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The Immune-Boosting Effects of Probiotics: A comprehensive systematic review

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Abstract

Probiotics are live microorganisms that, when given in sufficient quantities, benefit the host's health, especially by supporting the equilibrium of the gut microbiota. These good bacteria are essential for boosting immunity, reducing inflammation, and strengthening the integrity of the gut barrier. Recent studies reveal the gut microbiome's role in systemic inflammation. Probiotics, beneficial microorganisms, enhance immune health by strengthening gut barriers, modulating cytokine activity, and supporting immune responses. This review assesses probiotic efficacy in inflammatory diseases, highlighting mechanisms, strain-specific effects, and research gaps. This study highlighted the benefits of probiotics across various diseases. In respiratory infections, probiotics like Bifidobacterium lactis enhanced immune responses and shortened recovery times. For gastrointestinal issues, Bacillus strains alleviated symptoms in dyspepsia and ulcerative colitis, with improved remission and immune profiles. Dermatological benefits included reduced inflammation and improved skin in atopic dermatitis. Metabolic disorders saw improved glycemic control and reduced oxidative stress, particularly in diabetes and NASH. Probiotics also positively influenced mental health in cardiovascular disease and inflammatory markers in kidney disease. Neurologically, probiotics reduced migraine symptoms, while in infectious diseases, Lactobacillus fermentum enhanced healing in lactational abscesses. Cancer treatments benefitted from reduced inflammation and oral mucositis severity. Probiotics show promise in managing various diseases by enhancing immune function, reducing inflammation, and supporting microbiome balance, offering complementary therapeutic benefits for respiratory, gastrointestinal, metabolic, dermatological, and neurological conditions.

Introduction

Inflammatory diseases characterized by chronic immune dysregulation and tissue damage and represent a significant burden on global health, [1]. Probiotics, defined as live microorganisms that confer health benefits when administered in adequate amounts, have emerged as a promising therapeutic approach for modulating inflammatory responses [2]. In recent years, the intricate relationship between probiotics, gut microbiome and systemic inflammation has been observed and getting substantial attention within the scientific community.

Our gut is a complex environment and home of diverse microbial communities also referred to as gut microbiome that has a huge impact on our overall health. This microbial community and probiotics have a strong impact on immune system, boost immunity, reduce infections and maintain gut health [3]. Mechanistically, these probiotics increase the mucus secretion, increase production of IgA in gut and activate tight junctions, strengthen the intestinal barrier, and stop invading pathogens from intestine to blood circulation [4]. The probiotics increase the synthesis of cytokine by interacting with various immune cells like B cells, dendritic cells and macrophages and create balance between anti-inflammatory cytokines and pro-inflammatory cytokines which helps regulate immune responses [5]. Studies suggested that probiotics improve various disease conditions like gastrointestinal disorders (e.g. ulcerative colitis, irritable bowel syndrome, gastroenteritis, traveler's diarrhea) and several metabolic diseases (e.g. obesity, diabetes, respiratory infections) allergy and urinary tract and vaginal infections [6]. It has been suggested that a healthy gut flora may the future of healthcare and help us discover new avenues for preventative medicine and improving overall health [7]. This systematic review evaluates the efficacy of probiotics in inflammatory conditions, synthesizing evidence from randomized controlled trials and their effects on various diseases.

Methods

Literature Search and Selection Criteria

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A comprehensive literature search was performed using the electronic database PubMed/MEDLINE. The search strategy incorporated a combination of free-text keywords related to probiotics and inflammatory diseases, using Boolean operators.

First, records were identified from the NCBI PubMed databases, resulting in 6088 entries. Of these, 243 records are removed before screening because they lack full-text availability. Next, 5845 records are screened, and 5808 are excluded due to lack of associated data or not being randomized controlled trials conducted within the last five years. From the remaining records, 37 reports are sought for retrieval, with 5 reports not retrieved, leaving 32 reports assessed for eligibility. During eligibility assessment, 7 reports were excluded because they either did not focus on probiotics, lacked a defined probiotic dose, investigated non-specific diseases or non-probiotic interventions, or incorporated an anti-inflammatory diet instead of probiotics. Ultimately, 25 studies are included in the final review after this systematic selection process. (table 1, figure 1).

Discussion

In this review, we found that the various probiotics and synbiotics significantly improve the health by reducing inflammation, increasing immune response and modulating gut microbiota which ultimately beneficial effects in various diseases like cancer and diabetes. The effect of probiotics is also given as follows

Respiratory Disease

Respiratory tract infections (RTI), have a huge burden on healthcare systems worldwide. it is caused by various bacterial (Haemophilus influenzae, Streptococcus pneumoniae and Moraxella catarrhalis) and viral (rhinovirus, coronavirus) infections [8].

Studies suggested that various probiotics decrease RTI by improving mucosal barriers and immune system. They regulate both adaptive and innate immunity, accelerate synthesis of IgA production, and decrease inflammation. Some Clinical evidence shows probiotics lower infection incidence, duration, and antibiotic use, making them a safe adjunct for respiratory health [9]. The administration of probiotic Bifidobacterium lactis (Probio-M8) adjunctively with Symbicort Turbuhaler with a dose of 2 sachets of 3×10^{10} colony forming units (CFU) per sachets daily in asthma patients for 13 weeks activates gut-lung axis and improves of various anti-inflammatory pathways alleviates symptoms of asthma [10]. In influenza-induced ARTIs pediatric patients, administration of nasal-spraying probiotic "LiveSpo Navax" significantly reduced recovery time by 2 days and increased treatment effectiveness by 58%, while decreasing viral load, bacterial concentration, and pro-inflammatory cytokines [11].

Gastrointestinal Disorders

The digestive system (gastrointestinal) is not only a single passage from the mouth to the anus, but also a link between the body and the external environment. Gut-associated lymphoid tissue (GALT), which is present in the intestinal mucosa, is the largest immune organ in the human body. By stimulating the interaction between the immune system and the local microorganisms, GALT maintains the balance between beneficial microorganisms and resistance to pathogenic microorganisms [12]. The pilot trial of Wauters, L. 2021 demonstrated that the spore-forming probiotics Bacillus coagulans MY01 and Bacillus subtilis MY02 significantly improved symptoms in patients with functional dyspepsia compared to placebo, with a higher clinical response rate and comparable safety profiles. Beneficial immune and microbial changes suggest potential mechanisms for treatment efficacy [13]. The supplementation of probiotic capsules containing nine Lactobacillus and five Bifidobacterium species (3×10^{10} CFU) significantly lower Partial Mayo scores and C-reactive protein and increased hemoglobin and IL-10 levels and ultimately decreased remission rates of mild-to-moderately active ulcerative colitis patients [14]. Similarly in ulcerative colitis patients' administration of probiotic Lactobacillus and Bifidobacterium species (3×10^{10} CFU), thrice daily for 6 weeks significantly enhanced SIBDQ (short inflammatory bowel disease questionnaire) scores and improve quality of life [15]. Consumption of Escherichia coli Nissle 1917 (EcN) (2.5×10^{9} CFU) daily for 8 weeks decrease Inflammatory Bowel Disease Questionnaire (IBDQ) scores and enhanced clinical response and endoscopic remission ulcerative colitis patients [16]. Liquid-form of Bacillus clausii spores (LiveSpo CLAUSY; 2 billion CFU/5 mL ampoule) at high doses (4-6 ampoules/day) significantly shortened recovery time by 3 days and improved treatment efficacy in children with persistent diarrhea patients [17]. Administration of *Saccharomyces boulardii* CNCM I-745 (600 mg/day contains1×10^{9} CFU per capsule) 3 capsules of 200 mg each significantly improved symptoms of viral acute diarrhea, with 70% of patients showed improvement after 4 days [18]. The consumption of multi-strain probiotic in COVID-19 associated diarrhea patients reduces duration of diarrhea up to 4 days and lower incidence of hospital-acquired diarrhea [19].

Dermatological Disease

The skin is a home to a vast community of bacteria known as the surface skin microbiome, which together create an intricate system inside a complex ecosystem. This intricate web of microbes is essential for preventing serious illnesses and preserving the health of the skin. Probiotics are living microorganisms with health advantages; their use has made them a viable option for people who seek beautiful, healthy skin [20] Through microenvironment modulation, these beneficial bacteria can significantly improve the skin's microbiota. Probiotics increase the development of beneficial microbes and prevent the growth of dangerous ones, creating an environment that is less prone to infections. Moreover, they strengthen the skin's protective layer, making it better able to hold onto moisture and defend against invaders. Administration of Lactobacillus rhamnosus GG (1×10^{10} CFU daily) for 12 weeks in children with atopic dermatitis (AD) reduce scoring atopic dermatitis (SCORAD) index and improved quality of life scores [21]. Similarly, the consumption of probiotic mixture L. plantarum PBS067, L. reuteri PBS072 and L. rhamnosus LRH020 (1×10^{9} CFU) daily for 56 days in adults with mild-to-severe atopic dermatitis improved skin smoothness, moisturization, and reduced inflammatory markers and SCORAD score [22].

Metabolic and Endocrine Disorders

Recent literature suggested that various metabolic and endocrine disorders are also improved by using probiotics which enhance immune responses, modulate gut microbiota, and reduce systemic inflammation. In a pilot study, *Bacillus subtilis* strain DE111 (1×10^{9} CFU and 15 mg capsule per day) for 4-week increases anti-inflammatory immune cell populations in healthy adult individuals [23]. In a 24-week study, obese patients with type 2 diabetes received synbiotics consisting of *Lactobacillus paracasei* strain Shirota and *Bifidobacterium breve* strain Yakult, along with galactooligosaccharides, at a dosage of 5 billion CFU per day improve gut microbiota composition, increasing Bifidobacterium and total lactobacilli, along with higher fecal acetic and butyric acid levels, suggesting beneficial effects on the gut environment despite unchanged inflammatory markers [24].

In an 8-week randomized, placebo-controlled trial, women with type 2 diabetes mellitus (T2DM) were given *Lactobacillus rhamnosus* GG (ATCC 53103) at a dose of 10×10^{9} CFU/day increases the expression of mucin 2 and 3A genes, indicating improved intestinal barrier function. Additionally, daily fat consumption, body weight, and body fat were considerably reduced in the probiotic group [25]. In gestational diabetes mellitus, the supplementation of probiotics mixture (*Lactobacillus acidophilus, Lactobacillus casei, Bifidobacterium bifidum* and *Lactobacillus fermentum*) 2×10^{9} CFU/g per day for 6 weeks leading to better glycemic control, lipid profiles, inflammation, and oxidative stress markers [26]. In patients with nonalcoholic steatohepatitis (NASH), supplementation of probiotics *Lactobacillus acidophilus and Bifidobacterium lactis* (1×10^{9} CFU each) for 6 months, leading to better (AST to Platelet Ratio Index) APRI scores [27]. In patients with metabolic-associated fatty liver disease (MAFLD), multi-strain probiotics (Lactobacillus fermentum, Lactobacillus reuteri, Lactobacillus plantarum, daily for 60 days) significantly improved liver function and lowered uric acid levels [28]. In women with polycystic ovary syndrome, 2 g of *Bacillus coagulans* synbiotic daily for 12 weeks improved inflammatory markers (C-reactive protein) but did not significantly affect lipid profiles or atherogenic indexes [29].

Cardiovascular Diseases

In patients with coronary artery disease, co-supplementation with *Lactobacillus rhamnosus* GG (1.9×10^{9} CFU) and inulin (15 g) for 8 weeks significantly decreased depression (Beck's Depression Inventory score), anxiety (The State-Trait Anxiety Inventory score), and inflammatory markers (hs-CRP, TNF-α), improving overall mental health of these patients [30].

Kidney and Urological Disorders

In end-stage renal disease patients on haemodialysis, high-dose probiotic supplementation (1×10^{11} CFU/day) for 6 months significantly reduced indoxyl sulfate (breakdown of dietary tryptophan) levels [31]. In haemodialysis patients, synbiotic supplementation (15 g prebiotics, 5 g probiotics) for 12 weeks significantly decreased hs-CRP, interleukin-6, endotoxin, and anti-HSP70 [32].

Neurological Conditions

The gut-brain axis, a complex communication network between the gut microbiota and the CNS, is being studied extensively. These probiotics can positively influence brain function by inhibiting harmful bacteria, regulating neurotransmitters, and reducing inflammation [33]. Study suggested that the supplementation of synbiotics (12 probiotics and fructooligosaccharides) for 12 weeks in migraines patients significantly reduce in migraine frequency, painkiller use, gastrointestinal issues, serum zonulin, and Hs-CRP levels and concluded that this Synbiotics may serve as a complementary treatment to alleviate migraine characteristics and improve inflammatory and gut permeability markers [34].

Infectious Diseases and Related Complications

The administration of *Lactobacillus fermentum* CECT5716 in patients with lactational breast abscesses (3-6 cm) during needle aspiration. significantly increase cure rate and may accelerate healing in lactational breast abscesses [35].

Cancer

Dysbiosis, an imbalance in gut microbiota, may contribute to cancer development. Probiotics, live microorganisms, offer potential benefits in cancer prevention and treatment by modifying the immune system, reducing inflammation, and directly fighting malignancies [36]. The supplementation of probiotic cocktail for 8 weeks on oral mucositis in nasopharyngeal cancer patients, significantly reducing OM severity [37]. The synbiotic supplement containing 10^9 CFU/day for 8 weeks on breast cancer patients significantly increases in adiponectin levels and reductions in TNF-α and hs-CRP, indicating improved inflammatory markers related to recurrence [38].

In this review we found that probiotics have shown a promising role in managing a range of health conditions through mechanisms such as reducing inflammation, enhancing immune responses, and modulating gut microbiota. In asthmatic patients, probiotics have been associated with reducing lung inflammation, potentially improving respiratory health. Similarly, in cases of functional dyspepsia, they may lead to beneficial immune and microbial changes, indicating a broader impact on gut health. Specific populations, including those with oral mucositis (OM) due to nasopharyngeal cancer, have experienced reduced severity of symptoms linked to improved immune response and altered gut microbiota structure. Atopic dermatitis has also demonstrated beneficial effects through modulation of both gut and skin microbiomes, thereby improving disease severity and quality of life. In obese patients with Type 2 diabetes mellitus, while inflammatory markers showed little change, there was an improvement in gut environmental conditions. These findings suggest that probiotics may offer a multifaceted approach to enhancing health and managing disease, particularly in chronic conditions with inflammatory components.

There are several pathways given below by which the probiotics can affect our metabolism (table 2). These pathways are given below

The Gut-Immune Axis: An Intentional Partnership

The gastrointestinal system (GI tract) is not only passageway of digestive system that extends from mouth to anus but also a system by which the body is connected with the external environment. The gut-associated lymphoid tissue (GALT) is largest immune organ of the human body and located in intestinal mucosa. By stimulating the interaction between the immune system and the local microbiota, GALT maintains equilibrium between good microorganisms and resistance against pathogenic microbes [12]. Research indicated that the body could improve gut health and boost immunity when it receives enough probiotics. There are several theories on the mechanism of action of probiotics and their impact on immune system regulation (figure 2).

Probiotics compete with harmful microorganisms for adhesion sites on the intestinal epithelium, which inhibit colony formation and subsequent infections. The use of probiotics can improve mucus production and strengthen intestinal tight junctions, forming a physical barrier that keeps toxins and infections out. Probiotics modify the immune response due to the interaction with immune cells in the stomach, such as dendritic and macrophage cells. This mutual action controls the generation of pro- and anti-inflammatory responses, resulting in tolerance to good bacteria and prevention of hazardous infections. Metabolites formed by probiotics have the capacity to modulate the immune system. The short-chain fatty acids (SCFAs) such as Acetate, butyrate, and propionate, that can be produced during the breakdown of dietary fibers. These SCFAs can interact with immune cells and control their behaviour. [39].

Pathogen competition for adhesion sites:

Probiotics inhibit the growth of harmful bacteria and prevent their multiplication in gastrointestinal tract. The probiotic strains such as *Lactobacillus* (*Lactobacillus casei Shirota*) strain and *Bifidobacterium* species (such as *Bifidobacterium breve* and *longum)* are the most commonly used [40]. By employing two strategies, these probiotic microbes gain a competitive edge: first strategy is by raising the acidity level of the intestine in which the bacteria require neutral or slightly alkaline environment to flourish. *Lactobacillus* and *Bifidobacterium* species break down the carbohydrates and produce lactic acid during the digestion. Due to acidic environment in the intestines, pH is lowered, and harmful bacteria are prevented from proliferating and settling in specific regions [41].

In the second strategy, probiotic strains secrete bacteriocin (ribosomally synthesize peptide with antibacterial properties) which prevent the multiplication of pathogenic bacteria by disarraying their essential biological processes or disrupting their cell membranes, both of which lead to microbial death [42]. Several probiotic strains can also create organic acids including propionic acid, acetic acid, and hydrogen peroxide, these compounds also have antimicrobial activity [43].

Probiotics and Gut Barrier Function: Mechanisms of Protection and Integrity by increased synthesis of mucin.

The gut mucosa is the main and a very complex defence mechanism of the body. The gut mucosal barrier is a complex and dynamic entity that helps in the defence of the body against infections. The mucus barrier, mainly composed of mucin glycoproteins, traps and neutralizes harmful bacteria before they reach the epithelial lining [44]. Strains like *Lactobacillus* and *Bifidobacterium* increase mucin production, enhancing the viscosity of mucus and augmenting the barrier to pathogens, toxins, and viruses. They also compete with pathogens for nutrients and produce antimicrobial compounds that contribute to the defense of the protective mucus barrier [45]. Goblet cells control the secretion of mucus in the intestine, and their interaction with probiotics modulates immune functions, reducing unwanted inflammation and maintaining gut and systemic health [46].

Probiotics and Gut Barrier Function: Mechanisms of Protection and Integrity by upregulated expression of tight junction proteins:

As a transitional barrier, the intestinal epithelium senses environmental elements essential to survival while preserving a fine balance between immune tolerance and protection. To maintain this equilibrium, tight junctions (TJs) are crucial protein complexes that control cellular and chemical mobility [47]. Probiotics are essential because they strengthen the intestinal barrier by upregulating TJ proteins such as zonula occludens (ZO) and occludin [48]. Occludin supports the adhesion of ductal epithelial cells by forming the structural backbone of tight junctions [49]. Probiotics also reduce intestinal permeability and increase adhesive forces. Tight junctions are further stabilized by ZO proteins, which are connected to the actin cytoskeleton [50]. By strengthening epithelial connections and reducing paracellular gaps, increased expression of ZO-1 and ZO-2 proteins inhibits pathogen invasion [51]. Furthermore, probiotics indirectly enhance the gut barrier by supporting the organization and activity of the actin cytoskeleton, which is a complex network of protein filaments that serves as the foundation for epithelial cells [52].

Immune system modulation by chemokines and cytokines synthesis

These probiotics suppress pro-inflammatory cytokines such as interleukin-6 (IL-6) and Tumour necrosis factor-alpha (TNF-α), increases the production of IL-10 (anti-inflammatory cytokine). Immunological homeostasis, or the immune system's ability to respond to threats without going into overdrive and damaging other organs, depends on the delicate equilibrium. [53]. Probiotics, an integral part of the gut microbiome, collaborate with immune cells which line the gut. This contact causes the production of cytokines and chemokines, which operate as chemical messengers and help to coordinate immune responses by recruiting immunologically relevant cells to specific regions [23]. Probiotics can influence the total immune response, which affects the generation of signalling molecules required for a balanced and effective defence against infections. Several probiotics have been demonstrated to be efficient at modulating the production of specific cytokines, demonstrating their complex character. Probiotics play an important function in cellular health by intelligently managing the immune system, stressing the complexities of controlling the body.

Immune system modulation by augmented antigen presentation through antigen-presenting cells (APCs):

Dendritic cells serve as immune system sentinels, constantly removing antigens, or foreign molecules, from the intestinal lumen to enhance antigen presentation. Probiotic stimulation increases dendritic cell transfer efficiency of antigens. These activated dendritic cells enter the gut mucosa and move on to the immune cell population known as gut-associated lymphoid tissue (GALT). Dendritic cells in gut-associated lymphoid tissue (GALT) transfer the collected antigens to T and B cells, enabling the adaptive immune system to create a more potent response against putative gut-associated pathogens [54].

Immune system modulation by activity of regulatory T cells (Tregs):

Probiotics have the capability to regulate the function of T cells, a crucial part of the adaptive immune system. Research has indicated that specific probiotic strains may lend a helping hand to control the role of T lymphocytes. As a primary and anti-inflammatory mediator of inflammation, the immunosuppressive regulator T-regulatory cells (Tregs) improve immunological tolerance to commensal gut microorganisms. Maintaining immune system homeostasis is critical to halting the advancement of chronic inflammatory bowel disorders [55].

Immune system modulation by immunomodulatory metabolites production:

Immunomodulatory metabolites which help in immune system control can potentially be produced by probiotics. Our gut microbiota is largely influenced by our diet. Prebiotics are a kind of fiber that promotes the growth of good bacteria but which the body is unable to digest. They are required for the right consumption of nutrients. Probiotic bacteria in our colons can rapidly break down complex carbohydrates like fructooligosaccharides (FOS) and inulin [56].

Probiotics act as immunomodulators by generating short-chain fatty acids (SCFAs):

Probiotics facilitate anaerobic fermentation by converting dietary fibers beneficial compounds, particularly short-chain fatty acids (SCFAs) [57]. In blood circulation these SCFAs have a significant impact on gut and immune function. They act as important signalling molecule that regulate immune system by promoting T regulatory cells (Tregs) populations and increase immune tolerance [58]. The three examples of SCFAs are acetate, propionate, and butyrate and each having a distinct function. The elevated level of butyrate and propionate are strong anti-inflammatory and immune-boosting properties [59], the propionate support colonocyte nutrition and help to reduce inflammation [60], additionally Butyrate plays important role in maintenance and integrity of intestinal barrier. Studies suggested that various probiotic strain like *Bifidobacterium longum, Faecalibacterium prausnitzii and Lactobacillus plantarum* and produce butyrate, propionate respectively which helps to reduce inflammation, allergy responses and promotes gut health [5,61-62].

Probiotics enhance the integrity of the Gut Barrier:

In addition to being a passive pathway, the digestive system exhibits a fascinating and dynamic interaction between the internal and exterior environments. The primary defence system against numerous potential threats to the body is the intricate and diverse gut barrier. The complicated barrier serves a variety of critical functions, some of which are more intriguing than others. The digestive tract's intestinal barrier serves as a very sensitive intermediary, tightly monitoring the absorption of nutrients from digested food to ensure their distribution to the body's cells and tissues [63]. Furthermore, it works as a powerful defence mechanism, blocking the discharge of harmful bacteria and their toxins from within the gut into the bloodstream, so reducing systemic inflammation and infection [64]. Further, the intestinal barrier plays a key function in maintaining immunological homeostasis by developing tolerance to helpful bacteria such as Lactobacillus and Bifidobacterium, as well as keeping the body safe from harmful agents of pathogenesis [65]. Such careful balance is critical for avoiding secondary infections and autoimmune responses. Probiotics are vitally important for gut health since they can increase the potency of the intestinal barrier. Probiotics support a healthy intestinal environment by fortifying the gut barrier. As it has been shown in figure 2.

The relationship between chronic inflammation, the gut microbiome, and the impact of probiotics:

Inflammatory bowel disease (IBD) and other chronic illnesses can be caused by low-grade chronic infections and dysbiosis, or an imbalance in the gut microbiota. By promoting immune and digestive health, maintaining a healthy gut microbiome may help prevent these illnesses [66]. Probiotics have anti-inflammatory effects by regulating cytokine production and collaborating with immune cells to regulate inflammation [67]. They also promote the production of short-chain fatty acids (SCFAs), which strengthen the body's defenses against infections by enhancing regulatory T cells and suppressing pro-inflammatory cytokines [68].

The Impact of Probiotics Beyond Digestive Health:

In addition to promoting gut health, probiotics boost immunity in several organs, reducing the risk of diseases like respiratory infections. Understanding their mechanisms and strain specificity are essential for their therapeutic effects. Some effect of probiotics as given follows.

Probiotics in Respiratory Tract Infections:

Probiotics have been shown to significantly lower the incidence and length of respiratory tract infections (RTIs). Authors suggested that probiotics may be able to lower the frequency of upper respiratory tract infections (RTIs) that necessitate antibiotic treatment and prevent one or more RTI episodes. Additionally, they were able to reduce the duration of upper respiratory tract infection (URTI) symptoms by approximately 1.22 days [69]. Probiotics' effectiveness in treating respiratory tract infections (RTIs) varies, and their effects may differ based on the type of infection. Studies show that adult rhinovirus infection is less common when Lactobacillus rhamnosus GG is present. Additionally, it has been demonstrated that using a variety of Lactobacillus strains helps shield kids from respiratory infections [70]. Probiotics potential for reducing respiratory conditions like COVID-19. Oral probiotics containing *Lactobacillus*, reduce the incidence of respiratory failure in COVID-19 cases. Age, health, and personal risk factors can all affect the optimal probiotic strain and dosage for preventing respiratory tract infections [9].

Probiotics in Skin Infections:

By generating substances like lactic acid and bacteriocins that target pathogenic microorganisms, probiotics show their antibacterial properties. They additionally minimize inflammation, encourage wound healing, and control the skin's immune response. According to research, probiotics can help produce new blood cells, strengthen the skin's protective layer, and prevent inflammatory skin infections.

Probiotics also have the potential to improve wound healing by promoting beneficial bacteria and lowering infection rates, and they may help treat acne vulgaris by enhancing communication between the gut, skin, and body microbiomes [71].

Probiotics in genital infections:

The vaginal cavity's bacterial balance is essential for preventing illness. By outcompeting dangerous bacteria like Gardnerella vaginalis and Candida albicans, probiotics—especially Lactobacillus strains—help restore this equilibrium. Lactobacillus creates lactic acid to keep the environment slightly acidic, which suppresses bad bacteria and encourages good ones. Probiotics also boost the vaginal immune system's defenses against infections. Probiotics aid in the fight against infections and fortify the vaginal immune system. When administered orally or intravenously, Lactobacillus rhamnosus has proven to be an effective treatment for bacterial vaginosis (BV). Additionally, Lactobacillus acidophilus and Lactobacillus rhamnosus lessen vulvovaginal candidiasis (VVC) [72]. Use of probiotics to treat UTIs than for BV and VVC, they may help prevent UTIs by preventing harmful bacteria from adhering to the urethra. The strain, dosage, and mode of administration all affect how effective probiotics are; oral treatments are more effective for BV than vaginal suppositories are for VVC [73].

Probiotics in nervous system disorders:

A complex network of communication between the central nervous system (CNS) and the gut microbiota, known as the gut-brain axis, is essential to good health. Probiotics have the potential to indirectly affect brain function by suppressing harmful bacteria and lowering inflammation. Their advantages go beyond improving digestion; they also influence immunological responses and lessen long-term inflammation associated with neurological conditions. Additionally, probiotics have an impact on the synthesis of neurotransmitters that are essential for mood regulation, such as serotonin and GABA [74]. Probiotics may improve the stress response and reduce the symptoms of anxiety and depression by influencing the vagus nerve, a crucial connection between the gut and the brain. probiotics may help treat severe neurological disorders like Alzheimer's disease (AD) and autism spectrum disorder (ASD) by improving cognitive function and reducing inflammation. To prove clear therapeutic benefits, more research is required as probiotic efficacy varies by strain, dosage, and individual condition [75].

The Role of probiotics in cancer:

Recent studies have demonstrated the connection between human health and the gut microbiota, demonstrating how dysbiosis can lead to the development of cancer by causing immunological dysfunction, metabolic problems, and chronic inflammation. Researchers are looking into using probiotics, which are healthy live microorganisms, to prevent and treat cancer. By encouraging Th1 cells and inhibiting regulatory T cells (Tregs), they can improve immune responses [76]. Short-chain fatty acids (SCFAs), which are also produced by probiotics, have anti-inflammatory, anti-cancer, and anti-new blood vessel effects. Furthermore, some probiotic strains have demonstrated the capacity to eradicate cancer cells directly, indicating a possible use for them in upcoming cancer treatments [77]. Investigating the effects of probiotics on cancer types is a developing area of study. Probiotic therapy, which helps to strengthen the intestinal barrier, reduce inflammation, and restore microbial balance, has demonstrated positive responses to colorectal cancer, which is frequently linked to an imbalance in gut flora [78]. According to research, probiotics may also affect breast cancer by altering immune response and estrogen metabolism. Despite encouraging outcomes from preclinical and clinical research, there are still significant obstacles to overcome. Clinical application is hampered by variations in probiotic strains, disparities in research methodologies, and a lack of knowledge about their mechanisms. Future advancements depend on the identification of strong anti-cancer probiotic strains. Furthermore, it is necessary to create widely recognized probiotic formulations and carry out extensive randomized controlled trials to verify their efficacy and safety [79]. Overall, the gut microbiota offers a useful target for cancer treatment. By altering the gut flora, probiotics can improve immunological response and possibly prevent the growth of tumors. To ensure successful clinical use in the future, more research is required to fully realize the therapeutic potential of probiotics in cancer prevention and treatment [80].

Conclusion

Probiotics are an effective and adaptable way to support human health in a variety of systems. They are useful in treating skin infections, promoting vaginal health, modulating gut-brain communication, and even preventing and treating cancer due to their capacity to alter the immune response, restore microbial balance, and inhibit harmful pathogens. Probiotics have an impact on vital biological functions like immune regulation, neurotransmitter synthesis, and inflammation control. They may also have therapeutic benefits for diseases like bacterial vaginosis, acne, urinary tract infections, neurological disorders, and colorectal and breast cancers. However, despite promising preclinical and clinical results, challenges such as dosage optimization, strain variability, and insufficient understanding of underlying mechanisms hinder their widespread clinical use. To confirm the safety and effectiveness of probiotic strains, future studies must concentrate on identifying particular strains with specific therapeutic effects and carrying out extensive randomized trials. Realizing probiotics' full potential could greatly improve therapeutic and preventative approaches in a variety of medical specialties.

Conflict of Interest

None

Author Contribution

Abhishek Kumar Mishra: Concept, design, writing, final corrections and approval.
Dharmsheel Shrivastav: Writing, collection of data and materials, final corrections and approval.
Varun Kumar Sharma: Writing, reviewing, collection of data and materials
Sourabh Kumar Singh: Writing, collection of data and materials
Shilpy Singh: Writing, Collection of materials, Reviewing, critical review,
Jawahar Fudhayl Naif Alanazi: Writing, critical review, corrections, referencing
Rehab Owayn Alanazi: Writing, corrections, Tables, content, referencing
Manal S.A. Elsied: Writing, corrections, Tables, figures visualization, referencing
Mirza Masroor Ali Beg: Concept, design, figures visualization, writing, final corrections and approval.

References

1. Chen L, Deng H, Cui H, Fang J, Zuo Z, Deng J, Li Y, Wang X, Zhao, L. Inflammatory responses and inflammation-associated diseases in organs. Oncotarget, (2017); 9(6), 7204–7218.
2. Gebrayel P, Nicco C, Al Khodor S, Bilinski J, Caselli E, Comelli EM, Egert M, Giaroni C, Karpinski TM, Loniewski I, Mulak A, Reygner J, Samczuk P, Serino M, Sikora M, Terranegra A, Ufnal M, Villeger R, Pichon C, Konturek P, Edeas M. Microbiota medicine: towards clinical revolution. J Transl Med. (2022); 20(1):111.
3. Wu HJ, Wu E. The role of gut microbiota in immune homeostasis and autoimmunity. Gut Microbes, (2012); 3(1):4-14.
4. Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation. Therap Adv Gastroenterol, (2013); 6(1):39-51.
5. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. Cells. 2023 Jan 2;12(1):184. doi: 10.3390/cells12010184. PMID: 36611977; PMCID: PMC9818925.
6. Darbandi A, Asadi A, Ghanavati R, Afifirad R, Darb Emamie A, Kakanj M, Talebi M. The effect of probiotics on respiratory tract infection with special emphasis on COVID-19: Systemic review 2010-20. Int J Infect Dis, (2021); 105:91-104.
7. Wang X, Zhang P, Zhang X. Probiotics Regulate Gut Microbiota: An Effective Method to Improve Immunity. Molecules. (2021); 26(19):6076.
8. Calderaro A, Buttrini M, Farina B, Montecchini S, De Conto F, Chezzi C. Respiratory Tract Infections and Laboratory Diagnostic Methods: A Review with A Focus on Syndromic Panel-Based Assays. Microorganisms. (2022); 10(9):1856.
9. Zhao Y, Dong BR, Hao Q. Probiotics for preventing acute upper respiratory tract infections. Cochrane Database Syst Rev. 2022 Aug 24;8(8):CD006895. doi: 10.1002/14651858.CD006895.pub4. PMID: 36001877; PMCID: PMC9400717.
10. Liu A, Ma T, Xu N, Jin H, Zhao F, Kwok LY, Zhang H, Zhang S, Sun Z. Adjunctive Probiotics Alleviates Asthmatic Symptoms via Modulating the Gut Microbiome and Serum Metabolome. Microbiology Spectrum, (2021); 9(2):e0085921.
11. Tran TT, Phung TTB, Tran DM, Bui HT, Nguyen PTT, Vu TT, Ngo NTP, Nguyen MT, Nguyen AH, Nguyen ATV. Efficient symptomatic treatment and viral load reduction for children with influenza virus infection by nasal-spraying Bacillus spore probiotics. Science Report. (2023); 13(1):14789.
12. Wiertsema SP, Van BJ, Garssen J, Knippels LMJ. The Interplay between the Gut Microbiome and the Immune System in the Context of Infectious Diseases throughout Life and the Role of Nutrition in Optimizing Treatment Strategies. Nutrients, (2021); 13(3): 886.
13. Wauters L, Slaets H, De PK, Ceulemans M, Wetzels S, Geboers K, Toth J, Thys W, Dybajlo R, Walgraeve D, Biessen E, Verbeke K, Tack J, Van DWT, Hellings N, Vanuytsel T. Efficacy and safety of spore-forming probiotics in the treatment of functional dyspepsia: a pilot randomised, double-blind, placebo-controlled trial. Lancet Gastroenterology Hepatology, (2021); 6(10): 784-792.
14. Agraib LM, Yamani MI, Tayyem R, Abu SAT, Rayyan YM. Probiotic supplementation induces remission and changes in the immunoglobulins and inflammatory response in active ulcerative colitis patients: A pilot, randomized, double-blind, placebo-controlled study. Clinical Nutrition ESPEN, (2022); 51: 83-91.
15. Rayyan YM, Agraib LM, Alkhatib B, Yamani MI, Abu SAT, Tayyem RF. Does probiotic supplementation improve quality of life in mild-to-moderately active ulcerative colitis patients in Jordan? A secondary outcome of the randomized, double-blind, placebo-controlled study, European Journal of Nutrition, (2023); 62(7): 3069-3077.
16. Park SK, Kang SB, Kim S, Kim TO, Cha JM, Im JP, Choi CH, Kim ES, Seo GS, Eun CS, Han DS, Park DI. Additive effect of probiotics (Mutaflor) on 5-aminosalicylic acid therapy in patients with ulcerative colitis. Korean Journal of Internal Medicine, (2022); 37(5): 949-957.
17. Dang HT, Tran DM, Phung TTB, Bui ATP, Vu YH, Luong MT, Nguyen HM, Trinh HT, Nguyen TT, Nguyen AH, Van Nguyen AT. Promising clinical and immunological efficacy of Bacillus clausii spore probiotics for supportive treatment of persistent diarrhea in children. Scientific Reports, (2024); 14(1): 6422.
18. Salazar PMA, Cruz NRU, Trujillo TXA, Dominguez MJJ, Cruz NHI, Guzmán DJM, Guzmán RMJ, Vega GJO, Ascencio DKV, Zarate CMF, González PFY, Barbosa CFJ, Fuentes OC, Cervantes GG, Cervantes PE, Cervantes CGA, Cortés FAO, González OA. Effectiveness of Saccharomyces Boulardii CNCM I-745 probiotic in acute inflammatory viral diarrhoea in adults: results from a single-centre randomized trial. BMC Gastroenterology, (2023); 23(1): 229.
19. Ivashkin V, Fomin V, Moiseev S, Brovko M, Maslennikov R, Ulyanin A, Sholomova V, Vasilyeva M, Trush E, Shifrin O, Poluektova E. Efficacy of a Probiotic Consisting of Lacticaseibacillus rhamnosus PDV 1705, Bifidobacterium bifidum PDV 0903, Bifidobacterium longum subsp. infantis PDV 1911, and Bifidobacterium longum subsp. longum PDV 2301 in the Treatment of Hospitalized Patients with COVID-19: a Randomized Controlled Trial. Probiotics and Antimicrobial Proteins, (2023); 15(3): 460-468.
20. Grice EA, Segre JA. The skin microbiome. Nature Reviews Microbiology, (2011); 9(4): 244-53.
21. Carucci L, Nocerino R, Paparo L, De Filippis F, Coppola S, Giglio V, Cozzolino T, Valentino V, Sequino G, Bedogni G, Russo R, Ercolini D, Berni Canani R. Therapeutic effects elicited by the probiotic Lacticaseibacillus rhamnosus GG in children with atopic dermatitis. The results of the ProPAD trial. Pediatric Allergy and Immunology, (2022); 33(8): e13836.
22. Michelotti A, Cestone E, De Ponti I, Giardina S, Pisati M, Spartà E, Tursi F. Efficacy of a probiotic supplement in patients with atopic dermatitis: a randomized, double-blind, placebo-controlled clinical trial. European Journal of Dermatology, (2021); 31(2): 225-232.
23. Freedman KE, Hill JL, Wei Y, Vazquez AR, Grubb DS, Trotter RE, Wrigley SD, Johnson SA, Foster MT, Weir TL. Examining the Gastrointestinal and Immunomodulatory Effects of the Novel

Probiotic *Bacillus subtilis* DE111. International Journal of Molecular Sciences, (2021); 22(5): 2453.
24. Kanazawa A, Aida M, Yoshida Y, Kaga H, Katahira T, Suzuki L, Tamaki S, Sato J, Goto H, Azuma K, Shimizu T, Takahashi T, Yamashiro Y, Watada H. Effects of Synbiotic Supplementation on Chronic Inflammation and the Gut Microbiota in Obese Patients with Type 2 Diabetes Mellitus: A Randomized Controlled Study. Nutrients, (2021); 13(2):558.
25. Eliuz Tipici B, Coskunpinar E, Altunkanat D, Cagatay P, Omer B, Palanduz S, Satman I, Aral F. Lactobacillus GG is associated with mucin genes expressions in type 2 diabetes mellitus: a randomized, placebo-controlled trial. European Journal of Nutrition, (2023); 62(5): 2155-2164.
26. Babadi M, Khorshidi A, Aghadavood E, Samimi M, Kavossian E, Bahmani F, Mafi A, Shafabakhsh R, Satari M, Asemi Z. The Effects of Probiotic Supplementation on Genetic and Metabolic Profiles in Patients with Gestational Diabetes Mellitus: a Randomized, Double-Blind, Placebo-Controlled Trial. Probiotics and antimicrobial proteins, (2019); 11(4):1227-1235.
27. Escouto GS, Port GZ, Tovo CV, Fernandes SA, Peres A, Dorneles GP, Houde VP, Varin TV, Pilon G, Marette A, Buss C. Probiotic Supplementation, Hepatic Fibrosis, and the Microbiota Profile in Patients with Nonalcoholic Steatohepatitis: A Randomized Controlled Trial. Journal of Nutrition, (2023) ;153(7):1984-1993.
28. Lin JH, Lin CH, Kuo YW, Liao CA, Chen JF, Tsai SY, Li CM, Hsu YC, Huang YY, Hsia KC, Yeh YT, Ho HH. Probiotic Lactobacillus fermentum TSF331, Lactobacillus reuteri TSR332, and Lactobacillus plantarum TSP05 improved liver function and uric acid management-A pilot study. PLoS One. (2024); 19(7): e0307181.
29. Hariri Z, Yari Z, Hoseini S, Mehrnami A, Abhari K, Sohrab G. Effects of Synbiotic-Containing Bacillus coagulans (GBI-30) on the Cardiovascular Status of Patients with Polycystic Ovary Syndrome: A Triple-blinded, Randomized, Placebo-controlled Study. Clinical Therapeutics, (2023); 45(10): e193-e199.
30. Moludi J, Khedmatgozar H, Nachvak SM, Abdollahzad H, Moradinazar M, Sadeghpour Tabaei A. The effects of co-administration of probiotics and prebiotics on chronic inflammation, and depression symptoms in patients with coronary artery diseases: a randomized clinical trial. Nutritional Neuroscience, (2022); 25(8):1659-1668.
31. Lim PS, Wang HF, Lee MC, Chiu LS, Wu MY, Chang WC, Wu TK. The Efficacy of Lactobacillus-Containing Probiotic Supplementation in Hemodialysis Patients: A Randomized, Double-Blind, Placebo-Controlled Trial. Journal of Renal Nutrition, (2021); 31(2):189-198.
32. Haghighat N, Mohammadshahi M, Shayanpour S, Haghighizadeh MH. Effects of Synbiotics and Probiotics Supplementation on Serum Levels of Endotoxin, Heat Shock Protein 70 Antibodies and Inflammatory Markers in Hemodialysis Patients: a Randomized Double-Blinded Controlled Trial. Probiotics and Antimicrobial Proteins, (2020); 12(1):144-151.
33. Appleton J. The Gut-Brain Axis: Influence of Microbiota on Mood and Mental Health. Integrative medicine (Encinitas, Calif.), (2018); 17(4): 28-32.
34. Ghavami A, Khorvash F, Heidari Z, Khalesi S, Askari G. Effect of synbiotic supplementation on migraine characteristics and inflammatory biomarkers in women with migraine: Results of a randomized controlled trial. Pharmacological Research, (2021); 169:105668.
35. Zhang Y, Gao Y, Qin J, Li X, Jiang F, Cai Y, Feng H, Gu X, Gao M, Wang L, Lin Y, Fan Y, Xu B, Wang E, Shao Q. Breast microecology improvement using probiotics following needle aspiration in patients with lactational breast abscess: a multi-center randomized double-blind controlled trial. Scientific Reports, (2022); 12(1): 16692.
36. Zhang YJ, Li S, Gan RY, Zhou T, Xu DP, Li HB. Impacts of gut bacteria on human health and diseases. International Journal of Molecular Sciences, (2015); 16(4): 7493-519.
37. Xia C, Jiang C, Li W, Wei J, Hong H, Li J, Feng L, Wei H, Xin H, Chen T. A Phase II Randomized Clinical Trial and Mechanistic Studies Using Improved Probiotics to Prevent Oral Mucositis Induced by Concurrent Radiotherapy and Chemotherapy in Nasopharyngeal Carcinoma. Frontiers in immunology, (2021); 12: 618150.
38. Raji LM, Zarrati M, Najafi S, Yazdani B, Cheshmazar E, Razmpoosh E, Janani L, Raji LM, Shidfar F. Effects of synbiotic supplementation on serum adiponectin and inflammation status of overweight and obese breast cancer survivors: a randomized, triple-blind, placebo-controlled trial. Support Care Cancer, (2021); 29(7): 4147-4157.
39. Latif A, Shehzad A, Niazi S, Zahid A, Ashraf W, Iqbal MW, Rehman A, Riaz T, Aadil RM, Khan IM, Özogul F, Rocha JM, Esatbeyoglu T, Korma SA. Probiotics: mechanism of action, health benefits and their application in food industries. Frontiers in Microbiology, (2023); 14: 1216674.
40. Petrariu OA, Barbu IC, Niculescu AG, Constantin M, Grigore GA, Cristian RE, Mihaescu G, Vrancianu CO. Role of probiotics in managing various human diseases, from oral pathology to cancer and gastrointestinal diseases. Frontiers in Microbiology, (2024); 14:1296447.
41. Wang Y, Wu J, Lv M, Shao Z, Hungwe M, Wang J, Bai X, Xie J, Wang Y, Geng W. Metabolism Characteristics of Lactic Acid Bacteria and the Expanding Applications in Food Industry. Frontiers in Bioengineering and Biotechnology, (2021); 9: 612285.
42. Thuy TTD, Lu HF, Bregente CJB, Huang FA, Tu PC, Kao CY. Characterization of the broad-spectrum antibacterial activity of bacteriocin-like inhibitory substance-producing probiotics isolated from fermented foods. BMC Microbiology, (2024); 24(1): 85.
43. Ibrahim SA, Ayivi RD, Zimmerman T, Siddiqui SA, Altemimi AB, Fidan H, Esatbeyoglu T, Bakhshayesh RV. Lactic Acid Bacteria as Antimicrobial Agents: Food Safety and Microbial Food Spoilage Prevention Foods, (2021); 10(12): 3131.
44. Okumura R, Takeda K. The role of the mucosal barrier system in maintaining gut symbiosis to prevent intestinal inflammation. Seminars in Immunopathology, (2024); 47(1):2.
45. Qin D, Ma Y, Wang Y, Hou X, Yu L. Contribution of *Lactobacilli* on Intestinal Mucosal Barrier and Diseases: Perspectives and Challenges of *Lactobacillus casei*. Life (Basel), (2022); 12(11): 1910.
46. Phillippi DT, Daniel S, Nguyen KN, Penaredondo BA, Lund AK. Probiotics Function as Immunomodulators in the Intestine in C57Bl/6 Male Mice Exposed to Inhaled Diesel Exhaust Particles on a High-Fat Diet. Cells, (2022); 11(9): 1445.
47. Peterson LW, Artis D. Intestinal epithelial cells: regulators of barrier function and immune homeostasis. Nature Reviews Immunology, (2014); 14(3): 141-53.
48. Latif A, Shehzad A, Niazi S, Zahid A, Ashraf W, Iqbal MW, Rehman A, Riaz T, Aadil RM, Khan IM, Özogul F, Rocha JM, Esatbeyoglu T, Korma SA. Probiotics: mechanism of action, health benefits and their application in food industries. Frontiers in Microbiology, (2023); 14: 1216674.
49. Kuo WT, Odenwald MA, Turner JR, Zuo L. Tight junction proteins occludin and ZO-1 as regulators of epithelial proliferation and survival. Annals of the New York Academy of Sciences. (2022); 1514(1): 21-33.
50. Bauer H, Zweimueller-Mayer J, Steinbacher P, Lametschwandtner A, Bauer HC. The dual role of zonula occludens (ZO) proteins. Journal of Biomedicine and Biotechnology, (2010); 2010: 402593.
51. Maaty SE, Elashtokhy MMA, Amin MK, Hassan AS, Zabermawi NM, Qattan SYA, Shafi ME, Algopishi UB, El-Shaboury GA, Farsi RM, Mahgoub S. Probiotic potential and bioactive properties of Lactococcus lactis MSH-08 isolates from fermented dairy products: Antimicrobial, antioxidant, and anticancer activities. Applied Food Research, (2025); 5(1): 100763.
52. Dikeocha IJ, Al-Kabsi AM, Ahmeda AF, Mathai M, Alshawsh MA. Investigation into the Potential Role of Propionibacterium freudenreichii in Prevention of Colorectal Cancer and Its Effects on

the Diversity of Gut Microbiota in Rats. International Journal of Molecular Sciences, (2023); 24(9): 8080.
53. Pourrajab B, Fatahi S, Sohouli MH, Găman MA, Shidfar F. The effects of probiotic/synbiotic supplementation compared to placebo on biomarkers of oxidative stress in adults: a systematic review and meta-analysis of randomized controlled trials. Critical Reviews in Food Science and Nutrition, (2022); 62(2): 490-507.
54. Donaldson DS, Else KJ, Mabbott NA. The Gut-Associated Lymphoid Tissues in the Small Intestine, Not the Large Intestine, Play a Major Role in Oral Prion Disease Pathogenesis. Journal of Virology, (2015); 89(18): 9532-9547.
55. Goldmann O, Nwofor OV, Chen Q, Medina E. Mechanisms underlying immunosuppression by regulatory cells. Frontiers in Immunology, (2024); 15: 1328193.
56. Carlson JL, Erickson JM, Lloyd BB, Slavin JL. Health Effects and Sources of Prebiotic Dietary Fiber. Current Developments in Nutrition, (2018); 2(3): nzy005.
57. Siddiqui MT, Cresci GAM. The Immunomodulatory Functions of Butyrate. Journal of Inflammation Research, (2021); 14: 6025-6041.
58. Luu M, Riester Z, Baldrich A, Reichardt N, Yuille S, Busetti A, Klein M, Wempe A, Leister H, Raifer H, Picard F, Muhammad K, Ohl K, Romero R, Fischer F, Bauer CA, Huber M, Gress TM, Lauth M, Danhof S, Bopp T, Nerreter T, Mulder IE, Steinhoff U, Hudecek M, Visekruna A. Microbial short-chain fatty acids modulate CD8$^+$ T cell responses and improve adoptive immunotherapy for cancer. Nature Communications, (2021); 12(1): 4077.
59. Li M, van Esch BCAM, Wagenaar GTM, Garssen J, Folkerts G, Henricks PAJ. Pro- and anti-inflammatory effects of short chain fatty acids on immune and endothelial cells. European Journal of Pharmacology, (2018); 831: 52-59.
60. Hosseini E, Grootaert C, Verstraete W, Van de Wiele T. Propionate as a health-promoting microbial metabolite in the human gut. Nutrition Reviews, (2011); 69(5): 245-258.
61. Mills S, Yang B, Smith GJ, Stanton C, Ross RP. Efficacy of *Bifidobacterium longum* alone or in multi-strain probiotic formulations during early life and beyond. Gut Microbes, (2023); 15(1): 2186098.
62. Geng P, Zhao N, Zhou Y, Harris RS, Ge Y. *Faecalibacterium prausnitzii* regulates carbohydrate metabolic functions of the gut microbiome in C57BL/6 mice. Gut Microbes, (2025); 17(1): 2455503.
63. Farré R, Fiorani M, Abdu Rahiman S, Matteoli G. Intestinal Permeability, Inflammation and the Role of Nutrients. Nutrients, (2020); 12(4): 1185.
64. Vancamelbeke M, Vermeire S. The intestinal barrier: a fundamental role in health and disease. Expert Review of Gastroenterology & Hepatology, (2017); 11(9): 821-834.
65. Ji J, Jin W, Liu SJ, Jiao Z, Li X. Probiotics, prebiotics, and postbiotics in health and disease. MedComm, (2023); 4(6): e420.
66. Manichanh C, Borruel N, Casellas F, Guarner F. The gut microbiota in IBD. Nat Rev Journal of Gastroenterology and Hepatology, (2012); 9 (10): 599-608.
67. Dalmasso G, Cottrez F, Imbert V, Lagadec P, Peyron JF, Rampal P, Czerucka D, Groux H. Saccharomyces boulardii inhibits inflammatory bowel disease by trapping T cells in mesenteric lymph nodes. Gastroenterology, (2006); 131(6): 1812-1825.
68. Salvi PS, Cowles RA. Butyrate and the Intestinal Epithelium: Modulation of Proliferation and Inflammation in Homeostasis and Disease. Cells, (2021); 10(7): 1775.
69. Zhao Y, Dong BR, Hao Q. Probiotics for preventing acute upper respiratory tract infections. Cochrane Database of Systematic Reviews, (2022); 8(8): CD006895.
70. Du T, Lei A, Zhang N, Zhu C. The Beneficial Role of Probiotic *Lactobacillus* in Respiratory Diseases. Frontiers in Immunology, (2022); 13: 908010.
71. Gao T, Wang X, Li Y, Ren F. The Role of Probiotics in Skin Health and Related Gut-Skin Axis: A Review. Nutrients, (2023); 15(14): 3123.
72. Falagas M, Betsi GI, Athanasiou S. Probiotics for the treatment of women with bacterial vaginosis. Clinical Microbiology and Infection, (2007); 13(7): 657-64.
73. Schwenger EM, Tejani AM, Loewen PS. Probiotics for preventing urinary tract infections in adults and children. Cochrane Database of Systematic Reviews, (2015); 2015(12): CD008772.
74. Lu S, Zhao Q, Guan Y, Sun Z, Li W, Guo S, Zhang A. The communication mechanism of the gut-brain axis and its effect on central nervous system diseases: A systematic review. Biomedicine & Pharmacotherapy, (2024); 178:117207.
75. Ansari F, Neshat M, Pourjafar H, Jafari SM, Samakkhah SA, Mirzakhani E. The role of probiotics and prebiotics in modulating of the gut-brain axis. Frontiers in Nutrition, (2023); 10: 1173660.
76. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. Cells, (2023); 12(1):184.
77. Thananimit S, Pahumunto N, Teanpaisan R. Characterization of Short Chain Fatty Acids Produced by Selected Potential Probiotic *Lactobacillus* Strains. Biomolecules, (2022); 12(12): 1829.
78. Ha S, Zhang X, Yu J. Probiotics intervention in colorectal cancer: From traditional approaches to novel strategies. Chinese Medical Journal, (2024); 137(1): 8-20.
79. Thu MS, Ondee T, Nopsopon T, Farzana IAK, Fothergill JL, Hirankarn N, Campbell BJ, Pongpirul K. Effect of Probiotics in Breast Cancer: A Systematic Review and Meta-Analysis. Biology (Basel), (2023); 12(2): 280.
80. Sun J, Song S, Liu J, Chen F, Li X, Wu G. Gut microbiota as a new target for anticancer therapy: from mechanism to means of regulation. NPJ Biofilms Microbiomes, (2025); 11(1): 43.

Table and Figures

S.No.	Year	Study Type	Setting	Study Duration	Disease	Sample Size	Intervention	Dose	Effect	Reference
1	2021	Randomized, double blind, and placebo controlled human trial	Municipal Hospital China	3 Month	Asthmatic patients	55	*Bifidobacterium Lactis Probio-M8 Powder and Symbicort Turbuhaler*	3×10^{10} CFU/Sachet/Day	Reducing lung inflammation	10
2	2021	Single-Centre, Randomised, Double-Blind, Placebo-Controlled Pilot Trial	University Hospitals Leuven, Belgium	8 Weeks	Functional Dyspepsia	68	*Bacillus Coagulans My01 and Bacillus Subtilis My02,*	$2\cdot5\times10^{9}$ CFU Per Capsule	Potentially beneficial Immune and microbial changes	13
3	2021	Randomized, Double-Blind, Placebo-Controlled Trial	Wuyuan, Jiangxi, China	7 Weeks	Oral Mucositis In Nasopharyngeal Cancer	85	*L. Plantarum Mh-301, Lactis Lpl-Rh, L. Rhamnosus Lgg-18, L. Acidophilus*	One Capsule of (probiotic cocktail (containing B. animalis subsp. Lactis LPL-RH 10^{9} CFU, L. plantarum MH-301 strain 10^{9} CFU, L. acidophilus strain 10^{9} CFU, L. rhamnosus LGG-18 strain 10^{9} CFU) 2 Times A Day	Increase immune response and modifying the structure of gut microbiota.	37
4	2022	Randomized, Double-Blind, Controlled Trial	Italy	12 Weeks	Atopic Dermatitis	100	*Lactobacillus Rhamnosus Gg (Lgg)*	1×10^{10} CFU/Daily	Modulation of gut and skin microbiome	21
5	2021	Randomized Controlled Trial	Juntendo University Hospital And International Good Will Hospital Japan	24-Week	Obese Patients With Type 2 Diabetes Mellitus	88	*Lactobacillus Paracasei Strain Shirota (Previously Lactobacillus Casei Strain Shirota) And Bifidobacterium Breve Strain Yakult, And Galactooligosaccharides*	3.0 G Dry Powder Containing 3×10^{8} CFU Living *Lactobacillus Paracasei* Yit 9029 (Strain Shirota:Lcs) organisms, 3×10^{8} Living *Bifidobacterium Breve Yit* 12272 (Bbry) organisms, and 7.5 gm galacto-oligosaccharide per day	Improved the gut environment	24
6	2023	Double-Blind, Randomized, And Controlled Clinical Trial	Vietnam National Children's Hospital	70 Weeks	Acute Respiratory Tract Infections	43	*Nasal-Spraying Probiotic Livespo Navax Having 5 billion Of Bacillus Subtilis* and *B. Clausii Spores In 5 Ml*	2.5×10^{8} Bacillus Spores Per Each Nasal Cavity/ Time×3 Times/ Day Directly into nasal cavity	Reduce influenza viral infections	11
7	2023	Double-Blind, Placebo-Controlled Clinical Trial	Universidade Federal De Ci^Encias Da Saúde De Porto Alegre (Ufcspa) And Hospital Santa Casa De Porto Alegre, Brazil	26 Weeks	Non-alcoholic Fatty Liver Disease and Non-alcoholic Steatohepatitis (Nash)	48	*Lactobacillus Acidophilus, Bifidobacterium Lactis*	Lactobacillus Acidophilus 1×10^{9} CFU and Bifidobacterium Lactis 1×10^{9} CFU 1 Capsule/D With 1 Glass Of Water	Improve Ast to platelet Ratio and improve Gut Microbiota.	27
8	2022	Double-Blind, Four-Arm Parallel Randomized Controlled Trial	Imam Ali Cardiovascular Hospital in Kermanshah University of Medical Sciences, Kermanshah, Iran	8 Weeks	Coronary Artery Diseases	96	*Lactobacillus Rhamnosus G (Lgg)*	A Capsule/Day, Contained 1.9×10^{9} CFU Of Lactobacillus Rhamnosus G], Inulin (15 G/Day), Co-Supplemented (Lgg and Inulin	Beneficial Effects on Depression, Anxiety, And Inflammatory Biomarkers	30
9	2022	Double-Blinded Randomized Controlled Trial	Jordan University Hospital, Amman, Jordan	113 Weeks	Ulcerative Colitis	24	*Lactobacillus, Bifidobacterium Species*	3×10^{10} CFU of probiotic capsules (Nine Lactobacillus and Five Bifidobacterium Species	Induce remission and improve clinical parameters	14
10	2020	Randomized, Double-Blind, Placebo-Controlled Trial	Dialysis Center of Emam Khomeini Hospital, Ahvaz, Iran	12 Weeks	Haemodialysis Patients	75	*Lactobacillus Acidophilus T16, Bifidobacterium Bifidum Bia-6, Bifidobacterium Lactis Bia-6, And Bifidobacterium Longum Laf-5*	2.7×10^{7} CFU/Gm Each	Improving inflammatory markers, endotoxin, and anti-hsp70 levels	32
11	2021	Single-Centre, Randomized, Double-Blind, Placebo controlled, Parallel Group	Complife Italia SRL	8 Weeks	Atopic Dermatitis	80	*L. Plantarum, L. Reuteri, L. Rhamnosus*	1×10^{9} CFU L. Plantarum Pbs067, 1×10^{9} CFU L. Reuteri Pbs072 and 1×10^{9} CFU L. Rhamnosus Lrh020, Excipients such as corn starch (26 Mg) and vegetable magnesium stearate (1 Mg)	Improve Skin Conditions and Reduce Inflammation	22
12	2024	Randomized, Double-Blind, Controlled Clinical Trial	Gastroenterology Department At The Vietnam National Children's Hospital, Vietnam	113 Weeks	Persistent Diarrhea	100	*Bacillus Clausii Spore Probiotics (Livespo Clausy*	2 billion CFU /5 ml Ampoule at high dosages of 4–6 Ampoules a day	Reducing diarrhea symptoms, inflammatory cytokines, and iga levels.	17
13	2021	Randomized Double-Blind Controlled Trial	Isfahan University of Medical Sciences, Isfahan, Iran,	30 Weeks	Migraine	69	*Lactobacillus Casei, Lactobacillus Acidophilus, Lactobacillus Rhamnosus, Lactobacillus Helveticus, Lactobacillus Bulgaricus,*	Each500 mg capsule have 10^{9} CFU of each (*Lactobacillus Casei, Lactobacillus Acidophilus, Lactobacillus Rhamnosus, Lactobacillus Helveticus, Lactobacillus Bulgaricus,*	Reduce migraine frequency, pain, and inflammation	34

S.No.	Year	Study Type	Setting	Study Duration	Disease	Sample Size	Intervention	Dose	Effect	Reference
							Lactobacillus Plantarum, Lactobacillus Gasseri, Bifidobacterium Breve, Bifidobacterium Longum, Bifidobacterium Lactis, Bifidobacterium Bifidum, And Streptococcus Thermophilus, And Fructooligosaccharides (Fos)	*Lactobacillus Plantarum, Lactobacillus Gasseri, Bifidobacterium Breve, Bifidobacterium Longum, Bifidobacterium Lactis, Bifidobacterium Bifidum, And Streptococcus Thermophilus*)		
14	2023	Interventional Double-Blind Randomized Clinical Trial	Jordan University Hospital, Amman, Jordan	52 Weeks	Ulcerative Colitis	40	*Lactobacillus Rhamnosus , Lactobacillus Acidophilus, Lactobacillus Reuteri, Lactobacillus Paracasei, Lactobacillus Casei, Lactobacillus Gasseri, Lactobacillus Plantarum) And Bifidobacteria (Bifidobacterium Lactis, Bifidobacterium Breve, Bifidobacterium Bifidum, Bifidobacterium Longum, Bifidobacterium Infantis*	Oral viable capsules of probiotic contain ($1×10^{10}$ CFU /g) Of Lactobacillus (Lactobacillus Rhamnosus , Lactobacillus Acidophilus, Lactobacillus Reuteri, Lactobacillus Paracasei, Lactobacillus Casei, Lactobacillus Gasseri, Lactobacillus Plantarum) And Bifidobacteria (Bifidobacterium Lactis, Bifidobacterium Breve, Bifidobacterium Bifidum, Bifidobacterium Longum, Bifidobacterium Infantis) species three times a per day	Improved social, bowel, emotional, and overall quality of life	15
15	2023	A Randomized, Placebo-Controlled Double-Blind Study	Puerta De Hierro Hospitals, Tlajomulco De Zuñiga, Mexico	52 Weeks	Acute Inflammatory Viral Diarrhea	46	*Saccharomyces Boulardii*	3 Capsules ($1×10^9$/100 ml CFU Of Floratil 200mg/Day)	Improve diarrhoea.	18
16	2022	A Multicentre, Double-Blind, Randomised, Placebo-Controlled Study	Kangbuk Samsung Hospital, Sungkyunkwan University School Of Medicine, Seoul, Korea	8 Weeks	Ulcerative Colitis	133	*E. Coli Strain Nissle 1917*	One Capsule Containing $2.5×10^9$ CFU and One Capsule/Day from Day 1 To Day 4 And Two Capsules/ Day From Day 5	Effective exacerbation and endoscopic remission	16
17	2021	Parallel-Arm, Randomized, Double-Blind, Placebocontrolled	Food And Nutrition Clinical Research Laboratory (Fncrl) At Colorado State University,	4 Weeks	Obese And Healthy Control	44	*Bacillus Subtilis Strain De111*	A Capsule contain $1×10^9$ CFU Taken Once Daily	Increasing anti-inflammatory immune cell	23
18	2023	Randomized, Controlled, Single Center, Open label Trial	Department Of Internal Medicine, Gastroenterology And Hepatology, Sechenov University, Moscow, Russian Federation	18 Weeks	Covid-19-Associated Diarrheal	200	*Lactobacillus Rhamnosus Gg (Lgg), Bifdobacterium Bifdum, Bifdobacterium Longum Subsp. Longum Pdv 2301 Pdv 0903*	Florasan-D Containing 10^9 CFU Of Lactobacillus Rhamnosus Pdv 1705, 10^9 CFU Of Bifdobacterium Bifdum Pdv 0903, 10^9 CFU Of Bifdobacterium Longum Subsp. Infantis Pdv 1911, And 10^9, Bifdobacterium Longum Subsp. Infantis Pdv 1911, 10^9 CFU of Bifdobacterium Longum Subsp.Longum Pdv 2301	Decrease COVID-19 associated diarrhoea and antibiotic related complication	19
19	2021	A Randomized, Double Blind, Placebo Controlled Trial	Division Of Renal Medicine Tungs Taichung Metroharbor Hospital Taichung Taiwan, Republic Of China	26 Weeks	Haemodialysis Patients	56	*Lactococcus Lactis Subsp. Lactis Ll358, Lactobacillus Salivarius Ls159, And Lactobaccillus Pentosus Lpe588*	100 billion ($1 × 10^{11}$ CFU/Day)	Decrease in serum levels of indoxyl sulfate level	31
20	2022	Multicentre, Randomized, Double-Blind, Controlled Clinical Trial	Xiyuan Hospital Of The China Academy Of Chinese Medical Sciences, China	4 Weeks	Lactational Breast Abscess	110	*L. Fermentum Cect5716*	One Sachet of L. Fermentum Cect5716 once a Day	Shorten healing time	35

S.No.	Year	Study Type	Setting	Study Duration	Disease	Sample Size	Intervention	Dose	Effect	Reference
21	2024	Placebo-Controlled, Double-Blinded, Randomized Clinical Trial	Aging And Disease Prevention Research Center At Fooyin University Hospital, Taiwan	14 Weeks	Individual with abnormal liver function test and uric acid	120	*Lactobacillus Fermentum Tsf331 Lactobacillus Reuteri Tsr332 Lactobacillus Plantarum Tsp05*	6.7×10^9 CFU Of Either L. Fermentum Tsf331, L. Reuteri Tsr332, Or L. Plantarum Tsp05. The 3 Mix Capsule Contained A Total 6.7×10^9 CFU, Combining L. Fermentum Tsf331, L. Reuteri Tsr332, And L. Plantarum Tsp05. The 3 Mix and Pe0401 Capsule Was Composed Of A Total 6.7×10^9 CFU, Including L. Fermentum Tsf331, L. Reuteri Tsr332, L. Plantarum Tsp05, and 200 Mg Totipro1 Pe0401 Postbiotic Powder. L. Fermentum Tsf331 (Bcrc 910815 = Cgmcc 15527) and L. Reuteri Tsr332 (Bcrc 910816 = Cgmcc 15528) Were Isolated From The Gut Of Healthy Humans, Whereas L. Plantarum Tsp05 (Bcrc 910855 = Cgmcc 16710) Was Isolated From Kimchi. Totipro1 Pe0401 Was A Fermentation Product Derived From Probiotics	Improved liver function and reduced uric acid levels	28
22	2021	Randomized, Triple-Blind, Placebo-Controlled Clinical Trial	Private Oncology Clinic Tehran, Iran	2 Weeks	Breast Cancer	76	*Lactobacillus Casei, Lactobacillus Acidophilus, Lactobacillus Rhamnosus, Lactobacillus Bulgaricus, Bifidobacterium Breve, Bifidobacterium Longum, And Streptococcus Thermophiles*	10^9 CFU/G each (*Lactobacillus Casei, Lactobacillus Acidophilus, Lactobacillus Rhamnosus, Lactobacillus Bulgaricus, Bifidobacterium Breve, Bifidobacterium Longum, And Streptococcus Thermophiles*)	Improve reduce inflammation	38
23	2023	Triple-Blinded, Randomized, Placebo-Controlled Clinical Trial	Shahid Beheshti University Of Medical Sciences Tehran, Tehran, Iran.	12-Week	Polycystic Ovary Syndrome	72	*Bacillus Coagulans*	2 G Of Bacillus Coagulans	Improve inflammatory	29
24	2019	Randomized, Double-Blind, Placebo-Controlled Clinical Trial	Department Of Microbiology and Immunology, School Of Medicine, Kashan University Of Medical Sciences, Kashan, Iran.	6 Weeks	Gestational Diabetes Mellitus	48	*Lactobacillus Acidophilus, Lactobacillus Casei, Bifidobacterium Bifidum, Lactobacillus Fermentum*	Lactobacillus Acidophilus, Lactobacillus Casei, Bifidobacterium Bifidum, Lactobacillus Fermentum (2×10^9 CFU/G Each)	Improve glycemic control, lipid profile, and inflammatory markers	26
25	2023	Randomized, Placebo-Controlled Trial	Istanbul Faculty Of Medicine, Istanbul University, Istanbul, Turkey	8 Weeks	T2dm	34	*Lactobacillus Rhamnosus*	10×10^9 CFU/Day *Lactobacillus rhamnosus* GG (ATCC 53103)	Improve mucin gene expression	25

Table 1: An overview of 25 chosen studies assessing how probiotics affect inflammatory diseases in people that were found using a systematic review that adhered to PRISMA guidelines and particular inclusion and exclusion criteria

S.N.	Strain of Bacteria	Function	References
1	*Lactobacillus acidophilus*	Aids digestion and may prevent diarrhea.	26
2	*Lactobacillus rhamnosus*	Supports gut health and prevents antibiotic-associated diarrhea.	21
3	*Lactobacillus casei*	Aids immune function and may alleviate lactose intolerance.	26
4	*Lactobacillus plantarum*	Improves intestinal health and reduces IBS symptoms.	28
5	*Lactobacillus reuteri*	May alleviate newborn colic and promote intestinal health.	28
6	*Bifidobacterium bifidum*	Boosts digestive health and may reduce IBS symptoms.	26
7	*Bifidobacterium longum*	Supports intestinal health and immunity	61
8	*Bifidobacterium lactis*	Promotes digestive and immunological health	10
9	*Bifidobacterium breve*	Improves newborn gut flora and reduces constipation.	40
10	*Streptococcus thermophilus*	Aids in lactose digestion	34
11	*Saccharomyces boulardii*	Prevents and treats diarrhea, especially antibiotic-associated diarrhea.	18
12	*Lactococcus lactis*	Enhances intestinal health and immunity	31
13	*Escherichia coli Nissle 1917*	Helps manage ulcerative colitis	16
14	*Bacillus coagulans*	Supports digestive issues and gut health	13
15	*Bacillus subtilis*	Supports gut health and immune function	23
16	*Lactobacillus gasseri*	May improve intestinal health and weight management.	15
17	*Bifidobacterium infantis*	Promotes digestion and immunity, particularly in newborns.	15
18	*Lactobacillus helveticus*	May enhance mood and cognition.	34

Table 2. Different strains of probiotics which beneficial for human health and its treatment with these probiotics can significantly improves the symptoms of disease and reduces risk factors.

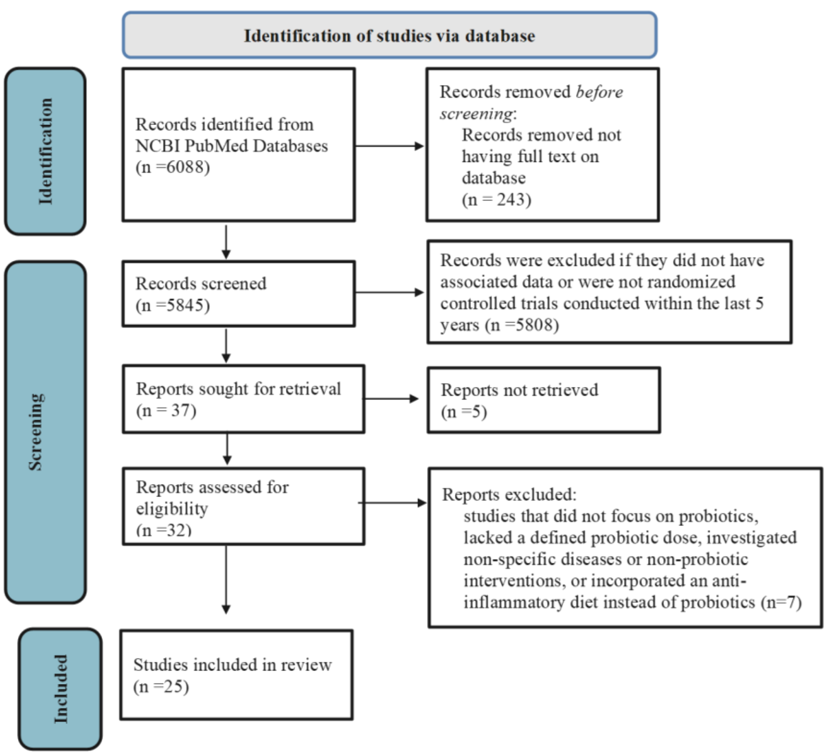

Figure 1: PRISMA diagram of selected studies: Systematic review on PubMed/MEDLINE database based on PRISMA guidelines, 6,088 articles were found; 5,808 were eliminated after applying filters ("Full Text," "Associated Data," "RCT," and "Last 5 Years" total 25 study enrolled.

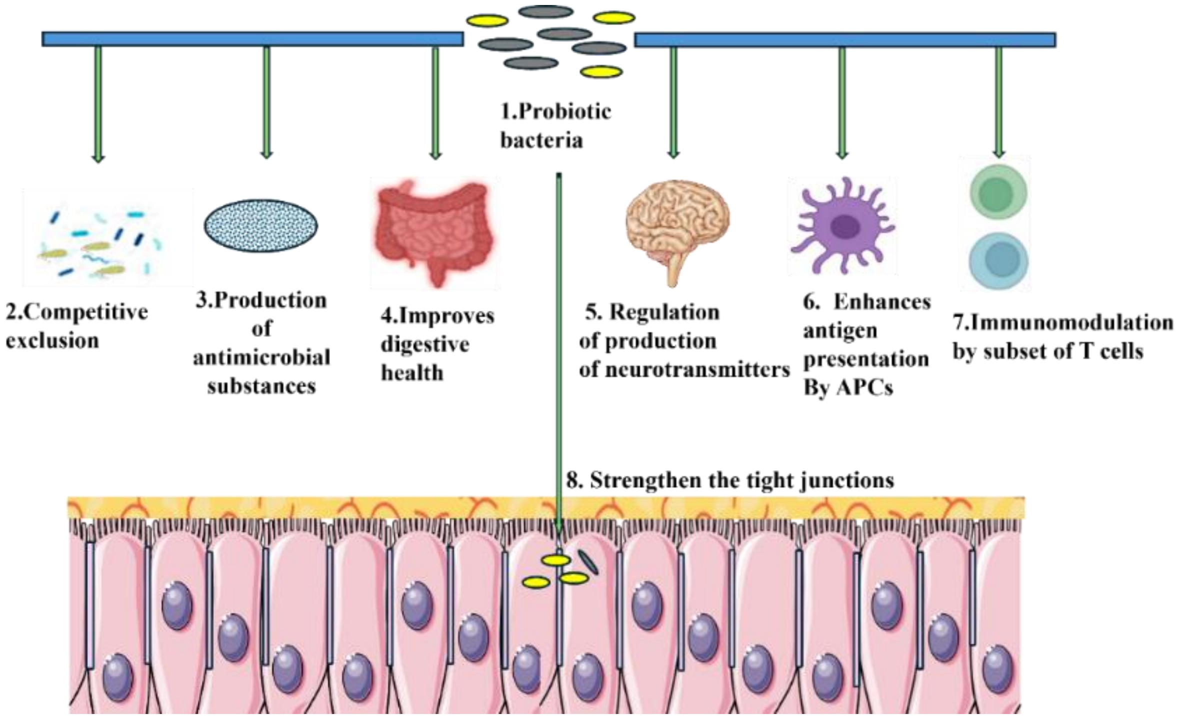

Figure 2: Several probiotic-influenced pathways, such as immune modulation, inflammation reduction, gut microbiota regulation, and barrier integrity enhancement, improve health outcomes for a variety of physiological systems and diseases.

Additional data may be available on request (681-701).