Food Science and Engineering
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Review

Bioactive Potential of Probiotic Bacteria-A Comprehensive Review

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Received: 13 March 2024; **Revised:** 10 September 2024; **Accepted:** 11 October 2024

Abstract: Probiotics are living microorganisms that, when consumed in adequate amounts, confer health benefits to the host. Probiotic microorganisms have been used as "food additives" in the functional food industry, which has experienced explosive expansion in recent years. The vast biodiversity of terrestrial and marine environments offers a rich source of untapped microbial diversity, which can hold the key to discovering new strains with unique probiotic properties. They have gained significant attention and recognition for their importance in various biomedical sectors. Therapeutic substances such as vitamins, bacteriocins, enzymes, immunomodulatory chemicals, and short-chain fatty acids are produced by probiotic strains and are essential for sustaining the homeostasis and metabolic processes of consumers. Recent advancements in the field of microbiology have led to significant breakthroughs in understanding the potential benefits of bacterial probiotics beyond the applications associated with gut health. By comprehending the methods by which probiotics modify the typical gut microbiota and offset anomalies in microbial communities, it will be easier to employ probiotics in diet control and disease prevention. A valuable development in the realm of immunization has been the design of probiotic-based vaccines and there is growing evidence that supplementing with probiotics might enhance the body's immune system's response against oral and systemically delivered vaccinations. In the future, the efficacy of probiotics may be enhanced for more nutritionally relevant and clinically effective settings by investing in large-scale intervention and population-based research, which will allow them to be adaptable to each person's biology and microbiota. In this context, this review presents a comprehensive description of food sources fortified by probiotics, their bioactive potential, possible advantages of probiotics in the treatment and prevention of specific diseases, as well as the present and potential directions of probiotic research through application studies.

Keywords: probiotics, lactic acid bacteria, bioactive compounds, gut health, inflammatory bowel disease, vaccines

Abbreviations

AAD	Antibiotic-Associated Diarrhea
CFU	Colony Forming Units
EcN	*Escherichia coli*. Nissle
FDA	Food and Drug Administration
IBD	Inflammatory Bowel Disease
IBS	Inflammatory Bowel Syndrome

DOI: https://doi.org/10.37256/fse.5220244592

LAB Lactic Acid Bacteria

1. Introduction

In the past two to three decades, efforts to improve human health have focused on methods for modifying the natural intestinal flora with live microbial supplements, now known as “probiotics”. Probiotics are a group of live microbial strains that have been shown to have beneficial impacts on the human body when consumed in large quantities [1]. The word “probiotics” is derived from the Greek word “pro bios,” which means “for life,” as opposed to the word “antibiotics,” which means “against life” [2]. Probiotics have been investigated as an antibiotic therapy substitute and account for the largest and fastest-growing section of the global market for functional foods, which accounts for 65% of the market’s enormous overall value of US $75 billion. *Bifidobacteria, Lactobacilli*, and *Enterococci* are examples of lactic acid bacteria that are typically the active ingredients in probiotic products. The preservation of normal and healthy intestinal flora, defense against infections, reduction of lactose intolerance, and immune system activation are just a few of the health benefits attributed to probiotics. Data from the Food and Agriculture Organization of the United Nations (FAO) and World Health Organization (WHO) suggest that probiotic strains must stay intact through the upper intestinal tract to ensure health-promoting effects, once they reach their site of action. For instance, it has been suggested that the so-called “minimum therapeutic” level of viable probiotic microbes should be at least 106 CFU/g of viable cells during the course of the product’s shelf life [3].

Probiotic strains may render significant differences in the resolution of globally prevalent issues impacting mankind. However, industrial manufacturers have encountered technological and marketing challenges due to the long-term sustainability and durability of probiotics. Technologies that address the stability and survivability concerns of probiotics in novel dietary settings hold great promise for the future. Recent studies suggest that innovative probiotic formulations and microencapsulation are considered to be some of the effective and cutting-edge methods for enhancing the vitality of probiotics. Expanding the range of food types into which probiotic components may be successfully introduced is difficult but can be solved by utilizing food-grade raw materials such as physically or enzymatically modified starches. In addition, new developments in food and drug control release systems are also offering new prospects for the future scenario [4]. Anyhow, the cost of production remains as a barrier between manufacturers and customers, substantial effort has been devoted to developing probiotics at affordable prices.

2. Probiotics demand

Although there are many different types of plant-based milk, like soymilk, rice milk, and coconut milk, which are the main carrier matrices employed in the development of probiotic foods, the capacity of these to maintain adequate probiotic levels throughout their product life makes them generally safe for consumption and a suitable vehicle for probiotic delivery. However, studies that are focusing on the evaluation of the functional efficacy of probiotics in these products with special reference to gastrointestinal survival, adhesion to intestinal epithelium, and immunomodulation are rare, and these aspects need to be further assessed [5]. Vegetarianism, the cholesterol level of milk, and lactose intolerance all have contributed to a rise in the demand for non-dairy probiotic products. Therefore, proper development of these as probiotic carriers is a challenge for both the industry and science sectors as well as a top research goal for food design [6].

The probiotic industry is rapidly expanding, as it seeks rising interest among business, consumers, and researchers. In the current market, India only represents less than 1% of the global probiotics market [7]. Dairy products and certain Supplemental probiotics make up the majority of probiotic foods present in the Indian market [8]. Juices, smoothies, cereal, nutrition bars, and infant toddler formula are the newest entrants to the industry, which has extended beyond these most popular probiotic items. The per capita consumption of packaged, store-bought probiotic products in India is 300 grams, and it is also strongly skewed toward metropolitan areas (around 1 kilogram), with almost no consumption occurring in rural areas. Due to their distribution networks and product penetration, Amul, Mother Dairy, Nestlé, and Britannia currently account for 80% of all packaged curd [9]. However, the biggest obstacle for probiotic manufacturers is the absence of standards and the requirement to validate product claims, as well as the lack of knowledge among lower middle class urban and rural populations which may be mitigated in the future.

3. Food sources fortified by probiotics

Growing consumer interest in health and well-being has an impact on eating patterns and food preferences as well. Consumers now recognize that a proper diet can provide a healthy and balanced nutrition profile in addition to just addressing their energy demands. Marketing and consumer acceptability of novel foods depend heavily on the concept of added value in food, food quality, and food functions. While manufacturing successful probiotic meals, adopting the most appropriate food delivery mechanisms for the microorganisms is an important consideration. Controlled human studies are desperately needed to confirm the advantages of probiotics in human diets for health. Healthy persons, people at high risk of disease, and people looking for dietary-management approaches are important target populations for these studies. Publicly supported studies on probiotics as foods or supplements would be advantageous for all of these populations [10]. A suitable balance of substances in them, in addition to their basic nutritional worth, aids in the prevention and treatment of illnesses and disorders. Products that include probiotics or lactic acid bacteria are becoming more and more important within this category.

The dairy business is the major food industry in which probiotics are used in various dairy products such as ice cream, yoghurt, cheese, and fermented milk [11]. Eventhough, it is widely acknowledged that dairy products containing probiotics have positive effects, for a substantial portion of consumers, the main negatives of using fermented dairy products are their high cholesterol content, lactose intolerance, and allergy to dairy products. As a result, to lessen adverse effects emerged by the usage of dairy products as delivery system for probiotics, both the scientific community and consumers are paying attention to probiotic food products generated from the fermentation of grains, fruits, and vegetables. The strains of *Bifidobacterium lactis, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus plantarum, and Lactobacillus rhamnosus* are most frequently used in the production of novel vegetable probiotic products [12]. According to an additional research, it is identified that fruit and vegetable juices might be the next class of food matrices to operate as probiotic bacteria carriers. However, probiotics may benefit from a protective habitat provided by the physical composition of non-dairy carriers which lessens their exposure to severe gastrointestinal conditions [13].

4. Probiotic bacteria

Microbiome is essential for host health and changes to the ecological balance of microorganisms can result in disease. Therefore, it makes sense to assume that using bacteria that are a part of the microbiome would aid in the restoration of equilibrium. Long ago, before identifying the mechanics underlying microbial metabolism and signaling, doctors and other healthcare professionals began the practice of administering intestinal bacteria as probiotics to treat gastro-intestinal diseases. Eventhough, this area of research is crucial for the advancement of human health there is currently a limited body of knowledge surrounding the usage of probiotics [14].

Probiotic bacteria are frequently added to foods as live dietary supplements, but they are also found in fermented foods that are intended for human consumption. Strengthening of the intestinal barrier, alteration of immune response, and antagonism of pathogens through production of antimicrobial compounds or competition for mucosal binding sites are some of the molecular mechanisms by which probiotics positively affect human health. The study of probiotic bacteria must consequently take into account recent advancements in the microbial ecology of the human gut. A thorough understanding of the make-up and function of the human gut microbiota can also reveal molecular markers that can be used as prior standards for effective probiotic therapy and to predict a person's susceptibility to certain probiotic supplements.

A number of studies discuss the probiotic benefits of lactic acid bacteria. *L. acidophilus, Lactobacillus johnsonii, Lactobacillus fermentum, L. rhamnosus, L. plantarum, Lactobacillus reuteri, Lactobacillus salivarius, Lactobacillus paracasei, Lactobrueckii subsp. bulgaricus, Saccharomyces boulardii, S. thermophilus, B. lactis*, *Bifidobacterium longum*, and *Bifidobacterium breve* are some of the species expressing probiotic effects [15]. The yeast *Saccharomyces cerevisiae* and other non-pathogenic *Escherichia coli* and *Bacillus* species are other less popular probiotics. The clearest clinical evidence for probiotics focuses on their ability to modulate the host immune system (through stimulation or control) and improve gut health [16]. Since probiotics have not yet been subjected to published evaluation for the treatment of COVID-19, their role in covid treatment is unknown. The ability of different probiotic strains to reduce the viral load via different mechanisms of action is also being studied by many researchers worldwide [17]. Since probiotic strains are not known to be harmful and have a high upper limit of tolerance, they can be safely marketed as a healthy dietary additive.

5. Classification of probiotics based on ecosystem

Probiotics are majorly found in fermented food products and supplements. However, probiotics can be categorized as soil-based and marine depending on their respective environments [18]. The most researched soil-based probiotics are species in the genus *Bacillus*, which produce spores that can withstand extreme circumstances such as radiation, high temperatures, and stomach acid. Soil-based probiotics are renowned in certain sectors for being harmful. There are concerns that probiotics based on spores might spread throughout the human intestine.

A set of naturally occurring microorganisms found in the marine environment known as marine probiotics appears to improve aquatic life forms' development, resilience to stress, reproduction, resistance to disease, and water quality through their biological activity [18]. *Lactobacillus*, yeasts, and *Bacillus* sp. have no negative side effects when administered by aquatic species since they are non-pathogenic and non-toxic microorganisms. The review by Mohapatra et al. emphasizes how probiotics aid fish in coping with many forms of physical, chemical, and biological stress [19]. Additionally, probiotics are known to be crucial in the development of innate immunity in fish, assisting them in their battle against pathogenic microorganisms as well as environmental stress. Some of the reported species of soil based and marine bacterial strains with probiotic potential, their beneficial effects, and their mode of action are recorded in Table 1.

Table 1. List of probiotic strains with their beneficial effects and mode of action

Bacteria species	Source	Beneficial effect	Mode of action	References
Bacillus subtilis	Soil, human intestine	Boost immunity and strengthen intestinal health of human	Fights against undesirable bacterial forms and toxins	[20]
Bacillus coagulans	Soil, fermented foods	Considerably lowers the symptoms of depression, bloating, and stomach discomfort in IBS patients.	Strains of *Bacillus coagulans* have the ability to decrease redox processes in the stomach and intestine by consuming free oxygen	[20]
Vibrio diabolicus	Deep sea	Boost the rate of survival in Shrimp larvae	Eliminate pathogenic vibrio from shrimp.	[21]
Bacillus licheniformis	Wet soil, sea water	Strengthen the fish's immune system and shield them from bacterial diseases	Synthesise antimicrobial peptides	[22]
Pseudoalteromonas ruthenica	Harsh marine conditions	Provide resistance to disease, regulate immunological responses, and alter the diversity of gut microbes	Strengthen the host's defences against diseases and heat stress	[23]
Phaeobacter inhibens	Sea water	Protect shellfish against the pathogen *Vibrio coralliilyticus*	Suppresses the expression of virulence factors of pathogen in shellfish	[24]
Psychrobacter nivimaris	Cold saline environments	In aquatic fish, alter the immune system and provide resistance to diseases	Produce immuno-stimulatory products	[25]

6. Biological activity of probiotics

Numerous experimental researches have discovered that probiotics have particular effects on immune cells with antiallergic potential, epithelial cells, and the intestinal lumen. Enhancement of antigen degradation, improvement of gut barrier function, and induction of regulatory and pro-inflammatory immune responses are among these effects [26]. According to Fuller, effective probiotic bacteria should have the following qualities: (i) It should be a strain that can increase the host animal's growth or resistance to disease. (ii) It should not be poisonous or harmful. (iii) It must exist as living cells, preferably in huge quantities. (iv) It should be able to adapt to and survive in the environment of the gut, including resistance to low pH and organic acid. (v) It should be stable and capable of lasting under storage and field circumstances for extended periods of time [27]. Production of inhibitory substances, stimulation of immunity, alteration of host gene expression, blocking of adhesion sites, competition for nutrients, and degradation of toxin receptors are some of the ways by which probiotics affect our bodies [2]. Research that supports the use of various probiotic strains in a range of ailments is still in the infantary stage. Probiotics have been linked to gut health and are mostly used to cure gastrointestinal illnesses. However, a number of probiotics are meant for oral hygiene as well.

Probiotic genomic and proteomic studies have identified a number of genes and specific compounds derived from probiotics, which mediate immunoregulatory effects [28]. Probiotics also enhance the immunological responses to vaccination when consumed at an adequate level. Studies on the biological effects of probiotics on host immunity showed that they control the actions of intestinal epithelial cells, mucosal immune cells, and systemic immune cells. Probiotics demonstrated therapeutic potential against a variety of illnesses, including those that are immune response-related, such as allergies, dermatitis, and viral infection [29]. Antibiotic-sensitive probiotics were found to exhibit zones of inhibition with varying widths against distinct antibiotics. Table 2 represents the antibacterial properties of various probiotic microorganisms. Future research will help to better understand the influence of colonizing microbes and probiotics on human health.

Table 2. Antimicrobial activity of probiotic microorganisms

Probiotic microorganism	Antimicrobial activity	References
Lactobacillus paracasei subsp. *paracasei* A20	Showed inhibitory activity against pathogenic bacteria *Candida albicans, Escherichia coli, Staphylococcus aureus*	[30]
Bacillus coagulans MTCC 5856	Inhibited pathogenic bacteria, including *Escherichia coli* and *Staphylococcus aureus*	[31]
Lactobacillus plantarum ACA-DC 146	Shown substantial inhibitory action against *Penicillium anomala* and *Aspergillus fumigatus* moulds.	[32]
Lactobacillus fermentum ME-3	Indicated inhibitory action against *Salmonella enteritidis, Shigella sonnei, Staphylococcus aureus* and *Escherichia coli*	[33]
Bacilus velezensis JW	Exhibited antibacterial action against fish pathogenic bacteria *Aeromonas hydrophila, Aeromonas salmonicida, Lactococcus garvieae, Streptococcus agalactiae,* and *Vibrio Parahemolyticus*.	[34]

6.1 *Bioactive compounds from probiotic bacteria*

Probiotics deliver an assortment of health benefits that are attributed to a variety of bioactive compounds. These bioactive substances are the subject of current research into their health effects and the particular advantages which may differ based on the probiotic strains and the health state of the individual. Bacteriocins, metabolic enzymes, amino acids and peptides, short chain fatty acids, vitamins, antioxidants, anti-inflammatory and immune-modulating agents, and exopolysaccharides are examples of bioactive molecules generated by probiotic bacteria [35]. When these chemicals work together, they boost gut health and physiological function. Additionally, these bioactive ingredients can bind to different neurotransmitters, which have distinct effects on various physiological effects [36]. Table 3 represents the major bioactive compounds found in various probiotic strains.

Table 3. List of bioactive compounds in various probiotic strains

Bacterial strain	Bioactive compounds	Reference
Bacillus coagulans	organic acids, bacteriocins	[37]
Lactobacillus plantarum	nzymes, vitamins, amino acids, oligosaccharides	[38]
Lactococcus lactis	Nisin	[39]
Butyricicoccus pullicaecorum	Butyric acid	[40]
Pediococcus acidilactici	phenolics, organic acids, free fatty and amino acids	[41]
Bifidobacterium longum	Acetic acid	[42]

6.2 *Significance of probiotics in disease cure*

Recent researches have provided some insight into the roles, that nonpathogenic-probiotic bacteria play in maintaining human health. Probiotics, prebiotics, and symbiotics are increasingly used in medical care. This acceptance has been facilitated by the development of well-designed, controlled clinical trials examining the effects of probiotics on human health, a growing understanding of the mechanisms of action through which these agents work, and the development of molecular techniques for identifying and analyzing complex bacterial communities within mammalian intestines.

Identification of appropriate microbes is the primary stage in selecting potential probiotics to cure specific diseases. Existing techniques such as gene sequencing, oligonucleotide probes, genetic fingerprinting, and specific primer selection and molecular methods, like temperature gradient gel electrophoresis, denaturing gradient gel electrophoresis, and fluorescence in situ hybridization, are used to identify and characterize probiotics. The capacity to examine fully sequenced genomes has accelerated the use of genetic approaches to elucidate the functions of probiotics in curing human disease.

Probiotics and prebiotics are currently being heavily marketed for their advantageous impact on human health.

The potential health advantages of probiotic bacteria have drawn a lot of interest, especially in the areas of gastrointestinal health and immune system modulation. It has been shown that probiotic and prebiotic therapy is a viable treatment options for maintaining and repairing the gut ecosystem [43]. The composition of the healthy colonic microbiota may be enhanced by consuming prebiotics such as inulin and oligofructose, as well as lactic acid bacteria and other beneficial live microorganisms. Administering inulin and oligofructose together, helps the bacteria to survive in the large intestine throughout their passage through the upper gastrointestinal tract [2]. Researches have shown that probiotics can be therapeutically beneficial in treating a variety of illnesses, including rotavirus diarrhea, celiac disease, irritable bowel syndrome, *Helicobacter pylori* infection, and diarrhea. *S. boulardii* has been proven to have benefits in the prevention of antibiotic-associated diarrhea (AAD), whereas probiotics have been demonstrated to have clinically significant advantages in the treatment of rotavirus-induced diarrhea. Researches focusing on the way by which microbes function inside the human body in different contexts has demonstrated how effectively they modify the gut environment in order to prevent illness.

It has been demonstrated that a number of probiotic strains can help patients with inflammatory bowel disease avoid relapses. Since the gastrointestinal tract is home to a wide variety of microbial species that either directly or indirectly modulate host metabolism and immune response, it is also possible to investigate the impact of the intestinal microbiota, one of the targets of probiotic therapies to treat inflammatory disorders or immune-mediated diseases. Thus, it is not surprising that probiotics have demonstrated potential for mitigating the symptoms of inflammatory disorders such as multiple sclerosis, rheumatoid arthritis, type 1 diabetes, and inflammatory bowel disease, among others.

Colorectal cancer is the fourth most common cause of cancer-related death and the third most common malignant disease. Adenocarcinomas account for 95% of all cases of colon cancer. Depending on the stage, surgery may be performed either before or after chemotherapy and radiation. Research on the gut microbial environment is still underway since it is believed to be crucial for the onset, progression, and evolution of the disease as well as the emergence of post-operative complications. Strong intestinal bacterial pathogenicity and a fulminant inflammatory response in the host are two introgenic characteristics associated with colorectal cancer treatment that can adversely affect the course of the disease. The capacity of probiotics to affect gut flora seems to be a useful strategy for reducing these issues in surgical patients. Lactic acid bacteria contained in dairy-based probiotic meals have shown positive effects on colorectal cancer (CRC) patients [44]. Strains of the genera *Lactobacillus*, *Bifidobacterium*, and *Propionibacterium* were identified to reduce post operative complications and promote the wound healing process in CRC patients.

The connection between the gut microbiota and the brain is facilitated by a multitude of processes and signals, including immunological, endocrine, and neurological linkages, which significantly lower postoperative complications in tumor localization by 16.7% in the ascending colon and 33.3% in the rectum [44]. According to a research, it is identified that altering the intestinal microbiota using probiotic formulations may have a major impact on the brain organization and development, behavior, as well as mood and cognition in human beings. Understanding the impact of gut microbiota on neurological function is a promising development that has the potential to revolutionize neuroscience which may lead to the discovery of novel etiologies for neurodegenerative and psychiatric illnesses in the future [45].

Several research studies have demonstrated the beneficial effects of probiotic strains in the management or avoidance of specific pediatric illnesses. Some probiotics have been used to treat acute gastroenteritis, prevent antibiotic-associated diarrhea, treat *Clostridium difficile*-associated diarrhea, and prevent nosocomial diarrhea in children. More meticulously designed, large-scale, strain-specific, and targeted dose-response studies are required in pediatric treatment. Regrettably, there exists a lack of general agreement for most diagnoses, specific strains, dosages, and treatment plans. Another study covers the effect of probiotic supplements on children with food allergies, human immunodeficiency virus, diarrhea, irritable bowel syndrome, and Crohn's disease [46]. A comprehensive analysis of randomized, double-blind, placebo-controlled trials showed that strains of *Lactobacillus* are beneficial in lowering the intensity and length of acute infectious diarrhea in babies [47]. Moreover, *B. lactis* BB-12 injection during pregnancy and after delivery has demonstrated immunomodulatory effects, which may shield newborns from atopic illnesses [48]. Furthermore, supplementing with *L. casei* was found to significantly lower the incidence of respiratory and gastrointestinal tract illnesses in children [49].

Apart from modulating gastro-intestinal ecosystem and immunological functions, probiotics can help to prevent a number of conditions such as necrotizing enterocolitis, ventilator-associated pneumonia, dental decay, periodontal disease, halitosis, diarrhea, ulcerative colitis, and colon cancer. Probiotics also help with the reduction of stress and hypertension, lactose intolerance, cholesterol reduction, sucrase-isomaltose insufficiency, and the metabolism of xenobiotics [2]. The most often used probiotics, *Lactobacillus* and *Bifidobacterium* species, have the ability to treat or prevent dental caries, periodontal disease, and urogenital infections. *In vitro* and animal studies have shown that probiotic bacteria inhibit the colonization of enteropathogenic microorganisms. There is mounting evidence that probiotics may also be useful in the management of allergies as well as intestinal, liver, and metabolic diseases. Probiotics are generally recognized for their favorable effects on gut permeability control, host intestinal microbiota normalization, gut immunological barrier function enhancement, and maintenance of a healthy balance between pro- and anti-inflammatory cytokines. Nevertheless, the positive effects of probiotics may not always be supported by the findings of thoroughly conducted clinical investigations. Even when results from randomized, placebo-controlled trials indicate that a particular probiotic has beneficial effects, it should be highlighted that advantages are usually not transferable to other probiotic formulations [50].

6.3 *Probiotic vaccines*

Probiotic bacteria have emerged as potential candidates for vaccine delivery and adjuvant systems, offering unique advantages in terms of safety, stability, and immune stimulation. The latest studies are focussed on the application of probiotic strains, including *L. acidophilus, Bifidobacterium, Lactococcus lactis,* and *E. coli* Nissle (EcN), in the development of probiotic vaccines. *L. acidophilus* has shown promise as a delivery system for oral vaccines. Bermúdez-Humarán et al. developed a recombinant *L. acidophilus* strain expressing a protective antigen from a pathogenic bacterium [51]. The engineered *L. acidophilus* strain induced a specific immune response and provided protection against the targeted pathogen in an animal model, which highlights the potential of *L. acidophilus* as a probiotic vaccine platform, offering a safe and effective means of antigen delivery.

Bifidobacterium has been investigated as a mucosal vaccine adjuvant to enhance immune responses. Shokryazdan et al. utilized *B. longum* as an adjuvant for an influenza vaccine in chickens [52]. The study demonstrated that *Bifidobacterium*-treated groups exhibited significantly higher antibody titers and improved cellular immune responses compared to the control group. These findings suggest that *Bifidobacterium* has the potential to improve vaccine efficacy as a mucosal adjuvant. *L. lactis* has been explored as a live vaccine vector for various diseases. Researchers developed a recombinant *L. lactis* strain to express an antigen from *Mycobacterium tuberculosis* [53, 54]. Oral immunization with the recombinant *L. lactis* strain induced a specific immune response and conferred partial protection against tuberculosis in a mouse model. This highlights the potential of *L. lactis* as a probiotic vaccine vector, offering an oral delivery platform for targeted immune responses [55].

E. coli Nissle (EcN) has been investigated as a live vaccine against various pathogens [56]. Guyard-Nicodème et al. developed a genetically modified EcN strain expressing a protein from *Campylobacter jejuni* [57]. Oral immunization with the recombinant EcN strain induced humoral and cellular immune responses, providing protection against *Campylobacter* infection in chickens. These findings demonstrate the potential of EcN as a live probiotic vaccine candidate, harnessing the advantages of a well-characterized bacterial strain. *L. acidophilus, Bifidobacterium, L. lactis*, and *E. coli* Nissle have shown promising results in antigen delivery, adjuvant activity, and live vaccine vectors. These findings open up new avenues for the development of safe and effective probiotic-based vaccines, offering innovative strategies to combat infectious diseases.

7. Fundamental researches on clinical application of probiotics

Probiotic bacteria have gained recognition for their potential health benefits, and numerous studies have explored the applications of specific strains in various areas of human health. An overview of the literature on the applications of four specific probiotic strains: *L. acidophilus* NCFM, *B. breve* B-3, *S. thermophilus* TH-4, and *L. plantarum* WCFS1 highlights the effectiveness of these strains in improving gut health, immune modulation, lactose intolerance, gastrointestinal protection, and inflammatory bowel diseases. *L. acidophilus* NCFM has been investigated for its potential in improving lactose digestion and reducing symptoms of lactose intolerance. Hemalatha et al. conducted a study that demonstrates significant improvements in lactose digestion and reduction of symptoms in lactose-intolerant individuals by consuming *L. acidophilus* NCFM [58].

Kawahara et al. suggested that supplementation with *B. breve* B-3 enhanced immune parameters and natural killer cell activity in elderly individuals, indicating its potential as an immune-modulating probiotic [59]. *S. thermophilus* TH-4 has been studied for its potential in gastrointestinal protection. Chen et al. identified that administering *S. thermophilus* TH-4 significantly reduces non-steroidal anti-inflammatory drug (NSAID)-induced intestinal inflammation and promotes the healing of gastrointestinal lesions in a rat model. *L. plantarum* WCFS1 has been investigated for its ability to promote gut barrier function [60]. In another study Martín et al. demonstrated that *L. plantarum* WCFS1 improved gut barrier integrity, reduced inflammation, and ameliorated colitis symptoms in a mouse model of colitis, suggesting its potential therapeutic application in inflammatory bowel diseases [61].

Probiotic bacteria have gained significant attention for their potential immunomodulatory effects, with several strains showing promising results in modulating the immune system. *L. rhamnosus* GG (LGG) has been extensively studied for its immunomodulatory properties. Kekkonen et al. conducted a study on healthy adults and found that LGG supplementation enhanced natural killer cell activity, which plays a crucial role in immune defense against pathogens [62]. This suggests that LGG can potentially strengthen immune response. Furthermore, Yan et al. investigated the impact of LGG on immune function in children with atopic dermatitis [29]. The study revealed that LGG supplementation reduced disease severity and improved immune markers, indicating its potential in managing immune-related disorders.

B. longum is another probiotic strain that has shown promising immunomodulatory effects. Ménard et al. [63] conducted a study on healthy elderly individuals and indicated that *B. longum* supplementation improved the immune response by increasing the production of anti-inflammatory cytokines. This suggests that *B. longum* can potentially enhance immune function in the aging population. Additionally, Konieczna et al. demonstrated that, *B. longum* treatment reduced the severity of colitis in mice by modulating immune cell populations and cytokine profiles [64]. These findings suggest the potential of *B. longum* in modulating immune-mediated inflammatory diseases.

L. plantarum is known for its diverse health benefits, including immunomodulation. Another study on children with atopic dermatitis identified that *L. plantarum* supplementation resulted in reduced disease severity and decreased levels of pro-inflammatory cytokines. This suggests that *L. plantarum* may alleviate allergic inflammatory responses through its immunomodulatory activity [65]. Furthermore, Lan et al. investigated the immunomodulatory effects of *L. plantarum* in a mouse model of allergic asthma [66]. The study indicated that *L. plantarum* suppressed airway inflammation and regulated immune cell responses, indicating its potential as a therapeutic option for allergic respiratory conditions.

Another study investigated the scientific basis for the use of certain probiotic strains such as *L. rhamnosus* GG, *S. boulardii*, *B. lactis* BB-12, and *L. casei* in treating various ailments. The study demonstrated the effectiveness of strains in treating various illnesses, offering insights into their modes of action and possible therapeutic applications. *L. rhamnosus* GG has shown immense potential in the prevention and treatment of gastrointestinal illnesses such as diarrhea, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD), Furthermore, *L. rhamnosus* GG has been linked to improvements in IBS and IBD patients' overall quality of life as well as they proved their efficacy in treating symptoms associated with gastrointestinal diseases [67].

Research has been done on the potential of *B. lactis* BB-12 to modulate the immune system, prevent respiratory tract infections, and enhance gut health. According to a randomized controlled trial, it was identified that supplementing with BB-12 reduced the incidence of oral candida infections in the older population [68]. The probiotic yeast strain *S. boulardii* has been shown to be beneficial in treating and preventing *Clostridium difficile* infection and diarrhea brought on by antibiotics. Supplementing with *S. boulardii* lowered the risk of antibiotic-associated diarrhea in adult patients [69]. In a randomized, double-blind, placebo-controlled clinical investigation, *L. casei* was shown to be beneficial in reducing IBS symptoms [70]. The potential of *L. casei* to enhance immune system modulation, lower respiratory infections, and improve gastrointestinal health has also been studied. Overall, the reviewed studies highlight the disease resisting potential of specific probiotic strains. However, further research is needed to fully understand the underlying mechanisms and optimize the use of these probiotic strains in different clinical settings.

8. Conclusion

There are several factors driving the demand for probiotics. Scientific researches on the potential benefits of probiotics continue to expand, uncovering new applications and health benefits. Research has shown that the gut microbiota plays a crucial role in digestion, immune function, and even mental health. Probiotics help in maintaining a healthy balance of gut bacteria, which is essential for optimal health. The increasing prevalence of digestive disorders, such as irritable bowel syndrome and inflammatory bowel disease has led many individuals to seek alternative or complementary therapies. Studies suggest that probiotics may have positive effects on various health conditions, including allergies, cardiovascular health, and mental health disorders. Harnessing the power of soil-based as well as marine probiotic bacteria bacteria researchers are developing innovative health-promoting products that contribute to human well-being. In conclusion, the demand for probiotics is expected to remain strong due to increasing consumer awareness of gut health, the prevalence of digestive disorders, the impact of antibiotic use on gut microbiota, and ongoing scientific research uncovering new potential benefits. As a result, the probiotics market is likely to expand, with more products being developed and marketed to meet the growing consumer demand. This review recommends that further research and exploration are essential to fully understand and unlock the potential of these fascinating microorganisms.

Conflict of interest

The authors declare no competing financial interest.

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