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EEFECTS OF PROBIOTICS ON GUT AND SYSTEMIC HEALTH:A REVIEW

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Abstract:

Probiotics are live microorganisms that provide significant health benefits when consumed in adequate amounts, primarily by modulating gut microbiota. These beneficial microbes, including Lactobacillus, Bifidobacterium, Lactococcus, Saccharomyces, and Escherichia coli strains, contribute to various aspects of human health, including gastrointestinal, immune, metabolic, and neurological functions. They exert their effects through mechanisms such as antimicrobial production, immune modulation, gut barrier enhancement, and the restoration of microbial homeostasis. Probiotics have shown promise in the prevention and management of a wide range of conditions, including gastrointestinal disorders, liver diseases, respiratory issues, skin conditions, and neurological disorders. In particular, probiotics have been implicated in the modulation of the gut–liver axis, offering therapeutic potential for diseases such as Non-Alcoholic Fatty Liver Disease (NAFLD), Cirrhosis, and Alcoholic Fatty Liver Disease (AFLD). Additionally, emerging evidence highlights their role in neurodegenerative diseases like Alzheimer's and Parkinson's, and mental health conditions such as depression and anxiety, via the gut–brain axis. This review highlights the multifaceted actions of probiotics and their potential as a natural therapeutic strategy in improving systemic health and mitigating disease risk.

Keywords: Probiotics,gut microbiota, gut flora,beneficial bateria,metabolic health.

1. Introduction:

The human microbiota, particularly the gut microbiome, plays an integral role in maintaining health and preventing disease (Hill et al., 2014). Probiotics, which are live microorganisms that confer health benefits upon consumption, have emerged as a critical tool in modulating this microbiota and improving overall well-being (Sanders et al., 2019). Common probiotic species include Lactobacillus, Bifidobacterium, and other lactic acid bacteria, which are typically found in fermented foods like yogurt, kefir, and sauerkraut, as well as in dietary supplements (O'Callaghan & van Sinderen, 2016). These microorganisms have been shown to positively influence several physiological systems, including the gastrointestinal, immune, and metabolic systems, by promoting microbial balance, enhancing gut barrier integrity, and modulating immune responses (Plaza-Díaz et al., 2017). Probiotics exert their effects through diverse mechanisms such as antimicrobial production, pathogen exclusion, immune
modulation, and the restoration of gut microbiota homeostasis (Oelschlaeger, 2010). These actions have broad implications, ranging from alleviating gastrointestinal disorders like irritable bowel syndrome (IBS) and diarrhea (Ma et al., 2018), to preventing liver diseases like non-alcoholic fatty liver disease (NAFLD) and cirrhosis (Wan et al., 2016), to supporting mental health through modulation of the gut–brain axis (Mayer et al., 2015). The gut microbiota not only affects gut health but also plays a key role in systemic diseases, including liver, respiratory, and neurological disorders (Schwabe & Tabas, 2020). The bidirectional relationship between the gut and liver, known as the gut–liver axis, as well as the gut–brain axis linking the gut and the central nervous system, are central to many of these effects (Cryan & Dinan, 2012). Probiotics, by modulating the composition and activity of the gut microbiota, have shown therapeutic potential in managing these conditions (Marco et al., 2021). This review provides an overview of the functions and mechanisms of action of probiotics, exploring their therapeutic applications in a variety of conditions, including gastrointestinal diseases, liver diseases, respiratory conditions, skin health, and neurological disorders (Guarner & Malagelada, 2003). The growing body of evidence suggests that probiotics can be a powerful tool in promoting health and preventing disease, offering a holistic, natural approach to healthcare (Azad et al., 2018).

2. Functions of probiotics:

Probiotic microorganisms commonly used in human nutrition belong primarily to the genera Lactobacillus, Bifidobacterium, Lactococcus, Streptococcus, Enterococcus, as well as beneficial species from Bacillus, Saccharomyces, and non-pathogenic Escherichia coli strains. These microorganisms contribute to gut, immune, and metabolic health through diverse mechanisms. Species of Lactobacillus, naturally present in the gut, colon, and vagina, are obtained mainly from yogurt and fermented foods, and provide benefits such as reducing diarrhea (L. acidophilus), supporting treatment of irritable bowel syndrome and inflammation (L. casei, L. plantarum), lowering cholesterol, modulating immunity, and combating genitourinary infections (L. rhamnosus) (Hill et al., 2014; Sanders et al., 2019). Bifidobacterium species, found in breast milk and the colon, improve gastrointestinal health, reduce inflammation, regulate immune responses, and help manage diarrhea and allergic conditions (B. infantis, B. bifidum, B. longum) (O'Callaghan & van Sinderen, 2016). Other lactic-acid bacteria such as Streptococcus thermophilus and Enterococcus faecium exhibit antioxidant, anti-inflammatory, and immune-stimulatory properties (Salminen et al., 2021). Additional probiotic organisms—Bacillus subtilis, B. coagulans, Saccharomyces boulardii, and E. coli Nissle 1917—support intestinal health by improving microbial balance, enhancing immunity, resisting pathogens, and aiding conditions like ulcerative colitis, diarrhea, and H. pylori infection (Czerucka et al., 2007; Cutting, 2011). These beneficial microbes are commonly delivered through fermented foods such as yogurt, kefir, cheese, kombucha, sauerkraut, tempeh, miso, natto, and specialized fortified products (Marco et al., 2021).

3. Mechanism of actions of probiotics:

Probiotics exert multiple mechanisms of action that contribute to maintaining intestinal and systemic health. Their effects include antagonism through antimicrobial

production, competition with pathogens for adhesion sites and nutrients, modulation of host immune responses, and inhibition of bacterial toxin production (Oelschlaeger, 2010; Plaza-Díaz et al., 2017). Many strains also demonstrate co-aggregation ability, forming a protective microbial barrier that prevents pathogenic colonization of epithelial surfaces. By adhering to epithelial cells, probiotics block pathogen attachment and activate intracellular signaling cascades that modulate immunity through the release of soluble components and stimulation of various immune cell types (Hill et al., 2014). They produce low–molecular-weight antimicrobial substances, including hydrogen peroxide, short-chain fatty acids, and bacteriocins, which inhibit pathogen replication; notably, Lactobacillus species generate both peptide bacteriocins and class III high-molecular-weight antimicrobial proteins, while Lactobacillus and Bifidobacterium species deconjugate bile acids that exert potent antibacterial activity (O'Callaghan & van Sinderen, 2016). Some probiotics also compete for essential nutrients such as iron, giving lactic-acid bacteria an advantage, as seen with Lactobacillus delbrueckii, which binds iron hydroxide and limits its availability to pathogens (Sanders et al., 2019). Immunologically, probiotics enhance immunoglobulin production, activate macrophages, and stimulate interferon-γ, influencing both innate and adaptive

immune systems through metabolites, cell-wall components, and microbial DNA recognized by intestinal epithelial and immune cells (Plaza-Díaz et al., 2017). Cell-wall components of lactic-acid bacteria increase macrophage activity, reactive oxygen species, lysosomal enzymes, and cytokine production, while yeast-derived glucans stimulate the reticuloendothelial system, promoting detoxification through toxin inactivation and adsorption (Czerucka et al., 2007). Probiotics also correct gastrointestinal dysbiosis and strengthen the intestinal barrier by enhancing tight-junction proteins such as occludin and ZO-1, reducing claudin-2, increasing beneficial commensal populations, suppressing NF-κB inflammatory pathways while inducing heat-shock proteins and reducing MCP-1, and

upregulating mucus-associated genes MUC2, MUC3, and MUC5AC, thereby improving mechanical, biological, immune, and chemical barrier functions (Bron et al., 2017; Martín et al., 2015).

4. Gut - Liver axis

The gut–liver axis refers to the anatomical and functional bidirectional relationship between the gastrointestinal tract and the liver, primarily connected through the portal venous system, which transports nutrients, metabolites, and microbial products directly from the intestine to the liver (Tripathi et al., 2018). When the intestinal barrier is compromised due to dysbiosis, infection, or inflammation, intestinal permeability increases, allowing bacterial components such as lipopolysaccharides, toxins, and other harmful metabolites to translocate into the portal circulation. This results in constant hepatic exposure to toxic substances and microbial products, which may initiate or aggravate hepatic inflammation and injury; pre-existing dysbiosis can further amplify these pathological processes (Albillos et al., 2020). The relationship is bidirectional, as the liver not only receives microbial signals but also regulates gut microbial composition through the secretion of bile acids, antimicrobial peptides, and immunoglobulin A, all of which shape intestinal homeostasis and control bacterial overgrowth (Schwabe & Tabas, 2020). This dynamic interplay makes the gut–liver axis central to the development and progression of liver diseases, including non-alcoholic fatty liver disease, alcoholic liver disease, and cirrhosis.

5. Role of Probiotics in Non-Alcoholic Fatty Liver Disease (NAFLD)

The gut–liver axis plays a critical role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD), and growing evidence supports the contribution of gut dysbiosis as a causal factor (Bäckhed et al., 2004; Le Roy et al., 2013). Probiotics help restore a healthy balance of commensal bacteria, modulating the gut microbiota and influencing metabolic health (Everard & Cani, 2013). High-fat and high-carbohydrate diets promote NAFLD development, whereas certain probiotic strains—particularly Lactobacillus species—have been shown to reduce high-fat-diet–induced obesity and lower serum cholesterol levels (Everard & Cani, 2013). Additionally, probiotics can slow the progression of diet-induced hepatic steatosis by regulating adipokines such

as leptin and resistin and by reducing inflammatory biomarkers (Ma et al., 2018). Alterations in the gut microbiota can increase intestinal permeability and activate Toll-like receptors (TLRs), triggering

inflammatory pathways within the gut–liver axis; thus, restoring microbial homeostasis with probiotics is considered a promising therapeutic strategy for NAFLD (Bäckhed et al., 2004; Le Roy et al., 2013). Furthermore, probiotics exert anti-inflammatory effects by reducing tumor necrosis factor-α (TNF-α) through the downregulation of the NF-κB signaling pathway, supporting their hepatoprotective role (Wan et al., 2016).

6. Role of Probiotics in Alcoholic Fatty Liver Disease (AFLD)

In alcoholic fatty liver disease (AFLD), the gut–liver axis plays a central role, with chronic alcohol intake leading to increased intestinal permeability, endotoxemia, and elevated production of inflammatory mediators such as tumor necrosis factor-alpha (TNF-α) (Szabo & Bala, 2010). Individuals with chronic alcohol consumption often exhibit significant alterations in gut microbiota, characterized by reduced levels of beneficial bacteria including Bifidobacteria, Lactobacilli, and Enterococci (Mutlu et al., 2012). Probiotic supplementation, particularly with Lactobacillus species, has
been shown to reduce alcohol-induced gut leakiness, improve dysbiosis, and attenuate steatohepatitis by restoring mucosal integrity and decreasing systemic endotoxin levels (Kirpich et al., 2008). By lowering circulating endotoxins, probiotics help suppress pro-inflammatory cytokines such as TNF-α and interleukin-6 (IL-6), resulting in significant improvements in liver function parameters and reducing the toxic burden on the liver (Bull-Otterson et al., 2013). These findings highlight the therapeutic potential of probiotics in managing AFLD through modulation of the gut–liver axis.

7. Role of Probiotics in Cirrhosis

In cirrhosis, several physiological disturbances contribute to alterations in gut microflora and dysfunction of the intestinal epithelium, including decreased gut motility, reduced secretion of protective factors such as secretory IgA, lysozyme,
mucus, and gastric acids, along with increased intestinal pH, reduced bile acid flow, and excessive alcohol intake (Quigley, 2010). These disruptions promote bacterial overgrowth and intestinal permeability, leading to bacterial translocation and impaired host immune defenses (Wiest & Garcia-Tsao, 2005). Probiotic strains such as Lactobacillus and Bifidobacterium have demonstrated beneficial effects in cirrhotic patients by attenuating liver injury, reducing bacterial translocation, and normalizing inflammatory markers including TNF-α, as well as improving antioxidant levels such as glutathione (Liu et al., 2004). The mechanisms underlying these protective effects include the ability of Lactobacillus species to enhance the growth of beneficial anaerobic and gram-positive bacteria while suppressing gram-negative pathogens (Guarner & Malagelada, 2003). Additionally, probiotics increase the production of short-chain fatty acids (SCFAs), reduce intestinal pH, stimulate epithelial growth factors, promote healthy microflora proliferation, and inhibit pathogen adherence and invasion, collectively contributing to

improved gut barrier integrity and reduced complications of cirrhosis (Guarner & Malagelada, 2003; Bajaj et al., 2014).

8. Probiotics to Bind Toxins and Carcinogens

Probiotics have the ability to bind and immobilize toxic compounds within the gut lumen, thereby reducing the harmful effects of dietary toxins and contributing to improved gut and liver health (Ouwehand & Salminen, 1998). Lactobacillus rhamnosus strains, in particular, have demonstrated strong binding capacity for various mycotoxins that disrupt the intestinal mucosal barrier, and in Caco-2 cell models they can attenuate mycotoxin-induced impairments in epithelial differentiation and intestinal integrity (Haskard et al., 2001). Additionally, probiotic supplementation has been shown to mitigate the hepatotoxic effects of aflatoxin—one of the most potent dietary liver carcinogens—by reducing its bioavailability, enhancing detoxification, and lowering biomarkers associated with liver cancer risk (El-Nezami et al., 2006). These findings support the therapeutic role of probiotics as a natural strategy to counteract toxin-induced intestinal and hepatic injury.

9. Gut–Lung Axis

The microbiota of the upper and lower respiratory tracts differs markedly across anatomical sites; the nostrils are dominated by Firmicutes and Actinobacteria, while the oropharynx contains primarily Firmicutes, Proteobacteria, and Bacteroidetes (Man et al., 2017). The lungs harbor a distinct but low-biomass microbiome composed mainly of Bacteroidetes, Firmicutes, Prevotella, Veillonella, and Streptococcus, whereas the gut is rich in Bacteroides, Faecalibacterium, and other anaerobes (Budden et al., 2017). Despite these compositional differences, the gut and respiratory epithelia share a common embryonic origin and exhibit similar mucosal immune functions, and early-life microbial colonization of both systems follows parallel developmental patterns—a relationship known as the gut–lung axis (Dang & Marsland, 2019). The gut microbiota is strongly influenced by factors such as diet, medications, feeding practices, and mode of delivery, all of which shape susceptibility to respiratory diseases. For example, early exposure to acid-suppressive medications, antibiotics, frequent fast-food consumption, cesarean delivery, and formula feeding are associated with an increased risk of childhood asthma, whereas high dietary fiber intake, vaginal birth, and breastfeeding are associated with reduced asthma risk (Arrieta et al., 2015;
Metsälä et al., 2015). Collectively, these findings highlight the deep immunological interconnection between gut and lung health.

10. Role of Probiotics in Asthma

Asthma is a chronic inflammatory disorder characterized by reversible airflow limitation and airway hyperresponsiveness, and increasing evidence suggests that the gut microbiota plays a significant role in its development and severity (Arrieta et al., 2015). Early-life gut dysbiosis is strongly associated with higher asthma risk, as reduced microbial diversity—commonly observed in formula-fed infants—has been linked to immune dysregulation, whereas breastfeeding supports a more diverse and protective microbiome (Stokholm et al., 2018). Specific bacterial taxa also influence asthma susceptibility: decreased abundances of Bifidobacterium, Akkermansia, and Faecalibacterium combined with increased Candida and Rhodotorula levels have been
associated with heightened risk of allergies and asthma (Fujimura et al., 2016). Probiotic supplementation, including Lactobacillus rhamnosus, Lactobacillus casei, and Bifidobacterium breve, has shown potential in preventing or mitigating asthma and allergic responses by modulating immune pathways (Hougee et al., 2010). Disruption of gut microbiota by antibiotics may exacerbate Th2-dominant inflammation by increasing IL-4 and IL-13 production, reducing lung regulatory T cells (Tregs), and enhancing Th1/Th17 responses and eosinophilic infiltration (Russell et al., 2012). In contrast, probiotics may counteract these effects by increasing PPARγ expression in dendritic cells, elevating lung CD4+ T cells and CD4+Foxp3+ Tregs, reducing activated CD11b+ dendritic cells, lowering MMP-9 levels, and limiting inflammatory cell infiltration into the airways (Zhang et al., 2014). These findings highlight probiotics as a promising strategy for asthma prevention and management through modulation of the gut–lung immune axis.

11. Role of Probiotics in COPD

Chronic obstructive pulmonary disease (COPD) is increasingly recognized as a condition influenced not only by lung inflammation but also by gut dysbiosis. Cigarette smoke exposure alters mucin gene expression and cytokine production in
the gut, leading to increased expression of Muc2, Muc3, and Muc4, elevated levels of CXCL2 and IL-6, and reduced production of IFN-γ and TGF-β (Sze et al., 2018). Smoke-induced dysbiosis also disrupts epithelial barrier integrity by enhancing NF-κB activation through increased p65 phosphorylation and reduced IκBα levels (Wang et al., 2021). Probiotics have emerged as promising modulators of this gut–lung interaction in COPD. They can suppress macrophage-driven inflammation by regulating cytokines such as IL-1β, IL-6, IL-10, IL-23, TNF-α, CXCL-8, and HMGB1, while simultaneously enhancing innate immune responses (Kwon et al., 2019). Additionally, probiotic supplementation has been shown to increase natural killer (NK) cell activity and elevate the number of CD16+ cytotoxic cells, contributing to improved immune surveillance and reduced airway inflammation (Timmerman et al., 2007). Together, these findings highlight the potential of probiotics to counteract cigarette-smoke–induced gut inflammation and modulate systemic immunity in COPD.

12. Role of Probiotics in Cystic Fibrosis

Cystic fibrosis (CF) patients often require frequent antibiotic treatment, which can disrupt gut microbiota and promote systemic inflammation by increasing the proportions of Th17 cells, $CD8^+IL\text{-}17^+$ and $CD8^+IFN\text{-}\gamma^+$ lymphocytes, as well as IL-17-producing γδ T cells (Bruzzese et al., 2014). This immune activation contributes to chronic intestinal and pulmonary inflammation. Probiotic supplementation has been shown to mitigate these effects by reducing IL-8 production by intestinal epithelial cells and lowering levels of the gut inflammatory biomarker calprotectin (Bruzzese et al., 2007; Weiss et al., 2010). These findings suggest that probiotics may play a supportive role in managing intestinal inflammation in CF, potentially improving gut health and modulating systemic immune responses.

13. Role of Probiotics in Lung Cancer

Disruption of gut microbiota, such as through antibiotic use, has been shown to negatively influence antitumor immunity in lung cancer by upregulating VEGFA expression, downregulating pro-apoptotic genes like BAX and CDKN1B, and
reducing the production of IFN-γ, granzyme B (GZMB), and perforin (PRF1) by $CD8^+$ T cells (Routy et al., 2018). Such dysbiosis suppresses chemotherapy-induced Th17 responses and diminishes the presence of antitumor $CD3^+$ T cells and Th1 cells within the tumor microenvironment. Probiotic supplementation can counteract these effects by upregulating mRNA expression of IFN-γ, GZMB, and PRF1, enhancing chemotherapy-induced Th1 and Tc1 antitumor responses, and promoting infiltration of IFN-γ–producing γδ T cells into tumor lesions (Sivan et al., 2015). These findings highlight the potential of probiotics to restore gut-mediated immune surveillance and improve anticancer immunity in lung cancer.

14. Role of Probiotics on Skin Health

Probiotics, particularly lactic acid bacteria, have been shown to improve skin health by modulating immune responses and reducing inflammation, thereby decreasing
hypersensitivity reactions and inflammatory mediator production (Guéniche et al., 2010). Wound healing, a key aspect of skin repair, occurs in three overlapping phases: the inflammatory response, cell proliferation, and remodeling of the extracellular matrix, processes that can be positively influenced by probiotics (Peral et al., 2009). In various skin disorders, probiotics exert distinct mechanisms of action. In atopic dermatitis, they block integrin signaling and stimulate immune responses, while in allergic contact dermatitis, they reduce inflammation and enhance immune modulation (Han et al., 2018). In psoriasis, probiotics help prevent transepidermal water loss, modulate gene expression, and provide anti-inflammatory and immunostimulatory effects. In photoaging, probiotics regulate transcriptional activation and suppression of genes, while also exhibiting anti-inflammatory properties. In acne, probiotics produce bacteriocins and competitively inhibit pathogenic bacteria, maintaining a balanced cutaneous microbiome.

These multifaceted actions highlight the potential of probiotics in the prevention and management of diverse skin conditions.

15. Effect of Probiotics on the Immune System

Probiotics play a crucial role in modulating both innate and adaptive immune responses. They enhance humoral immunity, strengthen the intestinal immunologic barrier, stimulate nonspecific host resistance to microbial pathogens, and downregulate hypersensitivity reactions (Azad et al., 2018). Oral administration of lactobacilli, such as Lactobacillus casei, L. bulgaricus, and L. acidophilus, activates macrophages and enhances phagocytosis, exerting immunostimulatory effects in healthy individuals while downregulating inflammatory responses in allergic individuals (Gill et al., 2001). Specific strains exhibit distinct immunomodulatory properties: L. paracasei lowers IL-5, IL-8, and IL-10 levels, L. plantarum promotes Th1-type immune responses, and L. casei suppresses pro-inflammatory cytokines while modulating Th1-mediated immunity (Miettinen et al., 1996; Kalliomäki et al., 2003). Lactobacillus rhamnosus GG combined with hydrolyzed casein reduces IL-4 production, indicating that probiotics can modify antigen structure and immunogenicity (Isolauri et al., 2000). Lactobacillus species also enhance oral tolerance by upregulating Foxp3 expression and downregulating Th1-mediated
responses, which may be beneficial in autoimmune conditions such as rheumatoid arthritis. Additionally, oral probiotics normalize fecal urease concentrations, stabilize gut microbial environments, and prevent the generation of inflammatory mediators, as seen in rotavirus-associated diarrhea, where elevated fecal urease predisposes the gut mucosa to ammonia-induced damage (Guarino et al., 2015). Overall, probiotics exhibit a multifaceted capacity to regulate immune homeostasis and protect against inflammation and infection.

16. Gut-Associated Lymphoid Tissue (GALT) and Probiotics

Gut-associated lymphoid tissue (GALT), which includes Peyer's patches, isolated lymphoid follicles, and mesenteric lymph nodes, is a critical component of the immune system primarily located in the gastrointestinal tract (Macpherson & Harris, 2004). GALT serves as a primary site for antigen sampling and initiation of immune responses, playing a pivotal role in maintaining gut homeostasis by regulating immune reactions to dietary antigens and commensal microbiota while protecting the
host from mucosal pathogens (Mowat & Agace, 2014). Probiotics can positively influence GALT by modulating the gut microbiota, stimulating both innate and adaptive immune responses, and enhancing the integrity of the intestinal barrier, thereby promoting overall gut health and immunological balance (Doré & Blottière, 2015).

17. Role of Probiotics on the Nervous System via the Gut–Brain Axis

The gut–brain axis is a complex bidirectional communication system linking the central nervous system (CNS) and the enteric nervous system (ENS) with the gastrointestinal tract through neuronal, hormonal, and immunological pathways (Cryan & Dinan, 2012). Afferent and efferent neurons transmit signals via the autonomic nervous system (ANS), ENS, hypothalamic–pituitary–adrenal (HPA) axis, sympatho-adrenal axis, and descending monoaminergic pathways. The ENS, composed of the myenteric and submucosal plexuses, regulates gut motility, secretion, and absorption, while the ANS controls systemic functions such as heartbeat,

digestion, bile secretion, and mucosal immunity (Furness, 2012). Gut microbiota-derived molecules, including lipopolysaccharides (LPS), peptidoglycan, and flagellin, interact with pattern-recognition receptors (PRRs) such as Toll-like receptors (TLR2 and TLR4) on epithelial and immune cells, producing cytokines, hormones, and neurotransmitter-like signals that influence CNS functions (Carabotti et al., 2015). In a healthy state, gut microbiota promote the production of short-chain fatty acids (SCFAs), gut-derived peptides, neurotransmitters, and regulatory T and B cells, maintain intestinal barrier integrity, reduce LPS translocation, and support blood–brain barrier (BBB) function, thereby enhancing brain immune homeostasis and cognitive functions. Conversely, gut dysbiosis leads to increased intestinal permeability, translocation of microbial metabolites and molecular patterns, elevated pro-inflammatory cytokines, reduced SCFAs, and activation of microglial and astrocyte cells, contributing to neuroinflammation and the progression of neurological disorders. Probiotics, by restoring microbial balance, can modulate these processes, reinforcing gut barrier integrity, reducing neuroinflammation, and supporting CNS and ENS function (Mayer et al., 2015).

18. Role of Probiotics in Alzheimer's Disease

Alzheimer's disease (AD) is a neurodegenerative disorder primarily affecting older adults, characterized by progressive dementia and loss of cholinergic neurons. Neuropathologically, AD is associated with extracellular amyloid-β accumulation, senile plaques, and intracellular neurofibrillary tangles (Querfurth & LaFerla, 2010). Patients with AD exhibit gut dysbiosis, including reduced populations of butyrate-producing bacteria such as Butyrivibrio, Eubacterium, Clostridium sp. strain SY8519, Roseburia hominis, and Faecalibacterium prausnitzii, alongside increased proinflammatory taxa, including Bacteroides vulgatus, B. fragilis, and Eggerthella lenta (Zhuang et al., 2018). This imbalance promotes neuroinflammation and cerebral amyloid-β accumulation. Dysbiosis in AD is characterized by reduced Firmicutes and Bifidobacterium, increased Bacteroidetes, and an elevated abundance of potentially pathogenic bacteria such as Escherichia/Shigella, which correlates with enhanced proinflammatory mediators (IL-1, CXCL2, NLRP3) and amyloid pathology. Probiotic supplementation with strains such as Lactobacillus acidophilus, L. casei,

Bifidobacterium bifidum, and L. fermentum has been shown to reduce amyloid-β accumulation, decrease matrix metalloproteinase activity, lower proinflammatory cytokines (e.g., IL-6, TNF-α), and improve cognitive function, spatial memory, and synaptic integrity in experimental models (Akbari et al., 2016; Bonfili et al., 2017). These findings suggest that modulation of the gut microbiota via probiotics may represent a promising adjunctive strategy in AD management.

19. Role of Probiotics in Parkinson's Disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder primarily resulting from the loss of dopaminergic neurons in the substantia nigra pars compacta, manifesting as both motor and non-motor symptoms (Kalia & Lang, 2015). A hallmark of PD pathology is the accumulation of misfolded α-synuclein (Lewy bodies) in the substantia nigra, with evidence suggesting that this aggregation may originate in the enteric nervous system and propagate to the central nervous system via the vagus nerve (Braak et al., 2003). The etiology of PD involves oxidative stress, environmental toxins, metabolic dysfunction, genetic factors, and neuroinflammation.

Gut microbiota dysbiosis, including alterations in Lactobacillus and Bifidobacterium populations, has been implicated in PD pathogenesis through the gut–brain axis (Scheperjans et al., 2015). Probiotic supplementation, such as with Lactobacillus plantarum PS128, has been shown to alleviate motor deficits, reduce corticosterone levels, mitigate nigrostriatal dopaminergic loss, and decrease oxidative stress and neuroinflammation, highlighting the potential of microbiota-targeted interventions in PD management (Chang et al., 2019).

20. Role of Probiotics in Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune disorder characterized by T cell–mediated immune responses against myelin antigens, leading to axonal damage, demyelination, and progressive neurological disability, with clinical manifestations including blurred vision, motor dysfunction, and sensory disturbances (Reich, Lucchinetti, & Calabresi, 2018). Alterations in gut microbiota in MS patients can modulate immune homeostasis by affecting regulatory T cells (Tregs), which suppress proinflammatory T cell activation, while elevated levels of circulating Th1 and Th17 cells contribute to increased blood–brain barrier (BBB) permeability and central nervous system inflammation (Cekanaviciute et al., 2017). Probiotic supplementation has been shown to provide synergistic benefits with conventional MS therapies by modulating immune responses and reducing the expression of MS susceptibility alleles such as HLA-DQA1. Combined administration of Lactobacillus casei, Bifidobacterium spp., and Lactobacillus fermentum has demonstrated favorable effects on the Expanded Disability Status Scale (EDSS), systemic inflammation markers, insulin resistance, and malondialdehyde (MDA) levels, suggesting that probiotics may serve as a valuable adjunctive strategy for improving clinical outcomes in MS patients (Kouchaki et al., 2017).

21. Role of Probiotics in Depression

Depression is a prevalent, recurrent, and debilitating neuropsychiatric disorder characterized by low mood, loss of interest, feelings of guilt, hopelessness, sleep and appetite disturbances, and sexual dysfunction (Malhi & Mann, 2018). Major

depressive disorder (MDD) is associated with elevated levels of proinflammatory cytokines and alterations in gut microbiota composition. Specifically, an increased abundance of genera such as Anaerostipes, Blautia, Clostridium, Klebsiella, Lachnospiraceae incertae sedis, Parabacteroides, Parasutterella, Phascolarctobacterium, and Streptococcus, alongside decreased levels of Bifidobacterium, Dialister, Escherichia/Shigella, Faecalibacterium, and Ruminococcus, has been reported in individuals with MDD (Kelly et al., 2016). Probiotic supplementation with Lactobacillus helveticus, L. plantarum, and Bifidobacterium longum has demonstrated improvements in depression- and anxiety-like behaviors, while L. rhamnosus has been shown to reduce depression scores. Overall, Lactobacillus and Bifidobacterium species enhance cognitive performance and memory in stressed individuals by reducing proinflammatory cytokine production and cortisol levels, thereby alleviating depression and anxiety symptoms (Majeed et al., 2018).

22. Role of Probiotics in Migraine

Migraine is a complex neurological disorder frequently associated with gastrointestinal symptoms, including nausea, vomiting, dyspepsia, and bowel disturbances (Kang et al., 2017). Epidemiological studies indicate a higher prevalence of migraine in individuals with gastrointestinal disorders such as irritable bowel syndrome and celiac disease, suggesting a significant gut–brain axis involvement (Martin et al., 2018). Increased intestinal permeability may allow proinflammatory substances to reach the trigeminovascular system, thereby triggering migraine attacks. Modulation of gut microbiota through beneficial strains of Lactobacillus and Bifidobacterium may help reduce inflammation, enhance gut barrier integrity, and maintain intestinal homeostasis, ultimately contributing to migraine prevention and symptom alleviation (Sacco et al., 2020).

Conclusion:

In conclusion, probiotics play a pivotal role in maintaining and improving overall human health by modulating the gut microbiota and influencing multiple physiological systems. They contribute to the prevention and management of

metabolic disorders, liver diseases, respiratory conditions, skin disorders, and neurological and psychiatric illnesses through mechanisms that include enhancement of gut barrier integrity, regulation of immune responses, reduction of inflammation, and modulation of the gut–brain axis. Regular supplementation with specific probiotic strains, such as Lactobacillus and Bifidobacterium, has demonstrated beneficial effects on metabolic, immune, and neurocognitive functions, highlighting their potential as adjunctive therapeutic

agents. Overall, probiotics offer a promising, natural, and holistic approach to promoting systemic health and mitigating disease risk across a broad spectrum of conditions.

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