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Impacts of gut microbiota on human health and diseases

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Abstract

Numerous microorganisms that are important to the health of their host are found in abundance in the human gut. They can, however, also be potentially dangerous because of the alteration in their composition that occurs when the gut ecosystem experiences aberrant changes as a result of the use of antibiotics, sickness, stress, age, poor dietary practices, and lifestyle choices. Dysbiosis of the gut micro biota on humans has harmful health effects that can result in a number of chronic disorders. The potential of probiotics to treat certain disorders has led to much research into them. They are typically thought of as helpful microbes; additionally, when their products are supplied to humans in sufficient doses, they act as health adjuvants. Probiotics can prevent the beginning of disease through a number of processes, including altering gut bacteria, producing short-chain fatty acids, reducing intestinal pH, producing antimicrobial compounds, and suppressing epithelial binding growth. Additionally, they help to inhibit the invasion of pathogenic organisms, regulate the transfer of food antigens, enhance intestinal barrier performance, and alter host immunological responses. Probiotic tests have revealed encouraging outcomes in the prevention of diseases such as diarrhea, irritable bowel syndrome, colon cancer, and Crohn's disease. Numerous epidemiological and experimental investigations, particularly those focusing on the gut microbiota, have contributed to shed light on the role of probiotics as preventative agents. This review provides a potential target for the illness prevention and treatment by summarizing and discussing the roles and potential mechanisms of gut bacteria in human health and disorders.

Keywords: Probiotics; Dysbiosis; Inflammation; Immune response; Prevention

1. Introduction

Probiotics are sometimes referred to as health-promoting beneficial bacteria that offer their host certain advantages when consumed in sufficient quantities. The gastrointestinal (GI) tract of humans stores billions of gut bacteria necessary for immunity, nutrition absorption, and digesting. Numerous experimental researches have shown how probiotics are beneficial for human health. Probiotics, for instance, reduce the risk of numerous infectious diseases, both communicable and noncommunicable [1]. As antibiotic-resistant bacteria proliferate, infectious diseases also represent a serious threat to human health. Hospital stays are getting longer due to the rise in infections caused by microorganisms that are multidrug resistant. As a result, morbidity and mortality rates are also rising [2]. From a human health standpoint, nutritional advantages are highly effective in preventing fatal diseases like inflammatory bowel disease, obesity, diabetes, colon cancer, and intestinal disorders [3]. Scientific studies have also demonstrated the benefits of using probiotics preventatively. Clinical studies have validated the efficacy of probiotics and suggested probiotic doses for individuals suffering from particular disorders [4]. Among all probiotics, *Lactobacillus* and *Bifidobacteria* species are distinctly recognized microbes that can reduce GI discomfort. These probiotics have the ability to produce vitamin B,

promote a reaction that lowers cholesterol, and produce antioxidants, which can help prevent heart disease, diabetes, GI tract infections, and ulcers. In addition, they raise the quantity of helpful microorganisms, suppress harmful microbes, control the host's defense system, boost the delivery of nutrients, and lower the risk of disease development [5]. In general, this work aims to review and discuss the impact of the probiotics against common human diseases (e.g., intestinal diseases, allergic diseases, obesity, colon cancer, and diabetes) and on maintaining health.

2. Mechanisms of Action of Probiotics

The exact mechanisms by which probiotics accomplish their beneficial actions have not been well documented.

However, there are several postulated mechanisms that explain many of their favorable effects. Major Probiotic mechanisms of action include enhancement of the epithelial barrier, increased adhesion to the intestinal mucosa, concomitant inhibition of pathogen adhesion, competitive exclusion of pathogenic microorganisms, production of anti-microorganism substances, and modulation of the immune system [6,7].

2.1. Enhancement of the Epithelial Barrier

The intestinal epithelium is in constant contact with the contents of the lumen and the changing dynamic intestinal flora. The intestinal barrier is the main defense mechanism used to maintain the integrity of the epithelium and protect the organisms from the environment. Probiotics may improve intestinal barrier function by modulating phosphorylation of the cytoskeletal and tight junctional proteins, thereby affecting intercellular mucosal interactions and cellular stability. Intestinal barrier function is supported by several interconnected systems including mucus secretion, chloride and water secretion, IgA secretion, and binding of epithelial cells at apical junctions by tight junction proteins [6,8]. Several studies have shown that enhancing the expression of genes involved in tight junction signaling is a possible mechanism to improve the integrity of the intestinal barrier. For example, *lactobacilli* modulate the regulation of several genes encoding adherence junction proteins such as E-cadherin and β-catenin, in a T84 cell barrier model. Moreover, culture of lactobacilli and intestinal cells positively modulates epithelial barrier function, as they differentially affect the phosphorylation of adherence junction proteins and the abundance of protein kinase C (PKC) isoforms, such as PKCδ [9,10].

2.2. Increased Adhesion to Intestinal Mucosa

Adhesion to intestinal mucosa is regarded as a prerequisite for colonization and is important for the interaction between probiotic strains and the host. Adhesion of probiotics to the intestinal mucosa is also important for modulation of the immune system and antagonism against pathogens.

Lactobacilli represent various surface determinants (adhesins) involved in their interactions with intestinal epithelial cells (IECs) and mucus. IEC secretes mucin, a complex mixture of glycoproteins, the main component of the mucous membrane, to prevent the attachment of pathogenic bacteria [11,12].

2.3. Competitive Exclusion of Pathogenic Microorganisms

Competitive exclusion refers to the situation in which one species of bacteria competes for receptor sites in the intestinal tract more vigorously than other species. The mechanisms used by one species of bacteria to exclude or reduce the growth of another species are varied, including the following mechanisms: creation of a hostile microecology, elimination of available bacterial receptor sites, production and secretion of antimicrobial substances and selective metabolites, and competitive depletion of essential nutrients [6]. To gain a competitive advantage, bacteria can also modify their environment to make it less suitable for their competitors. The production of antimicrobial substances, such as lactic and acetic acid, is one example of this type of environmental modification [13]. Specific adhesiveness properties due to the interaction between surface proteins and mucins may inhibit the colonization of pathogenic bacteria and are a result of antagonistic activity by some strains of probiotics against adhesion of gastrointestinal pathogens [14]. Some lactobacilli and bifidobacteria can produce antimicrobial peptides known as bacteriocins, which prevent the proliferation of selected pathogens. The term "colonization resistance" refers to the use of probiotics to prevent or treat enteric pathogens [6]. In particular, some of these compounds produced by *L. plantarum* and *L. acidophilus* have been shown to inhibit the growth of Helicobacter, *C. difficile*, rotaviruses, and multidrug-resistant Shigella spp. and E. coli in some gastrointestinal conditions [15] and have activity against a number of uropathogens [16].

Some probiotic metabolites appear to play a role in the modulation of diverse signaling and metabolic pathways in cells. Indeed, components of the probiotic metabolome have been reported to interact with multiple targets in some

metabolic pathways that regulate cellular proliferation, differentiation, apoptosis, inflammation, angiogenesis, and metastasis [17].
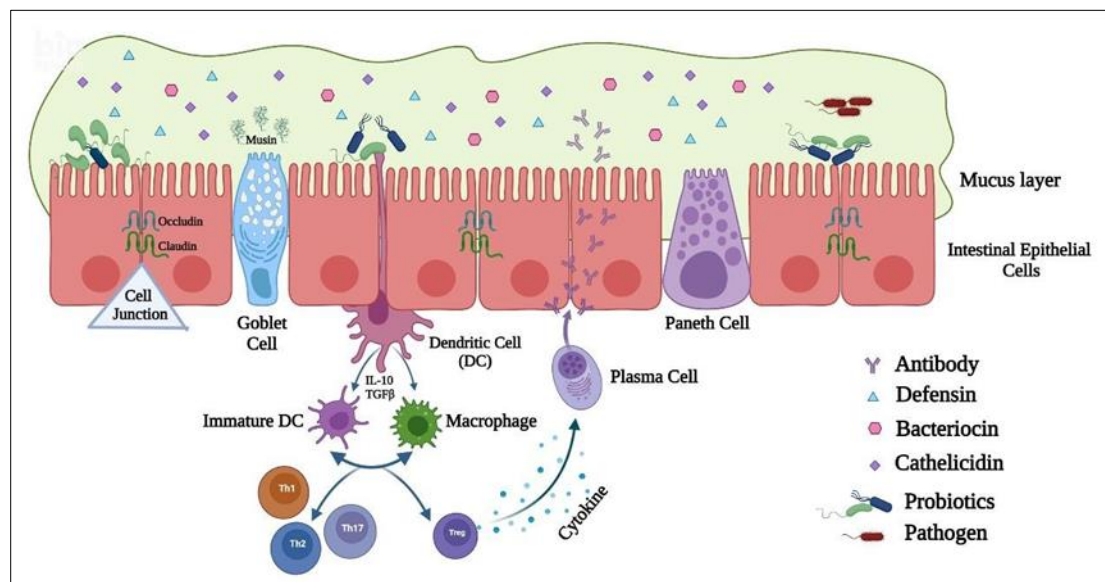
Figure 1 Mechanisms of action of probiotics

2.4. Production of Antimicrobial Substances

One of the proposed mechanisms involved in the health benefits afforded by probiotics includes the formation of low molecular weight compounds (<1,000 Da), such as organic acids, and the production of antibacterial substances termed bacteriocins (>1,000 Da). Organic acids, in particular acetic acid and lactic acid, have a strong inhibitory effect against Gram-negative bacteria, and they have been considered the main antimicrobial compounds responsible for the inhibitory activity of probiotics against pathogens. The undissociated form of the organic acid enters the bacterial cell and dissociates inside its cytoplasm. The eventual lowering of the intracellular pH or the intracellular accumulation of the ionized form of the organic acid can lead to the death of the pathogen.

Many lactic acid bacteria produce antibacterial peptides, including bacteriocins and small AMPs. The common mechanisms of bacteriocin-mediated killing include the destruction of target cells by pore formation and/or inhibition of cell wall synthesis [6]. Several bacteriocins produced by different species from the genus Lactobacillus have been described. The inhibitory activity of these bacteriocins varies; some inhibit other lactobacilli or taxonomically related Gram-positive bacteria, and some are active against a much wider range of Gram-positive and Gram-negative bacteria as well as yeasts and molds. For example, the probiotic *L. salivarius* subsp. *salivarius* UCC118 produces a peptide that inhibits a broad range of pathogens such as *Bacillus, Staphylococcus, Enterococcus, Listeria,* and *Salmonella species.* Lacticin 3147, a broad-spectrum bacteriocin produced by *Lactococcus lactis subsp.*, inhibits a range of genetically distinct *C. difficile* [8]*.* Other biologically active compounds produced by lactic acid bacteria include hydrogen peroxide, diacetyl, and short-chain fatty acids. The release of these compounds by probiotic organisms results in a beneficial modification of the microflora [18].

2.5. Modulation of the Immune System

Probiotics confer immunological protection to the host through the regulation, stimulation, and modulation of immune responses. They modulate the immune system via the production of molecules with immunomodulatory and anti-inflammatory functions that are capable of stimulating immune cells. These immunomodulatory effects are due to the interaction of probiotic bacteria with epithelial cells and DCs and with monocytes or macrophages and lymphocytes [19].

One of the major mechanisms of action of probiotics is the regulation of host immune response. Thus, the immune system is divided into the innate and adaptive systems. The adaptive immune response depends on B and T lymphocytes, which bind to specific antigens. In contrast, the innate system responds to common structures, called pathogen-associated molecular patterns (PAMPs), shared by a majority of pathogens [20].

The changes in microbial populations in the gastrointestinal tract (GIT) caused by probiotics increase the production of short-chain fatty acids (SCFA) and cause immunomodulation, which improves energy metabolism as well (Anwar and Rahman 2016). When SCFA is produced through the microbial fermentation of carbohydrate in the intestine, the SCFA metabolites act on leukocytes and endothelial cells through activating G-protein-coupled receptors (GPCRs) and inhibit histone deacetylase. Besides the interaction with various receptors, SCFAs promote the generation of IgA by B-immune cells, inhibit the NF-κB transcription factor, and reduce chemokine and cytokine production (Delgado et al. 2020). Probiotics have been evaluated for in vivo effects, such as increased peripheral immunoglobin production, stimulation of IgA secretion, and decreased proinflammatory cytokine production [21].

3. Gut Microbiota and Common Diseases

3.1. Allergies

Allergies are hypersensitive immune reactions brought on by certain elements, such as food, dust, or cold. Around the world, 20% of the population currently experiences allergies-related illnesses, and the number is rising [22]. Through the mucosal immune system, any dysbiosis in the microbial florae disturbs homeostasis and encourages allergic disorders. The Th2 phenotype increases the production of IL-4, IL-5, IL-13, and IgE by B cells; as a result, mast cells are activated, and they in turn increase the risk of allergy-related diseases. Allergic diseases occur through Th2 response activation because of the destabilization of the Th1/Th2 cytokine balance. However, Th1 responses and DCs can be deactivated by toll-like receptors and proteoglycan proteins, which can be regulated by probiotics. IgA thus turns on and blocks allergen antigens. But more research into this process is needed [22–24].

3.2. Colorectal Cancer

The third-most deadly cancer in the world right now is colorectal cancer (CRC). Adenocarcinoma is a well-defined chain of events brought on by oncogene and growth suppressor gene mutations, activations, and deletions [25]. Three distinct factors, including chromosomal instability (CIN), microsatellite instability (MSI), and the CpG island methylator phenotype, can contribute to the development of colon cancer (CIMP). A large variety of chromosomes or a lack of chromosomes in CIN might result in genetic instability and illnesses like colon cancer [26]. APC and TP53 deactivation, activation of oncogenes (KRAS and BRAF), and loss of heterozygosity for the long arm of chromosome 18 (18q LOH) can all lead to adenocarcinoma transitions, which account for 85% of adenocarcinoma transitions in CIN and colon carcinogenesis [27]. Malignant cells are a hallmark of MSI. More than 95% of cases of Lynch syndrome, a type of hereditary non-polyposis colorectal cancer (HNPCC), occur. DNA methylation, also known as CpG transcription, is the addition of a methyl group to cytosine in the fifth position. DNA methyltransferases catalyze this process through covalent bonding inside a CG dinucleotide sequence within a promoter region. CpG islands, which are typically found in regions surrounding gene promoters, are unmethylated while the majority of CpG sites in normal cells are extensively methylated. Global hypomethylation is linked to genomic fluctuation and chromosomal abnormalities, but hypermethylation within the promoter region may direct the deactivation of tumor-suppressor genes in the early stages of cancer [28,29]. The unique feature is explained by the colon's prevalence of enteric microbiota and the link between gut microbiota and cancer. The presence of *Fusobacterium nucleatum*, *Streptococcus gallolyticus*, and *Providencia* in human large intestine cancer tumors, for example, has been linked to an increased risk of developing carcinoma. Two intestine pathogenic bacteria, Bacteroides and Clostridium, have been connected to the pathophysiology of CRC [30]. Several studies have suggested that taking probiotics on a daily basis can help enhance the quantitative and qualitative profile of the viscous microbiota, thereby lowering chronic inflammation [31]. Yogurt starter microorganisms have been shown in animal model studies to be able to block bacterial enzyme activity, which may be the underlying mechanism of the CRC-preventive effects of probiotics [32]. CRC cells are suppressed by *Propionibacterium freudenreichii*, a probiotic present in the human gut microbiota, via SCFA-mediated apoptosis [33]. Butyric acid prevents CRC by influencing the cell cycle, differentiation, and apoptosis of colon cancer cell lines [34]. Probiotics alter the gut microbiota's makeup. As a result, they have an impact on their host by strengthening the intestinal barrier, lowering the metabolism of procarcinogenic chemicals, and preventing pathogen proliferation [31].

3.3. Crohn's Disease

CD is a chronic granulomatous inflammatory disorder that can involve any part of the GI tract, predominantly the terminal ileum and adjacent colon [35]. The main clinical symptoms vary among individuals and include diarrhea, abdominal pain, weight loss, nausea, vomiting, fevers or chills, fistula, anal lesions [36]. Numerous patients with CD require surgery, and 70% of these patients develop mucosal recurrence 1 year after surgery. Thus, it may result in clinical relapse, leading to potential complications and requiring repeat surgery [37]. Dysbiosis in gut microflora leads to the disruption of the defense mechanism of the mucosal epithelial layer. When the mucosal epithelial layer is excessively exposed to bacteria, an alternative pathway of DC maturation and macrophage activation is triggered,

leading to the production of IL-12, which induces a TH1 cytokine response. Some antigens produced by bacteria can induce CD4+ T cells to differentiate into targeted cytotoxic T lymphocytes (CTLs), which release IL-17 to stimulate Th17 cells to produce inflammatory cytokines; however, these cytokines can cause persistent inflammation and fibrosis [35]. Probiotics can secrete a small amount of TGF-β to prevent macrophage activation and induce IL-22 production, which can cause Paneth cells to secrete antimicrobial peptides that prevent bacterial contact with epithelial cells. They also inhibit intestinal inflammation and promote epithelial cell proliferation via the JAK-STAT pathway. In addition, probiotics maintain the integrity of the epithelial barrier and prevent intestinal microbial invasion. Ultimately, they inhibit antigen-specific immune responses and restrict intestinal inflammation through IL-10 downregulation [35,38].

3.4. Type 1 Diabetes Mellitus

In both industrialized and emerging nations, diabetes mellitus (DM), a metabolic condition that has an impact on world health, is on the rise [39]. In 2010, 285 million adult patients had diabetes, and this number is predicted to reach 439 million by 2030 [40]. The interplay between gut bacteria and host immune cells is critical in the onset of type 1 diabetes (T1D). By changing immune cell activities, metabolites and antigens produced by gut microbes can speed up the development of T1D pathogenesis. Proinflammatory responses triggered by the immune system in response to beta-cell antigens result in T1D. As a result, there is an increase in the infiltration of immune cells like macrophages, which leads to the formation of inflammatory islets and an insulin deficit [41,42]. Pancreatic lymph nodes experience an autoreactive immune response when T cells become more hyperactive (PLNs). After then, CD4+T cells keep multiplying and transform into autoreactive CD4+ effector T cells (Teffs), which aid antigen presentation cells (APCs) in more swiftly recognizing antigens [43]. Teffs develop as a result of these interactions and are further activated by the complement system. These activated Teffs in the pancreatic islets release cytokines including IFN and IL-2, which stimulate cytotoxic CD8+T cells and draw in macrophages. However, insulitis manifests as a result of the development of inflammatory islets. The production of cytokines that induce cell death is also influenced by cytotoxic T cells and macrophages. In pancreatic beta cells, these toxins may result in abnormal proinsulin processing and endoplasmic reticulum (ER) stress [42,44]. However, probiotics, particularly *Lactobacillus acidophilus*, *Bifidobacterium lactis*, and *L. rhamnosus*, induce the production of SCFAs (e.g., butyrate) and IL-10, which have a protective effect on beta-islet cells [45]. Additionally, it might boost intestinal L cells' glucagon-like peptide 1 (GLP1) synthesis. The GLP-1 hormone encourages the release of insulin from pancreatic cells and lowers blood sugar levels (46). These results show the probiotics' ability to prevent T1D by preserving the gut microbiota-immune axis' balance. B cells and IgA support the immune system whereas probiotics influence adaptive immune responses by activating DCs [41]. Probiotics therefore seem to be helpful in T1D prevention.

3.5. Type 2 Diabetes Mellitus

One of the most prevalent metabolic diseases is type 2 diabetes mellitus (T2DM). It is brought on by a confluence of two fundamental factors: insufficient insulin release by pancreatic cells and ineffective insulin response in insulin-sensitive tissues. Cell death and malfunction have historically been connected [47]. A complex network of interactions between the environment and numerous molecular processes involved in cell biology underlies the development of T2DM, which results in cell dysfunction [48]. Overproduction of free fatty acids (FFAs) and hyperglycemia trigger the unfolded protein response (UPR), which causes ER stress and ultimately cell death (49). Cell death is brought on by the metabolic and oxidative stress brought on by the lipotoxicity, glucotoxicity, and glucolipotoxicity associated with obesity [48]. The body's ability to maintain physiological glucose levels is constrained by the reduction in insulin production that occurs when cells fail. Additionally, insulin resistance (IR) worsens glucose absorption in the muscle, liver, and adipose tissue. It also causes the liver to produce more glucose. Cell dysfunction is typically more severe than IR, even though both processes start early in the pathophysiology and contribute to disease progression; when both symptoms exist, hyperglycemia results, which accelerates the onset of T2DM [50]. Clinical investigations have discovered a link between LPS and T2D development [51]. For instance, the blood glucose levels of patients with T2D are reduced by the daily consumption of 200 ml of a shake containing 4×10^8 CFU/100 ml of *L. acidophilus*, 4×10^8 CFU/100 ml of *B. bifidum*, and 1 g/100 ml of fructo-oligosaccharides [52]. Additionally, Bifidobacterium animalis subsp. lactis 420 can reduce metabolic bacteremia and restrict bacterial translocation in tissues during the early stages of T2D [53].

3.6. Diarrhea

Diarrhea is a condition in which unusual frequent discharge of semisolid or watery stool occurs at least three times per day, followed by abdominal cramps, abdominal pain, fever, mucus in the stool, and nausea [54]. Several diseases and conditions can cause diarrhea including viruses, bacteria, parasites, medications, food intolerance, surgery, and other digestive disorders [55]. Each year, the number of identified cases of diarrhea ranges between approximately 1.7 and 5 billion [56]. However, probiotics likely reduce the symptoms and duration of diarrhea and even prevent this condition [55]. When the normal gut microflora is disrupted, some pathogenic organisms evade immune responses, proliferate,

and produce toxins (enterotoxin and cytotoxin) [57]. These toxins bind to receptors on the surface of enterocytes and increase the concentrations of cellular cAMP, cGMP, or Ca^{2+}, thereby activating various protein kinases. Cryptic cells secrete chloride in an increased form while villous cells reduce the absorption of sodium and chloride. Thus, protein kinases are activated to alter the electrolyte transport by enterocytes, resulting in diarrhea [58]. Some toxins stimulate enterochromaffin cells to release serotonin, which triggers the release of vasoactive intestinal peptide from local enteric neurons, causing diarrhea (58,59). Moreover, some toxins bind to specific receptors in the intestinal wall, stimulating the production of tumor necrosis factor-alpha and proinflammatory ILs, which contribute to inflammatory responses and fibrosis. Because of the increase in colonic wall permeability, diarrhea usually occurs [57]. When probiotics are introduced, they rebalance the former gut microflora. As a result, different inflammatory ILs, such as IL-8 and tissue necrosis factor, are activated, inducing appropriate transporter proteins and ion channels. These activities in gut microbiota reduce the duration or severity of diarrheal illnesses [57,58,60,61].

3.7. Obesity

A medical syndrome known as obesity is defined by the buildup of excessive amounts of body fat, mainly visceral fat. According to a UN agency, in 2016, there were 600 million (13%) obese people and 1900 million (39%) overweight people over the age of 18. While an imbalance between energy intake and expenditure leads to obesity, poor lifestyle choices also affect brain secretion processes and epigenetic variables. The absorption, storage, and use of energy from dietary intake are all significantly influenced by the gut flora. Over time, energy balance is impacted by obesity-associated bacteria, which increase the potency of calorie intake from consumed foods [62–64]. To clarify how the gut microbiota contributes to the development of obesity, several pathways have been proposed. For instance, the production of SCFA is influenced by the management of energy and the fermentation of dietary polysaccharides. Once produced, SCFAs activate molecular pathways that promote lipogenesis and raise lipid storage. Additionally, they stimulate responsive element-binding macromolecules, which inhibit compound protein enzymes and cause triglyceride buildup in host adipocytes by suppressing the fasting-induced adipocyte tissue [62,65]. Therefore, obesity-associated gut bacteria provide their host with extra energy from nondigestible carbs and proteins, resulting in a lean-associated gut microbiota [66]. Certain probiotics can inhibit the upregulation of a number of host targets involved in the onset of inflammation and obesity [67]. They alter the composition of the gut microbiota, improve gut health, and restore the microbial shift associated with obesity [68].

3.8. Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a GI illness characterized by chronic stomach pain or discomfort and bowel habit changes, such as diarrhea and constipation, without any obvious biological abnormalities [69]. It may affect up to 20% of the population and have negative social and economic impacts on patients [70]. This multifactorial disease is associated with different environmental, inherited, and psychological factors. Its mechanisms include disturbances in the epithelial barrier integrity, dysfunction in the gut–brain axis, and visceral hypersensitivity. As a result, it causes abnormal enteroendocrine signaling, dysbiosis in the gut microbiota, atypical changes in intestinal permeability, immune activation, and altered GI motility [71]. Traditionally, the main pathogenic mechanism of IBS includes an altered gut–brain axis, which is associated with the dysfunction of the GI autonomic nervous system [69]. Various psychological factors, such as somatization, anxiety, hostility, phobia, paranoia, physical and sexual abuse, acute stress, and depression, are related to the dysfunction of the gut–brain axis, which leads to the secretion of corticotrophin-releasing factor (CRF). To promote permeability, CRF stimulates the release of nerve growth factor by mast cells. Some toxic components from various foods such as gliadin can rearrange the cell cytoskeleton by reducing occludin/ZO-1 protein interaction, which increases monolayer permeability [72,73]. After invading the epithelial layer, pathogens may secrete proinflammatory cytokines (IL-8), which produce inflammation. When probiotics are introduced, their interaction with toll-like receptors induces the NF-κB pathway, which decreases inflammation by reducing IL-8. Different DC surface pattern recognition receptors interact with microbial factors, which determine DC maturation and later produce IL-1β, IL-6, and IL-23. Afterward, the triggered DCs modulate the differentiation of antibody T cells into Th1, Th2, Th17, or Treg. Treg cells induce Paneth cells to produce antimicrobial peptides and defensins. The proinflammatory cytokines from Th1 trigger IgG-producing plasma cells, which are derived from B cells. IgG enters the blood and eliminates pathogens by various mechanisms, such as opsonization, neutralization, and agglutination [69]. However, probiotics have beneficial effects on IBS. They prevent pathogenic invasion and inhibit the pathogenic bacterial overgrowth of the host. They also produce substances such as SCFAs and neurotransmitters and improve gut barrier function and receptor interactions. Other mechanisms of IBS may also exist, but they should be further investigated [71].

Limitations

Probiotics have many positive health impacts, but they might also have some negative ones. The most typical reaction to probiotic supplements based on microorganisms is an increase in gas production [72]. Biogenic amines, such as

histamine, tryptamine, and tyramine, are present in some probiotic foods, including yogurt, sauerkraut, and kimchi. Amines have the ability to activate the sensory nerve system, alter blood flow, and cause migraines in people who are sensitive to certain food additives [74]. Some bacterial strains used in probiotic supplements can cause the stomach to release histamine. The excess histamine is subsequently absorbed through the digestive tract's covering and into the blood circulation system, leading to adverse effects including a hypersensitive allergic reaction [75,76]. In rare instances, probiotic bacteria or yeasts can enter the bloodstream and cause infections in people with weakened immune systems [77]. Probiotics should also be avoided by those with severe pancreatitis since they increase the risk of death (78). Probiotic cells have been found to enter the circulation through a process termed bacteraemia that can result in sepsis in the event of young infants with a weakened immune system or serious illnesses. A very powerful immunological response, including heavy breathing, is produced by the body in this situation, which is usually fatal. Further immune reactions to bacterial activity are simply responses as there is no considerable increase in antibody production because the immune system is already compromised or fighting the sickness [79]. Research from experimental studies and meta-analyses on the efficacy of probiotics has produced conflicting findings [80]. Probiotics are therefore safe for a sizable section of the population, but they might not be appropriate for individuals who have underlying health disorders.

Future Perspective

Probiotics are only ever consumed as a food supplement, never as a medication [81]. Since most probiotics are unicellular bacteria, they may be easily cultured or grown by giving them the required media and crucial circumstances. According to what the cells need to employ them in functional foods, probiotics can be generated on a wide scale. Without making a substantial expenditure, it is simple to generate the conditions necessary for their growth in a medium. Large tanks known as bioreactors are used in enterprises to produce goods [82]. Different cells use various resources; thus, they are cultivated in various bioreactors that have been specially built for them. If the probiotic grows more than once in the medium it is being utilized in, its effectiveness will improve. Only when these cultures are consistently given the ideal conditions is this conceivable [83]. Along with the number of health benefits, probiotics also have some ambiguities [84]. Additionally, understanding the genetic makeup of probiotic bacteria might greatly help reduce instances of food poisoning. This is understandable given that food is unquestionably an essential carrier for nutrients as well as for the favorable growth of harmful germs. Given the increased concern over ensuring that the food ingested every day is both wholesome and secure [85], Understanding how the genes of prospective probiotics inhibit the gene expression and, as a result, the survival of well-known food-borne pathogens and their toxins, may provide fresh perspectives on the propensities of probiotics [86,87].

4. Conclusion

Probiotic dosage must be determined through in vivo/in vitro, clinical, or survey-based investigations in order to be precise and advised. Probiotics are likely to play a part in preventing human disease, according to empirical investigations. Additionally, there is enough evidence to show the effectiveness of probiotics in the treatment of many illnesses. It is possible to create more specialized illness prevention or treatment plans by comprehending the fundamental mechanics of diagnosing common diseases.

Compliance with ethical standards

Acknowledgments

Disclosure of conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

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