An Overview on the Function of Probiotics and Their Positive Effects on Enhancing Intestinal Immune Responses

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Abstract
Probiotics are alive and beneficial microorganisms that affect the body’s microbial flora when consumed by humans or animals and have beneficial effects on the health of the host. Nowadays, probiotics are considered a factor in the prevention of many infectious diseases and cancers. Given the particular importance of probiotics, this study aimed to narratively review previous studies on the mode of action of probiotics and the beneficial effects of probiotics on enhancing intestinal immune responses. Articles on this topic were searched in Google Scholar, Springer, Science Direct, and Clinical Trial databases, and systematic review articles examining the effects of probiotics on the function of the intestinal immune response were included in the study. The results of the research showed that probiotics can boost the body’s immune system, break down food due to their ability to produce enzymes, lower the pH of the environment, and secrete bacteriocins. Furthermore, the effect of probiotics on the modulation mechanisms of the innate defense responses of the intestinal epithelium, including the stimulation of trefoil factor 3, induction of antimicrobial peptide (AMP) secretion, stimulation of secretory immunoglobulin production, and stimulation of toll-like receptors increase in heat shock protein production, modulation of P-glycoprotein (P-gp) and regulation of mucins by probiotics. Therefore, probiotics are expected to be used as an adjunct treatment for many digestive and infectious diseases.

Keywords: Cellular immunity, Humoral immunity, Probiotics, Digestive system, Intestine

Background
It was once believed that the human digestive system was the only place for the digestion and absorption of nutrients. In recent years, it has become evident that the digestive system has many functions that are necessary for human health.1 The human digestive system is home to more than 500 known species of microbes. The human gut flora is metabolically active and has numerous beneficial effects on the host.2 The main function of the microbial intestinal flora is metabolic activity, which leads to the conservation of energy and absorbable nutrients. Moreover, it has important trophic effects on gut epithelial cells, immune function, and host protection from invading microbes. The human intestinal flora can be modified in three ways: antibiotics, prebiotics, and probiotics. Probiotics are microorganisms that have a health-promoting effect on their host if they are used sufficiently and are alive.3 The consumption of probiotic supplements results in the formation of beneficial colonies that can contribute to human health as well as the gut’s natural bacterial environment, while providing a basis for repairing and rebuilding the gut’s natural bacterial environment. Subsequently, these colonies are gradually replaced by the gut bacterial environment that can reconstruct itself. Therefore, probiotics are called biological restorers.3,4 The word probiotic, meaning life, which is the opposite of the word antibiotic, comes from the Greek, and it was first used by Lilly and Stillwell in 1965 to describe the substances secreted by one microorganism stimulating the growth of another microorganism.5 Parker was the first who used the word probiotic in its current meaning. He defined probiotics as organisms that effectively restore the microbial balance in the gut.6,7 The mechanisms of the beneficial effects of probiotics on the health of the human digestive system are not yet fully understood, but in general, by binding and colonizing the digestive system, probiotics inhibit the growth of pathogenic bacteria, improve the microbial balance in the gut, promote the function of the mucosal barrier of the digestive system, and stimulate the systemic and innate immune system of the host.8,9 Probiotics also possess immunomodulating properties, including
mechanisms for increasing macrophage or natural killer cell activity, modulating immunoglobulin or cytokine release, increasing the intestinal epithelial barrier, altering mucus secretion, competitively eliminating pathogenic bacteria, and lowering colonic pH. This review aimed to examine the mode of action of probiotics and their beneficial effects on strengthening the intestinal immune response and the health of the human digestive system.

The Role of Probiotics in Altering the Composition and Metabolism of the Gut Microflora

The microbial flora of the intestine in a person is often constant even though this microflora can vary in different people. However, the administration of probiotics leads to changes in stool microbial profile and metabolic activities in both neonates and adults. Although these changes are small, when prescribed for pathological conditions, they are generally sufficient to correct the disease process. In most cases, the administration of probiotics leads to an increase in the number of lactobacilli and bifidobacteria, a decrease in the activity of bacterial enzymes, and a decrease in stool pH.

Variation in the Activity of Bacterial Enzymes Gorbach-Goldin

In a study on 64 women, the administration of Lactobacillus Gorbach-Goldin (GG) led to the recovery of LGG in feces and the reduction of β-glucuronidase, nitroreductase, and glycocholic acid hydrolysis activity in feces. Moreover, the urinary excretion of p-cresol, a product of the intestinal Bacteroids fragilis, decreased. The activity of the mentioned enzymes in the feces remains low throughout the probiotic prescription period (four weeks), and this value returns to the original levels when probiotic consumption is stopped. A decrease was also observed in the activity of intestinal azoreductase and β-glucuronidase enzymes after the administration of Lactobacillus acidophilus.

Changes in pH

By producing lactic acid and short-chain fatty acids such as acetate and propionate, probiotics decrease the pH in the gut, making the gut environment unsuitable for colonization by pathogenic bacteria. In another study, it was reported that consuming Lactobacillus plantarum V299 in a fruit drink containing fermented barley increases the concentration of carboxylic acids, specifically acetic acid and propionic acid in the feces of healthy subjects. These short-chain fatty acids are a source of energy for the colonic mucosa cells. For example, an increased concentration of short-chain fatty acids in the intestinal lumen can be beneficial for the condition of the mucous membranes. The reason for the concentration increase in the above study is probably the changed composition of the microbial intestinal flora. In this way, L. plantarum may help increase the number of bacteria that produce acetic acid and propionic acid or inhibit bacteria that break down these compounds.

Probiotic Modulation of Intestinal Barrier Function

Gut epithelial tissue is the lining tissue that covers the small and large intestines. This columnar weave is simple and has no cilia. The epithelium is constantly exposed to the microbes and food that live in the gut and invading pathogens. Tight connections between the membrane proteins of the intestinal epithelial cells (IECs) ensure that they seal the intercellular space and prevent the entry of pathogens. The most important role of this tissue is digestion. This tissue also plays a role in the body's immunity. The gut has many immune cells that help repair the tissue and provide protection against microbial gut infections. In addition to the epithelial cells, the epithelium contains a type of immune cell called intestinal intraepithelial lymphocytes. These lymphocytes, which belong to the T-cell subclass, represent the first line of specific immune defense against gut microbes. Therefore, the fusion and destruction of these cells cause damage to the physical and immunological strength of the gut and, as a result, increase the risk of contracting infections and inflammatory bowel diseases (IBDs). Unfortunately, opportunistic pathogens can potentially break down junctional complexes between neighboring cells that decrease transepithelial electrical resistance, leading to a leakage in the intestinal tract. In paracellular permeability, in turn, causes intestinal disorders such as IBD.

The Increase in Tight Junctions

Junctions in IECs form a physical barrier against the penetration of substances from the intestinal lumen into the enterocytes and the bloodstream. Tight junctions (TJ) increase the integrity and decrease the permeability of the intestinal epithelial barrier. By affecting signaling pathways such as mitogen-activated protein kinase (MAPK) signaling, probiotics increase the expression of TJ proteins, including occluding, ZO-1, and claudin-1 and increase the integrity of the gut epithelial barrier. For example, by acting on tyrosine kinase receptors on the surface of epithelial cells, L. acidophilus activates the MAPK kinase cascade in the cytoplasm, and finally, MAPK enters the cell nucleus and increases the integrity of the intestinal epithelial barrier by increasing the expression of TJ proteins.

Increasing the Gut Epithelial Cell Survival

Probiotics prevent apoptosis of gut epithelial cells by affecting phosphoinositide 3-kinase (PI3K) signaling and activation of protein kinase B or AKT and increase the survival of these cells. For example, Lactobacillus
rhannosus activates PI3K by affecting tyrosine kinase receptors on the surface of epithelial cells, and this molecule mediates phosphorylation of the proapoptotic protein BAD through the activation of AKt. On the other hand, PI3K inhibits cell apoptosis in the mitochondrial pathway by activating the anti-apoptotic protein Bc12. Studies have also indicated that this bacterium inhibits apoptosis by activating the MAPK kinase cascade through the activation of the mitochondrial pathway.31,32

Modulation of Gastrointestinal Immune Responses by Probiotics
There is growing evidence that probiotic bacteria can modulate the adaptive and innate immunity of the components of the host immune system listed below (Figure 1).1,13,33

Regulation of Mucins by Probiotics
Mucin is one of the main glycoproteins that make up mucus. This molecule has an extremely diverse sugar part and a protein part with repeating units (proline, threonine, and serine). Mucin is produced in the body in two forms: secretory and membrane-bound. The interaction of sugar parts with water is responsible for creating lubricant properties in the mucous membrane and regulating the environmental pH. The branch-like structure of the sugar part prevents pathogens from penetrating and reaching the underlying cells.34 Mucin is secreted by goblet cells, leukocytes, and digestive tube cells, plays a role in the regulation of ion transport, and acts as a receptor in the membrane width state. This molecule is expressed in humans by 22 genes named “MUC” ranging from “MUC1” to “MUC22”. The MUC1 gene encodes the mucin found in the mucosa of the gastrointestinal tract (i.e., mucin 1). Among the different human mucin genes, MUC2 and MUC3 are dominant in the colon. The membrane-spanning mucin in the outer part prevents the penetration of bacteria to the lower layers, and in the inner part, it plays a role in the messaging pathway by being phosphorylated.34,35 These molecules regulate the differentiation and apoptosis of intestinal cells, inflammation, and cell adhesion. Certain probiotic strains have been reported to upregulate mucin expression, thus influencing mucosal properties and indirectly regulating the gut immune system.35,36 Table 1 presents the regulation of mucins by probiotics.

So far, studies on the interaction between probiotics and mucins have mainly demonstrated the ability of probiotics to adhere to mucins since adhesion ability is presented as one of the criteria for selecting bacteria as probiotics.

Trefoil Factor Stimulation
Trefoil factors (TFFs) serve as a signal for epithelial repair, migration of IECs, and their resistance to apoptosis. TFFs include TFF1, TFF2, and TFF3. TFF3 is assumed to be one of the gastrointestinal inflammation factors because the overproduction of TFF3 has been found in most cases of gastrointestinal inflammation such as necrotizing enterocolitis and IBDs.41,42 A recent study showed that dietary LGG supplementation does not have a significant regulatory effect on TFF gene expression in mice with dextran sulfate sodium-induced colitis.43 The intestinal cell layer was enlarged, and liver function improved. Interestingly, both overproduction and underproduction of TFF can compromise gut integrity. Therefore, although differential regulation of TFF levels occurs in modulation by probiotics, probiotics appear to play a role in regulating abnormal (higher or lower) to normal TFF levels.41,42

Induction of Secretion of Antimicrobial Peptides
Antimicrobial peptides (AMPs) are among the diverse groups of antimicrobial compounds that have received much attention due to the increasing resistance of pathogenic bacteria to common antibiotics and include bacteriocins and peptide antibiotics.44,45 Bacteriocins are compounds synthesized by ribosomes that are produced in bacteria and are active against bacteria closely related to the producing bacteria.46 When exposed to pathogens or microbial molecules, IECs secrete AMPs along with several immune cells.37 A deficiency in AMPs such as defensin has been identified as a cause of IBD such as Crohn’s disease and as a cause of inflammation.48,49 The studies indicated that increased hBD-2 may be associated with toll-like receptor (TLR) 2 and TLR5 expression in gut cells, suggesting that TLR may be involved in monitoring probiotic-induced effects.50-52 Lactobacilli and VSL #3 culture induce hBD-2 gene expression through imperfections of inflammatory ways, including NF-xB, MAPK, and activator protein 1.51,52 In 2015, Rezakhani et al examined bacteriocin effects based on AMPs in both

Figure 1. Modulation of Gastrointestinal Immune Responses by Probiotics
laboratory conditions and molecular calculations. The findings confirmed the antibacterial effects of *L. lactis* strain and the peptide and bacteriocin nature of the inhibitory metabolite produced by it.

**The Role of Probiotics in Strengthening the Body’s Immune System**

Probiotics, including lactobacilli, inhibit the growth of many types of pathological cells. This group of bacteria enhances the host’s immune response, has a preventive effect against cancer, and inhibits the growth of cancerous tumors. Probiotics affect the immune system at various levels, including increasing cytokine, immunoglobulin levels, mononuclease cell proliferation, and natural killer cell activity, activating macrophages, modulating autoimmunity, and stimulating immunity against pathogenic bacteria and named protozoa. The fact that the ingestion of probiotics has preventive and therapeutic effects on intestinal viruses is mainly due to the stimulation of the intestinal lymphatic tissue, which leads to an increase in the humoral immune response. The observation of increased immunogenicity of the rotavirus vaccine when co-prescribed with *Lactobacillus* and the clinical observations of the reduction in rotavirus shedding in populations receiving probiotics support the enhancement of this immune response from both treatment and prevention perspectives.

**Stimulating the Production of Secretory Immunoglobulin and Cytokines**

Immunoglobulin A (IgA) has been proposed as a non-inflammatory immunoglobulin antibody that acts as a pathogen receptor in the gut. When secreted into the luminal environment, IgA is generated into secretory IgA (SIgA), which adheres to the mucosa of epithelial cells. After pathogen infestation, it can prevent pathogens from contacting the epithelium by forming a hydrophilic membrane and epithelial glyocalyx secretion against the shell that is farthest from pathogens and consequently suitable bacterial communities in a specific area of the intestinal lumen. SIgA can also influence intracellular pathogens by inactivating bacterial lipoproteins and transporting them out of the epithelial lumen during epithelial transcytosis. Moreover, bacteria that have breached the epithelium can be eliminated by localized IgA in the lamina propria in two ways: either by redistribution into the lumen via plgR or by immune clearance as a result of binding of IgA to the Fc_RI receptor (CD89) on immune cells. Probiotics can stimulate the creation of IgA and consequently increase the barrier function. Probiotics also stimulate a subcategory of cells in the immune system to produce cytokines, which play a key role in triggering and regulating immune responses. Stimulating human peripheral blood mononuclear cells with *L. rhamnosus* strain GG in the laboratory increased the production of interleukin-4 (IL4), IL-6, IL-10, tumor necrosis factor (TNF), and interleukin -gamma. Other studies have revealed that the production of Th2 cell cytokines such as IL-2 and IL-10 rises with the consumption of lactobacilli. The production of mucosal immunoglobulins relies on some cytokines such as transforming growth factor (TGF). Some species and strains of *Lactobacillus* can stimulate the production of TGF to varying degrees. A group of researchers examined probiotic feeding *Lactobacillus* on the intestinal immune response of animals to surmount *Eimeria acervulina* infection and reported the positive influence of probiotics in stimulating the primary immune response against *Eimeria acervulina* by increasing the secretion of IL-2 and interferon-gamma. Using quantitative polymerase chain reaction, Ganguli et al in their study measured the expression of the IL-8, IL-1, and TNF genes in the intestine of the human fetus, which was close to the live bacterium *L. rhamnosus* GG. They noticed that *L. rhamnosus* GG markedly reduces the production of inflammatory cytokines in response to pathogenic bacteria and pro-inflammatory signals in human fetal IECs.

**Stimulation of Toll-Like Receptors**

To protect the intestinal lumen from pathogens, the

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**Table 1. List of Probiotic Strains That Regulate the Mucus Layer**

<table>
<thead>
<tr>
<th>Bacterial Strain</th>
<th>Mechanism</th>
<th>Increased (↑) or Decreased (↓) Gene/Protein Expression</th>
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<tbody>
<tr>
<td><em>Lactobacillus plantarum</em> 299v</td>
<td>In vitro (HT-29 cell lines), Lp299v reduces the adherence of enteropathogenic <em>E. coli</em> to mucosal epithelial cells by increasing the expression of mucins 2 and 3 at the mRNA level</td>
<td>↑MUC2-3 For both: gene expression↑</td>
</tr>
<tr>
<td><em>Escherichia coli</em> Nissle 1917</td>
<td>In vitro incubation of HT-29 cells with EcN increases the expression of several mucin genes. Milder effects were observed with inactivated bacteria, while stronger effects were shown with polarized cells</td>
<td>↑MUC 2-3 ↑MUC5A and SAC For: gene and protein expression↑</td>
</tr>
<tr>
<td><em>Lactobacillus casei</em> GG</td>
<td>Addition of LGG to Caco-2 cells in vitro reduces <em>E. coli</em> translocation through increased expression of MUC2 gene expression</td>
<td>↑MUC2 gene and protein↑</td>
</tr>
<tr>
<td>VSL#3 (probiotic mixture)</td>
<td>In vivo and in vitro experiments show that exposure to VSL#3 increases gene expression levels of MUC2 and only slightly those of MUC3. It also increased mucin gene expression in HT29 cell lines</td>
<td>↑MUC2-3 ↑MUC5A Gene expression↑</td>
</tr>
</tbody>
</table>

Note: EcN: *Escherichia coli* Nissle; GG: Gorbach-Goldin; LGG: Lactobacillus GG.
intestinal epithelium evolved and provided vigilance against potential pathogen invasion. IECs can express pattern recognition receptors such as TLRs and intracellular nucleotide-binding oligomerization domains to recognize different kinds of pathogenic bacteria based on their molecular patterns of pathogen-associated expression.\textsuperscript{18,65,66}

It has been reported that some harmless commensal bacteria can also stimulate pro-inflammatory signaling pathways,\textsuperscript{67,68} which may suggest a practical way that probiotics can maintain a “state of consciousness” in the host to monitor pathogen penetration.\textsuperscript{10,69}

\textit{Lactobacillus johnsonii} strain N6.2 was found to stimulate the expression of TLR-7 and TLR-9 in Caco-2 cells. Conversely, in the culture supernatant of \textit{Clostridium butyricum} TO-A containing human HT-29 colon cells, TLR-4 was down-regulated at both the mRNA and protein levels, suggesting that TLR-4 down-regulation may be highly correlated with butyrate content in the supernatant, suggesting that some probiotic species are more effective in inhibiting excessive or persistent inflammatory responses.\textsuperscript{70} A review demonstrated that balancing the TLR with probiotics promotes the activation and monitoring of innate defense such as the production of AMPs and cytokines by the host. As mentioned above, the stimulation of defenses in Caco-2 cells by \textit{Escherichia coli} Nissle 1917 (EcN) and \textit{L. plantarum} could be related to the expression of TLR2 and TLR5.\textsuperscript{71}

Finamore et al treated caco-2 cells with enterotoxigenic \textit{E. coli}, \textit{L. rhamnosus}, and \textit{L. rhamnosus} supernatants separately and in close proximity to each other and examined the effect on the TLR4 signaling pathway. Western blot analysis showed that \textit{L. rhamnosus} suppresses the activity of different TLR-4 signaling pathways in caco-2 cells.\textsuperscript{72} A study by Brito-Bermudez et al investigated the immunological effects of \textit{Bifidobacterium breve}-CNCM 4035 on human intestinal dendritic cells in response to \textit{Salmonella typhimurium}. They infected these cells with \textit{Salmonella}, then they were mixed with live probiotic bacteria during an experiment. Afterward, they analyzed the secretion of cytokines by the enzyme-linked immunosorbent assay and the expression of TLR genes by real-time polymerase chain reaction in another experiment with supernatant and after incubation. The results indicated that the supernatant in the dendritic cells of human intestinal cells challenged with S. \textit{typhimurium} causes a decrease in the amount of IL-6,12, but the live \textit{Bifidobacterium} was a stronger inducer for IL-10, IL-8, IL-6 . On the other hand, chronic fatigue syndrome caused TGF\textit{β} levels to return to the initial state in the presence of \textit{Salmonella}. It was also found that live \textit{Bifidobacterium} increases TLR2,9,4 in the presence of \textit{Salmonella}, but its supernatant increases TLR1,9,5,2.

Indeed, the results indicated that the increase of TLR9 is higher by the supernatant.\textsuperscript{73} Castillo et al evaluated the role of \textit{L. casei} in preventing \textit{S. typhimurium} infection in c/ BALB mice. Examination and measurement of cytokines on different days after treatment with probiotics and via immunohistochemical methods showed that injection of probiotics into healthy mice increases the expression of TLR2,9,4 genes and increases the production and secretion of interferon, TNF, and IL-10 in plaques. However, after infection with \textit{S. typhimurium} and after re-injection of probiotics, the host was assisted by modulating the inflammatory response, TNF levels decreased, and the production of IL-10, IL-6, and interferon increased in the lamina propria of the small intestine.\textsuperscript{74} In Soltan Dallal and colleagues’ study, the results showed that after treating healthy and uninfected HT29 cells with each of the two probiotic bacteria, the expression of the TLR-2-4 genes increased significantly. On the other hand, when the healthy HT29 cell was exposed to \textit{S. enteritidis} and incubated for six hours, the lipopolysaccharide of the cell wall of this bacterium was bound to these membrane receptors on the surface of the intestine (HT29) and the HT29 cell increased its TLR4 and TLR2 gene expression compared to the normal state, allowing the body to boost its immunity, produce immune cytokines, and fight the infectious agent.\textsuperscript{80}

**Increasing the Production of Heat Shock Protein**

The expression of heat shock proteins (HSPs) is stimulated by several kinds of stressors such as fever,\textsuperscript{75} infection, inflammation, heavy metals, and conditions causing injury and necrosis.\textsuperscript{76,77} Probiotics were reported to induce HSPs in the epithelium,\textsuperscript{86,79} and they are gutted. For example, soluble factors from the conditioned medium of \textit{L. rhamnosus} GG (CM) regulate the expression of both HSP72 and HSP25, which is hypothesized to be modulated through the MAPK pathway.\textsuperscript{80} In addition, \textit{Bifidobacterium breve}, \textit{Bacillus subtilis}, LGG, \textit{E. coli} Nissle, and \textit{L. plantarum} bacteria stimulate the expression of HSP27 in Caco-2BBc cells of the large intestine.\textsuperscript{82,81}

**Modulation of P-glycoprotein**

In the intestinal epithelial defense system, P-glycoprotein (P-gp) appears to be an important mediator for the influx of drugs/xenobiotics and bacterial toxins from the intestinal mucosa to the lamina propria.\textsuperscript{83,84} A new investigation suggested a novel process by which probiotics may mitigate IBD through P-gp regulation.\textsuperscript{85} In the Caco-2 cell model, culture supernatant of \textit{L. acidophilus} and \textit{rhamnosus} strains increased P-gp activity, as measured by verapamil-sensitive pydgidoxin [3H] and P-gp activity that was listed to be increased. This is mediated by increased multidrug resistance mutation 1/P-gp mRNA and protein expression.\textsuperscript{80,87}

**Conclusion**

Probiotics are living microorganisms that can have
beneficial effects on the body’s health when consumed in sufficient quantities in the form of medicines or food. Today, probiotics are considered an important factor for preventing many infectious diseases and cancers, treating digestive disorders, and reducing Helicobacter pylori. Treatment with probiotics is based on the hypothesis of healthy microbial flora. The use of specific species of healthy human intestinal microbial flora for modifying endogenous microbial flora constitutes the logic of probiotic treatment. Various studies have demonstrated that probiotic species are different from each other, and their effectiveness is also influenced by the matrix used to deliver them to the intestine. An ideal probiotic can remain permanently alive in the gut during passage through the digestive system and has beneficial effects on the health of the host. These microorganisms can boost the body’s immune system, break down food (due to the ability to produce many enzymes), lower the pH of the environment (due to the production of acidic compounds), and secret bacteriocins. On the other hand, the presence of probiotics in the gut as dietary supplements or components of the microbiota can directly prevent the activity of pathogenic bacteria through the competitive elimination of pathogens (e.g., competition for binding site, pathogens place, nutrients, and the like). Research indicates that among all the modulation pathways of probiotics, the presence of defense responses by gut epithelial cells, modulation of gut defense barrier function, innate and adaptive mucosal immune responses, and signaling pathways can play crucial roles in defense against gut pathogens. M cells in epithelial cell layers pick up probiotics or their metabolites and deliver them to dendritic cells located in the epithelial substratum. Therefore, probiotics stimulate the secretion of various types of cytokines from DC and macrophage cells located in the organ. They are digested, and the components of probiotics, especially DNA and peptidoglycan can trigger responses in the innate immune system. The metabolites caused by probiotics are recognized by sensitive receptors in the host’s immune cell such as TLRs and trigger a cascade in the cell to regulate immune function. Probiotics either adhere directly to the membrane of the epithelial cells and trigger a cascade in the cells, or they release soluble substances in which the immune cells are directly involved. Other mechanisms by which probiotics modulate the innate defense responses of the gut epithelium include the stimulation of trefoil factor 3, induction of AMP secretion, stimulation of secretory immunoglobulin production, stimulation of TLRs, enhancement of heat shock protein production, modulation of P-gp, and mucin adaptation. Although there is acceptable evidence for the probiotics’ role in improving the function of the intestinal immune response, human clinical trials are still limited, and more detailed planning is needed to achieve more effective treatments. Therefore, given the unique importance of probiotics, the mechanism of action of different probiotics should be explained more clearly so that the best type of probiotic can be selected for use against a specific pathogen.

Authors’ Contribution
All authors contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript. All authors reviewed the manuscript.

Competing Interests
The authors declare that they have no competing interest.

References


