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PROBIOTICS AS MICROBIAL HOMEOSTASIS REGULATORS AND IMMUNOMODULATORS: A REVIEW OF THEIR ROLE IN DISEASE RESISTANCE

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Abstract
Probiotics are microscopic living organisms, when consumed in adequate amounts results in health benefit to the host. They have been used for thousands of years in fermented foods, including yogurt, cheese, and soy. Probiotics balance the gut flora or bacteria in our gut, fight off bad bacteria, help to digest food, boost immunity, and can even have impact on mood and brain function. Their effects are further enhanced when simultaneously administered with the prebiotics or synbiotics. Probiotics provides benefit to people of all ages, from infants to seniors, and have the potential to assist the digestive, metabolic and immune systems. They are generally safe although some individuals may have mild adverse effects, and in rare cases, serious complications may arise, particularly in immunocompromised individuals. This review describes the history, classification and the potential beneficial effects, mechanisms of action as well as the safety aspects of probiotics, demonstrating their significance for human health.

INTRODUCTION
The notion of probiotics has a long, historical background, reaching at least as far back as when humans begun utilizing fermented foods. Ancient evidence indicates that civilizations consumed fermented dairy or grain products to obtain nutrition and nourished their bodies for health at least for centuries before science was ever involved. According to archaeological evidence, and milk fermentation was also practiced traditionally in Egypt, Mesopotamia, India and Greece, traditionally fermented foods have been used to enhance food security, nutritional value, and food safety (Ozen & Dinleyici, 2015). The term probiotic was proposed for the first time in the mid- 20th century and successively redefined since, reaching the currently acceptable FAO/WHO definition which stipulates that live microorganisms which when administered in adequate amounts confer a health benefit on the host (Hill et al., 2014). In recent studies, probiotics has seen a significant growth, motivated by developments in microbiome science, molecular methods, and large-scale clinical trials. Currently, the term probiotic refers to several genera (among them *Lactobacillus, Bifidobacterium, Enterococcus and Saccharomyces*) involved in multiple functions such as digestive comfort, immune system modulation and metabolic control among others (Latif et al., 2023). The research on probiotics is expanding with trends in their application in functional foods, in beverages and in supplements that

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indicate significant consumer interest and a fast-growing consumer market. The global probiotic markets are expected to grow in product categories such as non-dairy probiotic foods and encapsulated products that provides protection to probiotic strains and targeted delivery (El Sohaimy & Hussain, 2023). Advanced techniques like microencapsulation and fermentation process control have been proposed to enhance strains stability in processing and under gastrointestinal environment. Current scientific directions also include next generation probiotics, tailored probiotic therapy according to individual microbiome profiles and the potential health benefit of postbiotics and synbiotics as complementary approaches to health promotion (Sethuraman et al., 2024; Zhuang et al., 2025).

1. Microorganism as a probiotic

A microorganism can be considered probiotic only when it meets the internationally agreed upon scientific criteria based on the definition of probiotics by FAO/WHO, which identifies them as microscopic living organisms that give benefit to host health when consumed in an adequate amount. As reported by Binda et al. (2020), there are four basic prerequisites for the strain: it must be adequately characterized with clear taxonomic identity, it must be safe for the intended use, its use must be backed by at least one good quality clinical study showing beneficial effects on human health, and it must be present alive in an effective amount until the end of the shelf life of the product. Accurate strain identification is also required to attribute any detected health outcome to a single biological agent and hence, a polyphasic taxonomic approach using phenotypic (morphological, physiological, biochemical) and genotypic method is the best way to achieve the right classification and labeling (Donelli et al., 2013). Besides the above important active and functional property, other active property, such as survival during gastrointestinal transit, adhesion to intestinal epithelial cells, colonic transit, production of antimicrobial substances, modulation of the intestinal micro flora and resistance to technological treatments have been considered as favorable selection criteria. (Shewale et al., 2014). Together, these criteria provide the scientific basis for differentiating well-characterized probiotic strains from organisms without proven health benefits, and allow the appropriate use of 'probiotic' in scientific investigation, regulatory policy, and product labelling.

2. The Interplay of Probiotics, Prebiotics, and Synbiotics

Probiotics, prebiotics and synbiotics are converging elements that work together in the preservation and recovery of gut microbiota composition and host well-being. Live microorganisms that when administered in adequate amounts exert a beneficial effect on the host are referred as probiotics and they colonize the gut by producing antimicrobial substances and competing with pathogens and modulating the host immune system (Smolinska et al., 2025). Prebiotics are non-digestible food ingredients, such as inulin or fructo-oligosaccharides, that selectively stimulate the proliferation and/or activity of beneficial bacteria, like *Bifidobacterium* and *Lactobacillus*, leading to an increased production of short-chain fatty acids (SCFAs), which contribute to sustaining intestinal barrier function and have anti-inflammatory properties (Smolinska et al., 2025; Zhuang et al., 2025).Synbiotics are formulations that combine probiotics with prebiotics and are designed to enhance the survival, gut colonization, and metabolic activity of beneficial bacteria in the intestinal tract, and it has been suggested that their synergistic actions may be more potent than those of probiotics or prebiotics individually (Smolinska et al., 2025). Clinical evidence indicates that treatment with probiotics, prebiotics and synbiotics leads to enriched populations of beneficial taxa such as *Bifidobacterium* and *Lactobacillus*, promotes microbial diversity and modulates inflammatory markers (increased IL-10 and decreased TNF-α), once again indicating the complementary properties of these compounds and their ability to support gut homeostasis and the health of the host systemically (Zhuang et al., 2025). In general, probiotics bring beneficial microbes to your gut, prebiotics feed them and

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synbiotics do both, an approach that may be the most synergistic in modifying gut microbiota to help digestive, metabolic and immune functions.

3. Efficacy of Microbes for Gut Health

Several main types of probiotics are accessible in the literature like *Lactobacillus spp., Bifidobacterium spp., Enterococcus spp., Streptococcus spp., Escherichia coli and Saccharomyces spp.* The rod-shaped *Lactobacillus* (for the tubby-wheeled) are common inhabitants of our digestive and vaginal tracts and were first described in 1901, and that you can find lots of them in really well fermented foods (Table 01). The probiotics that are being used today belong to the genus *Lactobacillus*. This small army of bacteria is known as *lactobacilli* The Updated Taxon Acl Class for *Lactobacillus* unifies species that are phylogenetically related or share common ecological niches and metabolic properties based on lactobacilli. So this could help us unearth common mechanisms by which probiotics achieve their beneficial effects. (Czerucka & Rampal 2019)

The *Bifidobacterium species* substantially have a place at the top in probiotics to human beings for their ability to prosper and metabolize in the mid to distal large small intestines (Table 01), and to also produce bifidogenic (probiotic-compatible) that promotes maintaining the intestinal health of the person as well as being native to anaerobic conditions within the large bowel. The two major physiological effects of *Bifidobacterium* are a decrease in pro-inflammatory cytokines and the exclusion of pathogenic bacteria from the gut. (Sadiq et al., 2021)

Enterococcus adhering to the host in the gut and outcompeting it while also being able to survive is one of the critical role of other bacterial species such as the ubiquitous *Enterococcus* in the agri-food industry. These strains are reported to have high bacteriocin production and are stable to a broad range of (pH and temperature), which may suggest that they can be used as a natural protective agent in food industry, summarize in Table 01 (Shimizu et al., 2020).

Saccharomyces cerevisiae Probiotic foods for industrial application are constructed from the well-known non-pathogenic and strain of *Saccharomyces cerevisiae* (common). The probiotic activity of Saccharomyces strains has been widely studied and most probiotics have been used for diarrhea linked with antibiotic-associated enteropathogenesis. (Table 01) Perhaps superior gut survivability of S versus other probiotics, predispose them to enhanced survival of some *Saccharomyces* strains these also influence gut homeostasis and they have immunomodulatory actions, utilized for immune modulation of B-cell activity and immune system pathway modulation during infectious Andor chronic diseases. (Pais et al., 2020)

Saccharomyces boulardii, it's the only probiotic with yeast in its *S. boulardii* good luck, mate and these are the 5 best probiotics for diarrhea. It is also recommended for acne, for minimizing side effects of H-pyloric therapy and for prophylaxis of *Clostridioides difficile* recurrence (Szajewska et al., 2020)

The table 01 represents important probiotic microbes for human gut health and their main characteristics including mechanisms of action, dosage forms, main sites of action, and references. It shows bacterial probiotics (*Lactobacillus, Bifidobacterium, Enterococcus, Streptococcus, Escherichia coli*) and yeast probiotics (*Saccharomyces cerevisiae, Saccharomyces boulardii*) and their functional properties (pathogen-inhibition, immune-modulation, intestinal microbial balance). Dosage forms such as capsules and tablets, as well as functional foods, powders and microencapsulation formulations are available and may be used to deliver probiotics with the business purpose of carrying out survival and targeted delivery. This table provide the properties of probiotics, and how they can be applied in gut and systemic health

4. Differential Applications of Probiotics

Antibiotics-induced disturbance of gut micro biota may lead to health issues including antibiotic-associated diarrhea, inflammatory bowel disease and metabolic or neurological diseases. Probiotics are known to be effective to restore gut homeostasis and to improve immune function in the presence of adverse antibiotic effects. Recent investigations have highlighted the relevance of probiotic activity in male health and specifically in

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prostate inflammatory disorders. Probiotic supplementation has been shown in randomized controlled trials mean reductions in urinary bacterial counts in middle-aged men with recurrent urinary tract infections and thus it has been suggested that probiotics may contribute to reestablishment of urogenital microbial balance (Pacifici et al., 2021; Ferrari et al., 2024).

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Table 01: Pharmacodynamics and Delivery of Common Probiotic Microorganisms

Probiotic Microbe	Key Features / Mechanisms	Dosage Forms / Delivery Methods	Site(s) of Action	References
Lactobacillus spp.	Lactic acid and bacteriocin production; competition with pathogens; immune modulation.	Capsules, tablets, fermented foods, sachets, microencapsulation.	Gastrointestinal tract; some strains oral/vaginal.	Williams, 2010; Aleman & Yadav, 2021
Bifidobacterium spp.	Improves barrier function; produces SCFAs; reduces inflammation.	Fermented dairy, capsules, sachets, synbiotic combinations.	Large intestine; gastrointestinal tract.	Williams, 2010; Aleman & Yadav, 2021
Enterococcus spp.	Adheres to intestinal cells; survives variable pH/temperature; produces bacteriocin.	Fermented foods, tablets, encapsulated forms.	Gastrointestinal tract.	Aleman & Yadav, 2021
Saccharomyces cerevisiae	Resilient yeast with antimicrobial effects and immune modulation; survives gut conditions.	Supplement tablets/capsules; fermented yeast drinks.	Small & large intestine.	Guarner et al., 2005; Kumar et al., 2023
Saccharomyces boulardii	Yeast probiotic with evidence in diarrhoea management and immune support.	Capsules and powders (~10^9–10^{10} CFU/day).	Gastrointestinal tract.	Szajewska & Kołodziej, 2015; McFarland, 2010

The human microbiome is essential to female reproductive health, and dysbiosis of microbiota has been linked to diseases including polycystic ovary syndrome, endometriosis, pelvic pain, and infertility. Probiotic supplementation with *Lactobacillus* and *Bifidobacterium* strains could help maintain the homeostasis of uterine and vaginal microbiota, and they may be involved in the regulation for hormone-related skin disorders, e.g. acne during puberty or pregnancy. Moreover, estrogen declines during post-menopause can compromise collagen production and hasten skin aging; though studies on probiotics in this area are scarce, initial results indicate possible use for alleviating these changes (Ahmad et al., 2023).

Gut microbiota dysbiosis was recently proposed to be related to the pathophysiology of attention-deficit/hyperactivity disorder (ADHD) through the gut–brain axis. A randomized controlled trial investigating children aged 3–5 years from Vietnam found that probiotic supplementation with Lactobacillus casei Shirota (LcS) in fermented milk ameliorated some behavioral parameters, including the Conners' Parent Rating Scale (CPRS) total score, more so after four weeks of intake. Despite some post intervention and follow-up insignificant results, probiotics seemed to be of importance for the improvement of attention and auditory response control in children with ADHD, and could be considered as a replacement

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or complementary treatment choice (Allahyari et al., 2024; Nahidi et al., 2024).

In elderly individuals, age-related alterations in gut microbiota may affect brain function, inflammation, and health status (Fig 01). Systematic reviews summarizing the evidence from randomized controlled trials evaluating probiotics, prebiotics and synbiotics (PPS) suggest that these interventions may increase gut microbial diversity, the abundance of beneficial micro-organisms, including *Bifidobacterium* and *Lactobacillus*, and certain anti-inflammatory markers. In particular, probiotics exert significant promising effects on cognition in subjects with mild cognitive impairment, whereas the results on mortality, mood and frailty are still inconclusive. These results highlight the feasibility of probiotics in maintaining gut homeostasis along with some functional advantages in the aged population albeit with a strain of caution regarding the need for further large-scale clinical investigations (Zhuang et al., 2025; Hutchinson et al., 2021).

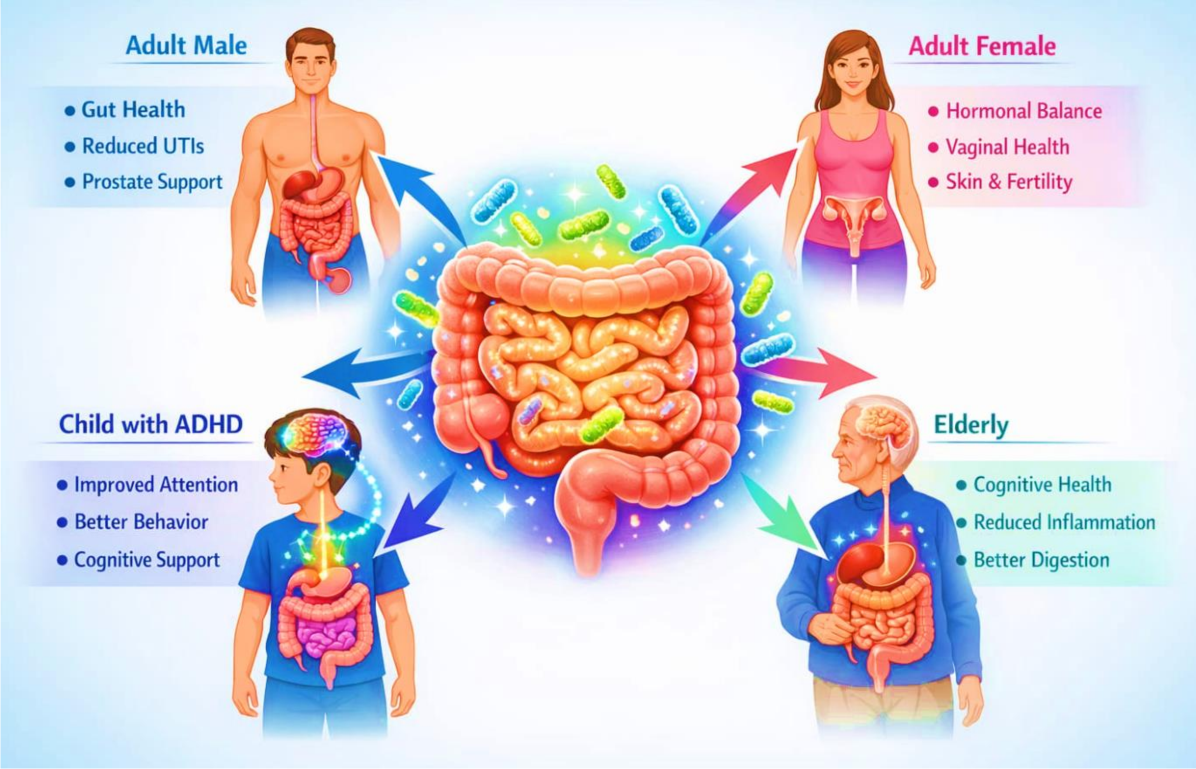

Fig. 01: Age-Specific Effects of Probiotics on Gut Health and Systemic Physiology

5. Probiotic-Rich Foods for Gastrointestinal Health

Yogurt is a food made of milk that has been fermented by the bacteria. The most common types of yogurts consumed globally based on cow's milk. The basis however is still country-dependent being milk rather from water buffalo, goats, sheep Horses Camels and Yak. Cow is used to produce thermophilic cultures S. salivary subpar for yogurt preparation. Also during manufacture lactic acid bacteria & bifidobacteria can be added. Yogurt is claimed to have health benefits such as decreasing or preventing osteoporosis, high blood pressure, severe diarrhea in children, and antibiotic-associated diarrhea (Nyanzi et al., 2020).

Cheese contain live cultures of *L. acidophilus* and *Bifidobacterium*, including those that are inoculated (such as some varieties of blue cheese), as well as natural aged cheeses also are great sources of probiotics (Patrignani et al., 2019).Kombucha Fermented tea (Kombucha) certain type of a black tea with sugar and yeast. The yeast is present in the presence of sugar and provides a film floating on top of the drink. A film

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can be made if you gather film in making a fresh kombucha drink. The taste of the slightly acidic form of kombucha comes from little amount of alcohol and gasses produced from acetic acid during fermentation (some small-tempering of carb based purpose alcohol) bacterial side with Acetarobacter called Gluconacetobacter xylene; or yeast may contain Candida-stellate and Saccharomyces. cerevisiae. Kombucha health benefits: antihypertension and anti-inflammatories response, lower atherosclerosis, antidiabetic properties, alleviate gout, rheumatism and arthritis (Selvaraj & Gurumurthy, 2022).Tempeh is made by fermenting soybeans to produce a cake, a traditional meal of the Indonesians. Tempe production is based on the controlled fermentation of soybeans by the white mycelium of the spore *Rhizopus oligosporus*, which binds the soybeans into a firm cake that can be cut, fried, or cooked like meat (Jang et al., 2021). The fermented soybeans used to make natto, a traditional Japanese food, are first steamed and then fed *B. subtilis* (Jang et al., 2021).Miso is a typical dish from Japan. It is a thick paste made from soybeans fermented with salt, koji (a type of mold) and sometimes seaweed, rice or barley. *L. acidophilus* and *Tetragenococcus halophilus* are two of the bacteria found in miso (Jang et al., 2021).Soy sauce Soy sauce, an old fermented condiment believed to have originated in western China in the Han Dynasty, is made by fermenting soybean past with salt-water and certain mould such as *Aspergillus oryzae* or *A. sojae*. This process of fermentation for flavor enhancement also produces various lactic acid bacteria which provide health benefits such as anti-diabetic, anti-hypertensive, anti-cardiovascular and anti-neuroinflammatory activities and blood cholesterol lowering (Sun et al., 2022). Just like those above, fermented soy products (e.g., natto and miso) have also been associated with decreased risks of cardiovascular diseases (Nosie et al., 2020).Evidences from epidemiological studies further suggest that consumption of fermented dairy and soy products also correlates with a decreased risk of obesity, metabolic syndrome, cancers of the colon, and cardiovascular disease (Sun et al., 2022). Sour red soup is a fermented food geared from southwest china. Its ingredients like tomatoes, red pepper, glutinous rice flour, white wine and other ingredients are naturally fermented during its making that is rich in minerals, organic acids, and more. It's also important for regulating the acid-base balance of the body and muscle and nerve excitability (Maftei et al., 2024)

6. Probiotic Mechanisms of Action

Probiotics promote host health through various interrelated mechanisms. They compete with pathogens for nutrients and adhesion space, produce antimicrobial substances, and reduce intestinal pH, which inhibits the proliferation of pathogenic bacteria (Plaza-Díaz et al., 2019; Liu, Wang & Wu, 2022). They also improve intestinal barrier function by stimulating mucin secretion and the expression of tight junction proteins to inhibit the translocation of pathogens (Latif et al., 2023; Chang et al., 2022). Probiotics engage with epithelial cells and immune cells to regulate the immune responses, such as anti-inflammatory cytokine production like IL-10 and TGF-β, and induce the differentiation of Treg cells as well as the production of IgA (Liu et al., 2022). They play a role in shaping the gut microbiota in which they facilitate good bacteria (e.g., Lactobacillus and Bifidobacterium) that produce short-chain fatty acids (SCFAs), known to promote barrier function, metabolism regulation and inflammation modulation (Plaza-Díaz et al., 2019; Chandrasekaran et al., 2024). Finally, probiotics generate metabolites that might modulate behavior, mood, stress, and neuro-signaling along the gut–brain axis (Latif et al., 2023).

7. Probiotics in Disease Prevention and Management

The human gut microbiota produces a large number of microorganisms, mainly bacteria, which contribute to the development and treatment of different diseases. Among the diseases, probiotics have been most extensively studied as therapeutic products in disorders of host gut microbial homeostasis and immune modulation. In gastrointestinal diseases, probiotics are restricted by a lack of clinical

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effectiveness as they are hindered by the barriers of delivering live organisms to the target sites, by production stability, and by an incomplete knowledge of mechanistic pathways. Emerging data indicate that imaging technologies and preclinical models, including organoids and human microbiota simulations need to be further refined and developed for better evaluation of solutions for modulating the gut microecology (Deshmukh, 2024; Wolfe et al., 2023). In addition to GI diseases, an abnormal gut microbiota has also been associated with some skin disorders, including psoriasis, acne and atopic dermatitis.

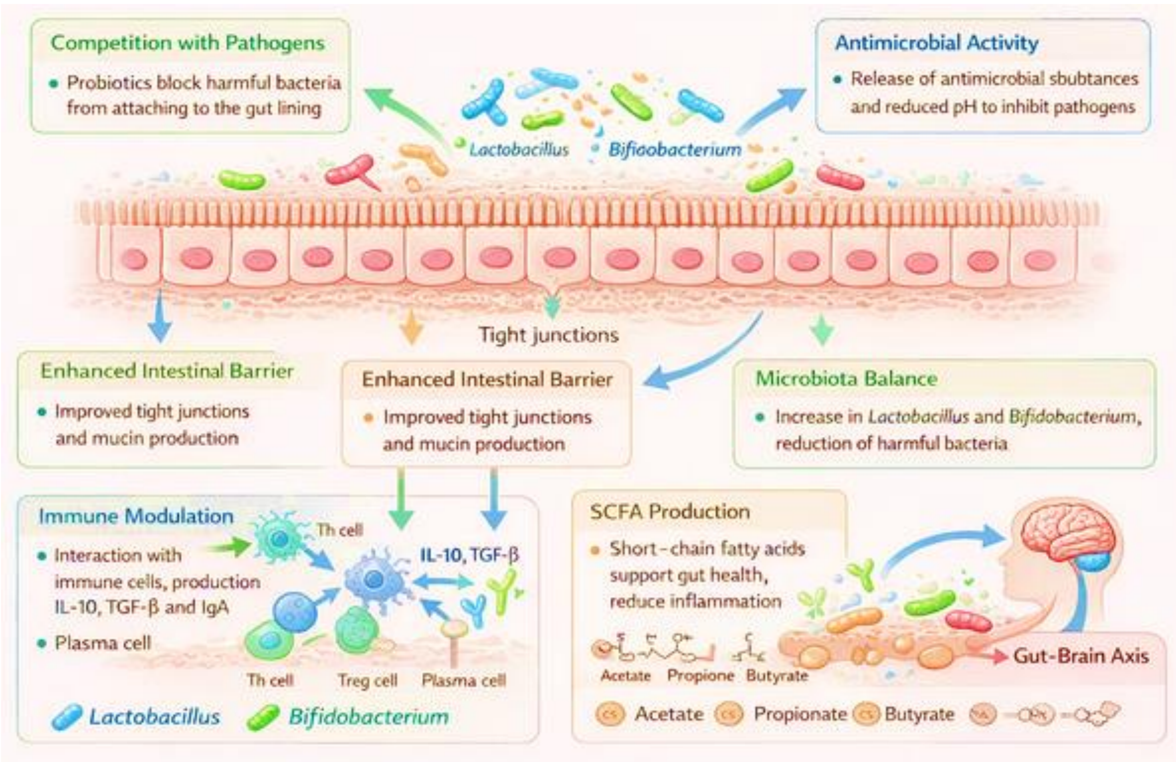

Fig 02: Multifaceted Mechanisms of Probiotic Action: Antimicrobial, Immunomodulatory, Barrier-Protective, and Neurogastroenterological Effects

Preliminary reports indicate that probiotics may have beneficial effects on symptoms related to these disorders through their action on gut and skin microbiomes, but they are still under development (López-Navarro et al., 2021). Probiotics and symbiotic have also been extensively studied in cardiometabolic disease. A meta-analysis including >5,000 adults indicated that supplementation with mainly *Lactobacillus* and *Bifidobacterium* strains could have potential to improve glycemic control and decrease levels of C-reactive protein in type 2 and gestational diabetes, with some improvements observed also in vascular function and dyslipidemia. However, when it comes to obesity, hypertension, and CVD, findings are more mixed, highlighting a need for well-designed RCTs (Sun et al., 2021). Concerning viral infections, probiotic strains, particularly multistrain preparations of *Lactobacillus, Bifidobacterium, Clostridium, Enterococcus, and Streptococcus spp.* can stimulate immune defenses and thus contributing to the reduction of the risk and severity of viral infections, as shown by in vitro and in vivo studies. While these organisms are promising for both digestive and respiratory viral diseases, the absence of standardized protocols precludes the possibility of comparison of results between studies (Lopez-Santamaria et al., 2021). Regarding upper RTI, there is some clinical evidence that probiotics might be useful to reduce

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the risk, although relevant antiviral mechanisms and the clinical applicability require further elaboration in devoted studies (Lehtoranta et al., 2020). Probiotics can also affect liver function through the gut–liver axis, with benefits for hepatic encephalopathy and metabolic-associated fatty liver disease having been reported. Nonetheless, the current evidence is not sufficient to allow clinical advice for the treatment of chronic diseases including cirrhosis, viral hepatitis, or primary sclerosing cholangitis (Malenkov et al., 2021). Meanwhile, interest has turned to the potential role of probiotics as vaccine adjuvants. While preclinical studies imply that probiotics-induced immune modulation could have an impact on the effectiveness of vaccines, clinical data are scarce especially for human vaccines (influenza, rotavirus). It seems that the capacity of probiotics to exert benefits in this setting is strain-dependent and related to dose and host factors, and targeted further trials are warranted (Peroni, 2021).

8. Potential Risks and Contraindications of Probiotics

Probiotics are safe for most healthy people, but side effects can occur related to the strain, dose, duration, and host factors (Hempel et al., 2012; Doron & Snydman, 2015). The most frequent minor side effects were bloating, flatulence, abdominal pain and mild diarrhea and most of them disappeared within a few days to a few weeks of the treatment (McFarland, 2015).Severe but very rare, complications can occur in the immunocompromised, severely ill, or those with serious underlying disease and may include sepsis, meningitis, endocarditis or other infections caused by the probiotic strains themselves (Doron & Snydman, 2015; Sanders et al., 2019). Fermented foods with biogenic amines (such as kimchi, sauerkraut and some aged cheeses) can also provoke headaches or migraine in some people (Reid, 2017). Altogether, probiotics are considered safe for the general population, although particular care should be taken in risk populations and medical advice should be obtained for high-risk subjects (Hempel et al., 2012; Sanders et al., 2019).

Conclusion

Probiotics contribute to the healthy functioning of our gut and body. They assist in better digestion, boost immunity and might also have an impact on mental well-being. Probiotics when combined with prebiotics or synbiotics can have enhanced efficacy. They can benefit people of all ages and aid in the treatment of a plethora of health conditions, but caution should be exercised in the latter. With on-going research, it will be possible to utilize probiotics in more targeted ways in the future. In general, probiotics are well-tolerated by most individuals and offer a natural approach to enhancing health and preventing disease.

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