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Research Article

Probiotics and Prebiotics: A Comprehensive Review of Their Role in Treating Infectious Diseases and Their Impact on the Gut Microbiome

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Abstract

Prebiotics have a significant effect on the treatment of infectious diseases because they alter the gut flora and boost immunity. Probiotics are advantageous living microorganisms that support the preservation of a healthy stomach environment. Prebiotics are indigestible dietary ingredients that help beneficial bacteria proliferate. The paper looks into the ways that probiotics and prebiotics work, including immune control, the production of antimicrobial chemicals, and pathogen competitive exclusion. They are widely recognized for their ability to treat and prevent gastrointestinal disorders, such as diarrhea and Clostridium difficile infections. Additionally, probiotics may help prevent urinary tract infections, reduce the duration and frequency of respiratory tract infections, and cure skin conditions like atopic dermatitis. Probiotics and prebiotics help fight antibiotic resistance by lowering the demand for antibiotics. Standardizing their use and comprehending strain-specific effects remain difficult despite a plethora of clinical investigations demonstrating their safety and effectiveness. Probiotics and prebiotics may help cure infectious illnesses, but more study is needed to develop specific procedures and regulatory frameworks.

Keywords: Antibiotic Resistance; Infectious Diseases; Prebiotics; Probiotics; Microorganisms

Introduction and Background

As the world's population ages, infectious diseases are expected to become more common and remain the leading cause of death and disability-adjusted life years. The current COVID-19 pandemic is predicted to cost $16 trillion annually, contributing to the estimated $60 billion annual financial impact of these epidemics. Even though vaccines are being created, it is still unknown how effective they will be in the long run, and interruptions in immunization programs could cause diseases that young children can prevent via vaccinations. Due to the emerging issue of antimicrobial resistance, new preventative and interventional strategies are required to lessen the burden of infectious diseases. Resilience to viral and inflammatory illnesses depends on maintaining and possibly repairing the human microbiome [1]. The host's health is impacted by the gut microbiota via immunological, physiological, and nutritional processes. Genetics, nutrition, environment, and inflammatory states are only a few of the factors that determine the type of bacteria. The idea of changing intestinal flora through fermented foods has become more and more popular as proof of the link between gut flora and health grows [2].

In contrast to probiotics, which are live microorganisms that can be healthy when consumed in sufficient quantities, prebiotics are indigestible food elements that encourage the growth and activity of particular bacteria outside the colon. Probiotics support commensal microbe growth and survival, change microbial populations, and have immunomodulatory effects. The immune system and commensal bacterium development are specifically supported by prebiotics. Their creation was intended to mimic the oligosaccharides present in human milk [3]. Microorganisms in the mouth, gastrointestinal tract, and skin are among those that are closely associated with humans. With 1500 distinct bacterial species, the gastrointestinal system has the highest concentration of commensal microbes. These microorganisms support digestion, defend the host, and boost immunity, among other vital health roles. After birth, the gut flora is quickly acquired and does not change over time. But the mucosal immune system has trouble discriminating infections from benign species. Immunosuppressive treatments, radiation, and antibiotics can all change the composition of the gut flora; therefore, introducing good bacterial species may be a way to stop disease before it starts [4].

Exposure to pathogens is one example of an external variable that affects homeostasis, the dynamic equilibrium that exists in biological tissues and organs. The metabolic products of the microbiota have a crucial role in immune-mediated disease vulnerability and host immunological homeostasis maintenance. As holobionts, mammals depend on the genomes of their hosts and microbes to function at their best. The microbiota is essential to health, and antibiotic-resistant chronic illnesses are a threat to world health [5]. Rapid mutations, changing climatic circumstances, a shortage of antiviral drugs, and worldwide migration have all contributed to a notable increase in virus generation during the past 20 years. Millions of deaths and millions of disabilities occur globally each year due to respiratory diseases. Over $40 billion is spent annually in the US on viral respiratory tract diseases. Compared to DNA viruses, RNA viruses-*coronaviruses* in particular-are more important [6]. In order to assess probiotics and prebiotics' efficacy in treating infectious disorders, this review covers immune system activation, illness prevention and therapy, and the mechanisms of action of each supplement.

Mechanisms of action

Probiotic microorganisms have a significant impact on the host, changing the gut luminal environment, immune system, and barrier function. They affect monocytes, dendritic, epithelial, B, T, and NK cells, among other immune cell types [7]. Experimental models suggest that probiotics work in different ways, and strains and species differ significantly from one another. These interactions, which include interactions across microbes, could explain the variability of probiotic effects as well as the differing outcomes observed in clinical trials. Understanding these pathways is vital for selecting optimal strains for various circumstances [8]. It is not always the case that probiotics colonize the digestive tract in order to work. Probiotics that integrate into the human gut microbiota include *Bifidobacterium longum*, whereas those that change or temporarily alter the preexisting microbial population, such as *Lactobacillus casei*, have an impact on the gut microbiota [9].

Prebiotics are good bacteria that improve intestinal health, stop pathogen growth, and aid in host nourishment. Short-chain fatty acids (SCFAs), polyamines, and energy-saving chemicals are also produced by fermenting indigestible fibers. Diarrhea and other symptoms of inflammatory bowel disease are lessened by prebiotics. They also boost the bioavailability of nutrients, promote satiety, and aid in weight loss while lowering the risk factors for cardiovascular disease. Beneficial bacteria are selectively multiplied and SCFAs are produced, which is how prebiotics enhance health [10]. Prebiotics are more advantageous than probiotics since they promote the growth of gut bacteria and may change the microbiota in the gut. Benefits for human health have been documented, yet changes happen at the strain and species level [11]. Figure 1 illustrates the prebiotic and probiotic mechanisms of action.

Immune system enhancement

Immune system recognition of "stranger" and "danger" chemical patterns is needed for pathogen protection. It combines humoral and cellular agents with host barriers, usually via innate and adaptive immunological systems. Innate immunity involves physical barriers such as skin, mucous membranes, and endothelia, while adaptive immunity is mediated by the microbiota, which acts as the body's first line of defense. The term "microbiome" refers to these bacteria's genetic makeup [12]. Probiotics are gut-dwelling bacteria that offer a number of defense mechanisms against intestinal disorders. They create chemicals like fatty acids and organic acids that function as inhibitors, colonize the gut, and hinder other pathogens by lowering their viability and altering the metabolism of bacteria. Additionally, probiotics prevent infections from consuming nutrients, which makes them suitable for usage in a variety of industries [13].

The ways in which probiotic strains act are varied, intricate, and strain-specific. Pathogen competitive exclusion, intestinal colonization capability, tight junction protein and mucin upregulation for improved intestinal barrier function, PAMP-PRR interaction, AMP production, and immune system control are among them [14]. Prebiotics in foods including wheat, oats, chicory, onion, asparagus, garlic, Jerusalem artichokes, and scallions help to multiply the bifidobacteria in excrement and encourage the growth of gut bacteria. Fermentation has provided these low-polymerized prebiotics with energy and calories. Three prebiotics that are frequently researched include xylooligosaccharides (XOS), fructooligosaccharides (FOS), and isomalto-oligosaccharides (IMO) [13].

Materials and Methods

The Cochrane Library, PubMed, Web of Science, Google Scholar, and Scopus were among the many online databases used to conduct a thorough search of the pertinent literature. We used PubMed to search MEDLINE and find English-language scientific papers published in the period between 2000 and 2024. Out of the 88 publications that our search turned up, ten were specifically picked to offer details on the probiotics' mechanisms of action. We also looked through the included papers' reference lists to find any other relevant literature.

Result

After deduplication, 78 records out of the total 88 were recovered. Sixty-three records were deemed potentially relevant after being evaluated according to the abstract and title. This systematic review comprised fifty-five trials. Considering the abstract and title, we were able to eliminate fifteen records and extract eight full-text publications.

Prevention of gastrointestinal infections

Early childhood acute diarrhea has been shown to be significantly reduced by probiotics, particularly in cases of rotaviral gastroenteritis. Treatment of antibiotic-induced diarrhea, especially those caused by the Clostridium difficile toxin, has shown promise using probiotics. Probiotics have been demonstrated in vitro to both guard against and prevent the germination of *C. difficile* toxin in mammalian cell lines. When Bifidobacterium and Lactobacillus species were combined, the percentage of elderly patients receiving antibiotics who experienced diarrhea positive for C. difficile toxin dropped to 2.9%. Children who take probiotics can effectively avoid rotavirus-induced diarrhea and experience less fever and vomiting during diarrhea episodes. Interferon gamma (IFN-g) production and CXCL10 gene expression can both be stimulated by probiotics. Probiotics have been shown in studies using animal models to increase the mucosa's synthesis of defense compounds, decrease pro-inflammatory cytokines, and increase anti-rotavirus antibodies. According to randomized controlled trials, the probiotic group's total eradication rate was roughly 10% greater than that of the control group [5]. Numerous studies have examined the management or avoidance of pediatric infectious diarrhea [15]. *Rotavirus* and *C. difficile*, which are extremely resistant to anti-infectious measures, are the main causes of diarrhea in children admitted to hospitals. One safe and efficient way to lessen this problem would be to take probiotics. According to a recent large randomized controlled trial, using *Lactobacillus GG* dramatically lowered the incidence of vomiting fits, gastrointestinal illnesses lasting more than two days, and gastroenteritis. In order to prevent hospital-acquired infections, *Lactobacillus GG* may be suggested as a viable precaution [16].

Respiratory tract infections

The human respiratory system, which includes the upper and lower respiratory tracts, is an essential organ in human physiology. As the lower respiratory system receives and releases oxygen, the upper respiratory tract has heaters, humidifiers, and filters. Respiratory tract infections can result from imbalances, although healthy respiratory tracts have microbial communities that are resistant to harmful microbes [17]. The development of the disease and exacerbations of asthma are both influenced by respiratory infections, particularly viral ones. Probiotics like LGG and Lactobacillus casei strains can help prevent asthma. These microbes have the ability to both prevent and cure viral and bacterial illnesses of the respiratory and gastrointestinal tracts, including influenza [18].

Mucosal surfaces in the nose, sinuses, throat, larynx, and major airways can become infected with acute upper respiratory tract infections, or URTs. Both bacterial infections like *Streptococcus pneumoniae* and *influenza viruses* are common. These infections, which make up 9% of consultations in general practice, are prevalent in young children, the elderly, and babies. They result in a rise in outpatient visits and the usage of antibiotics [19]. Each year, 200 million instances of viral community-acquired pneumonia (CAP) occur, with 24.5% of those cases being caused by rhinovirus, influenza virus, and respiratory syncytial virus (RSV). With the emergence of infectious diseases like SARS and MERS, viral pneumonia

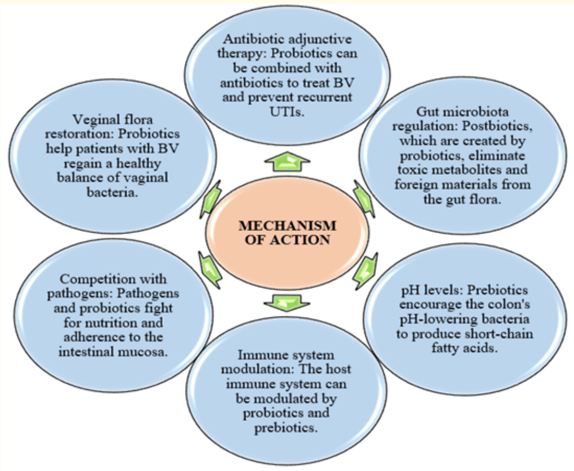

Figure 1: Prebiotics and Probiotics' Mechanism of Action.

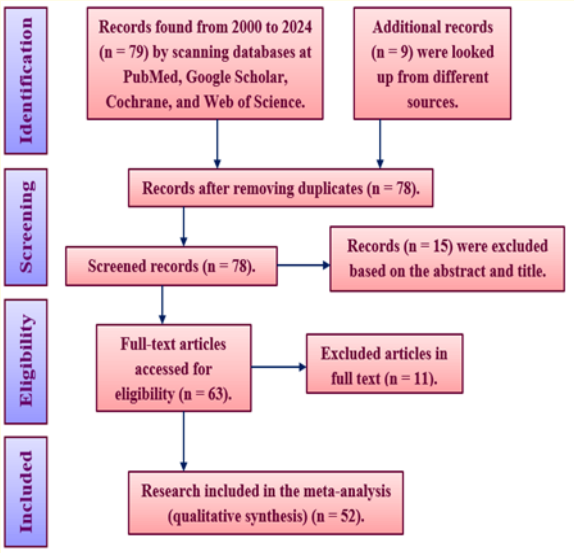

Figure 2: Flow chart according to the PRISMA protocol.

is increasingly seen as potentially lethal. Globally, the COVID-19 epidemic has taken the lives of about 1.9 million people. There are currently few effective antiviral medications, making current efforts to combat SARS-CoV-2 inadequate. According to preclinical studies, microbial agents like probiotics and prebiotics may be able to alter the gut flora and enhance the health of those who suffer from respiratory conditions. According to the gut-lung axis idea, the gut microbiota has a major impact on how the immune system responds to viral lung infections [20].

Urinary tract infections (UTIs)

A significant fraction of bacterial infections affecting the kidneys, ureters, bladder, and urethra are caused by urinary tract infections, or UTIs. They can cause severe complications such as kidney dysfunction, pyelonephritis, strictures, abscesses, and fistulas, as well as bacteremia and fever. Senior citizens are particularly vulnerable to high mortality rates [21]. More than 150 million people worldwide suffer from urinary tract infections (UTIs), the most prevalent kind of bacterial infection. Simple UTIs happen when there are no anomalies, whereas complex UTIs arise when there are genitourinary abnormalities, calculi, neurological disorders, renal failure, and pregnancy. In young, healthy women, simple infections are not uncommon [22].

Every year, UTIs—a common bacterial infection that affects 150 million people—occur. UTIs affect 50% of women, with recurring infections occurring in up to half of cases. The projected lifetime prevalence for men is 13.7%, which is a lower occurrence. The diagnostic criteria and reporting practices make it challenging to determine the true incidence [23]. The skin's and mucosal surfaces' bacterial ecology, which balances harmful and non-pathogenic microorganisms, forms an infection barrier. When the immune system's natural protective biofilm is weakened in immunocompromised hosts or in patients receiving antibiotic therapy, severe infections ensue. Through immune system modulation, which affects the generation of immunoglobulins and changes the body's immune response, and competitive theory, which overgrows harmful flora, probiotics can reestablish host-supportive bacterial flora [24].

Skin infections

The skin's surface, hair follicles, sebaceous glands, and perspiration all contain the microbiome, which is made up of bacteria, fungi, viruses, micro-eukaryotes, and phages. Age, gender, immune system, hormone balance, sleep habits, stress, metabolic parameters, hygiene, and environmental toxins are just a few of the many variables that could alter its makeup. In adults, the skin microbiota is stable and less complex than in babies. 45–80% of the skin microbiome is made up of the three most common bacteria: *Corynebacterium*, *Cutibacterium acnes*, and *Staphylococcus epidermidis*. The *Papillomaviridae*, *Polyomaviridae*, and *Circoviridae* families of viruses, *Malassezia spp.* of fungi, and dust mites have the ability to alter the skin microbiome [25]. Microorganisms, such as commensal bacteria, are essential to immune system maintenance and human health. Skin conditions including rosacea, psoriasis, acne, and atopic dermatitis can be brought on by the skin microbiome, which includes a variety of species. A wide range of ailments can be prevented and treated with probiotics, which are widely recognized for their medical uses. The skin's surface, hair follicles, sebaceous glands, and perspiration all contain the microbiome, which is made up of bacteria, fungi, viruses, micro-eukaryotes, and phages [26].

Maintaining homeostasis depends on the skin microbiota's regulation of inflammation and immune cells. It fluctuates daily and is influenced by various factors like temperature, food, exercise, humidity, stress, and pH. Certain types of bacteria, like *Corynebacterium* and *Staphylococcus*, are location-dependent in the skin's microenvironment. While the introduction of pathogenic species can result in illnesses, a healthy skin microbiota restricts the capacity of pathogenic bacteria to propagate infections [27]. Acne and atopic dermatitis are two skin disorders that can seriously lower someone's quality of life. These illnesses are caused by viruses, fungi, and complex bacteria. They are impacted by elements like temperature, hydration, heredity, and the concentration of sebaceous glands. There is currently no permanent solution for the side effects of current medications. Finding equilibrium again in the skin microbiome may help with treatment outcomes and lessen the requirement for systemic medicine. Upcoming studies ought to concentrate on novel therapeutic approaches that employ microorganisms to maintain the equilibrium of the host's environment [28].

Impact on antibiotic resistance

An important public health issue is antibiotic resistance, which is directly related to the use of antibiotics and the existence of resistant bacteria in intensive care units and hospitals. But the complete spread of resistance cannot be explained by the ecological effects of antibiotic classes. It's also unknown why some antibiotic classes have contradictory effects and why studies differ from one another. Over the past ten years, authors have confused ecological effects with spectrum activity without taking other aspects into account [29]. Antibiotic resistance has resulted from the improper and overuse of antibiotics, despite the fact that they are essential for treating infectious infections. Reducing inappropriate use in veterinary and human applications is one way to counter this. Stabilizing gut microbiota through probiotic use may have an effect by delaying the formation of antibiotic resistance. Probiotics can also reduce the chance of contracting viral infections and diarrhea brought on by antibiotics [30].

Safety and efficacy

Live organisms, or probiotics, have the potential to infect patients who are immunosuppressed, very sick, elderly, or immunocompromised. The Agency for Healthcare Research and Quality, however, did not find any indication of harm in its investigation. Bloodstream infections occurred in 0.5% of patients with hematopoietic cell transplants, according to 10-year observational research conducted at the Fred Hutchinson Cancer Research Centre. Antimicrobial resistance genes are a problem since probiotic strains have the ability to carry and transfer these genes to other bacterial species [13].

Discussion

Probiotics and prebiotics have been shown in numerous trials to be effective in treating viral infections. Probiotics are used to prevent infectious diseases in the same manner that immunostimulants and vaccinations do, but their use in aquaculture is forbidden and requires more safety study, according to J. García-Márquez., *et al.* [31]. Liu., *et al.* examined how, depending on the host, probiotics, prebiotics, and postbiotics improve immune system and gastrointestinal health by controlling immune response, modifying host immunity, and balancing microorganisms [32]. Manoj Kumar Yadav., *et al*. reported that probiotic microorganisms are utilized in healthcare and consumer goods to treat illnesses including cancer, HIV, and gastrointestinal disorders. They also provide health benefits like immune stimulation and pathogen inhibition. Collaboration is necessary to achieve further clinical validation [33]. In the study of M. Eslami et al. Probiotics and prebiotics are recommended treatment options for antiallergic diseases, which provide a clinical challenge because of immune system problems and decreased exposure to early microorganisms [34]. According to the Chuan-Sheng Lin, et al., recent research utilizing metabolomics, metagenomics, metatranscriptomics, and bioinformatics has shown how the gut microbiota influences immunity, modulates tissues, and promotes the formation of fermentable nutrients, among other things, in human health and disease [35].

M. Van den Nieuwboer., *et al*. determined that inadequate documentation in trials including probiotic and synbiotic interventions affects risk-benefit analysis and optimal dose-response correlations by omitting strain and dosage specifics. The main areas of future study should be meta-analyses and efficacy. [36] Mayes et al. noted that while the study shows that probiotic supplements are clinically safe for use in pediatric burn victims, more research is necessary to determine the advantages to health [37]. A.A. Amara, and A. Shibl A.A. Amara and A. Shibl came to the conclusion that this review explores the role that probiotics play in improving health, avoiding illness, and aiding in the treatment of existing conditions. It also provides a thorough inventory of probiotic strains, kinds, uses, and firms [38]. Even though we don't fully understand the makeup of microbial communities, Vieira et al. claim that prebiotics, probiotics, and certain bacteria can affect the gut immune system, which can be used to treat and control diseases [39]. According to the research of E. Jirillo., *et al.,* since genetically predisposed hosts are susceptible to developing bowel cancer or chronic inflammation, studying particular microbiota species may aid in the development of novel dietary therapies for gastrointestinal health [40]. Theodoros Kelesidis and Charalabos Pothoulakis identified *S. boulardii* as a useful biotherapeutic agent for gastrointestinal disorders; they also noted the need for caution in individuals with impaired immune systems and the possibility of larger-scale trials [41]. Gourbeyre., *et al.* highlighted probiotics' impact on the innate immune system, but more data is needed on adaptive immunity, with bacteria-specific and environment-dependent properties [42].

Challenges and future considerations

The effectiveness of probiotics and prebiotics is influenced by genetics and the microbiota's makeup. Inadequate oversight can raise safety concerns and regulatory problems. Immunocompromised people may experience adverse effects from probiotics, and the full extent of their therapeutic benefits is unknown. Short study durations, discordant methodology, and small sample sizes all contribute to the lack of clinical support. [43-46] Probiotics and prebiotics' effectiveness is influenced by genetics and the microbiota's makeup. Inadequate oversight can raise safety concerns and regulatory problems. Immunocompromised people may experience adverse effects from probiotics, and the full extent of their therapeutic benefits is unknown. Short study durations, discordant methodology, and small sample sizes all contribute to the lack of clinical support [47-52].

Conclusion

Probiotics and prebiotics are effective in managing and preventing infectious diseases by modulating gut microbiota and enhancing immune responses. They reduce infections, produce antimicrobial substances, and reduce antibiotic consumption, combating antibiotic resistance. Maximizing efficacy and improving precision in therapies require standardization in the formulation of probiotics and prebiotics as well as customized approaches to each patient's unique microbiota profile. When it comes to treating infectious diseases, probiotics and prebiotics are entirely useful, but before they can be completely included in traditional treatment, further research and legal requirements must be met.

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Conflict of Interest

The authors declare no financial or commercial conflict of interest.

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