



## EFFECTS OF FERMENTED PRODUCTS ON HUMAN HEALTH AND GASTROINTESTINAL MICROBIOTA

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### Abstract

The human microbiota is an ecosystem that contains thousands of symbiotic microorganisms. Fermented products have been a part of the human diet for about 10 thousand years and have reached their highest diversity today. Each fermented product includes a unique microbial population. In this study, the effects of fermented products on human health and microbiota were evaluated by researching information from the literature. Different microbial products are generated by fermentation. In addition to providing nutrients supporting intestinal microbiota, fermented products can provide characteristic microorganisms for temporary or long-term colonization in the intestines. The microbiota of fermented products benefits human health with the metabolites they produce by metabolizing nutrients (such as exopolysaccharides, short-chain fatty acids, vitamins, polyphenols, and peptides). Fermented products can serve as a means of safely transporting beneficial microorganisms to the intestines. The microbiota of fermented products can positively change brain function and behavior by communicating with the central nervous system through nutrients provided by both the products and the intestines, as well as changing the structural properties of the raw material. Fermented products can affect cognitive function through neurochemical modulation and serotonin conversion. A Western-style diet, low in fiber and high in animal fat and protein, disrupts the intestinal microbiota and causes inflammation. Fermented products consumed in the human diet provide therapeutic benefits. Since regular consumption of fermented products can affect the intestinal microbiota in the short and long term, they should be considered an essential part of the human diet.

**Keywords:** *Fermented product, Microbiota, Nutrition, Bioactive compound.*

## Introduction

The gastrointestinal (GI) microbiota consists of an ecosystem made up of thousands of symbiotic microorganisms, each with different functional activities. In healthy individuals, the number of beneficial microorganisms in the microbiota is much higher than that of harmful ones. There are approximately  $10^{14}$  microorganisms per g of content in the human GI tract.<sup>1,2</sup> Throughout human history, the most crucial function of microorganisms has been their use in food preservation via fermentation. Fermentation is the process by which microorganisms convert raw materials into new products. It is a process where alcohols, carbon dioxide, and organic acids are produced by microorganisms, primarily from sugars, usually under anaerobic conditions, to generate energy and organic compounds. The production of organic acids prevents the growth of undesirable microorganisms in fermented products, inhibits the activity of enzymes in the food system, and extends the product's shelf life.<sup>2</sup> There are varying opinions on the health benefits of fermented products, and research and discussions continue regarding their level of benefit. This review investigates and evaluates the changes that may occur in the gut microbiota through the nutrients provided by fermented products and their subsequent effects on human health.

### Development of the Microbiota in Humans

The GI microbiota development in humans likely begins at the time of birth and after, as the newborn is exposed to microorganisms from the mother during childbirth (from the intestines, mother's skin, breast milk, etc.).<sup>3,4</sup> During the breastfeeding period, the baby continues to acquire various microorganisms. In the growth phase, the intake of millions of microorganisms continues through food, beverages, and

environmental contact.<sup>5</sup> There are significant differences in the microbiota of babies fed with breast milk versus formula milk. Probiotic bacteria, such as *Bifidobacterium*, are found in higher numbers in the intestines of babies fed breast milk. *Bifidobacterium* can digest the prebiotic (oligosaccharides) components found in breast milk.<sup>6,7</sup> People who follow a plant-based diet have greater diversity in their GI microbiota. Diet plays a major role in shaping the GI microbiota. The microorganisms in the GI generally do not expend their energy on competition but instead adapt to live together.<sup>6,8,9</sup>

### Microbiota of Fermented Products

Traditional food fermentation is carried out by transferring microbiota from raw materials containing microorganisms or previously fermented products. Industrial food fermentation is carried out using defined microbial cultures. Most of the fermented products contain a local microbiota, potentially consisting of different microorganisms. The microbiota of fermented products may include various bacteria such as lactic acid bacteria (LAB), *Acinetobacter*, *Arthrobacter*, *Bacillus*, *Bifidobacterium*, *Brachy bacterium*, *Brevibacterium*, *Enterobacter*, *Enterococcus*, *Hafnia*, *Haloanaerobium*, *Halobacterium*, *Halococcus*, *Klebsiella*, *Kocuria*, and *Micrococcus*.<sup>6,8</sup> Yeast genera may include *Brettanomyces*, *Cryptococcus*, *Debaryomyces*, *Dekkera*, *Galactomyces*, *Geotrichum*, *Hansenula*, *Hanseniaspora*, *Hyphopichia*, *Issatchenkia*, *Kazachstania*, *Khuyveromyces*, *Metschnikowia*, *Pichia*, *Rhodotorula*, *Rhodosporidium*, *Saccharomyces*, *Schizosaccharomyces*, *Torulasporea*, *Torulopsis*, *Trichosporon*, *Yarrowia*, and *Zygosaccharomyces*.<sup>2,10,11</sup> Fungal genera may include *Actinomucor*, *Amylomyces*, *Aspergillus*, *Monascus*, *Mucor*, *Neurospora*, *Parcilomyces*, *Penicillium*, *Rhizopus*, and *Ustilago*.<sup>2,10,11</sup> Major microorganisms commonly detected in fermented foods and their reported physiological functions are summarized in Table 1.

**Table 1.** Major microorganisms associated with fermented foods, their metabolites, and reported health effects

Microorganism	Common fermented foods	Major metabolites	Reported physiological effects
<i>Lactiplantibacillus plantarum</i>	Vegetables, olives, sourdough, kefir	Lactic acid, bacteriocins, EPS	Antimicrobial activity, GI microbiota modulation
<i>Lacticaseibacillus rhamnosus</i>	Yogurt, fermented milk	SCFAs, EPS	Immune modulation, GI barrier protection
<i>Limosilactobacillus reuteri</i>	Fermented milk products	reuterin, organic acids	Antimicrobial activity, intestinal health
<i>Levilactobacillus brevis</i>	Kimchi, sauerkraut	Lactic acid, GABA	GI microbiota modulation
<i>Latilactobacillus sakei</i>	Fermented meat products	Organic acids, bacteriocins	Inhibition of pathogenic bacteria
<i>Bifidobacterium longum</i>	Fermented dairy products	Acetate, vitamins	GI microbiota balance, immune support
<i>Propionibacterium freudenreichii</i>	Swiss-type cheese	Propionate, vitamin B12	Metabolic regulation
<i>Lactococcus lactis</i>	Fermented milk, cheese	Bioactive peptides	Antihypertensive activity
<i>Leuconostoc mesenteroides</i>	Kimchi, sauerkraut	Dextran, lactic acid	Improved GI microbial diversity
<i>Saccharomyces cerevisiae</i>	Beer, wine, sourdough	Ethanol, CO <sub>2</sub> , vitamins	Improved digestion and nutrient bioavailability

SCFAs: Short-chain fatty acids, EPS: Exopolysaccharides GABA: Gama-aminobutyric acid, GI: Gastrointestinal.

There is a significant variation in the microbiota of fermented products. For example, the microbiota formed during the maturation of cheeses originates from the milk, ingredients used in cheese production, starter cultures added during production, and the cheese-making and maturation environment. The microbiota in the cheese processing environment contributes to developing the organoleptic characteristics specific to the cheeses. Bacterial genera common in all raw milk include *Enterococcus*, *Lactobacillus*, *Lactococcus*, *Leuconostoc*, and *Streptococcus*, however, this microbiota varies depending on the milk source. In cow's milk, dominant bacterial genera may include *Bacillus*,

*Lactococcus*, and *Acinetobacter*, while in camel's milk, dominant bacterial genera may include *Enterococcus*, *Lactococcus*, and *Pediococcus*. Most fermented products are consumed without further processing, such as heat treatment.<sup>2,11</sup> These products provide a high number and diversity of microbiota to the gut system.

### Health Effects of Fermented Products Benefits for Human Health

Consumption of different fermented products improves mood and brain activity by leading to the positive changes in the gut microbiota. Fermented products positively affect health

through the compounds they contain. Fermented soybeans and fermented cabbage are sources of nutrient components such as soluble fiber, linoleic acid, iron, zinc, and vitamins (including K, B9, B1, and B6). Fermented dairy products contain calcium, protein, and vitamins (such as B2, B9, and B12). Vitamins B7 (biotin), B11 (folic acid), and B12 (cobalamin) can be produced during the fermentation of dairy products by species of *Lactiplantibacillus plantarum*, *Lactobacillus delbrueckii*, *Limosilactobacillus reuteri*, and certain species of *Propionibacterium*, *Bifidobacterium*, and *Streptococcus*.<sup>12</sup> Folate produced in fermented products protects against certain cancers and cardiovascular diseases. Additionally, many metabolic processes use folic acid, nucleic acids, and amino acids as cofactors in forming B12. Fermented turnips are made from black carrots and contain vitamins A, B, and C, minerals, and polyphenols. Antioxidants produced by microbial esterases in fermented products protect against the harmful effects of free radicals. Fermented Kombucha and sweetened tea contain antioxidants with antagonistic effects against the progression of neurodegenerative diseases, diabetes, and some cancers. Fermented products like fermented cabbage and kimchi contain anti-atherogenic substances, such as propionic acid, that prevent lesions in artery walls.<sup>10,13</sup> Consumption of dietary fiber and flavonoids from fermented products can improve plasma cholesterol and triglyceride levels in the liver. Saponins, oligosaccharides, and phytosterols provided by fermented products may reduce cholesterol absorption in the gut. *Lactococcus lactis* found in fermented milk has been reported to reduce high systolic and diastolic blood pressure caused by hypertension, providing antihypertensive benefits.<sup>14</sup> However, a study also noted that consuming 50 grams of yogurt daily did not affect mortality or cardiovascular disease (CVD) risk.<sup>13</sup>

Probiotics in fermented products, in addition to altering the structural properties of the product, can also influence brain functions via the gut microbiota. Neurotransmitters produced in fermented products are neurochemicals that can affect cognitive function. Brain-derived neurotrophic factor (BDNF), glutamate, gamma-aminobutyric acid (GABA), and serotonin are involved in learning and memory functions.<sup>10</sup> Therefore, fermented products can improve cognitive function by providing neurotransmitters. A study found that LAB (such as *Lactobacillus*) added to animal feed affected animal behavior, with animals displaying social behaviors. In contrast, animals not exposed to microorganisms exhibited socially deficient behaviors.<sup>15</sup> As fermented product-derived microorganisms proliferate in the gut and compete with other microorganisms, their metabolites could positively change human behavior. Fermentation increases bioavailability of products by hydrolyzing raw materials and generating new components such as bioactive peptides, phytochemicals, and vitamins, which enhances the absorption of raw material components in the gut. Some food components that are not absorbed in the intestines, are converted into active forms by intestinal bacteria, increasing their absorption and positively affecting health. For example, short-chain fatty acids (SCFAs), produced from indigestible fibers and complex polysaccharides by colon-specific bacteria, serve as an energy source for colon epithelial cells, positively influencing host metabolism and the functioning of the central nervous system (CNS). Well-known SCFAs include acetate, propionate, and butyrate. The leading producers of these SCFAs are *Bifidobacterium* and the members of *Lactobacillaceae*. SCFAs are also produced in fermented products, although their amounts vary, and they are generally found as free fatty

acids (FFAs) that contribute to the organoleptic properties of fermented products like cheese. In Italian hard cheeses (such as Parmigiano Reggiano and Grana Padano), FFAs account for 25% of the triglyceride content. *Propionibacterium* in Swiss-type cheeses ferment lactose into SCFAs, such as acetate and propionate.<sup>10,15</sup> The gut microbiota ferments some polysaccharides with prebiotic properties into SCFAs.<sup>14</sup>

The microbiotas that are colonized in different regions of newborns play significant roles in the development and maturation of the immune, endocrine, and central nervous systems. The gut wall is skinny, with immune system cells located immediately on the inside. Nearly 80% of the immune system is located on the inner surface of our gut.<sup>6</sup> Many immune system diseases originate from the gut. Disruption of the microbiota balance in the body begins to stress and weaken the immune system. If bacteria had not entered the body during and after birth, the acquired immune system would not have been developed as the first defense against microorganisms. The body produces the ability to respond to microorganisms from the outside through the microbiota formed after birth. The innate or acquired immune system does not react negatively to the microbiota once the body recognizes it. The microbiota immune system permits, becomes essential for healthy living. There is a strong relationship between the brain and the gut microbiota, which has led to terms like "second brain" and "second memory" being used to describe the gut. The bacteria in the gut influence the development of depression. Serotonin, which is responsible for feelings of well-being, high self-confidence, and good sleep, is produced by the gut microbiota in about 70% of cases.<sup>16</sup> Therefore, maintaining balance in the gut microbiota offers individuals a more balanced, happier, and joyful life. Disruptions in the gut microbiota can lead to depression, anxiety (feelings of fear and worry), doubt, sleep disorders, stress-related disorders like irritable bowel syndrome (IBS), and neurodevelopmental disorders such as autism.<sup>16</sup> Interactions between humans and microorganisms play a key role in maintaining healthy living. Communication between the gut microbiota and the CNS occurs through nerves, hormones, and metabolic pathways.<sup>16</sup> The enteric nervous system (ENS) is directly connected to the CNS via the vagus nerve. Microbial activity in the GI system produces neurochemical metabolites that stimulate the ENS and, consequently, the brain.<sup>5</sup> Chronic diseases cause significant changes in the microbiota, exacerbating the course of the diseases. Differences in the composition and function of the gut microbiota have been linked to various chronic issues such as inflammatory, metabolic, neurological, cardiovascular, and respiratory diseases, as well as Type 2 diabetes and obesity.<sup>6,17,18</sup> The gut microbiota affects metabolism by producing active metabolites for hormones and neurotransmitters.<sup>19</sup> The reduction in bacterial diversity and abundance and changes in species balance are associated with metabolic syndromes.<sup>14</sup> Consumption of Kimchi, a probiotic-containing food, has shown anti-diabetic effects.<sup>10</sup> Dietary changes and probiotics affect the gut microbiota and its functions. The microbiota-brain-gut axis can be considered a treatment method for immune, hormonal, and CNS disorders.

### Digestion of complex organic compounds

Fermentation increases the digestibility of foods by converting starches into oligosaccharides, proteins into amino acids, polysaccharides into simple sugars, and lipids into fatty acids and glycerol. In fermented products like cheese, the concentration of essential nutrients and the bioavailability of

minerals, such as calcium, are increased by removing water.<sup>2,20</sup> The gut microbiota also helps digest complex foods like vegetables and meats.<sup>8,11</sup> Fermentation enables consumers who cannot tolerate certain raw foods to tolerate fermented products. In fermented dairy products, the microbiota significantly reduces the level of lactose, making it more likely that individuals with lactose intolerance can consume fermented dairy.<sup>8</sup> The lactase enzyme produced by the microbiota helps further reduce the remaining lactose during the fermentation, storage, consumption, and digestion of the fermented product. The lactase enzyme can be protected from the acidic conditions of the stomach due to its presence inside the microbial cell and the buffering properties of the fermented product. As a result, the lactase enzyme can continue its lactose hydrolysis function in the intestines. Fermentation can neutralize toxic compounds in raw materials, such as polyphenols (like paclitaxel and rotenone), phytates, and tannins. In fermented products like soybeans, trypsin inhibitors, lectins, and other toxic compounds can be reduced by up to 95%.<sup>21</sup> In the fermentation of grains, phytic acid, an anti-nutrient compound that can bind divalent mineral ions, is broken down. Extended fermentation of sourdough bread hydrolyzes fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), converting them into simpler compounds. Reducing FODMAP content in wheat and rye bread may improve tolerance in patients with IBS.<sup>14</sup> Relatedly, the digestibility of fermented products is increased, and the risk of allergic reactions and gastrointestinal discomfort is reduced. Fermentation can also decrease the levels of mycotoxins in fermented products. Mycotoxins pose serious threats to human health, with effects such as immunosuppression, carcinogenic, mutagenic, nephrotoxic, cytotoxic, neurotoxic, and teratogenic properties. Bacterial cell wall components (polysaccharides and peptidoglycans) of *Lactobacillus* species (such as *L. rossiae*, *L. fermentum*, and *L. sanfranciscensis*), *Bifidobacterium*, *Lactococcus*, and *Pediococcus* can bind mycotoxins.<sup>8,19</sup> Antifungal metabolites produced by LABs (such as lactic acid, phenyl lactic acid, hydroxyphenyl lactic acid, indole, and bioactive peptides) can reduce mold growth and mycotoxin formation. The GI microbiota also influences feelings of hunger and satiety.<sup>19</sup> Appropriate fermented products, particularly prebiotics, must be consumed to

maintain gut microbiota health. This requires diversifying food sources and consuming fiber-rich foods especially. In cases of problems such as underweight or obesity, disturbances in the diversity of gut bacteria should be suspected. An increase in carbohydrate content in the stool may indicate either an excessive intake of fiber or undigested fiber remaining due to insufficient gut microbiota. It is suggested that the microbiota of people living in industrialized societies may lack the capacity to break down fibers. In such cases, microorganisms capable of hydrolyzing fibers can be added to the diet through fermented products or in capsule form to enhance the capacity of gut microbiota to break down carbohydrates.

### Production of bioactive compounds

Bioactive peptides (such as casomorphins,  $\alpha$ -lactorphin, lactoferrins, and phosphopeptides) are specific protein breakdown products that positively affect body functions and health. Typically, each bioactive peptide molecule contains 3–20 amino acids. Best-known bioactive peptides are initially inactive within the structure of proteins and are released during fermentation due to protein hydrolysis. In addition to their positive contributions to digestion, endocrine functions, cardiovascular health, immunity, and nervous system, bioactive peptides have antimicrobial, antithrombotic, antihypertensive, analgesic, immunomodulatory, cholesterol-lowering, mineral-binding, and antioxidant effects on human health.<sup>22</sup> Bioactive peptides can lower blood pressure, improve metabolic syndromes, have anticancer effects, and regulate immune functions. Bioactive peptides that inhibit angiotensin-1-converting enzyme (ACE) can reduce hypertension. It has been reported that ACE-inhibitory bioactive peptides from milk proteins are produced in fermented dairy products by *Lactobacillus helveticus*, and in sausages by *Lactobacillus sakei* and *Lactobacillus curvatus*.<sup>10</sup> Amino acids and their derivatives with neurotransmitters (such as GABA) and immunomodulatory functions are also produced during fermentation. Some bioactive peptides and exopolysaccharides (EPS) produced in food fermentations can have antioxidant functions, prevent pathogens from adhering to the intestinal mucosa, and provide immune-boosting and hypocholesterolemic activities.<sup>12,19,22</sup> The principal bioactive metabolites generated during fermentation and their potential health effects are summarized in Table 2.

**Table 2.** Bioactive compounds produced during fermentation and their potential health effects

Bioactive compound	Producing microorganisms	Source fermented foods	Physiological effects
Short-chain Fatty acids	<i>Lactiplantibacillus</i> , <i>Lactocaseibacillus</i> , <i>Bifidobacterium</i> , <i>Propionibacterium</i>	fermented dairy, vegetables	energy source for colonocytes, anti-inflammatory effects
Bioactive peptides	<i>Lactococcus</i> , <i>Lactiplantibacillus</i> , <i>Lactocaseibacillus</i> , <i>Propionibacterium</i>	fermented milk products	antihypertensive, antioxidant effects
Exopolysaccharides	<i>Lactiplantibacillus</i> , <i>Leuconostoc</i> , <i>Bifidobacterium</i> , <i>Pediococcus</i>	yogurt, kefir	immune modulation, cholesterol reduction
Vitamins (B-group)	<i>Propionibacterium</i> , <i>Lactococcus</i> , <i>Bifidobacterium</i>	fermented dairy products	metabolic regulation
Polyphenol metabolites	<i>Lactiplantibacillus</i> , <i>Leuconostoc</i> , <i>Saccharomyces</i>	wine, fermented vegetables	antioxidant activity
Neuroactive compounds (GABA, serotonin precursors)	<i>Levilactobacillus</i> , <i>Lactiplantibacillus</i> , <i>Lactocaseibacillus</i>	fermented dairy and vegetables	modulation of the gut–brain axis
Organic acids (lactic acid, propionate)	<i>Lactiplantibacillus</i> , <i>Lactococcus</i> , <i>Propionibacterium</i>	fermented vegetables, dairy	inhibition of pathogenic microorganisms

GABA: Gama-aminobutyric acid

### Production of exopolysaccharides

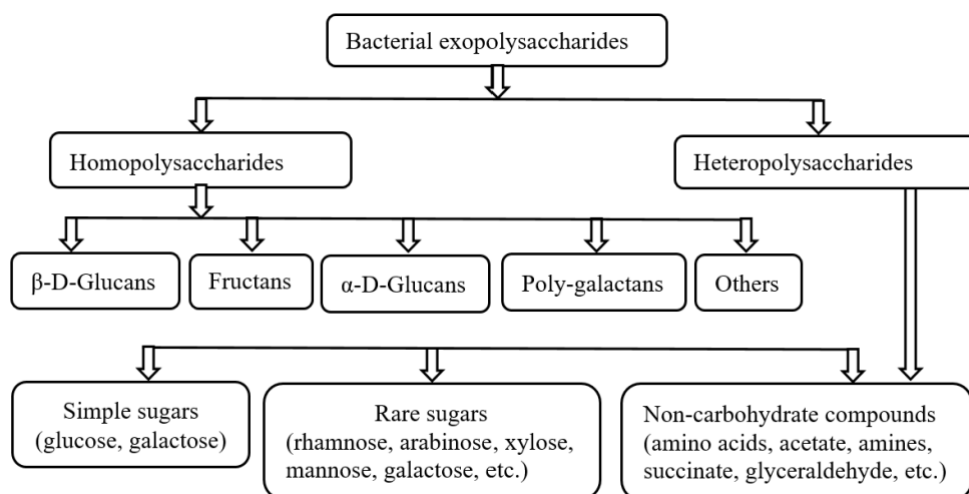
In many food fermentations, microorganisms produce high-molecular-weight exopolysaccharides (EPS) from simple sugars. Some species of *Bifidobacterium*, *Enterococcus*, *Lactobacillus*, *Leuconostoc*, *Pediococcus*, *Streptococcus*, and

*Zymomonas* produce EPS such as acetan, xanthan, and kefiran in fermented products.<sup>19</sup> Microorganisms produce EPS as a capsule or slime layer (glycocalyx) on the outer surface of the cell wall. Polysaccharides that accumulate inside the cells are known as intracellular polysaccharides.

EPS produced as a slime layer adheres less to cells and can be easily detached. Microorganisms synthesize EPS during the late logarithmic, logarithmic, and stationary phases, with maximum production occurring during the late logarithmic phase.<sup>19</sup> The EPS secreted by microorganisms differ in their monosaccharide composition and the presence of repeating side chains. EPS can generally be classified as homopolysaccharides (HoPs) and heteropolysaccharides (HePs). The general classification of EPS is shown in Figure 1. HoPs can be branched or unbranched and are composed of glucose or fructose. HoPs include  $\alpha$ -D-glucans (dextran, mutan, alternan, and reuteran),  $\beta$ -D-glucans, fructans (levan and inulin), poligalactans, gellan, xanthan, and kefiran. HePs are composed of sugars such as D-glucose, D-galactose, L-rhamnose, mannose, arabinose, and fructose. In some cases, N-acetylglucosamine, N-acetylgalactosamine, or glucuronic acid can also be found in the EPS structure. HoPs have a molecular weight greater than 106 Da (daltons), while HePs have a molecular weight between 104 and 106Da.<sup>12</sup>

Depending on various factors, EPS has stimulatory or suppressive roles on the immune system.  $\beta$ -glucans produced by *Pediococcus* in fermented products can lower serum cholesterol levels due to their ability to bind cholesterol,

providing cardiovascular health benefits.<sup>10</sup> In the intestines, EPS binds bile, part of cholesterol, to bacterial cell walls, reducing bile absorption. Decreased bile intake leads to the breakdown of serum cholesterol for synthesis in the liver, lowering serum cholesterol levels. When  $\beta$ -glucan-producing *Lactobacillus paracasei* was given to mice with a fermented product, a significant decrease in serum cholesterol levels compared to control mice was observed.<sup>23</sup> EPS-producing *Pediococcus damnosus*, when given to mice with fermented oats, caused a substantial decrease in total cholesterol levels.<sup>24</sup> EPS produced by *Bifidobacterium* also reduced cholesterol levels in diet-induced obese mice.<sup>25</sup> EPS produced by *Lactobacillus acidophilus*, *Lactobacillus gasseri*, *L. plantarum*, and *Lactocaseibacillus rhamnosus* have been found to possess antioxidant and antitumor activities.<sup>12</sup> EPS produced by *L. plantarum* have been reported to exhibit anti-diabetic activity by inhibiting  $\alpha$ -glucosidase and  $\alpha$ -amylase enzymes.<sup>12</sup> EPS obtained from a fermentation medium performed by a species of *Lactobacillus* has been shown to have dermal wound healing properties in mice.<sup>26</sup> EPS produced by *L. plantarum*, *Leuconostoc citreum*, *Lactobacillus johnsonii*, and *Bifidobacterium* species have been found to stimulate innate immunity.<sup>1</sup>



**Figure 1.** Classification of exopolysaccharides that bacteria can produce (Modified from Angelin and Kavitha (2020))

### Increase in the phenolic compound content

During fermentation, microbial populations enhance the bioavailability of polyphenols and increase the amount of flavonoids in fermented products. Flavonoids and phenolic acids comprise most dietary polyphenols and positively affect the gut microbiota due to their antioxidant properties. It has been reported that a mixture of eight legumes commonly consumed in China showed an increase in soluble phenolic compounds after 48 hours of fermentation with lactobacilli.<sup>29</sup> In plant and vegetable fermentations, the glycosyl hydrolases, esterases, decarboxylases, and phenolic acid reductases produced by LABs convert phenolic compounds, particularly flavonoids, into biologically active metabolites. These metabolites then react with anthocyanidins, transforming into antioxidants (pyranoanthocyanidins or 3-deoxypranoanthocyanidins). These antioxidants activate nuclear factor erythroid-related factor 2 (Nrf2), the primary regulator of mammal oxidative stress responses, providing antioxidant and detoxifying effects against oxidative and chemical damage. Consumption of fermented products reduces the severity of viral symptoms such as those from COVID-19 through the activation of the Nrf2 cellular oxidative stress response. During fermentation, the polyphenol content in red wine increases.<sup>30</sup> Red wine

polyphenols have been reported to reduce total cholesterol and blood pressure significantly.<sup>10</sup>

### Potential of Fermented Products to Affect Gut Microbiota

Fermented products can modulate the gut microbiota. In a study where participants consumed yogurt, kefir, fermented cheese, fermented vegetables, vegetable brine, and kombucha for seventeen weeks, an increase in microorganisms associated with fermented products (such as *L. acidophilus*, *Levilactobacillus brevis*, *Lactobacillus kefirianofaciens*, *Lactobacillus parabuchneri*, *L. helveticus*, and *L. sakei*) was observed compared to those who did not consume fermented products. At the same time, a decrease in microorganisms that are not associated with fermented products (such as *Streptococcus dysgalactiae*, *Prevotella melaninogenica*, *Enorma massiliensis*, *Prevotella multififormis*, *Enterococcus cecorum*, and *Bacteroides paurosaccharolyticus*) was noted.<sup>10</sup> Additionally, microbial metabolites such as short-chain fatty acids, isobutyric acid, isovaleric acid, and valeric acid were elevated in those consuming fermented products. Consumption of fermented dairy products has been shown to increase short-chain fatty acids (primarily butyrate) in the gut, reduce *Bilophila wadsworthia* in patients with IBS, and increase the number of Clostridiales species.<sup>10,31</sup> In another

study, IBS patients observed a significant increase in Lactobacillaceae density in feces after one month of kefir consumption.<sup>10</sup> In mice with the colorectal cancer, when milk and kefir were given separately, kefir resulted in enhanced colonization of probiotic bacteria and a reduction in pathogenic bacteria. On the other hand, milk consumption led to dysbiosis in the gut microbiota, as well as a decrease in the Firmicutes/Bacteroidetes and Ascomycota/Basidiomycota ratios.<sup>31</sup> Individuals infected with *Helicobacter pylori* tend to have fewer *Bifidobacterium* in their feces than healthy individuals; this reduction can be partially corrected by consuming probiotic yogurt.<sup>32</sup> Healthy individuals consuming yogurt for 42 days experienced an increase in the number and diversity of microorganisms in their gut microbiota, though the extent of changes varied among individuals.<sup>33</sup> In another study comparing the gut microbiota composition of individuals who consumed yogurt with those who did not, it was found that yogurt consumers had an increase in *Streptococcus*, *Ruminococcaceae*, *Christensenellaceae*, and *Lachnospiraceae* species.<sup>34</sup> After four weeks of consuming Camembert cheese, healthy individuals showed a significant increase in *Enterococcus faecalis* in their stool samples, while no *L. lactis* or *Leuconostoc mesenteroides* were detected.<sup>35</sup> Similarly, a study on healthy individuals consuming symbiotic fermented dairy products (such as yogurt) found an increase in Bacteroidetes (especially Bacteroidaceae and Prevotellaceae) and a decrease in Firmicutes (particularly Ruminococcaceae and Lachnospiraceae), with this effect reversing when fermented dairy consumption ceased.<sup>36</sup> Although fermented dairy products typically contain high load of Firmicutes, a decrease or absence of this phylum in some cases is noteworthy, suggesting a variable and complex relationship between fermented products and the gut microbiota. Therefore, monitoring the effects when incorporating fermented products or probiotics into the diet is essential. The effects of fresh and fermented kimchi on the gut microbiota of obese patients have been investigated; both types of kimchi caused variability in microbial populations, with an increase in Proteobacteria and Actinobacteria during consumption.<sup>37</sup> In patients with IBS, after consuming pasteurized and unpasteurized sauerkraut, significant improvements in symptoms and a decrease in gut microbiota composition (especially in Clostridiales) were observed. However, those who consumed unpasteurized sauerkraut had a higher number of lactic acid bacteria (*L. plantarum* and *L. brevis*).<sup>38</sup> Consumption of fermented soy milk resulted in a significant increase in the numbers of bifidobacteria and lactobacilli in stool populations, along with a decrease in Clostridiales.<sup>10</sup> This effect is thought to be due to ability of bifidobacteria to ferment oligosaccharides in soy. After administering the green tea fermented with *Aspergillus luchuensis* to mice, a significant increase in the butyrate-producing Clostridium XI and XIVa clusters was observed.<sup>10</sup> Following three weeks of coffee consumption, healthy individuals showed increased *Bifidobacterium* numbers in their stools.<sup>39</sup> In hypercholesterolemic patients, consumption of fermented plant extract led to an increase in *Bifidobacterium* and *Lactobacillus* numbers, while *E. coli* and *Clostridium perfringens* numbers decreased.<sup>40</sup> Consumption of raspberry juice fermented with *Lacticaseibacillus casei* enhanced the gut microbiota.<sup>10</sup> After consuming fermented fruit juice, significant increases in *Lactobacillus*, *Akkermansia*, and butyrate-producing bacteria were observed, while Bacteroides and *Ruminococcus* numbers decreased.<sup>41</sup> Unpasteurized sauerkraut, kimchi, kefir,

fermented sausages, yogurt, cheese, kombucha, and miso are fermented products that contain high numbers of live microorganisms (ranging from 10<sup>2</sup> to 10<sup>9</sup> cells per gram or milliliter). Most of these microorganisms remain alive as they pass through the digestive system. The daily consumption of fermented products containing "live" microorganisms allows for the temporary addition of new organisms to the gut microbiota.<sup>2</sup> Such microbial exposures are necessary for the normal development and activity of the immune and nervous systems. Microorganisms associated with fermentation can positively change the composition and functions of the microbiota in the gastrointestinal system.

Polyphenols in fermented products directly affect the gut microbiota. Some gut bacteria, such as lactobacilli, can use polyphenols as a nutrient substrate. Therefore, polyphenols increase the activity and proliferation of beneficial GI bacteria (such as commensal gut bacteria, lactobacilli, and bifidobacteria). Polyphenols from tea and red wine increase microbial diversity in the gut, lowering total cholesterol and blood pressure. In healthy individuals consuming a glass of wine daily, *Eubacterium rectale* became dominant during consumption.<sup>42</sup> Red wine polyphenols increased the numbers of *Bifidobacterium*, *Lactobacillus*, *Prevotella*, and butyrate-producing *Faecalibacterium prausnitzii* and *Roseburia*, while reducing the numbers of Gram-negative bacteria such as *E. coli* and *Enterobacter cloacae* that produce lipopolysaccharides (LPS).<sup>43</sup> Polyphenols from red wine, such as quercetin and resveratrol, have been found to increase the Firmicutes/Bacteroidetes ratio in the intestines of mice fed a high-fat diet, helping treat gut dysbiosis. Polyphenols inhibit pathogenic bacterial virulence factors, such as neutralizing gastric acid and inhibiting *H. pylori* urease. Some enzymes in the microbiota (such as esterases and demethylases) affect the bioavailability of polyphenols, converting them into forms that can be absorbed through the intestinal wall.<sup>10</sup> Polyphenols regulate the activities of beneficial bacteria by preventing pathogenic bacteria's growth. The consumption of fermented products rich in polyphenols has the potential to influence gut bacteria positively. The gut microbiota uses starch to produce acetate, which increases acidification and prevents the growth of bacteria that are less tolerant to acid. Acetate regulates the gut microbiota and may help reversing the gut dysbiosis to some extent. SCFAs, including acetate, butyrate, and propionate, increase mucus production in the colon and regulate pH, helping to maintain gut microbiota health. SCFAs stimulate host epithelial cells to produce mucus (primarily containing mucin proteins), which coats the intestinal epithelium and forms the thickest mucosal layer in the colon. Most of the gut microbiota resides on the mucosal surface, enabling bacterial adhesion and providing an energy source for the microbiota. Vinegar, which contains high amounts of acetate, can also affect the gut microbiota.<sup>44</sup> The microbiota of fermented products can survive gastric transit. In one study, *L. plantarum* isolated from cheese was exposed to gastric conditions (pH 2.2 and pepsin) for 90 minutes, followed by 150 minutes in synthetic duodenal fluid (pH 8.0, pancreatin and bile). The bacteria resisted digestive stresses during gastric transit and tolerated the bile.<sup>45</sup> *L. plantarum*, *L. brevis*, *L. mesenteroides* subsp. *mesenteroides*, and *L. mesenteroides* subsp. *dextranicum*, responsible for sauerkraut fermentation, has been shown to survive in gastrointestinal conditions containing low pH, bile salts, and digestive enzymes.<sup>10,11</sup> Consumption of 10-15 fermented olives coated with *L. paracasei* (10<sup>9</sup>-10<sup>10</sup> colony-forming units/olive) resulted in the isolation of a high number of this bacterium in

the stools of the consumers. *Lactobacillus* species were not found in stool samples before consuming the olives.<sup>46</sup> In this study, the ability of *L. plantarum* isolated from fermented products from vegetables, meat, and milk to survive in the gut depended on the strain type. It was also reported that strains from gut or fermented products performed better under digestive stresses than other bacteria, with higher survival rates in the digestive system. *L. casei* strains isolated from fermented dairy products survived in low pH (1.0, 2.0 and 3.0) and high bile concentrations.<sup>10</sup> Probiotic strains such as *L. rhamnosus*, *Propionibacterium freudenreichii* subsp. *shermanii*, and *Bifidobacterium animalis* subsp. *lactis* in capsules, when consumed with yogurt or low-fat cheese, showed more remarkable survival of *P. freudenreichii* and *B. animalis* strains with yogurt consumption.<sup>10</sup> *L. paracasei* and *L. rhamnosus* strains survived in a simulated gastric digestion model, but when consumed with cheddar cheese and fermented milk, they maintained higher viability in the intestines.<sup>8</sup> It was noted that the probiotic *L. reuteri* strain, when consumed with a fermented vegetable/fruit mixture, was protected by the mixture from stress caused by the small intestine, and *L. reuteri* survived.<sup>7</sup> Fermented vegetable/fruit drinks may appeal to vegetarian consumers and those with lactose intolerance. Fermented products can be used as carriers for high numbers of probiotic bacteria, which may positively affect gut microbiota and health. Research has shown that certain fermented product matrices may be more suitable for carrying specific probiotics than others.

When a high animal-protein diet is consumed, *Bacteroides*, which aids in protein digestion and has high bile tolerance, is more abundant in the gut, while *Prevotella* is more prevalent in high-sugar diets.<sup>47</sup> The fermentation of proteins by the gut microbiota can produce substances that cause discomforts such as toxicity, carcinogenesis, and immune disorders. In a study, individuals on an animal-based diet for five days, followed by the consumption of yogurt containing *Bifidobacterium longum*, showed a decrease in the number of *Bilophila*, *Odoribacter*, *Dorea*, and *Ruminococcus*, with metabolic disorders observed, and a reduction in *Bifidobacterium* numbers. On the other hand, when yogurt with added *Bifidobacterium* was consumed, the number of harmful bacteria in the gut microbiota decreased, and the gut microbiota was balanced.<sup>48</sup> It was stated that, due to *Bifidobacterium* producing hydrolase enzymes that hydrolyze bile, the proliferation of *Bilophila* and *Odoribacter* was limited. After seven weeks of consuming yogurt containing *B. animalis* subsp. *lactis*, *L. delbrueckii* subsp. *bulgaricus*, *L. lactis* subsp. *cremoris*, and *Streptococcus thermophilus*, the numbers of *Lactobacillus*, *Bifidobacterium*, *Lactococcus*, and *Streptococcus* strains increased in stools. However, these bacteria could not be detected after discontinuing the yogurt consumption.<sup>49</sup> This study showed that during fermented product consumption, the digestive system is exposed to the microbiota of fermented products, and the interaction with the gut microbiota can be either temporary or longer-term. Research indicates that the microbiota of fermented products can survive gastric transit. It has been pointed out that fermented products can alter gut microbiota populations, but there are often uncertainties about how these changes occur. Although studies have been conducted on various fermented products, comparisons of results are difficult due to varying parameters such as microorganism numbers and diversity in both healthy and patient models. Nevertheless, it was shown that the nutrients and microbiota in fermented products can affect gut microbiota. Recent studies have further highlighted the role

of fermented foods in shaping gut microbiota composition. For example, kefir and other fermented dairy products have been reported to modulate gut microbial diversity and promote intestinal health.<sup>50,51</sup> Similarly, traditional fermented foods such as tarhana harbor complex microbial communities dominated by lactic acid bacteria and may exert functional and prebiotic effects.<sup>52-54</sup> Further in-depth and descriptive human nutrition studies are needed to provide objective evidence of whether fermented products can change human gut microbiota. The effects on gut microbiota at the genus and species levels, as well as using advanced and sensitive tools for investigating fermented products and human gut microbiota, should be examined in artificial gut studies.

## Conclusion

Fermented products play a significant role in human life. While the primary function of fermented products is to extend the shelf life of seasonal foods, their associated health benefits are also considerably high. Complex organic compounds are partially hydrolyzed during fermentation, making them easier to digest, and fermented products become enriched with vitamins, antioxidants, and other compounds. The gut microbiota affects both physical and mental health. Many metabolic disorders are associated with disturbances in the gut microbiota. As lifestyle, including diet, influences the gut microbiome, fermented products should be positively modulated. Fermented products provide benefits to human health by performing one or more of the following functions as a result of the fermentation process: (i) increasing the nutritional value of the product with metabolites, including bioactive compounds, (ii) providing nutrients that support the proliferation of gut microbiota, (iii) the microorganisms provided by fermented products can survive gastric transit and become a component of the gut microbiota, even if temporarily, (iv) the microbiota in fermented products can inhibit harmful microorganisms in the gut by competing with them, (v) the microbiota in fermented products can inhibit the existing members of the gut microbiota by competing with them, or (vi) increasing the bioavailability of raw materials. Many fermented products contain microorganisms that are either added during production or can be found incidentally. The microbiota provided by fermented products can positively affect the gut microbiota by residing in the gut and/or interacting with the resident gut microbiota. Fermented products can serve as vehicles for safely delivering beneficial microorganisms, especially probiotics, to the gut. This review has provided information that clarifies the importance and potential necessity of specific fermented products in the human diet.

The possibility that fermented products may influence the gut microbiota is significant, and more clinical research should be conducted on this. The terms microbiota and nutrition are inseparable. Probiotics, prebiotics, and fiber-rich foods should be consumed to maintain a balanced microbiota. Fiber-rich fermented products that can provide prebiotics (fermented grains, fruits, and vegetables) should be included in the diet. Fibrous fermented products like kefir, pickles, and tarhana can provide significant prebiotics. If fermented products are insufficient in the diet, supplementing with probiotic products may be beneficial. A proper probiotic consumption results in a digestive system which is not only inhospitable to harmful bacteria, but also conducive to beneficial bacteria and selection of suitable fermented products and probiotics for an individual must be made with guidance of a dietitian.

### Conflict of Interest

There are no disclosed conflicts of interest for the author.

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