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PROBIOTICS AS A GUARDIANS OF GUT HEALTH AND GATEKEEPERS OF DISEASE PREVENTION

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Abstract

Probiotics are microorganisms, when administered in adequate amounts, provide significant health benefits to the host. Historically, ancient civilizations such as those in Egypt and India consumed probiotic-rich fermented dairy products like yogurt without understanding the microbial processes behind fermentation. Since their discovery, they have captured the interest of scientists due to their broad potential in supporting human health and disease presentation. Their influence extends across several systems. For examples they balance gut microbiota, and contribute to the integrity of the gut lining, enhance immune responses, inhibit the growth of harmful pathogens, and aid in nutrient synthesis. Modern research continues to uncover their role in managing various health conditions, including inflammatory bowel diseases, allergic disorders, metabolic imbalances, and even certain neurological and behavioral issues. Despite notable advancements, challenges remain in fully harnessing probiotics' clinical potential. One key obstacle is the strain-specific nature of their effects. Addressing this complexity is essential for optimizing their therapeutic application. This review highlights the crucial role of probiotics as both protectors of gut health and preventive agents against a range of diseases, while also underscoring the need for continued investigation into their targeted, strain-specific functions.

INTRODUCTION

Probiotics are microorganisms when administered in moderate amount and in correct route of administration cause benefits to the host organisms (Amara & Shibl 2015;Iqbal et al. 2014), but when used in high quantity may be harmful to host organisms. According to food and agricultural organization and world health organization probiotics has got attention because of its benefits to human beings and other organisms. Probiotic organisms belong to lactobacillus, Bifidobacterium, Saccharomyces, and some other genera and yeast (Vinderola et al. 2017). These microorganism species usually live in different tissue of the human body,

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especially in gastrointestinal tract. These species helps in the maintenance the gastrointestinal micro biota (Bezkorovainy 2018), helps in digestion process and immune system responses (Stavropoulou & Bezirtzoglou 2020).

The basic benefits of the probiotics is the capability to restore and keep the gastrointestinal micro biota in average amount, if the balance of the micro biota disturbs a disease develops which is known as Dysbiosis which system includes irritable bowel syndrome, allergies, obesity, and some the chances of the diseases(Su et al. 2020); moreover probiotics also have immunomodulatory effects,

probiotics increases the innate and adaptive immunity responses by regulating the production of cytokine a chemical regulator, promoting the activity of ,macrophages, and natural killer cells and help in the maturation of regulatory T cell (Ganjbakhsh 2017). All these components works in cooperation manner to create response against pathogens, reduces the inflammation during response and also involved in the prevention of the autoimmune diseases (Yousefi et al. 2019).

Probiotics are also involved in protection against pathogens through competition with pathogen in gastrointestinal tract by producing antimicrobial substances, and by strengthening the mucosal layer of the gastrointestinal tract. Probiotics also have been used for the decreasing the severity of the diarrhea and respiratory disease, beyond the protection from gastrointestinal diseases and immunity component completion experiments also highlighted that probiotics also beneficial to digestive system, and nervous system, due to gut brain close connection. Probiotics are used in diary items, and therapeutic regime to enhance human health (Araújo et al. 2020).

History of the probiotics

The ancient peoples of the Egypt India were using the probiotics in the form of yogurt or other dairy products, but did not know the fermentation causative agents (Gogineni 2013). They did know the fermentation is beneficial to human being. In 1905 stamen grigorov a discovered the lactobacillus in yogurt (Ummah 2019). 1907 Elie Metchnikoff give statement that lactic acid bacteria can increase life, this hypothesis gave the birth to modern probiotic. In 1910-1930 scientist isolated the bacteria which help in the fermentation of the yogurt, in 1953 the term probiotics was coined by Werner kollath (Ebner et al. 2014)(Brzozowski), initially it was believed that these substances help in growth of the microorganism, in 1965 on other definition was given ,which was that probiotics are the microorganism which in enhance the growth of the other microorganism.in 2001 another more commonly accepted definition was given by world health organism : probiotics are the microorganism when administered into the host body in limited level cause the benefits to the living host.

Review of the literature

Probiotics are living microbes usually bacteria that, when entered in the body of living organisms in moderate amounts, cause positive effects on health of the host(Reid et al. 2019). These probiotic microorganisms are mixed with different items, which include foods, dietary items (Jankovic et al. 2010)(Tripathi & Giri 2014). The usage of fermented foods goes back hundred and thousands of years, with various cultured forms for their benefits without knowing the detail about of microorganism (Tamime 2002). In early 20th century aureate Élie Metchnikoff found that Bulgarian formers were using to consume fermented milk had increased longevity. Metchnikoff concluded that some bacteria in fermented could abolish baneful gut microbes, increasing health and life of the consumer of the probiotics (Podolsky 2012)(Anukam & Reid 2008). This was main observation and invention of the probiotics which cause the foundation the current scientific usage of the probiotics.

Types of the probiotics on the basis of the species

Lactobacillus species

The most common species which is used as probiotics, this bacteria is gram positive having facultative anaerobic condition for respiration

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(Kullar et al. 2023), found the human gut and vaginal tissues (Kullar et al. 2023). These bacteria are also involved in fermentation of yogurt, etc (Ng et al. 2011). These bacteria have the capability the digestion of lactose sugar, inhibit the other bacteria (pathogen) by producing lactic acid, and increase the immune system, when any inflammation reactions occur and these bacteria reduce the response of the inflammation. Lactobacillus species produce by products which has the antimicrobial property. The Table 1 below outlines key effects of, Lactobacillus species.

Table 1 Health Benefits of Probiotics (Al-Yami et al., 2022)

System/Area	Health Benefit
Digestive System Health	Supports the prevention of diarrhea and constipation.
Immune System Function	Enhances immune responses and aids in the maturation of natural antibodies.
Female Reproductive Health	Reduces the risk of vaginal infections.
Oral Health	Helps prevent oral infections by reducing harmful bacterial populations.
Mental Health	Certain Lactobacillus species reduce symptoms of depression.

Bifidobacterium species

Bifidobacterium are gram positive species, respire in anaerobic condition (Poupard et al. 1973). These bacteria enhance the gut barrier, increase the immune system, and decrease the pathogen by producing inhibitor biochemical(Ashraf & Shah 2014). These bacteria are found the in the colon region of the intestine of the young children, and yogurt (Wieërs et al. 2020)t. These bacteria have role in balancing the bacteria which lives in the intestine by neutralizing the harmful bacteria, (Tojo et al. 2014) increasing the nutrition absorption in the in the small intestine, boosting up the immune system, and kill the damaging bacteria. The Table 2 below outlines key effects of, Bifidobacterium species.

Table 2 Common Bifidobacterium Species and Their Health Benefits (Derrien et al., 2022)

Species	Description
Bifidobacterium longum	Helps prevent diarrhea and allergies; reduces the risk of constipation.
Bifidobacterium bifidum	Strengthens the epithelial barrier in the small intestine to block pathogen entry into the bloodstream.
Bifidobacterium breve	Aids in preventing diarrhea and allergic reactions.
Bifidobacterium infantis	Reduces gut infections and supports intestinal health.
Bifidobacterium adolescentis	Assists in the digestion of dairy products.
Bifidobacterium lactis	Enhances immune system responses.

Saccharomyces boulardii

The saccharomyces species was first discovered by Henri Boulard in 1920.These are the yeast species rather than the bacteria, these probiotics required oxygen for its survival this yeast specie is found in fruit peels. This probiotics is used for the prevention of diarrhea (Vandenplas et al. 2009). The Table 3 below outlines key effects of Saccharomyces boulardii specie.

Table 3 Probiotic Benefits in Gastrointestinal Health (Kelesidis & Pothoulakis, 2012)

Benefit	Description
Prevention of digestive diseases	Helps prevent antibiotic-associated diarrhea.
Prevention of Clostridium difficile infection	Reduces the risk of C. difficile infection.
Enhancement of gut barrier	Strengthens the gastrointestinal lining, preventing pathogen entry into the bloodstream.

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Reduction of inflammatory responses	Decreases inflammation in the gut.
Microbiota balance in the GI tract	Supports the maintenance of a healthy gut microbiota.
Antibiotic-like effect	Produces antimicrobial proteins that inhibit pathogenic organisms.

Streptococcus thermophiles

Streptococcus thermophiles are gram positive bacteria producing lactic acid commonly used in milk products. They are naturally found in the milk but it can by also colonized artificially in human gastrointestinal tract which help in the lactase digestion by producing lactase enzyme (Gaughran 1947). This probiotics are common used in the fermentation of the milk into yogurt (Hutkins & Morris 1987)(Chaves et al. 2002). The Table 4 below outlines key effects of Streptococcus thermophiles specie.

Table 4 Health Benefits of Probiotics in Gut and Immune Function (Tarrah et al., 2018)

Benefit	Description
Lactose digestion support	Produces the enzyme β-galactosidase, aiding in the digestion of dairy products.
Gut health maintenance	Helps sustain a healthy gastrointestinal microbiota.
Immune system enhancement	Stimulates proteins involved in immune system regulation.
Improvement of intestinal barrier	Strengthens the gut epithelial cells, enhancing the intestinal barrier.
Gut microbiota balance	Aids in maintaining the balance of gut microbial populations.

Enterococcus faecium

Enterococcus faecium is a gram positive respire in facultative anaerobic respiration condition (Shehata et al. 2020).Some strain of this bacterium is used as probiotics because theirs effects on the epithelial of gastrointestinal tract, this barium found in the gastrointestinal tract of human being and animals, these bacteria have high tolerance in the environment where it live, this bacterium is involves in the production of lactic acid (Selim et al. 2021). The Table 5 below outlines key effects of Enterococcus faecium specie.

Table 5 Probiotic Benefits in Digestive and Immune Health (Mansour et al., 2014)

Benefit	Description
Maintenance of gut health	Improves digestion and overall gut function.
Diarrhea treatment	Reduces pathogenic diarrhea.
Enhanced immune response	Stimulates the body's immune responses.
Antimicrobial activity	Produces compounds that inhibit the growth of pathogens.
Improved nutrient absorption	Increases nutrient uptake in the gastrointestinal tract.
Reduction of inflammation	Decreases inflammatory responses in the body.

Bacillus species

These are rod shaped gram positive bacteria, these bacteria found in soil, water, and in oil well, and gastrointestinal tract of the human being and animals (Schallmey et al. 2004). This bacteria is used as probiotics because it can survive in harsh condition(Cutting 2011), these probiotics are involved in the production of many enzymes which helps in the digestion, enhances the immune responses, and gut health (Wieërs et al. 2020). The Table 6 below outlines key effects of Bacillus specie.

Table 6 Health Benefits of Common Bacillus Species (Jezewska-Frąckowiak et al., 2018)

Species	Benefits
Bacillus subtilis	Maintains gut health and produces enzymes that aid in digestion.
Bacillus coagulans	Enhances immune responses.

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Bacillus clausii	Helps prevent diarrhea.
Bacillus indicus	Supports the maintenance of gut epithelial cells.
Bacillus licheniformis	Improves the digestion process.

Escherichia coli Nissle

Escherichia coli nissle first discovered by Dr.Alfred Nissle in 1917 during world war first, from the soldier who was infected by the bacteria, this bacterium is considered one of the beneficial bacteria, and used in the as probiotics for the improvement in human health (Falzone et al. 2024), these bacteria bind to the epithelium of the intestine improving the gut health. The Table 7 below outlines key effects of Escherichia coli Nissle specie

Table 7 General Health Benefits of Probiotics (Łubkowska et al., 2023)

Benefit	Description
Gastrointestinal tract health	Helps balance and maintain the gastrointestinal microbiota.
Pathogen control	Inhibits and destroys pathogenic bacteria.
Immune system enhancement	Regulates and strengthens the immune response.
Diarrhea treatment	Reduces the risk and severity of diarrhea-related infections.
Vitamin production	Produces essential vitamins such as vitamin K and B-complex.
Fatty acid production	Supports the synthesis of beneficial fatty acids.

Mechanism of working of probiotics

Adhesion to the wall of intestine

Probiotics microorganisms get attached with the wall of intestine of the host by cell surface protein of the epithelial cells or use of the pili for the attachment to the wall of the intestine, some other probiotic bacteria use mucus binding protein which helps in the attachment even some other probiotic bacteria use sortase enzyme for the attachment to the wall of intestine. This attachment is helpful in exerting local effects in intestine (Wahlqvist et al. 2006)(Ummah 2019).

Competition with pathogen

After the getting attached with the epithelial tissue of the intestine make colony in intestine which inhibit the colonization of the pathogens in intestine, this is phenomenon is known as competitive exclusion which usually prevents the infections of E. coli.(Liverani et al. 2013). Probiotics also compete with pathogenic bacteria for nutrition which reduces the chances of colonization of the pathogenic bacteria still other probiotic bacteria produce antimicrobial substances which inhibit the growth of pathogenic bacteria.

Increases the barrier of the intestine

Probiotic microorganisms after getting attach with the tight junction protein increases the epithelial tissue tight junctions which decreases the absorption of the toxins and pathogens into blood stream(Zhang et al. 2020)(Bron et al. 2017). Some other probiotic bacteria increase the production of the mucus from goblet cells of the intestine which increase the barriers for the pathogenic bacteria.

Incensement in the immune response

Probiotics enhance the innate immunity helping in the activity of macrophages and dendritic cells which are involves in the first line of the defense(Maldonado Galdeano et al. 2019)(Oliveira et al. 2024). Probiotics enhance the T- helper cells, regulatory T cells which reduce the excessive inflammatory responses. Probiotics microorganism also increases the production of the immunoglobulin –A. Cytokine regulation some probiotics can express the expression of pro (Lescheid 2014)inflammatory cytokines regulating the inflammation(Maldonado Galdeano & Perdigón 2006) .

Antimicrobial Production

The probiotic microorganism produce some compounds which includes bacitracin, and Organic

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acids which lower the gut PH which inhibit the growth of the pathogenic bacteria, while bacitracin inhibits the growth of the same bacterial strain in small intestine (Denkova et al. 2016)(Gou et al. 2022). Nicin is chemical produced by lactobacillus which is antibacterial of gram positive bacteria, Reuterin is produced by other bacteria which are antimicrobial for gram positive, gram negative, yeast and protozoan species.

Production of Hydrogen Peroxide

Hydrogen peroxide produced by different metabolic pathways e.g pyruvate oxidase activity which has antimicrobial properties by damaging the cellular organelles and DNA of the pathogenic bacteria, in the presence of the of the enzymes and other biochemical the hydrogen peroxide increases overall the antimicrobial activities. (Zalán et al. 2005)(Gray 2019).

Metabolic Contributions

Probiotics also helps in the productions of vitamin -B group and vitamin –K which contributes the host nutrition(Salman & Mauriello 2023).Some other probiotic produces bile and some enzymes which increases the digestion of the lipids, Some other probiotic bacteria stimulating the appetite by secreting certain biochemical.

Detoxification

Certain probiotics strain neutralize the baneful compounds which includes heavy metals, carcinogens, mycotoxins, by binding with them thus reduce the rate of absorption into blood stream (Elsanhoty et al.) (Ansari et al. 2024) some others probiotic bacteria degrade the poisonous biochemical thus reducing the toxicity.

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Conclusion and future directions

Probiotics have risen as component which help in the maintenance and support human and animals' health in all over the globe. Probiotics have the ability to restore the gastrointestinal micro biota, increases the immune system responses and prevent the pathogen growth. Extensive research knowledge of the research shows that probiotic microorganism's help in the managing gastrointestinal tract diseases, prevent infections, maintain metabolism and even neurobehavioral health. These finding is focus on the important role of probiotics in diseases management. In spite of the progress have been made in the utilization of the probiotics for human being health still some problems are unsolved to utilized the full clinical benefits of the probiotics, one of the major problem is that strain specific nature of the probiotic effects, which complicates the generalization and require identification and characterization of each strain, moreover variation in the genetic makeup, age, diet , temperature ,and the population of the existing micro biota of the host individual effects the potential of the probiotics. The absence of the of standardized regulatory system, variability in the quality of the product, and discrepancies between the labeled and actual microorganism content in commercial probiotic formulation further complicate their clinical use.

Looking forward future research should be made on addressing these challenges through different strategic angles. Detail studies are necessary to evaluate that how a specific probiotic microorganism interact with tissue of the host. Personalized probiotics therapies should be made for specific individual micro biome profiles can be increase the potential and results, especially in complicated diseases. Advanced technologies should be involved such as met genomics, transcriptomics in research probiotics research to understand the probiotic and host interaction, and identify the benefits. Additionally the discovery of synbiotics, postbiotrics and genetically modified probiotics opens exiting new avenues for enhancing therapeutic applications.

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Conflict of Interest

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Author Contributions

M. Yousif and **D. Riaz** conceived the idea, conducted the literature review, and drafted the initial version of the manuscript.

A.A. Khalique and **G. Murtaza** contributed to the critical analysis and interpretation of content related to microbial and gut health mechanisms.

A. Ali and **F. Laraib** reviewed literature and contributed to refining the scientific context.

M.S. Akhtar and **M. Ullah** assisted in manuscript structuring, editing, and proofreading.

A. Maqsood contributed to the section on biotechnological applications and reference formatting.

S.A. Gull critically revised the manuscript for intellectual content, and served as the corresponding author.

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