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International Journal of Advanced Research in Food Science and Agricultural Technology

Journal homepage:
https://karyailham.com.my/index.php/fsat/index
ISSN: 3030-556X

Fermentation for Enhanced Biosynthesis and Bioavailability of Micronutrients, Prebiotics, Bioactive Peptides and Functional Fatty Acids in Food Products

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ARTICLE INFO

Article history:
Received 27 November 2024
Received in revised form 28 February 2025
Accepted 14 March 2025
Available online 28 March 2025

Keywords:
Fermentation; vitamins; minerals; bioactive compounds; prebiotics; conjugated fatty acids; bioavailability; lactic acid bacteria

ABSTRACT

Microorganisms in fermented foods and beverages are crucial in enhancing both nutritive and bioactive components. Fermentation can occur spontaneously or be initiated by adding specific starter cultures. This review highlights the contribution of fermentation to the enhancement of micronutrients (vitamins and minerals) and three major functional macromolecules: prebiotics (carbohydrates), bioactive peptides (proteins), and functional fatty acids. During fermentation, microorganisms produce important vitamins, particularly B vitamins, and unique compounds like Vitamin K2. Non-digestible carbohydrates such as fructo-oligosaccharides and galacto-oligosaccharides, which have prebiotic effects, are also produced, promoting gut health. Enzymatic hydrolysis of proteins during fermentation generates bioactive peptides with benefits ranging from antioxidant properties to blood pressure regulation. Additionally, fermentation promotes the production of fatty acids, including short-chain fatty acids (SCFAs) and conjugated linoleic acid (CLA), linked to anti-inflammatory and metabolic health benefits. Overall, microbial fermentation offers a natural, efficient way to enrich foods with bioactive and nutrient-dense compounds, presenting a promising approach to improving global nutrition, particularly in addressing micronutrient deficiencies and supporting gut health. Harnessing these processes could help combat malnutrition and promote overall well-being.

1. Introduction

Adequate food consumption does not necessarily guarantee sufficient and balanced nutrient intake. A healthy and balanced diet requires consuming nutrient-rich food, which can be achieved through fortification. Fortification aims to supplement or achieve target levels of nutrients in the population or specific population groups, particularly those affected by hunger and malnutrition. Malnutrition encompasses inadequate, excessive, or imbalanced intake of energy and nutrients. The double burden of malnutrition is the coexistence of undernutrition and overnutrition in the same

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https://doi.org/10.37934/fsat.4.1.927a

population [1]. While fortification can be achieved through processing and chemical synthesis, natural methods like fermentation offer a more efficient, socially rooted approach that is generally recognized as safe. Fermentation not only reduces unwanted by-products but also enhances bioavailability and often exceeds intended nutritional benefits.

Globally, there are 1.9 billion overweight adults and 462 million underweight adults. Furthermore, 144 million children under the age of five experience stunted growth, while 38.3 million are overweight [1]. The importance of food fortification is further emphasized during the COVID-19 outbreak. Undernourished individuals with metabolic health issues such as obesity and diabetes face a higher risk associated with COVID-19 [2]. The pandemic also caused significant disruptions across global food supply chains, impacting each stage from production to retail and influencing nutritional access worldwide.

Fermentation in food and beverage production, involves desired microbial growth and enzymatic conversion of food components, going beyond the strict biochemical definition tied to anaerobic processes. This broader definition includes aerobic fermentations (e.g., soy sauce, vinegar) and excludes foods processed solely by non-microbial means. Fermented foods may not always contain live microorganisms at the point of consumption, as some undergo treatments like baking or filtration (e.g., bread, beer). Products containing fermented ingredients, but which are not fermented themselves (e.g., salad dressing with vinegar), or those made through chemical means (e.g., synthetic vinegar), are not considered fermented foods under this definition [3].

Based on the consensus by The International Scientific Association for Probiotics and Prebiotics (ISAPP), fermented foods may support health through three major mechanisms; one being “nutrient modification”, while the other two are the alteration of gut microbiota and modulation of immune system (Figure 1) [3]. Although ancient, fermentation has always been regarded as a promising technique for enhancing the biosynthesis and availability of both micronutrients and non-nutrients in food [4]. Micronutrients are essential substances required in small quantities but vital for various physiological functions in the human body. They include vitamins (organic compounds) and minerals (inorganic compounds), that differ in terms of chemical structure and specific roles. Micronutrients are involved in energy metabolism, immune function, DNA synthesis, and many other processes.

Non-nutrients are bioactive compounds in food that, while not essential for survival, offer benefits beyond basic nutrition. These include bioactive peptides, prebiotics, and conjugated fatty acids, each providing unique health advantages. Interestingly, these compounds can be derived from common foods and "created" by microorganisms as part of their natural metabolism. Bioactive peptides, short amino acid chains, can exert beneficial physiological effects, such as antioxidant, antihypertensive, and antimicrobial properties. Prebiotics, non-digestible carbohydrates, selectively stimulate beneficial gut bacteria, supporting gut health. Conjugated fats, like conjugated linoleic acid (CLA), are modified fatty acids associated with health benefits, including anti-inflammatory and anti-cancer effects [5].

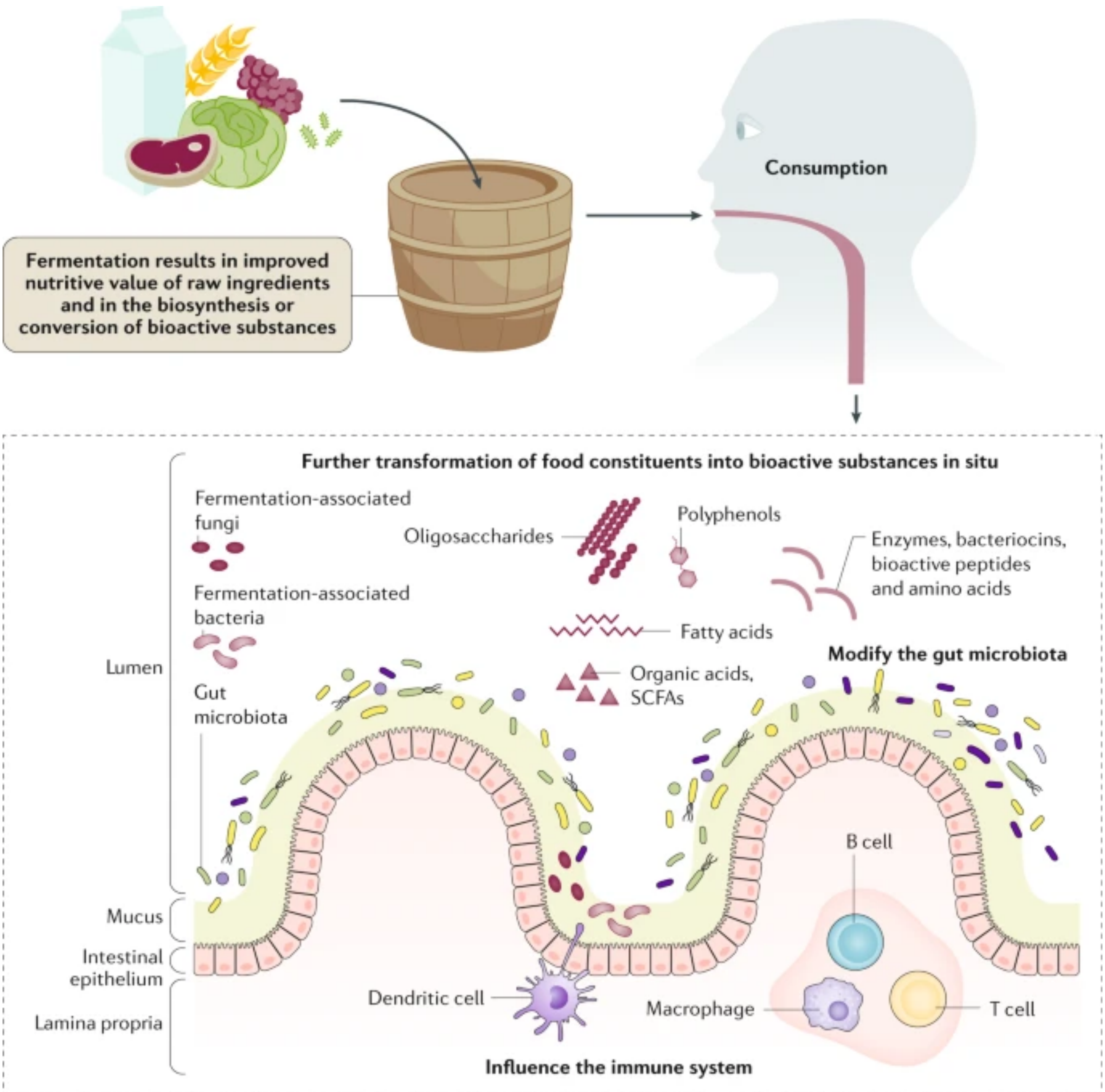

Fig. 1. Fermentation enhances food's nutritive value by transforming components and producing bioactive compounds like peptides and vitamins. Consumed microbes and compounds from fermentation interact with the gut microbiota, further producing beneficial substances such as organic acids and amino acids. These interactions support gut and immune health. The figure is adapted from [3]

Fermentation can occur spontaneously or with the use of starter cultures containing specific microbial species [6]. Microbes involved in fermentation can produce or activate certain vitamins, release minerals from complex compounds, generate bioactive peptides through enzymatic hydrolysis, and convert fatty acids into conjugated forms [7]. This transformation not only increases the content of these compounds but also improves their bioavailability, making fermented foods a valuable source of micronutrients and non-nutrients with potential health benefits [7].

Common microbes involved in fermentation include lactic acid bacteria (LAB), yeast (such as *Saccharomyces* species), and fungi (including *Aspergillus*, *Penicillium*, and *Fusarium*) [8–10]. For food safety assurance, the microbes used in fermentation must be categorized as Generally Recognized as Safe (GRAS) by the United States Food and Drug Authority (FDA). The selection of microorganisms determines their characteristics, such as probiotic properties, antioxidant activity, peptide production, or degradation of antinutritive compounds. The chosen strains should also exist in the intestinal flora for further breakdown [11].

This review aims to demonstrate that fermentation-based biofortification offers a promising approach to enhancing the nutritional value of food through the production of beneficial compounds. This review highlights microbial fermentation's potential to produce nutritional and non-nutritional compounds that have been linked to diverse health benefits. The choice of specific microorganisms and environmental factors that influence these processes can guide the optimization of fermentation conditions to maximize the production of desired compounds.

2. Impact of Fermentation on Micronutrients – Vitamins and Minerals

Micronutrients, as indicated by the term "micro," are essential nutrients required in small quantities that promote health benefits such as growth and immune system support, reducing the risk of infection [12]. They can be classified into four categories: water-soluble vitamins, fat-soluble vitamins, macro-minerals, and trace minerals.

Typically, minerals are not typically synthesized by microorganisms, but their bioavailability can be significantly enhanced through microbial actions. Microorganisms can break down antinutritional factors that bind to minerals, such as phytic acids, tannins, oxalates, enzyme inhibitors, lectins, and glucosinates [7] (Figure 2). Moreover, microbial activity can help produce organic acids, such as lactic acid and acetic acid. These organic acids play a crucial role in breaking down the cell walls of plant-based foods, thereby releasing and making minerals more readily available for absorption. Furthermore, microorganisms secrete digestive enzymes like proteases and lipases, which effectively break down food into smaller molecules, facilitating the enhanced absorption of minerals. These mechanisms have been demonstrated in multiple microorganisms, such as bacteria, fungi, and bacteria [13].

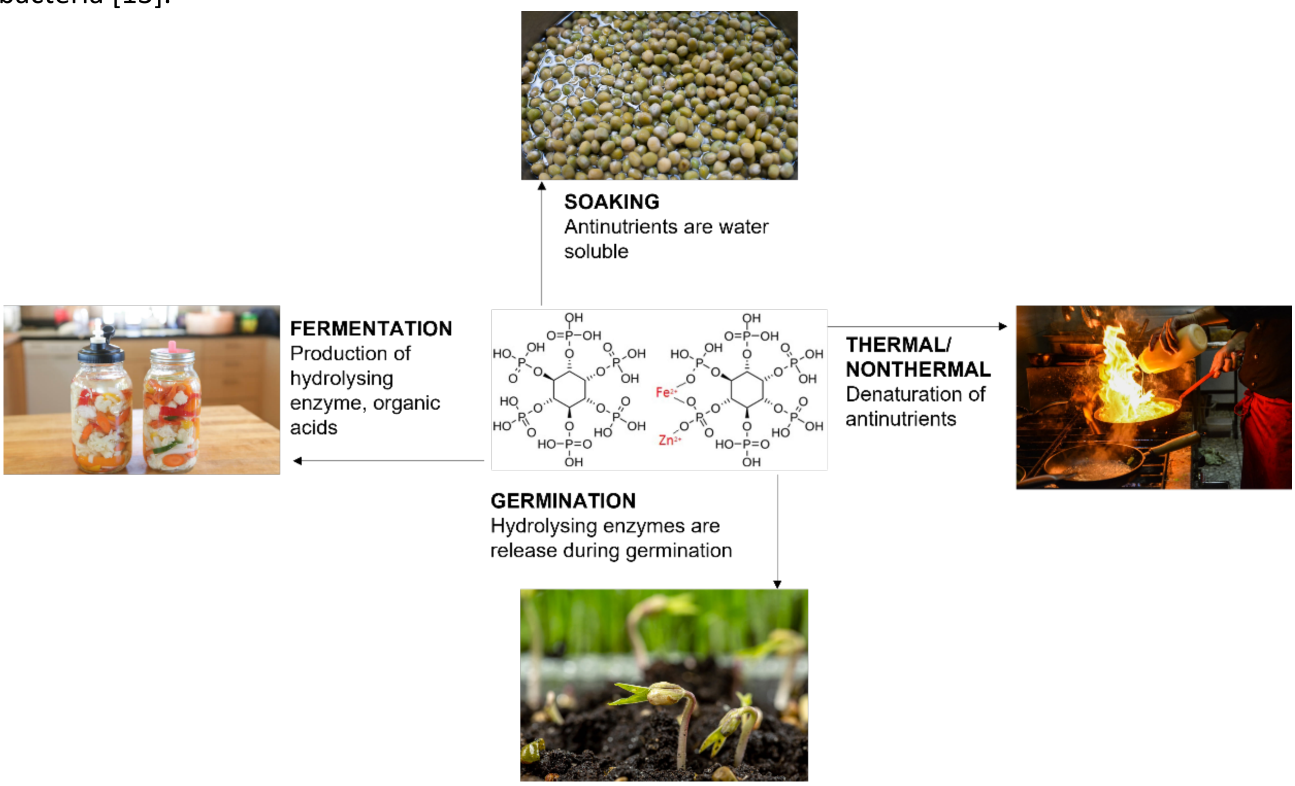

Fig. 2. The possible mechanisms of degradation of antinutrients in plant-based food [7]

Microorganisms possess the remarkable ability to synthesize certain nutrients *de novo*, including essential amino acids and vitamins such as the vitamin B complex (Figure 3). The production of microbial-based amino acids is well documented [14], including in fermented foods [15]. Similarly, the ability of microorganisms in fermented foods to enhance B-group vitamins and vitamin K was demonstrated by various researchers. From a microbial or fermented food perspective, riboflavin, folate, vitamin B12, and vitamin K are the most consistently elevated during fermentation. It should be noted however, that other B vitamins like thiamine, pyridoxine, niacin, and pantothenic acid show less consistency, as their levels can remain unchanged or even decrease during fermentation [16].

Riboflavin, or Vitamin B2, is an important co-enzyme, especially for the formation of flavin adenine dinucleotide ($FADH_2$) that participates as an electron carrier during the metabolic processes. The biosynthesis of riboflavin involves a series of enzymatic reactions, starting from the precursor molecule guanosine triphosphate (GTP). Microbes such as bacteria, yeasts, and fungi can produce B2, with certain bacterial species like *Bacillus subtilis* and *Ashbya gossypii* being efficient B2 producers. These microorganisms have specific genes encoding the enzymes responsible for the biosynthesis of B2 [17].

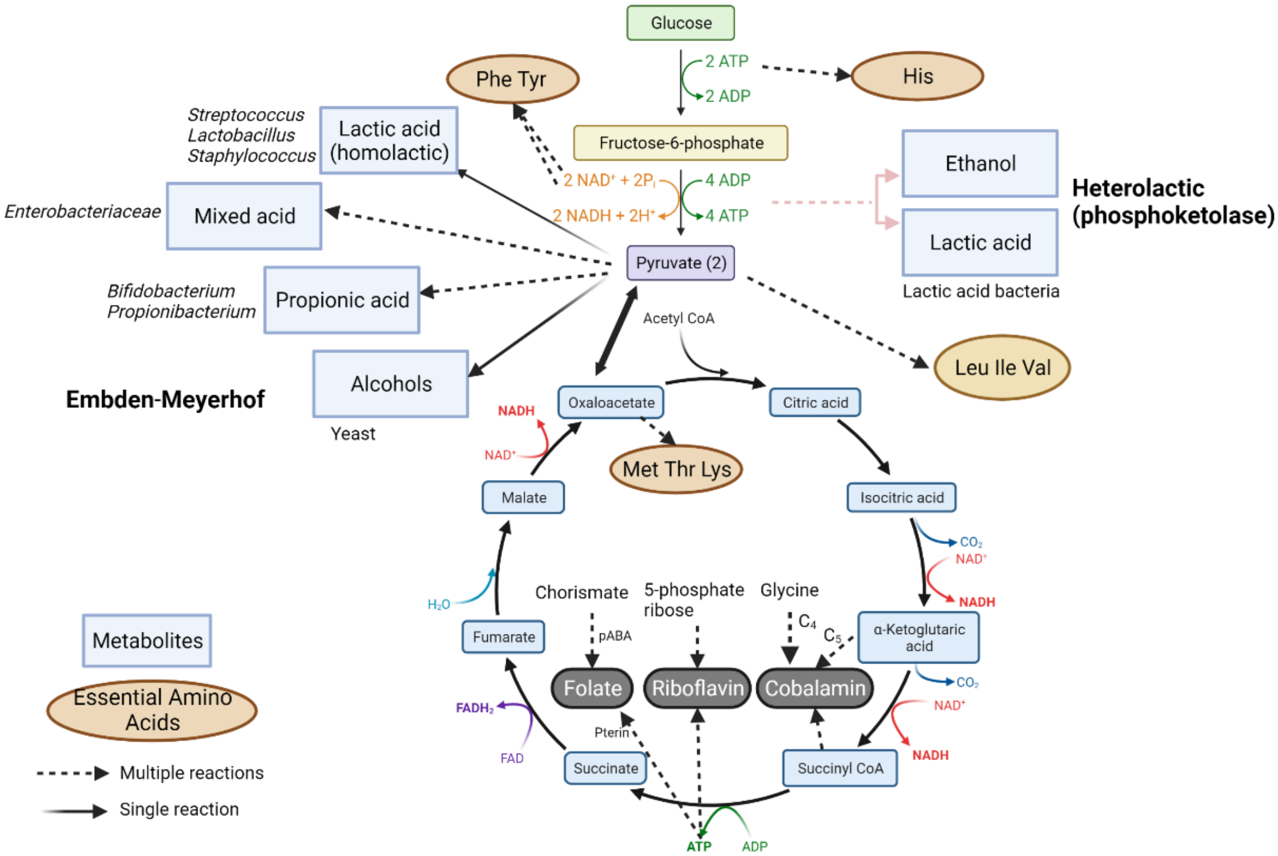

Fig. 3. The possible *de novo* biosynthesis of nutrients in microorganisms. The figure is based on our previous publication [8]

Folate (B9) is important for DNA synthesis, cell division, and red blood cell production. Like B2, B9 can be synthesised by microorganisms *de novo* through a biosynthetic pathway (Figure 3). This pathway involves a series of enzymatic reactions that convert p-aminobenzoic acid (PABA) and pteridine derivatives into tetrahydrofolate (THF), the active form of vitamin B9. LAB possess the necessary enzymes, including dihydropteroate synthase (DHPS), dihydrofolate reductase (DHFR), and folylpolyglutamate synthetase (FPGS), to catalyze these reactions.

The comprehensive review on the ability of microorganisms to produce cobalamin (B12) was performed by Fang *et al.,* [18]. Vitamin B12 is produced by bacteria (primarily LAB) during fermentation, with *Propionibacterium freudenreichii*, *L. reuteri*, *L. plantarum*, and *Bifidobacterium animalis* being notable producers. The biosynthesis of vitamin B12 involves complex pathways, including the conversion of precursors like uroporphyrinogen III. *L. reuteri* has approximately 30 genes responsible for vitamin B12 synthesis, with the hem gene positioned uniquely in the middle of the gene cluster [19]. This positioning likely enhances metabolic efficiency by coordinating both heme and B12 pathways, allowing efficient use of resources. Additionally, the clustering enables co-regulation, streamlining the gene's expression with other B12 genes and supporting a more synchronized biosynthesis process [19].

Vitamin K exists in multiple dietary forms, including phylloquinone (PK) and menaquinones (MKs). PK, also known as vitamin K-1, is predominantly found in green leafy vegetables, while MKs, including MK-4 to MK-13, are primarily synthesized by bacteria and present in smaller amounts of meat, dairy, and fermented food products. Bacterial synthesis of MKs was discovered in the 1930s, and most bacteria produce MKs with isoprenoid side chains of varying lengths. Bacteria utilize distinct biochemical pathways for MK synthesis, such as the pathway employed by LAB in food fermentations. In this pathway, the napthoquinone ring is synthesized from chorismate, and the isoprenoid side chain is separately formed before being joined to complete MK biosynthesis [16].

The specific bacterial strains and fermentation conditions influence the concentrations and forms of MKs in fermented foods. For instance, cheese and milk products are major dietary sources of long-chain MKs, particularly MK-8 and MK-9, produced by LAB strains. Other fermented foods like sauerkraut and natto also contain long-chain MKs. Propionibacterium strains primarily produce MK-9 and tetrahydromenaquinone-9 (MK-9 (4H)), while *Bacillus subtilis* natto is known for producing significant amounts of MK-7. *Lactococcus lactis* strains produce MK-7 to MK-9 but not MK-9 (4H) [20]. A large study examining vitamin K2 levels in 62 fermented dairy products found that thermophilic species like *Streptococcus thermophilus*, *Lactobacillus delbrueckii*, and *Bifidobacterium* do not produce vitamin K2. Fermented dairy products using only thermophilic cultures showed no long-chain menaquinones (MK-6 to MK-10). In contrast, products containing mesophilic LAB, particularly *Lactococcus* species, had high vitamin K concentrations exceeding 0.1 µg/g [20]. However, comprehensive data exists on MK contents across various foods and regional dairy consumption patterns are limited, highlighting the need for further research to accurately assess MK intake at the individual and population levels.

Table 1 highlights research showcasing the ability of various microbial producers to synthesize micronutrients during fermentation. The findings suggest that everyday foods can become significant sources of essential micronutrients or increase their bioavailability simply through fermentation, especially with optimal starter cultures. This microbial diversity is not limited to LAB or bacteria but also includes other types like yeast and fungi. For example, kombucha, a fermented tea, provides essential elements such as copper, iron, manganese, nickel, and zinc; vitamins B1, B2, B6, B12 and C; carbon dioxide; natural antibiotic compounds; D-saccharic acid-1,4-lactone (DSL); and hydrolytic enzymes [21].

Table 1
Examples of micronutrient biofortification in common fermented foods are listed below. This list is not comprehensive due to the vast amount of evidence and literature demonstrating the benefits of fermentation in enhancing micronutrient content

Nutrient	Food item (s)	Microorganisms	Findings
Riboflavin (B2)	Idli Batter	*Saccharomyces boulardii* SAA655	Optimal production at 28 ± 2°C for 14h [22]
	Fermented cocoa bean	*S.cerevisiae* and *Pichia kudriavzevii*	Reduction of fermentation duration from 96h to 72h [23]
	The mixture of cauliflower and white beans	*L. plantarum* Lp900	Optimal production at 30 °C for 44h [24]
	Quinoa sourdough	*L. plantarum* CRL 2107 and *L. plantarum* CRL 1964	Optimal production at 30^{0}C for 24h [25]
Folate acid (B9)	Yogurt	*L. bulgaricus* CRL871, *S. thermophilus* CRL803 and CRL415	Optimal production at 42^{0}C for 6h [26]
	Cheese	*Lactobacilli*, *Enterococcus*, and *Streptococcus*	Increased production after 30 days [27]
Cobalamin (B12)	Wheat bran	*P. freudenreichii* DSM 20271 and *Lactobacillus brevis* ATCC 14869	Co-fermentation increases production [28]
	Lupin tempeh	*P. freudenreichii* and *Rhizopus oryzae*	Optimal production at 30 ^{0}C for 2 days ([29]
	Indonesian tempeh	*Rhizopus oligosporus, Klebsiella* sp. and *Saccharomyces cerevisiae*	*S. cerevisiae* enhances vitamin B12 production in tempeh, while *Klebsiella* sp. increases daidzein and genistein levels during soybean fermentation [30]
Zinc	Fermented cassava tuber	-	Increased bioabsorption and reduced pH [31]
	Black-eyed pea (*Vigna unguiculata*) flour	*Aspergillus oryzae*	Optimal bioavailability at 30 ^{0}C for 96h [32]
Iron	Fermented kisra bread	LAB	Optimal production after 72h [33]

3. Effect of Fermentation on Non-nutrient/Bioactive Compounds

Fermentation is known to transform food crops into edible forms, enriching them with natural bioactive compounds such as non-digestible carbohydrates, proteins, and fatty acids. Bioactive compounds can be described as phytochemicals released from the food matrix, which contribute to various health benefits through their metabolism [34]. This concept, originally advocated by Hippocrates 2500 years ago with the statement "Let food be thy medicine and medicine be the food," is now embraced by increasingly educated consumers aware of the impact of their daily food intake. As awareness grows, fermented foods are increasingly incorporated into health-conscious diets as functional foods that support both preventive and therapeutic health strategies.

3.1 Non-Digestible Carbohydrate

Indigestible carbohydrates, also known as soluble fiber, are carbohydrates that cannot be digested by the human digestive system and instead bypass the absorption process in the upper part of the intestine. When these indigestible carbohydrates reach the lower gut, they have the ability to modify the composition and function of microorganisms in the human gut [35]. Consumption of prebiotics by probiotic bacteria leads to several changes, including an increase in the expression or alteration of the composition of short-chain fatty acids, a decrease in luminal colon pH, and a reduction in nitrogenous end-products [36]. These changes can contribute to numerous health benefits, such as improving intestinal health, strengthening the immune system, preventing cardiovascular-related conditions, and enhancing the gut's ability to absorb certain nutrients [37]. In this section, we will focus on two main types of prebiotics: fructooligosaccharides and galactooligosaccharides.

3.1.1 Prebiotics - Fructooligosaccharide (FOS) and galactooligosaccharides (GOS)

Prebiotics are compounds selectively utilized by beneficial gut microorganisms to confer health benefits and can be found in various fermented foods and beverages. Examples include fermented grains, vegetables, beer, and wine, which are known to contain prebiotic compounds such as β-glucans, oligosaccharides, and polyphenols. In some cases, prebiotics are synthesized *in situ* by the microorganisms involved in the fermentation process. For instance, exopolysaccharides with prebiotic properties are generated during the fermentation of dairy and cereal products [3]. Additionally, certain fermented foods and beverages may contain both live microorganisms (probiotics) and prebiotic substrates. However, for such products to be considered synbiotics, the combined presence of live microbes and prebiotics must demonstrate a proven synergistic health benefit [3].

The addition of prebiotics, particularly oligosaccharides, has been shown to promote the growth of LAB and increase the production of B-vitamins, especially folate [38,39]. Prebiotics can directly boost food health benefits and also indirectly support the activity of probiotics present in the food. Microbial fermentation can produce prebiotics by releasing specific enzymes, such as bacterial and fungal carbohydrases, which break down starches to release bioactive, non-digestible oligosaccharides or prebiotics. Table 2 summarizes studies examining the ability of microorganisms to increase the content of fructooligosaccharides (FOS) and galactooligosaccharides (GOS) in foods. The production of prebiotics *in situ* is more commonly practiced with GOS compared to FOS. Industrial production of FOS is typically carried out under controlled conditions using fungi, while GOS is often produced directly within dairy-based fermented foods, benefiting from the numerous LAB strains that naturally ferment such products.

Table 2
The prebiotic production from fermented food and beverages

Food item(s)	Microorganisms	Finding (s)	References
A) Fructooligosaccharides (FOS)			
Cashew apple juice	*L. acidophilus, L. casei, L. plantarum, Leuconostoc mesenteroides,* and *Bifidobacterium longum*	The juice contains increased vitamin B-complex and prebiotics like FOS and oligosaccharides	[38]
Natto	*Bacillus subtilis natto* CCT 7712	The optimal conditions for FOS formation (98.86 g/L) were a sucrose concentration of 300 g/L, pH 7.7, and agitation at 234 rpm	[40]
Various plant-based fermented foods	Lactic acid bacteria and fungi	Inulosucrase catalyzes the biosynthesis of FOS by elongating fructan chains through the addition of fructosyl units, forming β-2,1-glycosidic bonds	[41]

Sugarcane molasses	*Aspergillus tubingensis* XG21	High fructofuranosidase (FFase) activity and the ability to synthesize FOS from sugarcane molasses	[42]
Carrot juice	*A. niger*	Carrot juice was utilized as a matrix for producing FOS through the use of a fructosyltransferase enzyme from *A. niger*	[43]
B) Galactooligosaccharides (GOS)			
Whey cheese	*Trichoderma* sp.	The highest β-galactosidase activity at 55^0C	[44]
Wheat bran	*Penicillium sp.*	Highest β-galactosidase activity at the temperature 50^0C (1.60 $IU.mL^{-1}$)	[45]
Yoghurt	*L.bulgaricus* CRL450	Highest GOS production (41.3 %) at fermentation 45^0C	[46]
Fermented milk permeates with apple	*Pediococcus acidilactici*	Highest GOS production production (26.80 mg/100mL) at fermentation 30 °C for 48 h	[47]
Skim milk	*Lactobacillus*	Direct transformation of lactose into GOS in skim milk *Lactobacillus*, and utilisation of GOS by *Bifidobacterium* spp. that lead to the enhanced fermentation and nutritional characteristics	[48]
Fermented foods (from Argentina)	*Lactobacillus delbrueckii* subsp*. bulgaricus* CRL450	Out of 20 strains tested, 15 were able to grow on lactose and exhibited β-galactosidase activity, while 11 of them synthesized GOS	[46]
Yogurt	*Kluyveromyces lactis* (YNL-2, GODO*)* and *Lactobacillus acidophilus* La-5	Different types of yogurts with reduced lactose content and enriched with GOS were successfully developed	[49]
Tejuino	*Pantoea anthophila*	The β-galactosidases demonstrated significant transgalactosylation activity, predominantly forming β(1 → 3) and β(1 → 6) linkages	[50]
Sweet whey	*L. acidophilus, Streptococcus thermophilus, Bifidobacterium lactis, L. delbrueckii* subsp*. bulgaricus* and *S. thermophilus*	Transgalactosylation was higher in sweet whey compared to control and *L. bulgaricus* and *S. thermophilus* showed highest GOS yield	[51]

FOS are a type of inulin-type oligosaccharide commonly used as prebiotics due to their strong bifidogenic activity [52,53]. The high demand for FOS has led to ongoing research in search of new microbes that can produce fructosyltransferase (FTase) with excellent transfructosylation activity, which is crucial for FOS production. Some potent microorganisms involved in the industrial fermentation of FOS includes *Aspergillus* sp., *Penicillium* sp., *Aureobasidium pullulans*, LAB, and some bacterial species [54]. Both submerged and solid-state fermentation methods can be employed for cost-effective and efficient production of short-chain FOS. The food industry often uses FOS as low-calorie sweeteners due to their desirable properties of offer multiple health and functional benefits. FOS provide a mild sweetness without significantly impacting blood glucose levels, while improving the digestive health through the modulation of probiotics. Their stability during processing and pleasant taste profile make FOS an attractive choice for a wide range of products, from baked goods to beverages [55].

FOS can be synthesized through a transfructosylation reaction via two pathways: the enzyme ß-D-fructofuranosidase (FFase) or fructosyltransferase (FTase). The process involves two major steps. The first step, catalyzed by FFase (EC 3.2.1.26), irreversibly hydrolyzes the glycosidic bond of sucrose (GF) by cleaving the β (2,1) linkages. FFase acts as both a donor and an acceptor of a fructosyl residue, resulting in the production of glucose and the trisaccharide 1-kestose. The second step is a readily reversible reaction, where 1-kestose or another β (2,1) linked fructan can act as the fructosyl donor, while GF or any fructan can act as the acceptor. This reaction is catalyzed by FTase (EC 2.4.1.9), which specifically cleaves and reforms the β (2,1) linkage between fructosyl-fructose units [52,53].

The physicochemical characteristics of the substrate play a crucial role in FOS production during microbial fermentation. Studies by de la Rosa *et al.,* [56] and Ganaie *et al.,* [57] highlighted the high FOS production observed in sugar cane bagasse, which was attributed to its high-water absorption index (WAI) facilitating microorganism growth and cell immobilization. However, recent findings from [58] and [59] challenged the notion that physicochemical parameters alone determine FOS production. They observed that certain microorganisms, such as *A. tamarii* URM4634 and *Aspergillus niger* LBA 02, exhibited low WAI but still showed high enzyme activity. This suggests that factors beyond physicochemical parameters, including nutrient absorption and enzyme production, contribute to the complex process of FOS production during fermentation.

According to Davani-Davari *et al.,* [60], during the fermentation process, β-galactosidase can undergo transgalactosylation mechanism to produce GOS. The GOS can be produced through the binding of galactose molecules to lactose where 3-6 pieces of saccharides bind with β (1-4; 1-6) bonds to 2-5 parts of galactose units. Optimizing temperature is crucial for maximizing β-galactosidase activity and GOS production in different microbial strains. For instance, *Penicillium* sp. exhibited high activity at 50°C, while LAB strains, like *L. bulgaricus*, thrived at 45°C. Moreover, strain selection plays a vital role, with *P. acidilactici* showing enhanced β-galactosidase activity and GOS production [61].

3.2 Protein- Bioactive Peptide (BP)

Bioactive peptides (BP) are specific protein fragments that contribute to overall body health. The activity of these peptides is influenced by their inherent amino acid composition and sequence. Initially inactive in the parent protein, BP can be generated through microbial fermentation, leading to functional food benefits, as highlighted by Taniguchi *et al.,* [62]. Various microorganisms possess different proteolytic systems, and common probiotic strains like *L. plantarum*, *L. acidophilus*, *Aspergillus oryzae*, and *B. subtilis* are known to possess excellent proteolytic capabilities [63].

The fermentation of various food substrates using specific probiotic strains has been shown to increase the production of BP with potential health benefits. Ayyash *et al.,* [64] investigated the fermentation of camel milk using *L. lactis* KX881782 and observed a significant inhibition of α-amylase and α-glucosidase, indicating potential antidiabetic activity. Similarly, Flores-Medellín *et al.,* [65] found that fermented black bean with *B. subtilis* exhibited beneficial effects in obesity and type 2 diabetes mellitus. The mechanism of action of BP involves the inactivation of specific enzymes such as α-amylase, α-glucosidase, and dipeptidyl peptidase-IV (DPP-IV), as discussed by Yan *et al.,* [66]. Mazorra-Manzano *et al.,* [67] demonstrated an increase in angiotensin-I-converting enzyme (ACE)-inhibitory activity in cheese whey after fermentation, while Wu et al. [68] highlighted the inhibition as a mechanism for antihypertensive effects. Furthermore, Najafian and Babji [69] and Wu *et al.,* [70] reported antioxidant activities in fermented fish and salmon skin, respectively. By utilizing inexpensive ingredients like black beans and fish offcuts, fermentation can transform low-cost, readily available foods into nutrient-dense products with bioactive peptides that contribute to better health. This approach not only enhances the nutritional value of these foods but also makes them more accessible to broader populations, offering an affordable solution for combating conditions like obesity, type 2 diabetes, and hypertension.

The production of BP through microbial fermentation is influenced by the duration of fermentation, as observed by Sharma *et al.,* [71]. They found that the highest proteolytic activity (30.38 mg leucine/mL) in flaxseed milk supplemented with *L. plantarum* NCDC 374 was detected at 126 hours of fermentation, with a subsequent decrease in proteolytic activity at later stages. Similar trends were reported by Liu *et al.,* [72] in their study on defatted wheat germ (DWG) fermented with *B. subtilis* 10160. The peptide content increased from 0 hours (4.31 ± 0.59%) to 48 hours (29.68 ± 0.98%) and then decreased to 25.80 ± 1.49% at 72 hours of fermentation. This observation aligns with the findings of Ying and Voo [73], who emphasized that the fermentation process can enhance bioactive peptide levels in food and beverages through the proteolytic activity of microorganisms. Maffioli *et al.,* [74] discussed the interaction between endopeptidases and exopeptidases, noting that with longer fermentation durations, peptides produced by endopeptidases can further hydrolyze into amino acids, resulting in lower peptide levels (Figure 4).

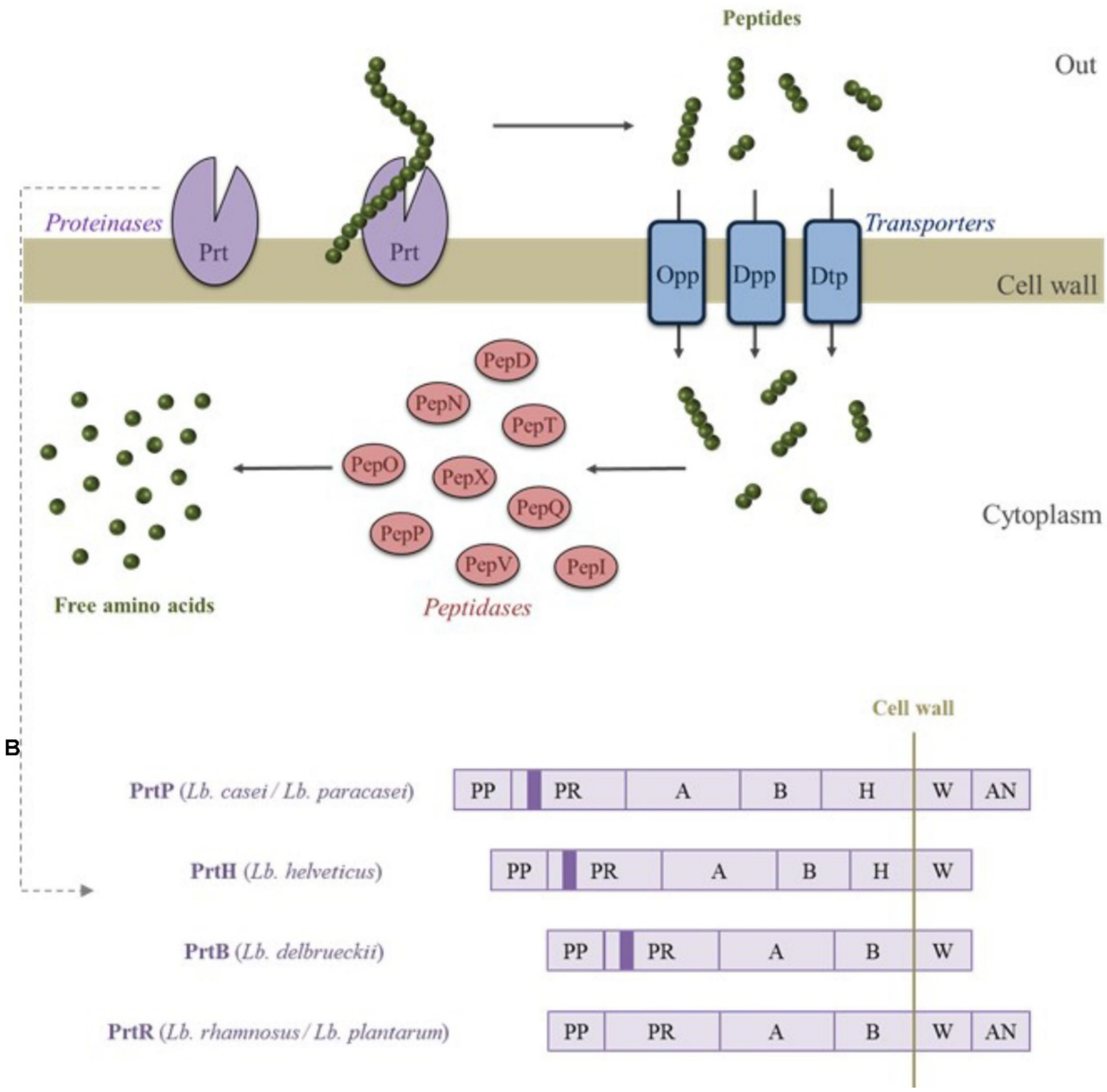

Fig. 4. (A) The proteolytic system of *Lactobacillus* spp. involves cell envelope proteinases (CEPs) and Prt enzymes that initiate protein hydrolysis. Peptides are transported inside the cell and further converted into free amino acids by peptidases. (B) The structure of CEPs from various *Lactobacillus* species, including different gene domains. The figure is adapted from [63]

Furthermore, Panchal *et al.,* [75] and Peres *et al.,* [76] both reported the highest proteolytic activity and bioactive peptide production in goat milk fermented with *L. fermentum* and *L. helveticus* IMAU80872, respectively, under specific fermentation conditions. It has been suggested by Ravenschot *et al.,* [63] that *Lactobacillus* strains develop proteolytic systems to hydrolyze proteins into various bioactive peptides (Figure 4). However, the BP profiles can vary among different *Lactobacillus* strains due to differences in CEP gene expression, CEP gene mutations, and enzymatic activities under specific optimum conditions.

3.3 Short-Chain Fatty Acids (SCFAs) and Conjugated Fatty Acids (CLA)

Short-chain fatty acids (SCFAs) are end-products of microbial fermentation in the gut and play a crucial role in host health. Acetate, propionate, and butyrate are the main SCFAs produced through the breakdown of dietary fibers and other complex carbohydrates by gut microbiota. SCFAs have diverse physiological effects, including energy metabolism, immune modulation, and maintenance of gut barrier integrity. However, various fermented foods, such as from dairy and vegetable-based fermented foods were shown to also be rich in these substrates. Dietary SCFA has been shown to exert multiple health benefits, such as reduced risk of metabolic perturbations, obesity, improved lipid synthesis and microbial composition [77].

Numerous studies have investigated the production of SCFAs through microbial fermentation in various food substrates. For instance, Jia *et al.,* [78] observed increased SCFA production (11.74 ± 0.08 mg mL^{-1}) during the fermentation of goat milk yogurt with *Lactobacillus rhamnosus* GG. Similarly, Hu *et al.,* [79] reported elevated levels of acetic acid, propionic acid, and butyric acid in carrot juice fermented with *L. rhamnosus* GG. However, Wang *et al.,* [80] argued that the correlation between SCFA production and *L. rhamnosus* strains may not be direct. They showed that the ability of *L. rhamnosus* strains to alleviate constipation symptoms was not directly linked to increased SCFA levels in the colon. The effectiveness of *L. rhamnosus* strains on constipation appeared to vary due to differences in strain-specific factors, such as cell surface molecules, metabolites, and their influence on gut motility-regulating peptides, neurotransmitters, and microbiota composition. Therefore, while SCFAs may play a role in fermentation, the therapeutic effects of different *L. rhamnosus* strains may arise through diverse mechanisms, suggesting that combinations of strains with varying properties could be more effective in addressing constipation symptoms [80].

Lee *et al.,* [81] demonstrated higher SCFA production in fermented rice liquors supplemented with barley compared to control alcoholic drinks. The supplemented group showed increased butyric acid (0.09 nmol/g dried fecal), propionic acid (0.11 nmol/g dried fecal), and acetic acid (0.45 nmol/g dried fecal) levels, while the control group had lower levels (butyric acid: 0.05 nmol/g dried fecal, propionic acid: 0.06 nmol/g dried fecal, acetic acid: 0.10 nmol/g dried fecal). Similarly, Pérez-Burillo *et al.,* [82] found that fermenting salami with citrus fibers enhanced SCFA production (acetate: 66%, propionate: 20%, butyrate: 58%) compared to the control.

These studies suggest that fermentation with dietary fiber can serve as an effective substrate for probiotics, leading to increased SCFA production [83]. The modulation of gut flora by fermented beverages has potential implications, as SCFAs have been found to activate G protein-coupled receptors (GPCRs) and influence glycemic response, improving glucose tolerance and insulin release [84]. Butyrate, a major SCFA derived from Acetyl-CoA through the glycolysis of dietary carbohydrates, plays a significant role in these physiological effects [85].

Fermentation also plays a role in the conversion of linoleic acid (LA) into conjugated linoleic acid (CLA), a beneficial modified fat. Microorganisms such as *Bifidobacterium, Enterococcus, Lactobacillus, Lactococcus, Propionibacterium*, and *Streptococcus* can convert LA into CLA through linoleate isomerase enzyme activity. CLA synthesis can occur through direct isomerization of LA or via 10-hydroxy-octadecenoic acid in certain *Lactobacillus*, *Propionibacterium*, *Bifidobacterium*, and *Clostridium*-like bacteria found in the human gut [86]. CLA production has been associated with reducing LDL cholesterol levels, enhancing immune function and osteogenesis, preventing hyperinsulinemia, and protecting against colon cancer [87].

The production of conjugated CLA through microbial fermentation has been investigated in various food products. For instance, Hwang *et al.,* [88] observed the production of cis-9, trans-11 CLA and trans-10, cis-12 CLA during the fermentation of soybean powder yogurt (SPY) with *L. plantarum*, while no CLA production was detected with *L. brevis* WCP02. Similarly, Özer and Kılıç [89] found efficient CLA production in semi-hydrated sausages fermented with *L. plantarum* AB20–961. Furthermore, Palachum *et al.,* [90] developed gummy jelly using guava pulp fermented with probiotic *L. plantarum* WU-P19. *L. plantarum* has been recognized as a probiotic capable of producing CLA [91], along with other microorganisms such as *Bifidobacterium, Lactobacillus, Streptococcus, Propionibacterium*, and *Clostridium* [86].

Temperature has been identified as a factor influencing CLA production during fermentation. Amiri *et al.,* [92] demonstrated that the highest CLA production (105.08 μg/ml) in whey cheese supplemented with *Bifidobacterium lactis* BB12 occurred at 34°C for 60 hours. In contrast, at the same fermentation duration (60 hours) but at 42°C, the CLA production was lower (67.66 μg/ml). The same team also showed that the highest CLA production during the fermentation of cheese whey with *L. acidophilus* was at 38°C for 60 hours (38.69 μg/ml), while at 34°C, the production was lower (19.01 μg/ml). Therefore, temperature plays a crucial role in microbial growth and metabolism during fermentation. The optimum temperature for the growth and metabolism of *L. acidophilus* in synthesizing CLA from linoleic acid (LA) is around 37°C [93]. The temperature also affects the isomerase capability of LAB in transforming LA into CLA, as high temperatures can denature the isomerase enzyme and reduce CLA production [94].

4. Conclusions and Future Prospects

Fermentation plays a crucial role in enhancing the biosynthesis and bioavailability of micronutrients, prebiotics, bioactive peptides, and functional fatty acids in food products. Through the action of diverse microorganisms, fermentation not only increases the nutrient density of food but also promotes the production of bioactive compounds that offer significant health benefits, such as improved gut health, enhanced immunity, and reduced risk of chronic diseases. The ability to modify the nutritional profile of common foods through fermentation processes highlights its potential as a cost-effective and sustainable strategy to improve public health.

Future directions in this field involve further exploration of the potential of different microorganisms and their interactions to enhance the production of these components. Additionally, investigating the impact of fermentation on other bioactive compounds and nutritional profiles would provide a more comprehensive understanding of the benefits of fermented biofortified foods. Advances in microbiome research and functional genomics can also contribute to a deeper understanding of the mechanisms involved in microbial fermentation and its impact on human health. Finally, efforts should be directed towards scaling up and translating these findings into practical applications, such as developing novel functional food products that can be easily incorporated into everyday diets, to address nutritional deficiencies and promote human health.

Acknowledgement
This research was supported by Universiti Putra Malaysia Inisiatif Putra Siswazah Grant, with a reference to UPM.RMC.8003/3/1/2024/GPI/9801000.

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