's diet with new bioactive compounds. The microbial community in most fermented foods and alcoholic beverages is dominated by acetic acid bacteria, lactic acid bacteria, non-lactic acid bacteria, gram-negative bacteria, filamentous molds, and alcohol-producing yeasts (Tamang et al., 2016). Microorganisms present in traditional fermented foods metabolize the constituents of raw materials during the fermentation process (Laya et al., 2023). Some microorganisms can increase the levels of vitamins, antioxidants, peptides, exopolysaccharides, organic acids, and other bioactive molecules in foods through fermentation. This process offers several health benefits and preservative properties, such as antioxidant and antimicrobial activities (Alkalbani et al., 2019; Kandylis et al., 2016; Mcgovern et al., 2004).

2.1. Bacteria

Lactobacillaceae bacteria are crucial for food fermentations, producing lactic acid from carbohydrates. This acid production lowers the pH, inhibiting spoilage organisms and pathogens, while also creating a tangy flavor, contributing to texture, and sometimes enhancing nutritional value. Different genera and species within Lactobacillaceae perform specific roles in various fermentations (Wang et al., 2021). Lactic acid bacteria are the most common bacteria isolated from various fermented foods. They share common characteristics such as being non-spore-forming, Gram-positive, catalase-negative (without cytochromes), anaerobic or aerotolerant, fastidious, acid-tolerant, and strictly fermentative (Lee et al., 2022). The main lactic acid bacteria genera isolated from various traditionally fermented foods are *Lactobacillus, Pediococcus, Enterococcus, Lactococcus, Leuconostoc, Oenococcus*, and *Streptococcus. Lactobacillus* is the predominant lactic acid bacteria in these foods, producing organic acids like lactic acid. This fermentation lowers the substrate's pH, inhibiting the growth of pathogenic, putrefactive, and toxigenic bacteria (Castellone et al., 2021; Lee et al., 2022, 2021).

Table 1
Comparative overview of traditional and industrial fermentation.

Aspect	Traditional Fermentation	Industrial Fermentation
Microbial Selectivity	Naturally occurring, diverse microbial communities	Selectively introduced microbial strains for targeted outcomes
Product Consistency	Variability due to environmental and regional factors	Standardized conditions ensuring uniform product quality
Bioactive Compound Production	Complex bioactive compounds resulting from diverse microbial interactions	Optimized production of specific bioactive compounds through controlled processes
Flavor Profile	Rich, variable, influenced by microbial diversity	More controlled and predictable flavors
Dominant Microbes	Halanaerobium, Halomonas, halophilic bacteria	Lactobacillus-related genera, primarily lactic acid bacteria
Fermentation Process	Natural progression influenced by environment and manual interventions	Systematic, engineered process with precise conditions
Application	Typically used for traditional food production with cultural significance	Widely used in modern food processing and large-scale production
Microbial Community Control	Open-system fermentation with natural succession of microorganisms	Closed-system fermentation with strict microbial management

Other important bacteria, particularly in fruit and vegetable fermentations, are the acetic acid-producing *Acetobacter* species. These bacteria play a significant role by converting ethanol (often produced by yeasts initially) into acetic acid. This contributes to the characteristic tangy or vinegary flavor of fermented products like vinegar, kombucha, and certain pickles. While lactic acid bacteria are primarily responsible for fermenting many dairy products and some vegetables, *Acetobacter* species dominate in environments with higher sugar concentrations and oxygen. The presence of oxygen distinguishes acetic acid fermentation from anaerobic lactic acid fermentation. *Acetobacter* species are also used in other fermented foods and beverages, contributing to their unique flavor profiles and preservation. Different species within the *Acetobacter* genus have varying tolerances to alcohol and acidity, making them suitable for different fermentation processes (Han et al., 2024).

2.2. Molds

In fermentation, molds function as both spoilage and preservation agents, typically following bacterial and yeast activity (Yang et al., 2022). These fungi degrade macromolecules through enzymatic action, enhancing texture, flavor, and nutritional value. Common genera include *Actinomucor, Aspergillus, Penicillium,* and *Rhizopus* (Tamang et al., 2016). Consequently, fungal fermented foods offer functional benefits such as enzyme production, anti-nutrient degradation, and improved mineral bioavailability (Laya et al., 2023; Lee et al., 2022). Specifically, *Rhizopus, Aspergillus*, and *Mucor* are used in mold fermentation to saccharify cereals, enriching them with peptides and amino acids. Furthermore, mold fermentation hydrolyzes glycerides, increasing free fatty acids, solubilizing fractions, and reducing anti-nutrients like stachyose and phytic acid (Nout & Kiers, 2005). Finally, these microorganisms significantly contribute to cheese and meat ripening, developing characteristic qualities and preventing rancidity through enzymatic activity and oxygen reduction (Diaferia & Berni, 2018).

2.3. Yeast

Yeasts, like bacteria and molds, can play both beneficial and detrimental roles in food fermentation. Beneficial yeasts, such as *Saccharomyces cerevisiae* (Parapouli et al., 2020), *Saccharomyces boulardii* (Abid et al., 2022), and *Candida milleri* (Kazemi et al., 2025), are essential for the production of many foods. *S. cerevisiae* leavens bread by producing carbon dioxide and is also used in alcoholic beverage production. *S. boulardii*, a probiotic yeast, is used in supplements and fermented foods to promote gut health. *C. milleri* contributes unique flavors to specific food fermentations (Moslehi-Jenabian et al., 2010). Beyond leavening bread and producing alcohol, beneficial yeasts contribute to the flavor and aroma of many fermented foods. They produce a variety of compounds, including esters, aldehydes, and organic acids, which contribute to the complex sensory characteristics of these products. In some cases, yeasts can also enhance texture. The specific yeast species used, in conjunction with fermentation conditions, significantly influences the final product's characteristics (Castellone et al., 2021; Lee et al., 2022).

Saccharomyces yeasts play a multifaceted role in food fermentation, impacting both the process and the final product. They ferment sugars, producing ethanol and carbon dioxide, which are crucial for alcoholic beverages and bread leavening. Furthermore, they generate a range of secondary metabolites that contribute to complex aromas and flavors. Importantly, some strains inhibit mycotoxin-producing molds, enhancing food safety. *Saccharomyces*' diverse enzymatic activities (lipolytic, proteolytic, pectinolytic, glycosidic, and urease) further influence flavor, texture, and other characteristics. These combined effects make *Saccharomyces* a vital microorganism in numerous fermentations, with specific contributions varying depending on the strain, substrate, and fermentation conditions (Lee et al., 2022).

3. Bioactive compounds in traditionally fermented foods and their applications

Fermented foods are a source of bioactive compounds because biosynthesis and biotransformation generate new compounds with bioactive potential. These compounds perform specific functions in the human body by influencing cellular activity, thus promoting health. Peptides, surfactins, bacteriocins, gamma-aminobutyric acid (GABA), exopolysaccharides, organic acids, fatty acids, vitamins, minerals, and polyphenols are some of the most prominent bioactive compounds isolated from various fermented foods (Table 2) (Laya et al., 2023).

3.1. Bioactive peptides

Bioactive peptides, short chains of amino acids released from parent proteins during processes like proteolytic cleavage or food protein maturation, are naturally produced in the body and used in foods to

Table 2
Bioactive compounds isolated from fermented foods and their medical applications.

Fermented Foods	Bioactive Compounds	Medical Applications (Bioactivity)	RRef
Fermented Vegetables	Bacteriocin	Antimicrobial Properties	(Tamang & Fleet, 2009)
Kimchi (Fermented cabbage)	Bacteriocin	Anti-viral effect	(Chang et al., 2008)
Kimchi (Fermented cabbage)	Pediocin	Anti -microbial, anticancer	(Chang et al., 2008)
Dahi	Nisin Z, pediocin	Anti-viral effect	(Darbandi et al., 2022)
Fermented cabbage product	Bacterriocin	Anti-oxidant property	(Gao et al., 2010)
Asian fermented soybean foods	Peptides, Enzymes.	Anti-oxidant property	(Ping et al., 2012)
Fermented kefir	Peptides, Amino acids.	Immunomodulatory and inhibitory properties	(Ping et al., 2012)
Koumiss	Peptides, vitamins	Inhibitory properties	(Chen et al., 2010)
Yoghurt	Peptides and amino acids.	Inhibitory properties	(Tillisch et al., 2014)
Fermented Kefir	Butyric acid, acetic acid, and propionic acid	Anti-cancer activity	(Melini et al., 2019)
Fermented Kefir	Organic acids	Antimicrobial activity	(Iraporda et al., 2017)
Dry-fermented sausage	Starter culture (P200S34) and protease (EPg222)	Angiotensin-converting enzyme inhibition, Antioxidant activity	(Song et al., 2018)
Fermented soybean	Isoflavin β	gE immunoreactivity	(Yang et al., 2023)
Fermented soybean paste	Histamine, Tyramine	Increased hepatic expression of IL-1β	(Yang et al., 2023)
Fermented soybean	Isoflavone (genistein and daidzein)	Level of progesterone increase	(Sapbamrer et al., 2013)
Fermented soybean	Aqueous extract of Hawaijar	Increase Glucose uptake, G6P production, and expressions of pPI3K, pAKT, mpAMPK	(Yang et al., 2023)
Fermented soybean	Lipoteichoic acid (LTA) Peptidoglycan (PGN	Reduce intestinal inflammation	(Yang et al., 2023)
Fermented soybean	Menaquinone-7,daidzin, genistein, and glycitin,	Angiotensin-converting enzyme inhibitor activity	(Kumar et al., 2017)
Fermented soy permeate	Isoflavones and α-galactooligosaccharides	Increase muscle glycogen content	(Vincent & Lefeuvre-orfila, 2013)
Chungkookjang	Genistin, Daidzein	Reduce DNA fragmentation	(Kim et al., 2007)
Cheonggukjang	Intact isoflavones (genistein, daidzein,and glycitein)	Decreased bone resorption activity	(Lee et al., 2017)
Cheonggukjang (natto)	Nattokinase	Increase digestion of fibrin, Digestion of plasmin substrate	(Kim et al., 2007)
Natto	Vitamin K2	Maintaining bone stiffness	(Katsuyama et al., 2002)
Miso	Lipopolysaccharide	PGD2 production via macrophage cells	(Sasaki et al., 2020)
Fermented soybeans	C-miso(a), S10-miso(b) and S9O1-miso(c)	Antioxidant effects, Anti-mutagenicity effects	(Vitaminol, 2006)
Misosoup, fermented soybeans, houba-miso	Isoflavone	Reduce hot flush severity	(Nagata et al., 2016)
Misoand natto	Isoflavones	Decrease blood pressure	(Nozue et al., 2017)
Soy Meju	Tetragenococcus halophilus EFEL7002	Antioxidant activity in human intestine	(Kim et al., 2022)
Thua-Nao	Daidzein Genistein	Reduce MCF-7 and HEK293 cancer cell growth	(Soybean et al., 2021)
Soy milk	Isoflavones 3-HAA	Decrease TG accumulation and total cholesterol within liver under oxidative stress	(Lin et al., 2005)
Tempeh	Anthocyanin and GABA	Antioxidant activity	(Hwang et al., 2018)
Kounou	Flavonoids, Polyphenols	Antioxidant activity	(Ronald et al., 2021)
Bozai (Boza)	Bacteriocin LF-BZ532	Antimicrobial activity	(Kingamkono et al., 2014)
Togwa	Lactic acid	Antimicrobial activity	(Kingamkono et al., 1999)
Fermented Tartary buckwheat	Monascus purpureus	Reduce liver glycogen content	(Bartkiene et al., 2023)
Fermented milk	Phenolic compounds	Antioxidant activity	(Fardet & Rock, 2018)
Fermented milk	Peptides and GABA	Anti-hypertensive activity	(Qian et al., 2011)
Yoghurt	Folate (vitamin B9), vitamin K, riboflavin (vitamin B2)	Increase of vitamin content	(Melini et al., 2019)
Fermented Quinoa	Phenolic compounds, GABA 1, peptides, CLA 2, folates (vitamin B9)	Antioxidant activity	(Melini et al., 2019)
Sourdough	Peptides and GABA	Anti-hypertensive activity	(Melini et al., 2019)
Lupin - tempeh	Folate (vitamin B9), vitamin K, riboflavin (vitamin B2)	Vitamin content	(Melini et al., 2019)
Fermented red cabbage	Phenolic compounds, GABA 1, peptides, CLA 2, folates (vitamin B9)	Antioxidant activity	(Melini et al., 2019)
Kimchi	Phylloquinone	Increase Vitamin content	(Kaprasob et al., 2018)

lower blood pressure, improve immunity, and promote heart health. They exhibit various biological activities beneficial to human health, including antihypertensive, antioxidant, immunomodulatory, antimicrobial, anticancer, anti-inflammatory, antithrombotic, and opioid-like effects (Antony & Vijayan, 2021; Aslam et al., 2020; Chelliah et al., 2021). Diverse bioactive peptides are synthesized during fermentation that can decrease blood glucose levels, improve insulin uptake, and inhibit key enzymes (α-amylase and α-glucosidase) involved in diabetes development and progression. These peptides include, but are not limited to, those derived from milk proteins (casein and whey), soy proteins, and cereal proteins. Examples include Val-Tyr-Pro and Ile-Lys-Pro (antihypertensive), and Leu-Tyr-Leu and Val-Pro-Glu-Pro (antioxidant). Numerous other bioactive peptide sequences exist and are continually being researched (Chelliah et al., 2021).

Hydrolyzed food proteins yield bioactive peptides that improve physiological functions and reduce chronic diseases like obesity and diabetes. These peptides regulate energy metabolism, fat accumulation, and appetite. Since excess fat accumulation increases the risk of cardiovascular disease, type 2 diabetes, and metabolic syndrome, managing obesity is crucial. Bioactive peptides can improve lipid and glucose metabolism, and reduce diabetes risk by inhibiting enzymes and enhancing insulin sensitivity (Chelliah et al., 2021; Laya et al., 2023).

3.2. Surfactin

Surfactin is a natural lipopeptide produced by *Bacillus subtilis*. It is found in fermented foods such as natto, Korean fermented soybean products, and African fermented locust beans. Surfactin's amphiphilic properties make it valuable for both food preservation and therapeutic drug development. Its ability to form micelles and vesicles enhances drug solubility and bioavailability (Zhang et al., 2017). Surfactin's broad antimicrobial activity (antibacterial, antifungal, and antiviral) makes it effective against various pathogens and enhances food safety by inhibiting spoilage organisms and foodborne pathogens (Zhen et al., 2023).

Surfactin can be classified into six major types, including hydroxylated and cross-linked fatty acids (e.g., mycolic acids), glycolipids, lipopolysaccharides, lipoproteins, lipopeptides, and phospholipids (Housaindokht et al., 2005). Due to their amphiphilic nature, these compounds are widely used industrially as emulsifiers (blending immiscible liquids), foaming agents (stabilizing bubbles), detergents (breaking down oils and dirt), wetting agents (enhancing liquid spreadability), dispersants (preventing particle clumping), and solubilizers (enhancing hydrophobic compound solubility) (Pardhi et al., 2022).

Surfactin has diverse physiological activities, including inhibiting fibrin clotting, lysing cells, and exhibiting antibacterial, antiviral (especially against enveloped viruses like influenza and HIV), antifungal, and antimycoplasma properties. It also has anti-inflammatory and hemolytic effects, making it valuable in medicine, agriculture, and biotechnology (Li et al., 2023). For instance, surfactin shows potential for controlling diabetes due to its role as an effective protease inhibitor and permeability enhancer, making it suitable for oral or intraintestinal insulin delivery for diabetic patients (Gedawy et al., 2018). Moreover, surfactin obtained from *B. subtilis* KLP2015 is considered an ideal candidate for the development of drugs aimed at treating obesity (Huang et al., 2021).

3.3. Bacteriocins

Bacteriocins, ribosomally synthesized antimicrobial peptides from lactic acid bacteria, offer broad-spectrum antimicrobial and diverse bioactivities (Simons et al., 2020; Tamang et al., 2016). These peptides exhibit anticancer and anti-inflammatory effects and may combat metabolic disorders by regulating glucose and influencing gut microbiota. This potential makes them valuable for functional food and nutraceutical development. Furthermore, bacteriocins are promising for natural food preservation and novel antimicrobial therapies, particularly against drug-resistant bacteria. Current research explores their use in treating infections, modulating gut microbiota, and addressing various health conditions, solidifying their key focus for the food and health industries (Heeney et al., 2019; Huang et al., 2021).

Bacteriocins provide a targeted antibiotic alternative, combating drug resistance while preserving beneficial microbes. They act as natural food preservatives against pathogens like *Listeria, Escherichia coli*, and *Staphylococcus*, thereby extending shelf life. Research explores their broader applications in food preservation and biofilm disruption, ultimately improving food safety and quality (Darbandi et al., 2022; Yang et al., 2014).

Naturally derived and generally regarded as safe (GRAS), bacteriocins are attractive food preservatives, meeting clean-label demands. Specifically, nisin and pediocin, from *Lactococcus lactis*, control pathogens like *Listeria* and *Clostridium* in dairy and meat, offering a natural alternative to synthetic additives and boosting food safety and extending product longevity (Lee et al., 2023; Shin et al., 2015). In addition to food preservation, bacteriocins offer targeted bacterial infection treatment, avoiding microbiome disruption and resistance common with broad-spectrum antibiotics. They specifically target pathogens like MRSA, *Clostridioides difficile*, and *Acinetobacter baumannii*, preserving beneficial bacteria (Tamang et al., 2016). Furthermore, bacteriocins offer personalized medicine potential and reduced side effects. They can enhance antibiotic efficacy against resistant strains and be developed into pharmaceuticals. Optimized production through genetic engineering supports commercialization. Despite challenges like resistance development, bacteriocins provide a promising solution against drug-resistant infections (Simons et al., 2020).

3.4. Gamma-amino butyric acid (GABA)

Gamma-aminobutyric acid (GABA) is a key non-protein amino acid that acts as the major inhibitory neurotransmitter in the brain. Its sedative properties, its ability to reduce stress, and its role in enhancing the quality of sleep are well-documented. The green and natural production of GABA in fermented foods, such as yogurt, kimchi, miso, and other soy products, has garnered great interest as a promising alternative to chemically synthesized counterparts. The precious biomolecule is widely generated through the decarboxylation of L-glutamic acid through the process of fermentation (Santos-Espinosa et al., 2020). GABA plays a vital role in the central nervous system by regulating neuronal excitability and promoting relaxation. It reduces anxiety, improves mood, enhances sleep quality, calms stress-related disorders, and regulates blood pressure and glucose metabolism. Additionally, GABA potentially improves insulin sensitivity, aids in managing type 2 diabetes, and contributes to weight management, highlighting its importance for mental and physical well-being (Sahab et al., 2020).

Fermentation enhances the bioavailability of GABA, making it more accessible for human absorption. GABA's functional properties extend beyond neurotransmission, improving mental health by reducing anxiety, enhancing mood, and promoting relaxation. It also influences metabolic functions, such as regulating blood pressure and improving insulin sensitivity. Research is growing on developing functional foods enriched with GABA to enhance public health and nutrition. GABA helps prevent obesity by regulating appetite, energy expenditure, and stress-related eating, reducing risk factors for cardiovascular disease, diabetes, and metabolic disorders. It also improves metabolic health by reducing insulin resistance and regulating fat storage and energy use. Animal studies show that GABA supplementation can reduce body fat percentage and increase lean muscle mass, aiding weight loss. Research supports GABA's potential in dietary strategies for weight management and metabolic health, though further studies are needed to fully understand its mechanisms and applications in obesity and related disorders (Bagus et al., 2021; Li et al., 2021; Patra et al., 2016; Rashmi et al., 2018; Rezazadeh et al., 2021; Sohrabipour et al., 2018).

Fermentation processes that yield high levels of GABA are mostly carried out with Lactic Acid Bacteria (LAB), which possess the enzyme glutamate decarboxylase (GAD) to decarboxylate L-glutamate into GABA (Yogeswara et al., 2020). Among the well-studied and productive GABA-producing LAB strains are *Lactobacillus brevis*, which commonly occurs in fermented foods like kimchi and sauerkraut, *Lactiplantibacillus plantarum*, which is widely used in certain fermented beverages, and *Lactobacillus paracasei*, which is often isolated from fermented fish and cheeses (Anumudu et al., 2024). Some LAB genera such as *Lactococcus, Pediococcus, Leuconostoc, Enterococcus*, and *Streptococcus* also have strains with the GABA-producing ability. Strain selection, fermentation conditions (pH, temperature, incubation time, initial L-glutamate level), and the development of fermentation technology, e.g., solid-state fermentation (SSF), electro-fermentation (EF), and cold stress treatment, play significant roles in the productivity of GABA (Cui et al., 2020).

The medicinal health impacts of GABA in fermented foods have been tried in human and animal trials. Human clinical trials reveal that GABA-enriched foods can increase sleep efficiency and reduce sleep latency, as indicated through the use of fermented rice germ extracts (Icer et al., 2024). Research also demonstrates that consumption of GABA-fortified beverages can moderate stress and anxiety through the enhancement of heart rate variability, even though additional research is warranted to confirm these impacts fully (Hepsomali et al., 2020). Additionally, antihypertensive properties have been observed, and GABA-enriched dairy products have been seen to have the capability of reducing systolic blood pressure in mildly hypertensive individuals (Beltrán-Barrientos et al., 2021). Some findings suggest GABA's role in the prevention of diabetes by stimulation of insulin secretion (Barakat & Aljutaily, 2025). In animal studies, supplementation with GABA has been established to have sleep-inducing, antidepressant, and neurologically improving effects (Almutairi et al., 2024). In poultry, studies exhibit improved feed conversion ratio, weight gain, and immune status, which indicates its prolonged metabolic effect (Attia et al., 2020).

3.5. Exopolysaccharides

Exopolysaccharides (EPS), complex carbohydrates from microbial fermentation, are recognized as safe (GRAS) and offer a wide range of benefits. They enhance food quality by improving texture, stabilizing emulsions, and extending shelf life (Osemwegie et al., 2020). Moreover, as prebiotics, they foster a healthy gut microbiome, which is crucial for digestion, nutrient absorption, immunity, and mental health. EPS also prevent spoilage, enhance sensory experiences, and contribute to nutritional value, making them prime ingredients for functional foods and nutraceuticals. Further research is underway to unlock their full potential (Angelin & Kavitha, 2020).

EPS-producing lactic acid bacteria (LAB) are vital for fermented food production, improving texture, stability, and sensory qualities. Specific LAB, such as *Lactobacillus, Lactococcus, Bifidobacterium, Leuconostoc*, and *Pediococcus*, contribute unique benefits to various foods, including yogurt, cheese, and fermented vegetables, enhancing flavor, probiotic properties, and overall quality (Ruas-madiedo et al., 2014). EPS also provide diverse health benefits, including antitumor properties through cancer cell inhibition and apoptosis promotion, metabolic regulation for diabetes management, potential obesity combat through appetite and lipid metabolism control, immunomodulatory effects that enhance immunity and reduce oxidative stress, and their use as therapeutic agent carriers to improve drug delivery (Choi et al., 2011; Dabiré et al., 2020; Zhao et al., 2022).

3.6. Free fatty acids and minerals

Fermented foods contain diverse free fatty acids. Short-chain fatty acids (SCFAs) like acetic, propionic, and butyric acid are prevalent in fermented dairy and vegetables, benefiting gut health. Medium-chain fatty acids (MCFAs) (lauric, capric, caprylic) occur in fermented coconut and some cheeses. Long-chain fatty acids (LCFAs) (oleic, linoleic, palmitic) are found in fermented meats, fish, and foods like natto. The specific fatty acid profile depends on the food, microbes, and fermentation (Silva et al., 2020).

For instance, short chain fatty acids (SCFAs) have been conferred anti-obesity properties in both animal models and humans. The branched short chain fatty acids (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 (Heimann et al., 2016). The production of short-chain fatty acids (SCFAs) and the maintenance of glucose homeostasis have significant implications for the management and prevention of altered glucose metabolism, type 2 diabetes (T2D), and obesity (Portincasa et al., 2022). SCFAs are produced in the gut through the fermentation of dietary fibers by beneficial gut microbiota. These SCFAs play a crucial role in regulating various metabolic processes, including enhancing insulin sensitivity and reducing inflammation, which are key factors in the development and progression of T2D. Additionally, SCFAs influence the release of gut hormones that regulate appetite and energy balance, thereby contributing to weight management. By promoting a healthy gut microbiota and improving metabolic health, SCFAs production and glucose homeostasis can be valuable strategies in addressing metabolic disorders such as T2D and obesity (Muhialdin et al., 2020).

3.7. Polyphenols

Fermented foods are rich in polyphenols 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. Phenolic profiles increase significantly after fermentation, resulting in higher levels of beneficial plant-based molecules in fermented foods compared to their raw counterparts. This also enhances their bioavailability and bioactivity, meaning they are better absorbed and utilized by the body. The increased bioactivity leads to more potent health effects, such as antioxidant, anti-inflammatory, and antimicrobial properties. This transformation enhances the overall health benefits of fermented foods, making them a valuable component of a healthy diet (Xu et al., 2015).

Polyphenol mechanisms of action are complex and vary by type, class, and fraction. Their structures, ranging from simple phenolic acids to complex flavonoids, interact uniquely with biological systems as antioxidants, enzyme modulators, or cell signaling influencers. Polyphenol fractions (free, conjugated, and bound) impact bioavailability and activity, as gut microbiota metabolizes them into compounds with differing effects. Fermentation converts phenolics into more bioactive compounds than their parent forms (Rudrapal et al., 2022). Furthermore, *in vitro* studies indicate that polyphenols significantly inhibit digestive enzymes, suggesting they may improve metabolic health by influencing nutrient digestion and absorption (Laya et al., 2022). As antioxidants, polyphenols neutralize free radicals, protect cells from oxidative damage, compete with toxins to maintain cell integrity, and inhibit harmful bacterial growth. They may also boost antimicrobial peptide secretion, enhancing immune defense (Li et al., 2021; Xue et al., 2022).

4. Fermented foods and their health benefits

4.1. Improve protein digestibility

Fermented foods contain a higher content of peptides and free amino acids due to proteolysis by microbial enzymes during fermentation. Free cystine, histidine, and asparagine are found in fermented cow and soy milk curd (Ghosh & Chattoraj, 2013). A study found that yogurt-like products obtained by fermentation with *Lb. rhamnosus* SP1, *Weissella confusa* DSM 20,194, and *Lb. plantarum* T6B10 showed improved protein digestibility (Lorusso et al., 2018). Fermentation can improve the protein digestibility of grains other than cereals, such as pulses, by reducing the levels of non-nutritive compounds that promote protein crosslinking (e.g., phenolic and tannin compounds) and by inhibiting digestive enzymes (e.g., trypsin and chymotrypsin inhibitors). Additionally, the production of microbial proteases during fermentation partially degrades proteins and releases some of them from the matrix (Çabuk et al., 2018).

Fermentation can enhance protein digestibility by reducing non-nutritive compounds in cereal matrices, but strains with high proteolytic activity may negatively affect protein quality. The combination of germination and sourdough fermentation improves in vitro protein digestibility. Longer fermentation time in lotus root leads to an increase in total protein content. Fermentation also alters amino acid and protein content in cereals, such as cornmeal, millet, maize, and sorghum. However, studies on sorghum kisra bread have shown no increase in lysine levels, but methionine and tyrosine levels do increase. Fermentation in uji production increases tryptophan content but decreases lysine content. Overall, the nutritional content of foods can vary, but the overall enhancement is often substantial (Çabuk et al., 2018; Melini et al., 2019; Sci et al., 2017).

4.2. Confer health-modulating compounds

A study found that fermentation-produced lactic acid can reduce pro-inflammatory cytokine secretion in macrophages and dendritic cells. Organic acids found in fermented foods can offer core health benefits by reducing reactive oxygen species burden in intestinal enterocytes, potentially affecting the small intestine. Certain bacteria in plant and dairy foods synthesize B vitamins, making microbial-derived products strain-dependent. Fermentation produces amino acids and derivatives, including GABA, which have neurotransmitter and immunomodulatory functions. Some polysaccharides act as prebiotics, fermented by gut microbiota into short-chain fatty acids (SCFAs), which support gut health by lowering pH, inhibiting pathogens, and fueling colonocytes (Bai et al., 2016; Makino et al., 2016; Pereyra et al., 2015; Russo et al., 2014; Wang et al., 2023).

4.3. Enhance vitamin content

Dietary intake is essential for vitamins, as the body cannot produce sufficient amounts. Food processing depletes vitamins, necessitating alternative strategies beyond WHO recommendations due to concerns about synthetic folic acid (Gorelova et al., 2017; Rossi et al., 2016). Fermentation is emerging as a sustainable, eco-friendly alternative to chemical synthesis for folate (vitamin B9) production, utilizing microorganisms to naturally enhance vitamin content (Revuelta et al., 2018). Vitamins A, B (B7, B11, B12), C, and E play crucial roles in healthy glucose metabolism and insulin resistance. Vitamin A protects beta-cells and improves glucose metabolism, while B vitamins, produced in fermented dairy by various bacteria, lower homocysteine levels, reducing oxidative stress and improving insulin resistance. Vitamins C and E, as antioxidants, reduce free radicals and improve insulin function, with vitamin C also enhancing glucose utilization (Fernández et al., 2015; Lezhen et al., 2023; Via, 2012; Yahaya et al., 2021)

Folate-producing lactic acid bacteria (LAB) offer a promising biofortification method for dairy and fermented foods, enhancing folate levels crucial for DNA synthesis and red blood cell formation, especially in populations reliant on these foods. This sustainable approach, utilizing naturally derived microorganisms, is particularly beneficial in regions with limited access to synthetic vitamins. Specific LAB and Bifidobacteria can significantly increase folate levels in fermented milk, potentially reaching over 200 μg/L in yogurt, contributing to the recommended dietary folate intake (Revuelta et al., 2018; Wouters et al., 2002). Fermented dairy products, particularly those using *Lactococcus* spp., are rich in vitamin K (menaquinones), which benefits bone and cardiovascular health. Selecting menaquinone-producing bacteria, including various LAB species, enhances vitamin K content. Microbial diversity in fermentation influences the specific vitamin K forms present. Additionally, fermentation significantly boosts vitamin B12 levels in dairy, crucial for nervous system and blood cell health (Fu et al., 2017; Manoury et al., 2013; Requirements et al., 2013; Zironi et al., 2014).

Fermentation naturally boosts vitamin content in cereals, particularly vitamin B12 in plant-based foods like tempeh, which is popular among vegans. Lupin serves as an alternative fermentation substrate, and co-culturing *Propionibacterium freudenreichii* and *Rhizopus oryzae* significantly increases B12 in lupin tempeh. Studies confirm that cereal products can be naturally fortified with active vitamin B12 through fermentation using *P. freudenreichii* strains (Kariluoto et al., 2018; Rooijackers et al., 2018). While lactic acid bacteria (LAB) possess folate synthesis potential, some fermented cereals like bensaalga exhibit low folate content and no fermentation impact (Microbiological, 2013). However, studies show that other microorganisms, such as *Saccharomyces cerevisiae, Candida milleri, Pseudomonas* sp., and *Janthinobacterium* sp., can significantly enhance folate levels in oat and barley matrices. Despite observed increases in folate during fermentation, research on LAB-fermented cereal vitamin content is lacking. Given humans' reliance on dietary and gut microbiota vitamin sources, particularly B-group vitamins from plant-based fermented foods, further investigation is warranted (Kariluoto et al., 2014) .

4.4. Supplying healthy gut microbes

Fermented foods like sauerkraut, kimchi, kefir, dry sausage, yogurt, cheese, kombucha, and misotypically contain numerous live microbes, a significant portion of which survive digestions, despite some being processed without live cultures. Fermented foods can boost dietary microbe intake up to 10,000-fold due to the live, proliferating bacteria and yeast (probiotics) they contain. These beneficial microbes support a healthy gut microbiome, improving digestion, immunity, and inhibiting harmful bacteria (Jenna et al., 2014). Daily consumption of live fermented foods introduces diverse, temporary microbes to the gut, in contrast to the heavily processed, sanitized diets common in Western societies (Plé et al., 2015). The hygiene hypothesis suggests these microbial exposures are essential for the normal development of the immune system and neural function (Stiemsma et al., 2015).

Fermented foods can indirectly counteract the hygienic Western diet and lifestyle by delivering high numbers of microorganisms to the gastrointestinal tract. These foods promote the long-term survival of organisms during distribution and storage, making them a practical vehicle for providing established probiotic strains to people in low-income countries (Anita et al., 2014; Kort et al., 2015). The delivery matrix of *Lactobacillus casei* BL23 in milk has been found to enhance health-modulating potential, as evidenced by reduced colitis levels in mice fed the milk-fed strain, and the modified cell-associated proteome of *L. casei* expressing certain proteins (Lee et al., 2015; Maria et al., 2024).

4.5. Increase in saponin and isoflavone production

Soybeans contain isoflavones, phytochemicals with health benefits, existing as β-glucosides, aglycones, malonylglucosides, and acetylglucosides, each impacting bioactivity. Isoflavone bioavailability varies greatly, with aglycones being more bioavailable than β-glucosides, though gut bacteria can convert the latter. Fermentation enhances bioavailability by increasing aglycone content, while malonylglucosides transform into other forms, affecting overall absorption. Understanding these variations is essential for developing functional foods that maximize isoflavone benefits, particularly by increasing aglycone levels (Cristina et al., 2012).

Asian fermented soybean products, including natto, miso, sufu, doenjang, chungkokjang, and thuanao, are rich in glycones and isoflavones, particularly Factor-II, which are enhanced by fermentation. Doenjang's isoflavones may prevent vascular diseases by increasing LDL-C receptor activation. Additionally, soybean saponins offer health benefits such as suppressing colon cancer, inhibiting lipid peroxidation, and preventing hypercholesterolemia. *Bacillus subtilis* fermentation enhances natto's saponin content, boosting its cholesterol-lowering, immune-supporting, and cancer-protective properties. Similarly, kinema, rich in Group B saponins, offers health benefits such as colon cancer suppression, lipid peroxidation inhibition, and hypercholesterolemia prevention, making both natto and kinema valuable for their health-promoting qualities (Chettri & Tamang, 2015; Meerak et al., 2007; Menaquinone-, 2005; Nishito et al., 2010; Stanley & Lazazzera, 2005).

4.6. Alleviate lactose intolerance

Lactose intolerance is a digestive disorder characterized by the inability to digest lactose, a sugar found in milk and dairy. This results from insufficient lactase enzyme in the small intestine, which normally breaks lactose down into glucose and galactose. Symptoms include gas, bloating, diarrhea, and abdominal pain. There are three types: primary (adult-onset), secondary (due to infection, disease, or medication), and congenital (varying by ethnicity). Undigested lactose causes osmotic imbalances, diarrhea, and through anaerobic fermentation, increased intestinal pressure (Swagerty et al., 2007).

Lactose intolerance is a condition where symptoms are triggered by the amount of lactose consumed and the degree of lactase deficiency. The severity of symptoms depends on the lactose content of the food or beverage and the individual's residual lactase activity. High-lactose foods trigger more symptoms, while lactose-free products or those low in lactose, like hard cheeses or yogurt, may be better tolerated. Understanding the relationship between lactose intake and lactase deficiency is crucial for managing dietary choices. Individuals diagnosed with lactose intolerance should assess their tolerance levels and adjust their lactose consumption accordingly (Management, 2015; Swagerty et al., 2007). Fermented dairy foods like yogurt are often well-tolerated by lactose-intolerant individuals, as lactic acid bacteria ferment lactose into lactic acid, lowering lactose content and improving digestibility (Savaiano & Hutkins, 2021).

4.7. Antimicrobial activity

Antimicrobial bioactive peptides, ranging from 1–100 amino acids, are used to inhibit bacteria, molds, yeasts, parasites, and some viruses by interacting with negatively charged microbial cell components. Their properties are influenced by size, charge, solubility, amphipathicity, hydrophobicity, and amino acid type/number. Smaller, positively charged, soluble, amphipathic, and hydrophobic peptides penetrate and disrupt microbial membranes more easily. Probiotic microorganisms also exhibit antimicrobial activity through competitive growth, inhibiting pathogenic bacteria multiplication. Probiotics create a favorable environment during fermentation, releasing bacteriocins that counteract pathogenic growth. Some strains may relieve constipation and facilitate the synthesis of essential micronutrients, improving carbohydrate metabolism (Caydam & Bor, 2014; Lei et al., 2019).

Fermented foods are enriched with anti-microbial end products such as various organic acids, ethanol and peptides or bacteriocins and several studies report the antiviral potential of fermented foods *in-vitro* and *in-vivo*. The probiotic bacteria and bioactive compounds in fermented foods possess antiviral activities against gut and respiratory and viruses. These active foods stimulate immune system function by increasing the synthesis of pro-inflammatory cytokines and T lymphocytes (CD3+, CD16+, CD56+) (Muhialdin et al., 2020). *Lactobacillus plantarum* LBP-K10 isolated from kimchi synthesized cyclic di-peptides that inhibited the growth of the influenza A (H3N2) virus (Kwak et al., 2013), while another study reported declined survival of feline calici-virus and murine noro-virus proliferation during dongchimi fermentation along with an increase in lactic acid bacteria (LAB) (Hwa et al., 2012). Likewise, soy extracts fermented with *Aspergillus fumigatus* F-993 or *A. awamori* FB-133 showed therapeutic potential by decreasing hepatitis A virus titers *in-vitro* (García-burgos et al., 2020).

According to the findings, the cell-free supernatant of yogurt has antiviral activity against RNA viruses such as enterovirus 71 and influenza, porcine epidemic diarrhea virus, and Coxsackie A and B viruses. Polyphenols, bioactive peptides, exopolysaccharides, linoleic acid, and vitamins are among the bioactive compounds found in fermented foods. Spanish sausage releases angiotensin-converting enzyme inhibitor (ACE-I) when *L. pentosus* and *S. carnosus* are used as inoculum for fermentation. The fermentation of *Ruditapes philippinarum* clams with *Bacillus natto* stimulates hyper-production of ACE-I peptide synthesis and exerts anti-cancer properties (Olaimat et al., 2020).

4.8. Anti-oxidative activity

Bioactive peptides (2–20 amino acids) are inactive within parent proteins but become active upon release via hydrolysis. Microbial fermentation is a novel production method, particularly in fermented dairy, legumes, cereals, meat, and seafood. These peptides have gained attention for their biofunctional properties and potential use in functional foods and nutraceuticals (Rizwan et al., 2023). Peptides with anti-oxidative activity are capable of minimizing oxidative stress caused by an overwhelming accumulation of reactive oxygen species in cells and tissues because of various environmental stress factors such as pollutants, UV rays, excessive calorie intake, heavy metals, and high-fat diets (Jomova et al., 2023). A significant increase in the level of reactive oxygen species can cause cell and tissue damage, which in turn contributes to aging and the development of neurological disorders. Anti-oxidative peptides prevent reactive oxygen species from causing damage by acting as direct radical scavengers and metal chelators, and by removing radical compound precursors (Pessione & Cirrincione, 2016).

4.9. Anticancer activity

Bioactive peptides, especially smaller ones, show promise in cancer treatment due to their antioxidant, anti-proliferative, and anti-mutagenic properties. They target multiple stages of cancer development, preventing it and combating tumor growth and metastasis by inducing apoptosis and inhibiting cell proliferation. These peptides, including anticancer peptides (ACPs), are being explored as new, selective cancer therapies. However, achieving tumor selectivity without harming normal cells remains challenging, as is predicting antitumor activity from ACPs structure. Despite diverse mechanisms of action, improving tumor cell killing is an ongoing research area (Gaspar et al., 2013; Ghadiri et al., 2024).

Bioactive peptides improve cancer immunotherapy by increasing tumor-associated antigen (TAA) expression on cancer cell surfaces and stimulating the release of "danger signals" from cancer cells. This dual mechanism contributes to the therapeutic potential of bioactive peptides against cancer. However, in vivo stability and efficacy are the main challenges. Recent research focuses on improving these factors through chemical modifications, nanoparticles, targeted delivery, and combination therapies. Combining peptides with chemotherapy, immunotherapy, or radiation therapy aims to create synergistic effects for more effective and less toxic cancer treatments. The goal is to develop peptide-based therapies that can be used as standalone treatments or part of a broader, multimodal approach to cancer management (Ghadiri et al., 2024; Sood et al., 2024)

4.10. Anti-obesity 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 (Moschonis & Trakman, 2023). Traditionally fermented foods can be an alternative to therapeutic properties attributed to bioactive compounds synthetized during fermentation processes and which may have various health benefits. Dajiang (Northeast China) (Zhang et al., 2018) and doenjang (Korea) (Misselwitz et al., 2019) are traditionally fermented condiments which showed anti-obesity activities attributed to bioactive components (dipeptides, linoleic acid, oleic acid, isofavones, soyasaponins, phytoestrogens, GABA, AA, probiotics LAB, and so on), which exert the biological effects (Shukla et al., 2016).

Bioactive peptides can help manage obesity by reducing body weight and lipid levels, thus improving hyperglycemic conditions and related diseases (Lee et al., 2012; Song et al., 2017; Yang et al., 2019). Some bioactive peptides, like lupin peptides, can regulate metabolic genes, such as altering SREBP2 and HNF1α transcription factors involved in cholesterol metabolism (Allison & Fontaine, 2003). Lupin and lupin proteins may improve LDL uptake in hepatocytes and inhibit cholesterol solubility by binding bile acids/salts. Doenjang's GABA may prevent obesity by influencing appetite (reducing food intake), lipid metabolism (reducing fat accumulation), gut microbiota (affecting metabolism/energy balance), and hormonal regulation (affecting appetite/metabolism/stress). However, further research is needed to confirm these mechanisms (Ibrahim et al., 2022). In addition, the anti-obesity effects of free amino acids have been reported by many researchers. Miso, a Japanese fermented food, may suppress high-fat diet-induced obesity due to bioactive compounds (isoflavones, lecithin, free fatty acids, bacteriocins, amino acids, and probiotics). Genistein, an effective anti-obesity agent, may inhibit adipogenesis by activating the AMPK signaling pathway (Hwang et al., 2005).

An *in vitro* study showed that thua nao (a Myanmar fermented food) has anti-obesity activity, potentially due to its amino acid and free fatty acid content, which can reduce blood cholesterol (Dajanta et al., 2011). Kimchi, a Korean fermented food, contains bioactive components (bacteriocins, EPS, GABA, amino acids, polyphenols, fatty acids, and probiotics) that may contribute to anti-obesity effects. EPS-rich fermented foods are known to lower blood cholesterol (Dajanta et al., 2011). The most important short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate, have demonstrated anti-obesity properties in both animal models and human subjects. Acetate influences host energy/substrate metabolism by stimulating gut hormone (GLP-1, PYY) secretion, affecting appetite, reducing lipolysis and inflammation, and increasing energy expenditure/fat oxidation (Sensitivity, 2019). Butyrate can improve insulin sensitivity by stimulating GLP-1 secretion (Round & Mazmanian, 2014). Propionate and butyrate (SCFAs from gut fiber fermentation) reduce cholesterol and triglycerides, benefiting obese patients at risk for cardiovascular disease. These SCFAs also influence appetite and energy metabolism, supporting weight management. Fiber-rich diets promote their production and a healthy gut, contributing to long-term health (Kandylis et al., 2016).

4.11. Anti-diabetic activity

Type 2 diabetes (T2D) is characterized by high blood glucose due to insulin deficiency, peripheral insulin resistance, or both (Galicia-garcia et al., 2020). Bioactive compounds from fermented foods, such as polyphenols, peptides, fatty acids, and probiotics, can inhibit key enzymes and provide promising treatments for T2D by enhancing immunity, reducing free radicals, and regulating homeostasis (Laya et al., 2023). Traditionally fermented foods, considered GRAS, offer health benefits beyond nutrition. Studies have shown that these compounds lower blood glucose, improve intestinal glucose permeability, and inhibit the formation of advanced glycation end products (AGEs), thus helping to manage diabetes (Portincasa et al., 2022; Rezazadeh et al., 2021; Zhao et al., 2022).

Consumption of omega-3 polyunsaturated fatty acids from traditionally fermented foods may reduce high-fat diet-induced high blood glucose and glycogen synthesis while improving insulin signals (Kobayashi et al., 2018). Other compounds can lower blood glucose responses to carbohydrate intake, improve hyperglycemic conditions, and treat hyperglycemia-induced diseases like obesity. Polyphenols act as antioxidants, quenching reactive oxygen species, protecting cells from oxidation, and preventing disease by regulating anti-inflammatory markers. They also inhibit receptors for advanced glycation end-products, reducing pro-inflammatory markers like IL-6 and TNF-α, which induce T2D. Additionally, polyphenols protect cells from damage by AGEs and inhibit dipeptidyl peptidase-4, lowering hepatic blood glucose levels (Lezhen et al., 2023; Parwani & Mandal, 2020).

Studies have shown that miso, a Japanese fermented food, possesses anti-diabetic properties due to its bioactive compounds, including bacteriocins, peptides, GABA, isoflavones, fatty acids, and probiotics (Cai et al., 2021; Takahashi et al., 2021). These peptides and isoflavones regulate insulin secretion and inhibit visceral fat accumulation, α-glucosidase, α-amylase, and dipeptidyl peptidase-4, thereby lowering blood glucose levels and the glycemic index (Jiang et al., 2018; Ken et al., 2010). GABA improves insulin resistance by increasing GLUT4 expression and decreasing gluconeogenesis and glucagon receptor gene expression (Rezazadeh et al., 2021). Kanjang/soy sauce also exhibits anti-diabetic effects due to its bioactive compounds. Clinical trials have demonstrated that *Lactobacillus acidophilus* La-5 and Bifidobacterium lactis BB-12 reduce TNF-α and fructosamine levels, further contributing to diabetes management (Laya et al., 2023).

4.12. Angiotensin-converting enzyme inhibitory activity

The inhibition of the angiotensin-converting enzyme (ACE) is one of the most notable functions of bioactive peptides. ACE is an exopeptidase that catalyzes the conversion of angiotensin I into angiotensin II, a powerful vasoconstrictor, as well as the degradation of brady-kinin, a vasodilator, both of which are required for blood pressure regulation. Excessive ACE activity results in increased angiotensin II production and, as a result, an increase in blood pressure. Angiotensin II contributes to the development of several physiological and pathophysiological conditions, including hypertension. Inhibiting ACE reduces the conversion of angiotensin I to angiotensin II, resulting in lower overall blood pressure (Zieli et al., 2020). The first ever reported mitigation of hypertension by oral administration of food-derived ACE inhibitory peptides has been reported (Kang et al., 2010).

There are many studies concerning ACE-inhibitory peptides and ACE-inhibitory activities of meat, fish, milk, fermented dairy products and eggs (He et al., 2013). A study reported the ACE-inhibitory activity of protein hydrolysate and protein fractions obtained from boza (a Central Asian beverage) and determined the effect of *in vitro* digestion on this activity. While the protein content of the post-digestion hydrolysate was lower than that of the boza, the hydrolysate's ACE-inhibitory activity was significantly higher ($p < 0.05$). Fractionation of the hydrolysate by molecular weight showed that all three fractions inhibited ACE activity. The IC50 values revealed a 3.5-fold increase in boza's ACE-inhibitory activity after simulated stomach digestion. These results indicate that boza is a good source of ACE-inhibiting peptides (Kancabas & Karakayab, 2012).

4.13. Immunomodulatory activity

Bioactive peptides with immunomodulatory properties enhance the host's defense system by modulating immune responses. These peptides, derived from food proteins or synthesized biotechnologically, influence both innate and adaptive immunity, improving the body's response to infections, inflammation, and other challenges. They promote the proliferation and maturation of immune cells, including lymphocytes (T and B cells), and induce natural killer (NK) cell activity. Furthermore, they enhance macrophage phagocytosis and boost antibody production, providing long-lasting protection against infections and contributing to immune memory (Akbarian et al., 2022).

4.14. Anti-hypertension activity

Hypertension, a prevalent degenerative disease affecting about a quarter of the global population, is a major risk factor for cardiovascular diseases (CVDs) such as heart attack, stroke, heart failure, and kidney disease. However, it is considered a controllable condition, and effective management can significantly reduce the risk of associated health problems (Roth et al., 2020). One key therapeutic approach for managing hypertension is the use of Angiotensin-converting enzyme (ACE) inhibitors, which play a crucial role in regulating blood pressure. ACE inhibitors limit the production of angiotensin II, preventing vasoconstriction and promoting blood vessel dilation, thus lowering blood pressure. Bioactive peptides from fermented food sources have been identified as natural ACE inhibitors, exerting their effects by binding to ACE and blocking the conversion of angiotensin I to angiotensin II, thereby reducing vasoconstriction and lowering blood pressure (Guo et al., 2023).

Bioactive peptides are derived from dairy proteins, fish, meat, eggs, soy, and other plant-based proteins. Their consumption during digestion or fermentation provides a natural approach to reducing blood pressure. These peptides are generally safe and offer multiple health benefits beyond blood pressure regulation, including antioxidant, anti-inflammatory, and cholesterol-lowering effects. The potential of using bioactive peptides as ACE inhibitors opens exciting possibilities for developing functional foods or nutraceuticals designed to manage hypertension. Incorporating these natural ACE inhibitors into dietary regimens can support long-term blood pressure control and reduce reliance on synthetic drugs (Akbarian et al., 2022).

4.15. Source of probiotics

Probiotics are live microorganisms that, when consumed in adequate amounts, confer health benefits by promoting the growth of beneficial gut bacteria. Common examples found in fermented foods include lactic acid bacteria (LAB) and certain Bacillus species, recognized as safe by the WHO (Alkalbani et al., 2019; Kandylis et al., 2016). Extensive research, including numerous in vivo studies, has demonstrated that probiotics positively modulate the gut microbiota (Topolska & Florkiewicz, 2021; Vadopalas et al., 2020). The increasing demand for functional foods has highlighted probiotics, prebiotics, and synbiotics (combinations of the two) as key examples. The definition of probiotics has evolved from describing growth-stimulating microbial secretions to its current understanding (Samedi & Charles, 2019; Topolska & Florkiewicz, 2021).

Probiotics, found in fermented foods like yogurt, kefir, sauerkraut, and kimchi, and also available as supplements, have multiple effects on the host's gut mucosa. They increase mucus production, enhance barrier integrity, and modulate the immune system by regulating cytokine production (Fijan, 2014). Studies show that probiotic microorganisms, such as *Lactobacillus* and *Bifidobacterium*, can reach the gastrointestinal tract (Fijan, 2014; Sanlier et al., 2019; Vitellio et al., 2019). Probiotics compete with pathogenic bacteria and produce immune-regulatory and neurogenic fermentation products (Dimidi et al., 2019). Lactic acid bacteria (LAB), particularly *Lactobacillus*, are widely used as starter cultures in dairy production and are being explored as bio-preservatives and antibiotic alternatives (Lashani et al., 2020).

Increased consumer awareness of the health benefits and therapeutic effects of different probiotic strains on gut microbiota, including improvements in neurological diseases and metabolic disorders, has driven demand for these strains (Table 3) (Amoah et al., 2022). These benefits result from the direct effects of the gut microbes and their fermentation products, which significantly influence body function and health (Bernardeau et al., 2017). Probiotics offer protection against inflammatory bowel diseases and gastrointestinal infections. They can also replace antibiotics in treating enteric infections, reducing antibiotic-related diarrhea. Furthermore, they regulate intestinal bacteria, inhibit harmful bacteria, support the immune system, and can be used to treat allergic diseases and infections during pregnancy. *L. acidophilus, Lactobacillus casei*, and *Bifidobacterium bifidum* are examples of probiotic LAB found in fermented milks. While dairy products are an excellent source of these strains, their commercial application is currently limited (Bernardeau et al., 2017; Giraffa et al., 2010).

The use of traditionally fermented foods for health promotion has become widespread, supported by evidence of their positive effects (De Carvalho et al., 2018; Lau et al., 2015). Recent studies show that fermented foods and beverages impact health due to prebiotics and probiotics. Experimental studies in humans and animals have shown that traditionally fermented foods modulate both immune response and metabolic function. These foods also positively influence body composition, blood pressure, brain health, and mental well-being, reducing stress, anxiety, depression, behavioral dysfunctions, and potentially cancer risks (Table 3) (Consumption, 2023; Simon et al., 2015; Yilmaz et al., 2022). The mechanism involves decreasing anti-inflammatory cytokines. Gut microbiota play a role in adiposity, glucose and lipid metabolism, and immune and cardiovascular system maintenance (Table 2) (Helmyati et al., 2021).

Probiotic supplements have gained attention for reducing the need for antibiotics and preventing drug-resistant infections (Das et al., 2022). Probiotics impact infectious diseases by affecting the epithelium, synthesizing antimicrobial substances, and competitive exclusion. Analyzing probiotic metabolic pathways guides industrial production of functional fermented milk. Recent research focuses on using millet and millet-based beverages as ingredients for probiotic products, promoting the growth of probiotic bacteria and providing dietary fiber, vitamins, and minerals (Bagheri et al., 2020).

Nutrient-rich grains, millets, and legumes contain prebiotic fibers, making them ideal for probiotic products by protecting probiotics. They provide essential nutrients and reduce chronic disease risks. *Lactobacillus* strains from oral and dietary sources show probiotic potential, particularly in millet-based products, for lactose digestion and sugar fermentation. Further research is needed to explore species-specific benefits and their impact on gut microbiome diversity and disease prevention (Karnwal & Malik, 2020). Probiotics in dairy and fermented foods offer health benefits, including lactose intolerance relief, cholesterol reduction, and cardiovascular disease prevention. They boost immunity, enhance disease resistance, and promote overall health through competitive exclusion and immune modulation. Native or commonly consumed probiotics are preferred for compatibility and effectiveness (Asadi et al., 2022; Hatami et al., 2022; KBD, 2020).

4.16. Source of prebiotics

First described in 1955, prebiotics are non-digestible food ingredients enhancing host health through selective stimulation of beneficial bacterial growth in the colon (Gibson et al., 2004). Non-digestible carbohydrates, such as galacto-oligosaccharides, fructo-oligosaccharides, and inulin, offer health benefits including reduced constipation, improved weight and glucose management, enhanced immunity, and increased calcium absorption. Prebiotics may also have anti-carcinogenic effects and produce short-chain fatty acids (SCFAs) with diverse biological roles. Furthermore, polyunsaturated fatty acids (PUFAs) in prebiotics may influence immunity and metabolism (Angelo et al., 2020; Seed et al., 2020). Prebiotics, substrates supporting host microorganisms for health benefits, are found in traditional fermented foods like grains, vegetables, beer, and wine, containing β-glucans,

Table 3
Probiotics isolated from fermented foods and their medical applications.

Fermented Foods	Probiotics	Medical Applications (Bioactivity)	Ref
Fermented milk	*Bifidobacterium animalis subsp. lactis*	Brain intrinsic activity	(Tillisch et al., 2014)
Fermented soy product	*Enterococcus faecium CRL 183, Lactobacillus helveticus 416*	Improved total cholesterol, non-HDL-C and LDL concentrations	(Randomized et al., 2016)
Fermented milk	*Aspergillus oryzae*	Hyperlipidemia	(Tillisch et al., 2014)
Chungkookjang	*Bacillus licheniformis*	Reduce obesity	(Back et al., 2013)
Kefir (dairy product)	*Lactobacillus johnsonii*	Anti- hypertension	(Marco et al., 2017)
Kimchi (fermented vegetables)	*Weissella cibaria JW15*	Anti-inflammatory	(Lee & Choe, 2019)
Kimchi	*Lactiplantibacillus plantarum LB5*	Antioxidant, Anti-inflammatory, Antibacteria	(Jeong et al., 2021)
Kimchi	*Lactiplantibacillus, plantarum 200,655*	Neuroprotective	(Jeong et al., 2021)
Sauerkraut (fermented vegetables)	*Lacticaseibacillus paracasei*	Antioxidant	(Shankar et al., 2021)
Sauerkraut	*Lacticaseibacillus Case*	Antioxidant, Immunomodulatory	(Shankar et al., 2021)
Sauerkraut	*Lactiplantibacillus plantarum*	Antibacterial activity	(Shankar et al., 2021)
Kimchi	*Lactobacillus sakei*	Anti-obesity	(Lee & Choe, 2019)
Kimchi	*Lactiplantibacillus plantarum LRCC5310*	Antidiabetic, Anti-inflammatory	(Youn et al., 2021)
Sauerkraut	*Lacticaseibacillus casei NA-2*	Antibacterial, antimicrobial	(Youn et al., 2021)
Fermented milk	*Lactococcus lactis strain NRRL B-50,571*	Anti-hypertensive activity	(Melini et al., 2019)
Fermented milk	*Lactobacillus rhamnosus strain PTCC 1637*	Antioxidant activity	(Melini et al., 2019)
Kefir (fermented milk)	*Weissella confusa DSM 20,194*	Improvement of protein digestibility	(Melini et al., 2019)
Quinoa (Fermented grain)	*Lb. plantarum strain T6B10 and L. rossiae strain T0B10*	Antioxidant activity	(S iler-marinkovic & Dimitrijevic, 2010)
Fermented wheat sourdough	*Lb. brevis CECT 8183*	Anti-hypertensive activity	(Fraberger et al., 2018)
Austrian traditional sourdough	*S. cerevisiae and Torulaspora delbrueckii*	FODMAP Reduction	(Fraberger et al., 2018)
Fermented sausages	*Bifidobacterium longum*	Antioxidant activity	(Song et al., 2018)
Fermented vegetables	*Lactobacillus pentosus*	ACE inhibitory	(Bartkiene et al., 2023)
Sausages	*Lactobacillus sakei*	Antioxidant activity	(Takeda et al., 2017)
Fermented milk	*L. helveticus CP790*	ACE inhibitory	(Tillisch et al., 2014)
Yogurt	*Lactobacillus delbrueckii subsp.*	Antihypertensive and opioid activities	(Lashani et al., 2020)
Dahi	*Lactobacillus delbrueckii ssp.*	ACE inhibitory	(Melini et al., 2019)
Cheddar cheese	*Lactobacillus casei*	ACE inhibitory	(Melini et al., 2019)
Cheonggukjang (fermented soya bean)	*Bacillus licheniformis-67*	Antidiabetic	(Melini et al., 2019)

Table 3 (*continued*)

Fermented Foods	Probiotics	Medical Applications (Bioactivity)	Ref
Fermented soymilk	*Lactobacillus paracasei ssp.*	Antimicrobial activity, antiosteoporotic	(Melini et al., 2019)
Boza (fermented cereal based beverage)	*Lactobacillus lacasei*	Cancer preventive, antioxidant, ACE inhibitory	(Melini et al., 2019)
Huang Jiu (Chinese rice wine)	*Aspergillus, Rhizopus, Mucor, Monascus*	ACE inhibitory, antioxidant, and hypo-cholesterolemic activity	(Rizzello et al., 2012)
Fermented Bitter bean	*Lactobacillus fermentum ATCC9338*	Antioxidative and antibacterial	(Muhialdin et al., 2020)
Fermented pea	*Lactobacillus plantarum 299v*	ACE inhibitory	(Muhialdin et al., 2020)
fermented navy bean milk	*L. plantarum 70,810,* L. *plantarum B1–6*	ACE inhibitory	(Melini et al., 2019)

oligosaccharides, and polyphenolic compounds. Fermented foods may include prebiotics synthesized by fermentation-associated microorganisms, such as exopolysaccharides from dairy and cereal fermentations (Cueva et al., 2015). Fermented foods, containing live microorganisms and prebiotic substrates, offer health benefits, with prebiotics like Galacto-oligosaccharides (GOS) enhancing beneficial bacterial and probiotic growth (Marco et al., 2021).

Beneficial gut microbiota (probiotics) utilizes prebiotics and oligosaccharide-based fibers as substrates, enhancing their growth and colonization. Prebiotics support beneficial gut bacteria, exclude infective microorganisms, provide immunomodulatory properties, and enhance gut barrier integrity (Oniszczuk et al., 2021). Research highlights the influence of fermented foods on health, addressing infections, allergies, diabetes, heart disease, neurological disorders, immunity, and overall well-being. These foods also impact personalized nutrition and psychological benefits via gut microbiota alterations, affecting mood, behavior, autism, and the gut-brain axis. Probiotics and prebiotics are extensively used in medical and dental fields for benefits like cancer risk reduction, gut and vaginal health, caries prevention, and periodontal care. Research also investigates their effects on immune health, skin, cholesterol, lactose intolerance, and sensorimotor behavior (Voidarou et al., 2021). Animal model studies indicate probiotics and prebiotics regulate host metabolism, encompassing inflammation, adiposity, satiety, energy expenditure, and glucose metabolism. However, robust, double-blind, placebo-controlled clinical trials confirming these effects in humans are scarce (Davis, 2016).

5. Industrial perspective of bioactive compounds fermentation

Industrial fermentation is a highly sophisticated bioprocess, focusing on mass production of bioactive molecules rather than food preservation (Sadh et al., 2018). It entails careful strain selection, elaborate process engineering, and strict regulatory compliance to create constant, safe, and low-cost ingredients. Unlike conventional fermentation, which focuses primarily on food shelf life extension, industrial fermentation focuses on the maximum recovery and utilization of health-related compounds through mass production (Niyigaba et al., 2025).

Scaling up to industrial manufacture from lab work brings with it several engineering challenges, not the least being the need for gigantic bioreactors of thousands to half a million liters (Crater & Lievense, 2018). These must provide the best fermentation conditions of efficient mixing, gas transfer—specifically oxygen in aerobic processes—and precise temperature control. Shear stress on microorganisms must also be regulated by engineers and stable operating conditions to be maintained for extended periods of time using batch or continuous fermentation processes (Silva et al., 2024). Industrial microbial strains must also possess both environmental stress tolerance and genetic stability with high productivity (Kuang et al., 2024).

Economic efficiency is at the heart of successful industrial fermentation, where companies strive to maximize yield while minimizing expense. This is possible through the implementation of optimized fermentation parameters including pH, temperature, and nutrient levels through the use of complex analytical and monitoring tools (Sawant et al., 2025). The culture of sustainability lies at the heart of this, with industries increasingly focusing on agricultural residues and food waste as cheap feedstocks to support circular economy processes. Besides, efficient energy-saving measures like optimized aeration, agitation, and sterilization keep operating costs low and improve profitability. Better automation, artificial intelligence, and waste valorization further enhance efficiency and sustainability of industrial fermentation (Pal et al., 2024).

6. Safety aspects and challenges of fermented foods

Fermented foods are a significant source of protein, vitamins, minerals, and other essential nutrients. However, the limited application of modern biotechnology hinders clinical exploration of their gut health benefits. Key aspects include safety, hygiene standards, and product preservation (Leeuwendaal et al., 2022). During natural fermentation, food-poisoning flora and coliforms may grow alongside beneficial lactic acid bacteria, requiring elimination for safety. Washing, soaking, and cooking treatments reduce microbial contaminants. Acid-producing microorganisms, such as lactic acid bacteria, produce organic acids (e.g., lactic, acetic, and fumaric acids) that act as preservatives. An inhibitory pH for bacterial growth ranges from 3.6 to 4.1 (Mafe et al., 2024). Molds used in some traditional fermentations produce antimicrobial glycopeptides that prevent food spoilage. In solid-state fermentations, low water activity also serves as an important preservative factor (Tanaka et al., 1985).

Despite these factors, some reports indicate poor sanitary quality in certain oriental fermented foods. Safe products are typically obtained by observing the following recommendations: (a) soaking substrates in acid at a low pH; (b) adequate cooking time; (c) maintaining hygienic conditions during production, handling, and storage; and (d) refrigerating products at 5 °C between production and consumption. Fermentation creates hostile environmental conditions that inhibit pathogenic microorganisms due to the presence of organic acids, inhibitory growth substances (e.g., diacetyl, acetaldehyde, mycosin, and bacteriocins), salt, nitrite, antimicrobials, lowered water activity, and carbohydrate depletion (Lemi, 2020). However, in unhygienic environments, these inhibitory conditions may not develop rapidly enough to prevent the growth of toxin-producing and spore-forming microbes such as *E. coli, Listeria monocytogenes, Yersinia enterocolitica, Staphylococcus aureus, Bacillus cereus*, and *Clostridium botulinum*. Therefore, producing nutritious and palatable foods free of microbiological health risks is crucial for enhancing the social role of traditional fermented foods in less developed countries (Bintsis, 2017).

While most food-fermenting microbes are safe, some fermented foods, particularly cheeses and low-acid products, can be contaminated with pathogens like *Listeria monocytogenes, Salmonella*, and *Clostridium botulinum* (Fernández et al., 2015). Certain microbes in long-ripened products can carry antibiotic-resistance genes. Fermented foods may also contain harmful metabolites. Alcohol and salt content should be considered. Biogenic amines (e.g., histamine, tyramine), produced by some microbes, can cause adverse effects; mitigation strategies include hygiene and decarboxylase-negative starter cultures (Barbieri et al., 2019).

Mycotoxin contamination is a significant risk in fermented foods produced with fungi. Domestication and careful strain selection have largely eliminated mycotoxin-producing lineages of *Aspergillus* and *Penicillium* from koji, cheese, and other fermented foods. Microbial metabolites, such as citrulline and reuterin, can be precursors to toxic compounds like ethyl carbamate and acrolein, which are found in alcoholic beverages and other fermented foods. However, the health risks associated with these compounds in fermented foods remain unclear (Marco et al., 2021).

7. Conclusion

Fermentation is a transformational pathway to improved nutrition and food security, particularly in undeveloped regions, by intricately coupling traditional knowledge and modern biotechnology to use local inputs and variable indigenous microbes for nutritious, safe, and acceptable food production and ultimately provoking personalized nutrition and sustainable development. This requires initiatives like establishing regional microbial strain banks for the isolation of beneficial microorganisms, developing region-specific starter cultures for enhanced safety and flavor, and implementing capacity-building programs that equip the local communities with essential information on controlled fermentation, hygiene, and quality control. Moreover, research is necessary to create fermentation processes capable of addressing specific nutritional deficiencies, to increase micronutrient bioavailability and maximize bioactive compound production like GABA for stress reduction and SCFAs for gut health, all specifically to address local needs. Besides food security, fermentation is crucial in global food production, increasing protein digestibility, anti-nutrient destruction, and creation of beneficial compounds like peptides, polyphenols, and probiotics. Advances in fermentation technology also enhance safety and efficiency of functional food production, bringing about uniformity and minimizing health risks. Even though traditional methods have their hygiene and microbial control issues, the use of standardized fermentation agents bridges this to some extent by achieving an important balance between tradition and science and positions fermentation to lead functional food technology innovation, improve global health outcomes, and drive the more sustainable, resilient food system through research and development.

8. Future perspectives

Fermentation, one of humanity's oldest biotechnological processes, is poised for a transformative future driven by growing global interest in health and sustainability. Integrating modern biotechnology, omics technologies, and precision fermentation can optimize the production of bioactive compounds such as probiotics, peptides, and exopolysaccharides. Genetic engineering and advanced synthetic biology tools will enhance strain development for diverse applications, including pharmaceuticals, cosmetics, and nutraceuticals, extending beyond traditional food uses. Fermentation's role in sustainable food systems is expanding, addressing food security and climate change through the upcycling of agricultural byproducts and waste reduction. Scaling up fermented product production in underdeveloped countries can improve nutritional security.

Follow-up studies have to give priority to safety, consistency, and quality, avoiding microbial contamination and standardization problems. The use of biotechnological advancements paves the way for new functional food possibilities, market penetration, and significant world health dividends. To understand the precise impact of fermented foods on human health, in-depth studies on their molecular mechanisms are needed. Future research has to put emphasis on how bioactive molecules interact with gut microbiota, modulate immune systems, and influence metabolic pathways. The objective is to purify individual compounds with activities like improved digestion and anti-inflammatory activity. Of utmost importance is to test the stability and bioavailability of the compounds under varied processing and storage conditions to ensure reproducible health effects in end products. Concomitant with this is safety and standardization, especially in traditional fermentation.

Essentially, research must develop solid methods for detection and prevention of contaminants, including undesired microorganisms and toxic by-products. Having uniform fermentation protocols from microbial cultures and process conditions will be essential to provide consistent quality and safety. Furthermore, understanding how the fermentation environment (oxygen, pH, temperature) influences the formation and stability of desired compounds will optimize production with both effectiveness and safety.

The future of fermented foods is in personalized nutrition and biotechnological innovations. Studies in personalized nutrition need to investigate how individual variation in microbiome composition, genetics, diet, and lifestyle affect the bioactivity of fermented foods' nutrients. This will allow individual tailoring of fermentation products to specific health needs, leading to targeted dietary interventions that maximize gut health while preventing disease. Meanwhile, biotechnological innovations hold promising prospects. Research needs to focus on developing genetically modified microbial strains in order to maximize the production of bioactive compounds with safety. New technologies like electro-fermentation, precision fermentation, and solid-state fermentation (SSF) can revolutionize the industry by making it more efficient and environmentally friendly. Understanding the influence of fermentation conditions on compound biosynthesis is key to optimizing large-scale production and sustainability.

Finally, the long-term impact and sustainable development of fermented foods depend on systemic analyses and robust structures. Long-term clinical trials will be required to test the effectiveness of fermented food compounds for preventing and managing chronic diseases like obesity, diabetes, and neurodegenerative diseases. These investigations need to explore how fermentation-derived metabolites modulate inflammation and metabolism-associated physiological pathways, establishing the best consumption patterns. Further, understanding synergistic effects and interactions of compounds in fermented foods will create multi-strain probiotic foods with enhanced health effects. This kind of progress demands close scrutiny of regulatory regulations to come up with harmonized international standards for safety, labeling, and health claims. Public opinions research is also necessary to guide industry practice and build consumer trust, with increased debate among researchers, policy makers, and industry actors necessary for the ethical commercialization of such technologies.

Ethical statement - studies in humans and animals

This manuscript is a review, and therefore an ethical statement is not applicable.

Authors contributions

Solomon Fitsum: Conceptualization; writing—original draft; data curation. Gebreselema Gebreyohannes: Writing—review and editing; Gebreselema Gebreyohannes and Desta Berhe Sbhatu: writing—review and editing; supervision. All authors are contributed equally.

CRediT authorship contribution statement

Solomon Fitsum: Writing – review & editing, Writing – original draft, Visualization, Validation, Formal analysis, Data curation, Conceptualization. **Gebreselema Gebreyohannes:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Data curation, Conceptualization. **Desta Berhe Sbhatu:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors have confirmed that there are no conflicts of interest.

Data availability

Data will be made available on request.

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