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Ethnic foods: impact of probiotics on human health and disease treatment

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Abstract

The human gut is inhabited by approximately 100 trillion of microflora, and there exists a reciprocal relationship between human health and the gut microbiota. The major reasons for the dysbiosis in the population of gut microbiota are attributed to changes in lifestyle, medication, and the intake of junk foods. In addition, the proportion of beneficial bacteria in the intestine decreases gradually with age and causes physiological disturbances, malfunctions of the immune system, and several metabolic disorders. Thus, finding safe solutions to improve the diversity of microflora is a big challenge. With an increase in health consciousness among the population, the demand for healthy and nutraceutical food products is growing gradually. Recent research has proved that consumption of probiotics promotes gut health and prevents from several metabolic and other diseases. Hence, in this present review, we will discuss the various probiotic bacteria present in ethnic foods. The importance of these probiotics in the prevention and treatment of gastrointestinal, respiratory, cancer, and metabolic disorders will be elucidated. In addition, we will highlight the importance of the development of new-generation probiotics to cater the needs of the current market.

Keywords Dysbiosis, Disorders, Ethnic food, Gut, Microbiota, Probiotics

Introduction

Ethnic foods have been major part of human diet for centuries. They exhibit unique functional, nutritional, sensory, and organoleptic properties that confer beneficial effects on host health [1–3]. The shelf-life of ethnic foods is reported to be quite longer than the raw foods such as meat, milk, and plants-derived products [4–6]. In the past, ethnic foods were developed without scientific

knowledge. The ethnic or fermented foods produced by plants or animal sources play a vital role in maintaining health and preventing diseases by producing organic acids, ethanol, or antimicrobial compounds to control the progress of harmful bacteria and prevent the spoilage of food products [7-10]. However, in recent times food scientists have probed the significance of probiotic bacteria for the development of several ethnic foods and beverages to meet consumer needs [11-13]. Probiotics are live microbes that when administered confer beneficial effects on host health and hold "generally recognized as safe status." Some of the probiotic bacteria include lactic acid bacteria (LAB, Lactobacillus (Lb.), Leuconostoc (Leu.)), Enterococcus (E.), and Bifidobacterium (B.) species, respectively [13-15]. Recent technological intervention has led to the industries for the commercial production and development of ethnic foods enriched with probiotic bacteria (10⁶–10⁷ colony forming units (CFU/mL)[16-18].

It was reported that probiotic bacteria utilize sugars present in food and produce organic acids (formic, lactic,

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acetic, propionic, and butyric acid), alcohol, bacteriocins, peptides, hydrogen peroxide, diacetyl, and carbon dioxide [19–21]. Thus, enhancing the mean life of ethnic food products by preventing the growth of pathogenic bacteria in the fermented foods [22, 23]. Probiotics adhere temporarily to the gut epithelial cells and cannot colonize for a longer period in the gastrointestinal (GI) tract because of the slow generation time in the intestine [24]. In this regard, ethnic foods are recommended daily to maintain the population of beneficial bacteria in the gut.

Among all the emerging foods available on the market nutritional, healthy, and functional foods are the only ones with proven health benefits. With the increase in health consciousness among the population across the world, there is a significant rise in foods which provide nutritional benefits, which are increasing tremendously. Any food to be classified as functional food must include either probiotic, prebiotic, dietary supplements, antioxidants or vitamins [25]. Probiotic-based functional foods and drinks are regarded as future foods with wide acceptance among consumers [26]. The international market for probiotic-based ethnic foods has doubled from 2017 to 2024 (i.e., from 42.55 billion USD to 94.48 billion USD) [27].

The byproducts produced by probiotic bacteria as a result of fermentation help in preventing and treating several intestinal diseases, such as irritable bowel syndrome, lactose intolerance, antibiotic resistance diarrhea, *Helicobacter pylori* (HP) infection, and inflammatory bowel syndrome, respectively [14, 28]. In addition to the above, ethnic foods are ready to eat and can be produced industrially by fermentation [29]. Thus, the ethnic fermented foods comprising active probiotic microorganisms are recommended by dieticians and medical practitioners to maintain good health [30]. The present review highlights the various ethnic and modern probiotic food products that are produced across the world, with special emphasis on their probiotic and functional attributes.

Differences between probiotics and fermented foods

Probiotics are specific microbes that confer beneficial effects on host health and wellbeing. Fermented food results from the transformation of sugars into organic acids by microbial processes. This process is still in practice to preserve the spoilage of food and agricultural products from contamination and help in long-term storage [14]. Not all fermented foods contain probiotic bacteria, and not all probiotics are fermented [31]. Usually, fermented foods contain beneficial bacteria or may be enriched with nutrients that confer beneficial effects on host health. It is difficult to say which bacteria are

present in fermented food. Probiotics contain known microbial species with proven health benefits. Specific bacterial strains may be employed during the process of fermentation, but the same species may get inactivated during the final stage of processing. In order to confer a fermented product as probiotic, there must be a live beneficial bacterium during its consumption. In addition to the above, the fermented product should not be contaminated with any pathogens. The quantity of fermented product is required to confer the health benefit [32]. Some fermented foods, such as sourdough and pickles, are processed in such a way that there will be no beneficial bacteria; however, other fermented products, such as kimchi, kombucha, yogurt, and yakult, contain live beneficial microbes that, when consumed in adequate amount, confer a beneficial effect on the host [33].

Dairy-based probiotics

Dairy-based probiotics have captured the market significantly across the globe, with great market value [34]. Currently, the challenges associated with the development of probiotic products include strain selection, finding a cheap and economical substrate to minimize the cost of manufacture, and enhancing the viability of probiotics. In addition, the strain selected for industrial scale must be able to produce metabolites that can confer beneficial effects on host health [35]. Hence, there is a great need to devise new molecular screening strategies to identify potent probiotic strains and blend them with dietary fibers to enhance their health-promoting properties. Lactic acid bacteria are the predominant probiotic bacteria reported in dairy-based probiotic products, because they enhance the shelf-life, and promote antimicrobial properties against pathogens, thus improving human health [36]. Some dairy-based probiotic products include ricotta cheese made of B. animalis subsp. lactis, and Lb. acidophilus, ($\geq 6 \log \text{CFU/g}$), yogurt made of B. animalis subsp. lactis, Lb. acidophilus (≥6 log CFU/g), cheddar cheese made of Lb. lactis subsp. lactis, Lb. helvetica, and Lacticaseibacillus (formally known as Lactobacillus) rhamnosus (≥8 log CFU/g) [35]. Probiotic ice-cream made of Lb. acidophilus and B. animalis subsp. lactis (≥ 6 log CFU/g) has been reported to enhance adhesion ability under the in vitro condition [36]. The addition of inulin to sheep milk ice-cream has promoted the survival of probiotic microbes by increasing the interaction between dietary fiber without affecting their physicochemical or sensory properties [37]. Chocolates made of milk or soymilk were reported to be effective for the delivery of probiotic bacteria such as Lb. acidophilus, Lacticaseibacillus paracasei, and B. animalis subsp. lactis [38].

Non-dairy-based probiotics

Non-dairy-based probiotic products include beverages made of fruits, which include pine apple juice comprising *Lb. acidophilus*, *Lactiplantibacillus* (formally known as *Lactobacillus*) *plantarum*, and *Lb. lactis* ($\geq 9-10$ log CFU/mL), and orange juice composed of *Pediococcus acidilactici* ($\geq 7-8$ log CFU/mL) [39], while pomegranate and Cornelian cherry juice comprised *Lactiplantibacillus plantarum* (≥ 9 log CFU/mL) [40]. Vegetable-blended beverages include beet, melon, and carrot, comprised *Lactiplantibacillus plantarum* CICC22696, and *Lb. acidophilus* CICC 20710 ($\geq 8-9$ log CFU/mL) [41, 42].

Fruits and vegetables-based non-dairy probiotic products

Fruits and vegetables are considered healthy as they are rich sources of anti-oxidants, polyphenols, phytochemicals, vitamins, sugars, and dietary fibers with taste and flavor [43]. Fruits and vegetables lack allergens like lactose and cholesterol, which adversely affect the health of the host. They serve as a perfect matrix for the growth of probiotic bacteria. In addition, the pH of the stomach is extremely acidic, which enhances the viability of probiotic bacteria. The predominant probiotics used in developing non-diary-based drinks include Lb. acidophilus, Lb. delbrueckii, Lacticaseibacillus casei, Lacticaseibacillus (formally known as Lactobacillus) paracasei, Lacticaseibacillus rhamnosus GG, Lactiplantibacillus plantarum, and B. bifidum species. The most commonly used fruits include apple, pineapple, cashew apple, cherry, grapes, guava, mango, orange, strawberry, sweet lime, etc., while carrot, beetroot, tomato, and cabbage are examples of vegetables [44].

The stability and viability of probiotic bacteria in fruit juice greatly depend on pH (organic acids), sugars, water activity, percentage of oxygen, the presence of antimicrobial compounds, preservatives, and other chemicals used in growing them. In addition to the above, the fruit juice processing steps include pasteurization, storage temperature, and packaging material. *Lactobacillus* species can survive up to pH 3.7 [43]. Non-diary-based probiotic health drinks can be developed either by the direct addition of probiotic strains or by the fermentation of juice with probiotics. The viability of probiotic bacteria was found to be 10^5 to 10^8 CFU/mL, after 4–12 weeks when stored at 4 °C [44].

Cereal-based non-dairy probiotic products

Cereals are considered staple foods across the world as they are rich in vitamins, minerals, carbohydrates, proteins, and fibers [45]. Fermentation of cereals has been widely reported across Asia and Africa to produce a wide variety of beverages and porridge. The most commonly used cereals are maize, sorghum, millets, oats, barley, wheat, and rye [46]. The most popular cereal-based fermented beverages include Boza (Bulgaria, Turkey, and Romania), Bushera (Uganda), Mahewu (South Africa), and Togwa (China and Japan) [47]. Boza is produced by the fermentation of cereals such as wheat, rye, or maize blended with sugar. Bushera is made by mixing sorghum or millet flour [46]. Mahewu is made from a multi-grain mix comprising maize, sorghum, malt, and wheat flour [47], while Togwa is produced by mixing maize, sorghum, and finger millet flour with probiotic bacteria [47]. All the cereal-based fermented drinks are rich in LAB and yeast species such as Lb. plantarum, Lactiplantibacillus acidophilus, Limosilactobacillus fermentum (formally known as Lactobacillus), Levilactobacillus (formally known as Lactobacillus) brevis, Lactococcus lactis subsp. lactis, Leu. mesenteroides, Enterococcus, Streptococcus, Saccharomyces cerevisiae, Candida tropicalis, Geotrichum penicillatum, and Geotrichum candidum [48]. All the cereal-based fermented drinks displayed good cell viability, ranging from 10⁶ -10⁸ CFU/mL. Maize porridge prepared by mixing maize flour with barley malt and fermented with probiotic strains such as *Limosilactobacillus* (formally known as Lactobacillus) reuteri, Lb. acidophilus, and Lacticaseibacillus rhamnosus GG displayed cell viability of 10^7 – 10^8 CFU/g after fermentation for 12 h at 37 °C [49].

Probiotic microbes present in ethnic fermented foods

Traditional ethnic fermented foods are broadly classified into fermented and non-fermented foods. Fermented foods are categorized as vegetables, cereals, meat, milk, legumes, and other fermented foods, while non-fermented foods are not explored yet. The most common microbes that are involved in the fermentation of ethnic foods belong to the genera *Lactobacillus*, *Leuconostoc*, *Lactococcus*, *Pediococcus*, *Enterococcus*, *Weissella*, *Bifidobacterium*, *Saccharomyces*, and *Streptococcus*. The above genera belong to LAB and are widely considered for the production of ethnic fermented foods [50]. Some of the most common ethnic fermented foods, along with their microbial distribution, are mentioned in Table 1.

Functional attributes of probiotic *bacteria* present in ethnic fermented foods

Probiotic bacteria present in ethnic fermented foods have been reported to regulate cancer, cardiovascular disease, inflammation, allergies, and other metabolic disorders, as mentioned in Table 2 [51]. The biological activity of probiotics is attributed to the release of end products resulting from fermentation, including organic

 Table 1
 Probiotic microbes reported in ethnic fermented foods

| Category | Ethnic fermented foods | Probiotic microbes | References |
|---------------------------------|--|---|-----------------|
| Cereal-based | Boza, Uji, Fura, Ricera, Ogi, Oat-based, Malt-based drink, | Limosilactobacillus fermentum, Limosilactobacillus reuteri, Lb. salivarius, Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Lb. pentosus, Lacticaseibacillus paracasei, Limosilactobacillus reuteri, Limosilactobacillus fermentum, Pediococcus acidilactici, P. pentosaceus, Weissella confusa, Limosilactobacillus reuteri, Streptococcus thermophilus, Streptococcus faecalis, Lb. delbrueckii, Levilactobacillus brevis, Leu. mesenteroides, E. faecalis, Lactococcus lactis, Lacticaseibacillus casei | [24, 45–49] |
| Fruits and Vegetables- based | Aubergine Makdoos, Kimchi, Kanji, Sauerkraut, Tempoyak, Ngari, Jiang-gua, Kitoza, Green pepper Makdoos, Mesu, Pickled green or Black olives, Vine leaves, Turkish Tarhana, Shatta | Lb. acidophilus, Lactiplantibacillus plantarum, Lacticaseibacillus rhamnosus, Levlactobacillus brevis, Weissella cibaria, Weissella paramesenteroides, P. acidilactici, P. pentosaceus, Saccharomyces cerevisiae, Lacticaseibacillus casei, Latilactobacillus sakei, Limosilactobacillus fermentum, Leu. mesenteroides, E. faecalis, Lactococcus lactis, Lacticaseibacillus casei, Staphylococcus cohnii, Staphylococcus carnosus, Staphylococcus xylosus | [24, 27, 43–45] |
| Dairy-based | Jameed, Tarhana, Keshik, Probiotic milk, Yogurt, Amasi, Doogh, Kafir, Shrikhand, Dahi, Khadi | Lb. delbrueckii, Lacticaseibacillus casei, Lacticaseibacillus paracasei, Lactiplantibacillus plantarum, Lb. acidophilus, Lb. kefir, Lacticaseibacillus paracasei, Lb. species, Weissella cibaria, P. pentosaceus, Streptococcus thermophilus, B. lactis, B. longum, E. faecium, Lactococcus lactis, Leu. pseudomesenteroides | [24, 27, 30] |
| Meat-based | Lang Satchu, Yak satchu, Arjia | Lacticaseibacillus casei, Lb. carnis, P. pentosaceus, E. faecium, Lb. species | [29] |
| Legume-based | Wadi, Kinema, Tungrymbai | Leu. mesenteroides, Limosilactobacillus fermentum, E. faecium | [28] |

Table 2 Functional attributes of probiotics present in ethnic fermented foods

| Probiotic strains | Function | Reference |
|--|--|--------------|
| B. animalis BB12, Saccharomyces cerevisiae Lyo | Prevention and treatment of diarrhea | [85, 86] |
| B. longum, Lb. acidophilus, Lb. casei subsp. rhamnosus, and Lb. helveticus | Boost immune response by producing lymphocytes, interleukin 1, 2 and 6, tumor necrosis factor, prostaglandin, γ -interferon, and serum proteins | [57–60] |
| B. infantis 35624 | Reduce abdominal pain | [93, 95, 96] |
| Lacticaseibacillus rhamnosus GG | Prevent the adhesion of pathogens to the intestine | [59] |
| Lb. acidophilus La5 | Inhibits Helicobacter pylori infection | [80, 81] |
| Lb. acidophilus | Decrease the chemically induced colon tumors | [57] |
| Lacticaseibacillus paracasei LP-33 | Reduce allergic rhinitis | [115] |
| Limosilactobacillus reuteri ATCC 55730 | Produce CD+4 T-Lymphocytes | [60] |
| Lb. acidophilus, Lb. buchneri P2, and B. longum BL1 | Reduce serum cholesterol | [62] |
| Escherichia coli Nissle 1917 | Used in treatment of colitis | [95, 96] |
| Lactiplantibacillus plantarum LP31 | Regulates the growth of food pathogens | [70-72] |
| B. longum | Promotes antitumor effect | [55] |
| <i>Lb.</i> UCC118 | Reduces colon cancer in mice | [54, 55] |
| Lb. acidophilus, Lacticaseibacillus subsp. rhamnosus, and B. bifidum | Reduce urinary tract infection | [95, 96] |
| Lb. acidophilus, Lb. bulgaricus, and Streptococcus thermophilus | Reduce lactose intolerance by producing $\beta\mbox{-galactosidase}$ involved in digestion of lactose | [116] |

acids, diacetyl, bacteriocins, CO_2 , and $\mathrm{H}_2\mathrm{O}_2$. The biological activity of probiotics greatly depends on the above factors [52]. The understanding of probiotics and their role has expanded in the last decade emphasizing their role in conferring therapeutic benefits. Thus, probiotics can be considered complementary to traditional drugbased therapy. An overview of the functional properties attributed to probiotic bacteria present in ethnic foods is mentioned in Fig. 1. The following are some of the applications of probiotics in regulating diseases along with their mechanisms.

Anticancer and anti-toxic activity

Recently, there has been a surge in people suffering from colon cancer in developed countries [53]. The major predisposing factors for the cause of cancer mutations, or abnormal expression of genes that regulate cell growth and division. Studies have shown that diet and antibiotic treatment can reduce the production of carcinogens and minimize the tumor induction process. It was predicated that traditional fermented foods rich in probiotic bacteria decrease the effect of chemical carcinogens by detoxifying the carcinogens [54]. Sometimes it will minimize the bacterial population in the intestine. Studies performed

on a mouse model clearly displayed that incorporation of *Lb. acidophilus* in the food decreased the chemically induced colon tumors [55]. It was predicted that intestinal bacteria would produce enzymes such as azoreductase, nitroreductase, β -glycosidase, and β -glucuronidase that would convert the procarcinogens to proximal carcinogens [56]. In addition to the above, the ability to neutralize the fecal mutagens can be considered an indicator to minimize the cancer-associated risk [57].

Boosting immune response

The major reason for GI tract infections is a change in gut microenvironment caused by dysbiosis in the intestinal microbiota [58]. It was reported that *Bifidobacteria* is the predominant bacteria inhabited in the large intestine, forming a barrier against pathogens by preventing their adhesion or colonization by decreasing the pH of the gut by releasing organic acids (acetic and lactic acid) [59]. Several probiotic bacteria, such as *B. longum*, *Lb. acidophilus*, *Lactobacillus casei* subsp. *rhamnosus*, and *Lb. helveticus* have been described to enhance the immune response by producing lymphocytes, interleukin 1, 2, and 6, tumor necrosis factor-alpha (TNF-α), prostaglandin, γ-interferon, and serum proteins [57, 60]. Probiotics

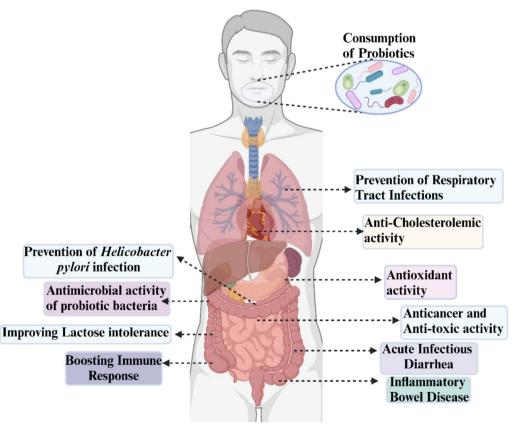


Fig. 1 Overview of the functional properties attributed by probiotic bacteria present in ethnic foods

modulate the immune response by elevating either pro or anti-inflammatory properties, thus influencing the innate and adaptive immune responses of the host [61].

Anti-cholesterolemic activity

Cholesterol is the major building block of tissue, but elevated levels of blood cholesterol are a major risk for coronary heart disease. It was reported that a diet supplemented with LAB reduces serum cholesterol levels. In vivo studies performed in pigs have demonstrated that dietary intake of *Lb. acidophilus* resistant to bile has decreased the serum cholesterol level [62]. Cholesterollowering ability was detected in people consuming fermented products containing probiotic bacteria [63, 64]. Fermented whole-grain foods were described to minimize the menace related to serum low- and high-density lipoproteins, diabetes, coronary heart disease, hypertension, obesity, and other inflammatory diseases [65].

Antioxidant activity

Humans have their own antioxidant systems which include superoxide dismutase, glutathione peroxidase, and uric acid, which defend against oxidative injury triggered by hydroxyl, superoxide, hydrogen peroxide, and peroxide radicals [66]. Fruits and vegetables are rich sources of antioxidant compounds such as vitamin C, glutathione, β -carotene, β -tocopherol, and phenolic compounds [67]. Lactic acid bacteria present in ethnic fermented foods exhibit free radical-scavenging activity [68]. Fermented foods such as tempeh, miso, or natto exhibit increased antioxidant properties [69].

Antimicrobial activity of probiotic bacteria

Probiotic bacteria such as Lactiplantibacillus plantarum KBB7-1, KO4-4, KC5-14, KBB11, Lb. delbrueckii subsp. bulgaricus KZM2-11-1, KZM 2-11-3 and Pediococcus pentosaceus KC 5-13, strongly inhibited the growth of pathogenic Gram-negative bacteria such as E. coli, Pseudomonas aeruginosa and Gram-positive bacteria such as Bacillus subtilis and Bacillus cereus [70]. In addition to the above the probiotic bacteria such as Lactiplantibacillus plantarum, Pediococcus pentosaceus, Latilactobacillus sakei were reported to prevent the development of filamentous mold's belonging to Aspergillus, Fusarium, and Penicillium species, respectively [71]. The antimicrobial property of the probiotic strains was attributed due to the release of antimicrobial agents such as lactate and acetate, which are active at low pH, in addition to the production of antimicrobial peptides by the probiotic bacterial species [72].

Prevention of Helicobacter pylori infection

Helicobacter pylori is a microaerophilic Gram-negative bacterium involved in damaging the mucosal layer of the GI tract [73]. It was reported that more than 50% of the world population is affected by this infection, with a high prevalence in developing countries rather than developed countries [74]. It causes peptic ulcers (PU) and gastric cancer (GC) if left untreated [75]. It was reported that HP infection and nuclear factor kappa-light-chain enhancer of activated B (NF-kB) cells-dependent chronic inflammation of the gastric mucosa are linked [76]. During the infection, HP antigens are released in the stomach and duodenum tract, which are identified by toll-like receptors (TLRs) present in the epithelial cell membrane, which trigger the stimulation of the NF-kB and c-Jun-Nterminal kinase (JNK) pathways, leading to the release of proinflammatory cytokines and chemokines [77]. Thus, the overproduction of CD4⁺ helper T cell (Th)-17 hyperactivation further elevates severe gastritis and enhances the chances of peptic ulcer and gastric cancer [78]. Antibiotic treatment (amoxicillin, clarithromycin, and mentronidazole) is suggested for the treatment of HP infection for two weeks. But due to its increased resistance to antibiotics, either triple or quadruple antibiotic therapy is recommended. In order to overcome the limitations and side effects associated with antibiotic treatment, novel treatment and therapeutic strategies are being considered, which include the application of probiotics [79]. It was reported that administration of Lb. acidophilus and Lb. bulgaricus has the ability to prevent the binding of HP bacteria to the gastric epithelium cells by down regulating the expression of the TLR4/NF-kB pathway and modulating the interleukin (IL)-8, cyclooxygenase 2 (Cox-2), and nitric oxide (NO)-dependent inflammatory responses, as mentioned in Fig. 2 [80, 81]. Thus, the application of probiotics as an alternate or in combination therapy with antibiotics is recommended to eradicate the HP infection.

Prevention of acute infectious diarrhea

The major reason for the acute infectious diarrhea is the infection caused by *Escherichia coli*, *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter jejuni*, *Clostridium difficile*, *Vibrio cholera* species, and other parasites such as *Giardia* or *Cryptosporidium* [82]. The above infections cause the release of enterotoxins, which trigger the activation of protein kinase, which causes a decrease in the release or absorption of GI fluids and electrolytes from the intestinal epithelial cells leading to watery stools and vomiting, depending upon the pathogen, inflammatory or non-inflammatory diarrhea [83]. Since there is no specific treatment for these infections, it is recommended

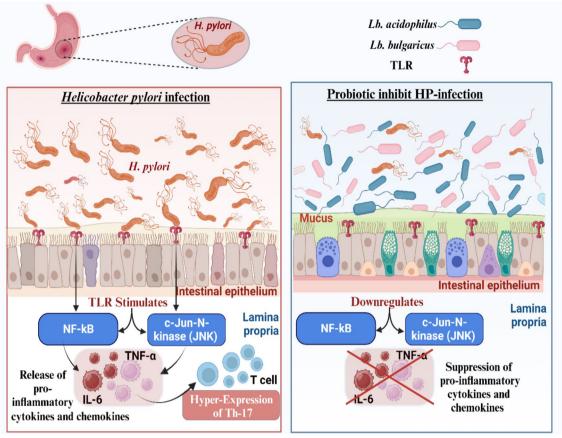


Fig. 2 Competitive binding of probiotic bacteria to the gastric epithelium cells to prevent the *Helicobacter pylori* infection and prevent the production of proinflammatory cytokines. TLR: Toll-like receptor, NF-kB: Nuclear factor kappa-light-chain enhancer of activated B cells, IL: Interleukin, TNF-α: Tumor necrotic factor-α

to give oral rehydration of salts (Na) as the first line of therapy [84]. Recent studies have shown that oral rehydration solutions should use probiotic strains such as Lb. acidophilus, Lb. bulgaricus, B. infantis, Streptococcus thermophilus, Lacticaseibacillus rhamnosus GG, Limosilactobacillus reuteri DSM 12246, and Saccharomyces boulardii with doses of Log 10¹⁰ CFU/day [85, 86]. Probiotics show direct and early effects by competing with pathogens for nutrition, binding to gut epithelial cells, neutralization toxins by producing antimicrobial peptides, and producing short-chain fatty acids, as mentioned in Fig. 3 [85]. In addition to the above, probiotics modulate oxidative stress and anti-inflammatory pathways and prevent the cytotoxic damage caused to gut epithelial cells [85]. Antibiotic treatment (metronidazole or vancomycin) is not recommended routinely due to the chances of the development of antibiotic resistance among the pathogenic microbes [86]. Hence, probiotics in combination with oral rehydration solutions are always recommended to overcome acute infectious or antibiotic-associated diarrhea.

Inflammatory bowel disease (IBD)

It is an immune-mediated disorder, and based on its severity, it is classified as ulcerative colitis, Crohn's disease, and inflammatory bowel syndrome [87]. In this condition, the mucosal immune response is aggravated by the gut microbiota due to genetic, immune, and environmental factors [88]. Patients suffering from IBD exhibit bloody stools, abdominal pain, anemia, weight loss, and diarrhea [89]. Recent clinical advancements in IBD detection have led to the development of therapeutic strategies that include antibiotics, aminosalicylates, and the use of biological immune modulators [90]. In addition to the above, vitamin D and iron levels need to be monitored regularly to overcome the problems associated with anemia [91]. The application of probiotics in the treatment of IBD was found to be effective in animal models [92]. Placebo study trails performed on patients suffering from IBD administered with tablet comprising B. infantis, Lb. acidophilus, E. faecalis, and Bacillus cereus displayed health benefits as mentioned in Fig. 4. Studies have shown that B. cereus creates an

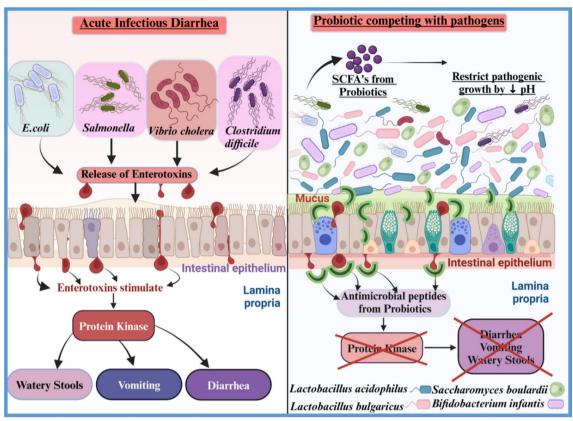


Fig. 3 Prevention of acute infectious or antibiotic resistance diarrhea by probiotic bacteria and their metabolic by products. SCFAs: Short-chain fatty acids

anaerobic environment for the growth of Bifidobacterium [93]. While the clinical studies performed on dextran sodium sulfate-induced acute colitis mouse model administered with propionic acid-producing Propionibacterium freudenreichii improved the production of mucin-2 (MUC-2) protein, which helped in restoring and enhancing the production of the goblet cells [94]. In addition to the above a cocktail mixture of probiotic bacteria comprising Lb. acidophilus, Lacticaseibacillus rhamnosus, B. bifidum, and B. lactis showed a reduction in the risk associated with the recurrence of urinary tract infection [95, 96]. Hence, there is a great need to design optimal probiotics that can overcome the above limitations. In this regard, the composition of the microbiome in patients suffering from IBD will help in identifying novel probiotic bacteria that can easily adapt and grow in the GI tract of infected patients. In addition to the above, their health benefits on the host will greatly depend on the nutritional sources, dietary or prebiotics supplements, and their dose, which are vital for promoting their long-lasting effect [97].

Prevention of respiratory tract infections (RTI)

The incidence and mortality rate caused by RTI are very high across the world [98]. It was reported that around 4 million deaths are reported every year due to RTI [99]. There are no effective vaccines reported for many respiratory pathogens, and the increase in drug resistance among the pathogenic microbes has made the treatment more challenging. Recently, many *Lactobacillus* species, such as Lacticaseibacillus rhamnosus GG, Limosilactobacillus fermentum CJI-112, Lacticaseibacillus paracasei strain Shirota, Lactiplantibacillus plantarum DK119, Lacticaseibacillus paracasei MCC1849, and Lactobacillus gasseri SBT2055 [100]. It was reported that oral supplementation with *Lactobacillus johnsonii* reduces Th2 type cytokines and lung inflammation in BALB/c mice [101]. Vaccines for Severe acute respiratory syndrome Coronavirus-2 (SARS-CoV-2) are available on the market but the rapid mutation rate of the virus makes the vaccine inefficient [102]. A low death rate was reported in Coronavirus disease 2019 (COVID-19) patients from Central Europe who consumed fermented vegetables rich in Lactobacillus species [103]. In addition, the oral administration of

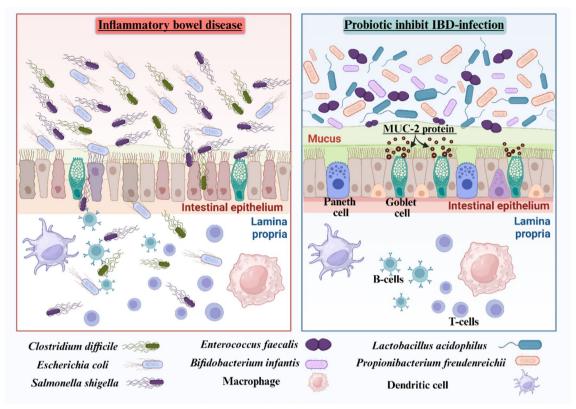


Fig. 4 Role of probiotics in stimulates the production of MUC-2 proteins which helps in development of goblet cells and inhibit the pathogen binding to gut during IBD and UTI infections. MUC-2: mucin-2, IBD: inflammatory bowel disease, UTI: urinary tract infection

probiotic bacteria has reduced the risk related of respiratory failure in COVID-19 patients by eightfold and minimized the mortality rate [104]. Several clinical studies have shown that oral supplementation with probiotics has decreased RTI infections [105].

Cystic fibrosis (CF) is an autosomal recessive disorder associated with lesions affecting predominantly the lungs and other organs of the body [106]. It was reported that patients suffering from CF have reduced diversity in their intestinal flora [107]. In clinical studies performed on patients suffering from CF, the oral supplementation of Lacticaseibacillus rhamnosus GG has reduced the symptoms in some patients [108]. The reason was attributed to the use of a single strain. Supplementation of probiotic capsules comprising multiple Lactobacillus species will be more beneficial to patients suffering from CF [109]. Immune check inhibitor drugs such as anti-PD-1/ anti-cytotoxic T lymphocyte-associated antigen-4 (CTLA4) antibodies are used as first-line treatments for lung cancer and tumors but they are associated with immune-related adverse effects when used in combination [94]. Hence, immunobiotics are recommended for the treatment of lung cancer [110]. Administration of probiotic Lacticaseibacillus rhamnosus GG inhibits the metastasis of tumor cells in the lungs in C57BL/6 mice [111]. Oral administration of Lacticaseibacillus casei YIT 9018 exhibited antitumor activity against Lewis lung carcinoma in C57BL/6 mice [112]. Thus, Lactobacillus can be considered a potent adjuvant in the treatment of lung cancer. While patients suffering from asthma have been reported to exhibit coughing, wheezing, chest tightness, and bronchial hyper-responsiveness, the reason was attributed to the imbalance of Th1/Th2 and the high level of IgE [113]. Application of inhaled corticosteroids, anti-leukotrienes, and β2 can improve the condition. But still, no specific treatment for asthma has been reported yet [114]. Numerous clinical studies have demonstrated that oral intake of probiotic *Lactobacillus* species such as Lactiplantibacillus plantarum K37, Limosilactobacillus reuteri, Lacticaseibacillus paracasei strain Shirota, Lacticaseibacillus paracasei HB89, and Lacticaseibacillus rhamnosus GG was found to be effective in ameliorating the symptoms associated with asthma [115]. The major mechanism by which the probiotic bacteria modulate the RTI is by transporting activated immune cells and cytokines (TNF-α, IL-6) from mesenteric lymph nodes, tissues, and the intestine to the lungs by circulation and promote the anti-inflammatory immune response.

While the short-chain fatty acids released by the probiotic bacteria promote hematopoiesis in bone marrow and transform macrophages and dendritic progenitor cells into Ly6C-monocytes, which reach the lung tissues and differentiate to produce anti-inflammatory activated macrophages [115]. *Lactobacillus* has proved to be a promising candidate for the treatment and prevention of RTI. Additionally, using single *Lactobacillus* species is rather ineffective in treating RTI; rather a combination of probiotics will be beneficial with better efficacy.

Improving lactose intolerance

The inability to digest lactose is prevalent worldwide. It was reported that lactose malabsorption in adults varies from 50 to 100% in Asia, Africa, and South America [59]. The reason for lactose intolerance was attributed to the lack of lactose-digesting enzyme lactase in the intestine. However, the undigested lactose will be fermented in the large intestine by the colon microbes to produce gas and cause watery stools. Individuals who are lactose intolerant can consume fermented dairy products, especially yogurt, which is rich in LAB (*Lb. acidophilus, Lb. bulgaricus*, and *Streptococcus thermophilus*), which aid

in digestion of lactose by producing β -galactosidase, as mentioned in Fig. 5 [116].

Antagonistic and enhanced shelf-life

Food products (meat, diary, fruits, and vegetables) fermented by LAB exhibit unique organoleptic properties such as aroma, flavor, and the production of organic acids which decrease the pH of preserved food [31, 58]. The probiotic strains extended the mean life of fermented foods by preventing the growth of pathogenic microorganisms by decreasing the pH, by producing organic acids, bacteriocins, and modulating the immune response [29, 117].

Application of probiotics in the food industry

With the increase in health consciousness among the population, there is exponential rise in the demand for probiotic-based products across the globe. Probiotics are one of the fastest-growing dietary supplements worldwide, and they are estimated to grow 7% annually, accounting for 64.3 billion USD by the end of 2023, and predicted to rise to 75 billion USD by 2025 [118–120]. Recently, the demand for non-dairy-based probiotics has also increased and is estimated to grow by around

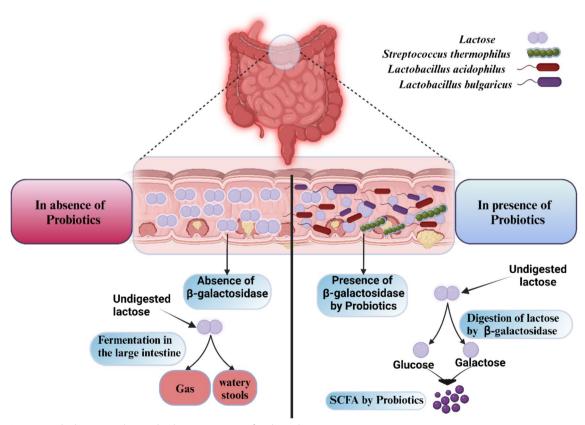


Fig. 5 Improving the lactose intolerance by the consumption of probiotic bacteria

26 billion USD by 2025 [118]. Some dairy-based products include yogurt, fermented dairy desserts, cheese, ice creams, and powdered milk. Non-dairy-based food products include fruit and vegetable juices, baby foods, cereals, and edible films [120].

Current trends in the development of probiotics

The biggest limitation for the use of probiotics in the food industry is their sensitivity to heat and processing conditions. Hence, in order to overcome the above limitation, researchers and food experts are working on innovative methods and techniques to safeguard the delivery of probiotics in the human gut [121]. One such method is the encapsulation of probiotics in edible films to promote thermal stability, viability, and shelf-life. Probiotic bacteria are subjected to encapsulation in biopolymers such as pectin, cellulose, seaweed, alginates, and chitin to enhance their viability and stability, and prevent their premature degradation [122]. The thermal stability of probiotic bacteria, for example, Lacticaseibacillus rhamnosus GG, Lb. acidophilus, and Lacticaseibacillus casei, was enhanced by encapsulating them either in sodium or calcium alginate ($\geq 7-8 \log CFU/g$) and mixing them in sour dough [123, 124].

An edible film comprising sodium carboxymethyl cellulose (CMC) and hydroxymethyl cellulose was developed by mixing Lacticaseibacillus rhamnosus with citric acid as a cross-linker [125]. Similarly, a CMC-based edible coating film was developed by mixing probiotic bacteria Lb. acidophilus, Lacticaseibacillus casei, Lacticaseibacillus rhamnosus, and B. bifidum and stored under refrigerated conditions. Of all the probiotic strains, encapsulated Lb. acidophilus exhibited more viability than other probiotic strains [126]. In addition, the straw berries coated with the above CMC edible film improved the physicochemical, antimicrobial, and shelf-life of the straw berries [127]. Similar results were reported in blueberries coated with alginate fiber comprising Lacticaseibacillus rhamnosus, which improved the freshness, shelf-life, and antimicrobial properties [128].

Safety issues associated with probiotics

There are several safety issues associated with the administration of probiotics which were reported by researchers and policymakers. Before considering a microbe to be used as a probiotic a full genome sequencing needs to be performed to assess the risks associated with that species [129]. The genome will be assessed for the presence of toxic, pathogenic, or antibiotic resistance genes to address the safety of probiotics [130, 131]. Other safety issues that should be taken into consideration during the administration of probiotics include performing microbiome profiling before and after the intake of probiotics to

understand the mechanisms and pathways that promote health, safety concerns and individuals or people who do not respond to probiotic therapy [132]. Assessing the danger associated with the horizontal gene transfer from the probiotic genome to the gut pathogens needs to be tested. Probiotic microbes associated with plasmids or mobile genetic elements associated with antibiotic resistance genes should not be commercialized. The effect of probiotics on the metabolism of drugs needs to be studied; this is rather a new area that needs to be explored further to study the interaction between the gut microbiome and xenobiotic compounds [133].

The efficiency of probiotic microbes depends on their long-term colonization in the gut. It was reported that B. longum subsp. longum AH1206 could survive for up to 6 months in the gut [134]. While the probiotic bacterial mixture comprising Akkermansia muciniphila, Clostridium butyricum, B. longum subsp. infantis, and Anaerobutyricum hallii could survive up to 4 weeks after their administration [135]. Lactiplantibacillus plantarum ATCC 202 and 195 survived for up to 6 months in the infant gut [136]. There are no long-term clinical studies on the impact of probiotics on human health. However, some short-term studies have demonstrated probiotics as opportunistic pathogens in immunocompromised, aged, or stressed individuals [137]. Hence, in order to overcome the above shortcomings, probiotic products must be subjected to quality assessments, which include microbiome profiling, screening of probiotics for antibiotic resistance genes, any possibility of invasive infections caused by their administration, resistance or sensitivity of probiotics to drugs, monitoring the effects of probiotics in vulnerable target populations, and finally labeling the formulation of probiotic products with their shelf-life [138, 139].

Globalization of ethnic foods

The globalization of probiotic-rich ethnic food products has become more prevalent. The popularity of ethnic or probiotic food greatly depends on its diversity, history, geographical values, and functional attributes [140]. The food industry is rather consumer-centric, which greatly depends on agriculture history of the nation. It clearly indicates that the food industry of any country depends on its agricultural and cultural diversity. In addition to the above, development of the food industry greatly depends on geographical, climatic, and ethnic diversity [140]. It was reported that countries with rather fast industrialization have less diversity in their food culture, unlike less industrialized countries. To overcome the food product shortage, people have developed diverse methods for the preparation and storage of food, and ethnic foods are one such example. With the increase in

transport and information technology, the rate of globalization has increased to higher levels. In this globalized era, global citizens want to try a variety of foods across the world, apart from learning their culture, history, and geography. In this globalized era, people are sick of eating the same food every day. Hence, these days' people are looking forward to trying new varieties of ethnic foods that hail from different regions and ethnic groups. Thus, the food industry must develop technologies to store, distribute, consume, and cook [141]. In this regard, ethnic foods across the world have a wide role to play in the development of the food industry. Recently, glocalization is the term that was introduced. It describes the process where the probiotic-rich ethnic foods from different countries are localized to better suit the culture, taste and food habits of their countries to enhance their consumption. However, during the localization of ethnic foods, their traditional knowledge should not be compromised (i.e., values that need to be preserved and things that need to be changed as per the regional requirement). In other words, research needs to be performed that can maintain the cultural and technical components without compromising the originality and important principles of food. In the global era, the truth and credibility of ethnic foods rich in probiotics (history, culture, and traditional technology) will become crucial for the development of the food industry. In this regard, research on molecular gastronomy with scientific data is required as a soft power to address the global community. Thus, before glocalization of any ethnic food's rich in probiotics to a new region, strategies need to be applied to localize ethnic foods according to their local taste and flavor to increase consumer acceptance. This strategy will be successful only when proper research and efforts are made to preserve their originality and taste without hampering the quality of the product [141].

Conclusions

The dysbiosis of the GI tract is the major reason for diseases in humans. In addition to the above, factor health consciousness among the population is also enhancing significantly, which has culminated in a rise in demand for safe and healthy foods. Ethnic fermented foods are rich in nutrition and enriched with beneficial bacteria to confer health benefits to consumers. Ethnic foods were reported to contain LAB and their metabolic byproducts with proven health benefits which has resulted in their application in the synthesis of both dairy and non-dairy food products. Recent studies have shown that the adhesion of beneficial bacteria to the gut greatly depends on the age, gender, and medical condition of the individual. In this regard, ethnic foods will serve as the best choice for the delivery of probiotic bacteria to confer synergistic

effects on host health. Based on the health benefits and industrial applications, novel ethnic foods enriched with probiotic bacteria can be developed. Concerning this, new molecular approaches need to be deployed for the selection of starter cultures. Technological advancement and applying the engineering concepts of bioprocessing and biotechnology need to be performed to improve the quality and health attributes of traditional ethnic foods. Further work needs to be focused on designing ethnic foods comprised probiotic bacteria that can prevent or treat a specific disease.

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