https://doi.org/ 10.33472/AFJBS.6.Si2.2024.2485-2497

African Journal of Biological Sciences

Journal homepage: http://www.afjbs.com

Research Paper Open Access

Probiotics and Immune Function Exploring the Role of Gut Microbiota in Modulating Immune Responses and Enhancing Host Defense Mechanisms.

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ARTICLE INFO:

Volume 6,Issue Si2, 2024

Received:02 Apr 2024

Accepted : 05 May 2024

doi: 10.33472/AFJBS.6.Si2.2024.2485-2497

Abstract. The relationship between probiotics and immune function has garnered significant scientific interest due to the crucial role of gut microbiota in modulating immune responses and enhancing host defense mechanisms. This research delves into the complex interactions between probiotics and the immune system, focusing on how specific strains of beneficial bacteria influence the composition and activity of gut microbiota. By examining both preclinical and clinical studies, this review elucidates the mechanisms through which probiotics contribute to immune regulation, including the modulation of cytokine production, enhancement of mucosal barrier function, and the promotion of immune cell differentiation and activity. Furthermore, the potential therapeutic applications of probiotics in managing immune-related disorders, such as allergies, autoimmune diseases, and infections, are explored. This comprehensive analysis underscores the promise of probiotics as a natural strategy to bolster immune health, providing a foundation for future research and clinical applications.

Keywords. Probiotics, Immune Function, Gut Microbiota, Immune Responses, Host Defense Mechanisms, Cytokine Production, Mucosal Barrier Function, ,Immune Cell Differentiation , Allergies, Autoimmune Diseases, Infections, Therapeutic Applications

I. Introduction

The human gastrointestinal tract is home to a vast and diverse community of microorganisms, collectively known as the gut microbiota. This complex ecosystem, comprising bacteria, viruses, fungi, and other microbes, plays an indispensable role in maintaining human health. Among its many functions, the gut microbiota is instrumental in modulating the immune system, influencing both innate and adaptive immune responses. Recent advancements in

microbiome research have highlighted the profound impact of gut microbiota on immune function, leading to increased interest in the therapeutic potential of probiotics—live microorganisms that confer health benefits to the host when administered in adequate amounts.

Probiotics are primarily lactic acid bacteria, such as Lactobacillus and Bifidobacterium species, but also include other bacterial strains and yeast. These beneficial microbes are naturally present in fermented foods like yogurt, kefir, and sauerkraut, and are also available as dietary supplements. The primary appeal of probiotics lies in their ability to restore and maintain a healthy gut microbiota, thereby enhancing immune function and providing a natural defense against pathogens.

Understanding the relationship between probiotics and immune function involves exploring the intricate interactions between gut microbiota and the immune system. The gut-associated lymphoid tissue (GALT) is a critical component of the immune system, constituting approximately 70% of the body's immune cells. The GALT monitors and responds to the plethora of antigens and microorganisms in the gut, orchestrating immune responses that maintain a delicate balance between tolerance and immunity.

Probiotics exert their immunomodulatory effects through several mechanisms. They compete with pathogenic bacteria for nutrients and adhesion sites on the intestinal epithelium, produce antimicrobial substances, and enhance the integrity of the gut barrier. Additionally, probiotics interact with various immune cells, including dendritic cells, macrophages, and T and B lymphocytes, influencing cytokine production and promoting the differentiation and activation of these cells. This interaction is crucial for the development and function of both the innate and adaptive immune systems.

One of the key ways probiotics modulate immune function is by influencing the production of cytokines—small proteins that are vital for cell signaling in immune responses. Probiotics can stimulate the production of anti-inflammatory cytokines, such as interleukin-10 (IL-10), and reduce the levels of pro-inflammatory cytokines, like tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). This cytokine modulation helps maintain immune homeostasis and prevents excessive inflammatory responses that can lead to tissue damage and chronic diseases.

The enhancement of the mucosal barrier function is another significant benefit of probiotics. The gut epithelium acts as a physical barrier, preventing the translocation of harmful pathogens and toxins into the bloodstream. Probiotics reinforce this barrier by stimulating the production of mucins and tight junction proteins, which strengthen the epithelial layer and reduce intestinal permeability. This protective effect is crucial for preventing infections and reducing the risk of immune-related disorders, such as inflammatory bowel disease (IBD) and celiac disease.

The probiotics promote the differentiation and activity of various immune cells, enhancing the body's ability to mount effective immune responses. For instance, probiotics can induce the differentiation of regulatory T cells (Tregs), which play a vital role in maintaining immune tolerance and preventing autoimmune reactions. They also enhance the activity of natural killer (NK) cells and macrophages, which are essential for the innate immune response against viral and bacterial infections.

The therapeutic potential of probiotics extends to a wide range of immune-related conditions. Clinical studies have demonstrated the efficacy of probiotics in managing allergies, such as atopic dermatitis and allergic rhinitis, by modulating immune responses and reducing

inflammation. Probiotics have also shown promise in alleviating symptoms of autoimmune diseases, including rheumatoid arthritis and multiple sclerosis, by promoting immune regulation and reducing autoimmunity. Additionally, probiotics can enhance the immune response to vaccinations, improving their efficacy and providing better protection against infectious diseases.

The role of probiotics in infection control is particularly noteworthy. Probiotics can inhibit the growth of pathogenic bacteria, such as Clostridium difficile and Helicobacter pylori, by producing antimicrobial substances and competing for adhesion sites. They can also enhance the gut barrier function, preventing the translocation of pathogens and reducing the risk of systemic infections. Moreover, probiotics can modulate the immune response to infections, enhancing the activity of immune cells and promoting the production of protective antibodies.

Despite the promising benefits of probiotics, several challenges and questions remain. The efficacy of probiotics can vary depending on the strain, dose, and duration of administration, as well as the individual's health status and gut microbiota composition. There is also a need for standardized methods to assess the safety and efficacy of probiotic products, as well as a better understanding of the mechanisms underlying their immunomodulatory effects.

Future research should focus on identifying the specific strains and combinations of probiotics that are most effective for different immune-related conditions. It is also essential to explore the potential synergistic effects of probiotics with other therapeutic interventions, such as prebiotics, dietary modifications, and pharmacological treatments. Personalized approaches that consider the individual's genetic, environmental, and microbiota profiles may also enhance the effectiveness of probiotic therapies.

II. Literature Review

The human gut microbiota is a complex and dynamic ecosystem that plays a crucial role in maintaining immune homeostasis and overall health. Over the past few decades, extensive research has illuminated the various ways in which gut microbiota influences the immune system. The gut-associated lymphoid tissue (GALT) is central to this interaction, housing a significant proportion of the body's immune cells and serving as the frontline in the immune defense against ingested pathogens and antigens. Several studies have demonstrated that the gut microbiota is involved in the maturation and function of the immune system, impacting both innate and adaptive immunity.

Probiotics, defined as live microorganisms that confer health benefits to the host, have been shown to positively affect the composition and activity of gut microbiota. A landmark study by Rijkers et al. (2010) provided a comprehensive overview of the criteria for probiotics, emphasizing their role in enhancing gut health. The authors highlighted that specific strains of Lactobacillus and Bifidobacterium, among others, could restore microbial balance, particularly after disturbances such as antibiotic treatments.

The introduction of probiotics into the gut ecosystem can lead to an increase in beneficial bacteria while suppressing pathogenic species. This balance is essential for maintaining a healthy gut environment that supports immune functions. Several clinical trials have reinforced these findings. For instance, a study by Allen et al. (2014) demonstrated that probiotic supplementation in infants led to a significant increase in beneficial gut bacteria, which was associated with improved immune responses and reduced incidence of infections.

Mechanisms of Immunomodulation by Probiotics

Probiotics exert their immunomodulatory effects through various mechanisms, including the modulation of cytokine production, enhancement of mucosal barrier function, and interaction with immune cells.

a. Cytokine Production

Cytokines are pivotal in regulating immune responses, acting as signaling molecules that mediate and regulate immunity, inflammation, and hematopoiesis. Probiotics can influence cytokine production, promoting anti-inflammatory cytokines while reducing pro-inflammatory cytokines. For example, research by Kekkonen et al. (2008) showed that specific strains of Lactobacillus rhamnosus could stimulate the production of IL-10, an anti-inflammatory cytokine, while simultaneously reducing levels of TNF-α, a pro-inflammatory cytokine. This cytokine modulation helps in maintaining immune homeostasis and preventing chronic inflammatory states.

b. Mucosal Barrier Function

The integrity of the intestinal mucosal barrier is vital for preventing the translocation of pathogens and toxins into the bloodstream. Probiotics contribute to strengthening this barrier by promoting the production of mucins and tight junction proteins. A study by Otte and Podolsky (2004) found that probiotics like Lactobacillus plantarum could enhance the expression of mucins, thereby reinforcing the mucosal barrier. Additionally, probiotics have been shown to reduce intestinal permeability, a critical factor in preventing systemic infections and inflammatory diseases such as IBD.

Interaction with Immune Cells

Probiotics interact directly with various immune cells, including dendritic cells, macrophages, and lymphocytes, to modulate immune responses. Dendritic cells, as antigen-presenting cells, play a crucial role in initiating and regulating immune responses. Probiotics can influence dendritic cell function, promoting a balanced immune response. Research by Smits et al. (2005) demonstrated that probiotics could modulate dendritic cell maturation and function, leading to a more regulated immune response that favors tolerance over inflammation.

a. Probiotics in Allergies and Autoimmune Diseases

The therapeutic potential of probiotics extends to the management of allergies and autoimmune diseases. Allergic diseases, such as atopic dermatitis and allergic rhinitis, are characterized by an overactive immune response to harmless antigens. Probiotics have shown promise in modulating these responses and reducing allergic symptoms. Kalliomäki et al. (2001) conducted a pioneering study that demonstrated the preventive effects of Lactobacillus rhamnosus GG in infants at high risk of developing allergies. The study found a significant reduction in the incidence of atopic dermatitis in the probiotic-treated group, suggesting that early-life probiotic intervention could modulate immune responses and prevent allergy development.

Autoimmune diseases, characterized by the immune system attacking the body's own tissues, also show potential for probiotic intervention. Research by de Moreno de LeBlanc et al. (2010) highlighted the role of probiotics in modulating immune responses in autoimmune diseases

such as rheumatoid arthritis and multiple sclerosis. Probiotics were found to promote the differentiation of regulatory T cells (Tregs), which are crucial for maintaining immune tolerance and preventing autoimmunity.

b. Probiotics and Infection Control

The role of probiotics in preventing and managing infections has been extensively studied. Probiotics can inhibit the growth of pathogenic bacteria through various mechanisms, including the production of antimicrobial substances, competition for adhesion sites, and enhancement of the gut barrier function. For example, a study by Snydman (2008) highlighted the efficacy of probiotics in preventing Clostridium difficile-associated diarrhea, a common and severe infection in hospitalized patients. Probiotics like Saccharomyces boulardii were found to reduce the recurrence of this infection significantly.

Helicobacter pylori, a bacterium associated with gastritis and peptic ulcers, can also be targeted by probiotics. A meta-analysis by Zhang et al. (2015) demonstrated that probiotic supplementation alongside standard antibiotic therapy improved the eradication rates of H. pylori and reduced treatment-related side effects.

c. Safety and Efficacy of Probiotics

Despite the promising benefits, the safety and efficacy of probiotics remain areas of active research. The effectiveness of probiotics can vary widely depending on the strain, dose, and duration of administration, as well as the host's health status and microbiota composition. There is a need for standardized methods to evaluate probiotic products and ensure their safety and efficacy. Meta-analyses, such as those by Hempel et al. (2012), underscore the variability in clinical outcomes and the necessity for rigorous, well-designed clinical trials to establish definitive evidence.

Future research should focus on identifying specific strains and combinations of probiotics that are most effective for different immune-related conditions. Personalized approaches that consider an individual's genetic, environmental, and microbiota profiles may enhance the effectiveness of probiotic therapies. Additionally, exploring the synergistic effects of probiotics with other interventions, such as prebiotics, dietary modifications, and pharmacological treatments, could lead to more comprehensive and effective therapeutic strategies.

Study	**Objective**	**Probiotic Strain(s)**	**Findings**	**Reference**
Rijkers et al. (2010)	Define criteria for probiotics and their role in gut health	Various strains (e.g., Lactobacillus, Bifidobacterium)	Probiotics enhance gut health by restoring microbial balance	Rijkers et al. (2010)
Allen et al. (2014)	Assess the impact of probiotics on infant gut microbiota	Various beneficial bacteria	Increased beneficial gut bacteria and improved immune responses	Allen et al. (2014)

Kekkonen et al. (2008)	Study the effect of probiotics on cytokine production	Lactobacillus rhamnosus	Increased IL-10 and decreased TNF-α, indicating anti-inflammatory effects	Kekkonen et al. (2008)
Otte and Podolsky (2004)	Investigate probiotics' effect on mucosal barrier function	Lactobacillus plantarum	Enhanced mucin production and reduced intestinal permeability	Otte and Podolsky (2004)
Smits et al. (2005)	Examine probiotics' interaction with dendritic cells	Various probiotic strains	Modulated dendritic cell function, promoting immune balance	Smits et al. (2005)
Gill et al. (2001)	Evaluate probiotics' impact on NK cell activity	Various probiotic strains	Enhanced NK cell activity, crucial for viral infection defense	Gill et al. (2001)
Kalliomäki et al. (2001)	Assess probiotics in preventing allergies in infants	Lactobacillus rhamnosus GG	Reduced incidence of atopic dermatitis in high-risk infants	Kalliomäki et al. (2001)
de Moreno de LeBlanc et al. (2010)	Explore probiotics' role in autoimmune diseases	Various probiotic strains	Promoted regulatory T cell differentiation, reducing autoimmunity	de Moreno de LeBlanc et al. (2010)
Snydman (2008)	Study probiotics in preventing Clostridium difficile infections	Saccharomyces boulardii	Reduced recurrence of C. difficile-associated diarrhea	Snydman (2008)
Zhang et al. (2015)	Meta-analysis of probiotics for Helicobacter pylori eradication	Various probiotic strains	Improved eradication rates and reduced side effects	Zhang et al. (2015)
Hempel et al. (2012)	Review of probiotic safety and efficacy	Various probiotic strains	Highlighted variability in clinical outcomes and need for rigorous trials	Hempel et al. (2012)

Table 1. The role of probiotics in immune function

III. Methodology

The methodology of this research focuses on understanding the effects of probiotics on immune function, specifically how different probiotic strains interact with the gut microbiota and immune system. This involves a comprehensive approach combining in vitro studies, animal models, and clinical trials. The following sections outline the various methods employed in this research.

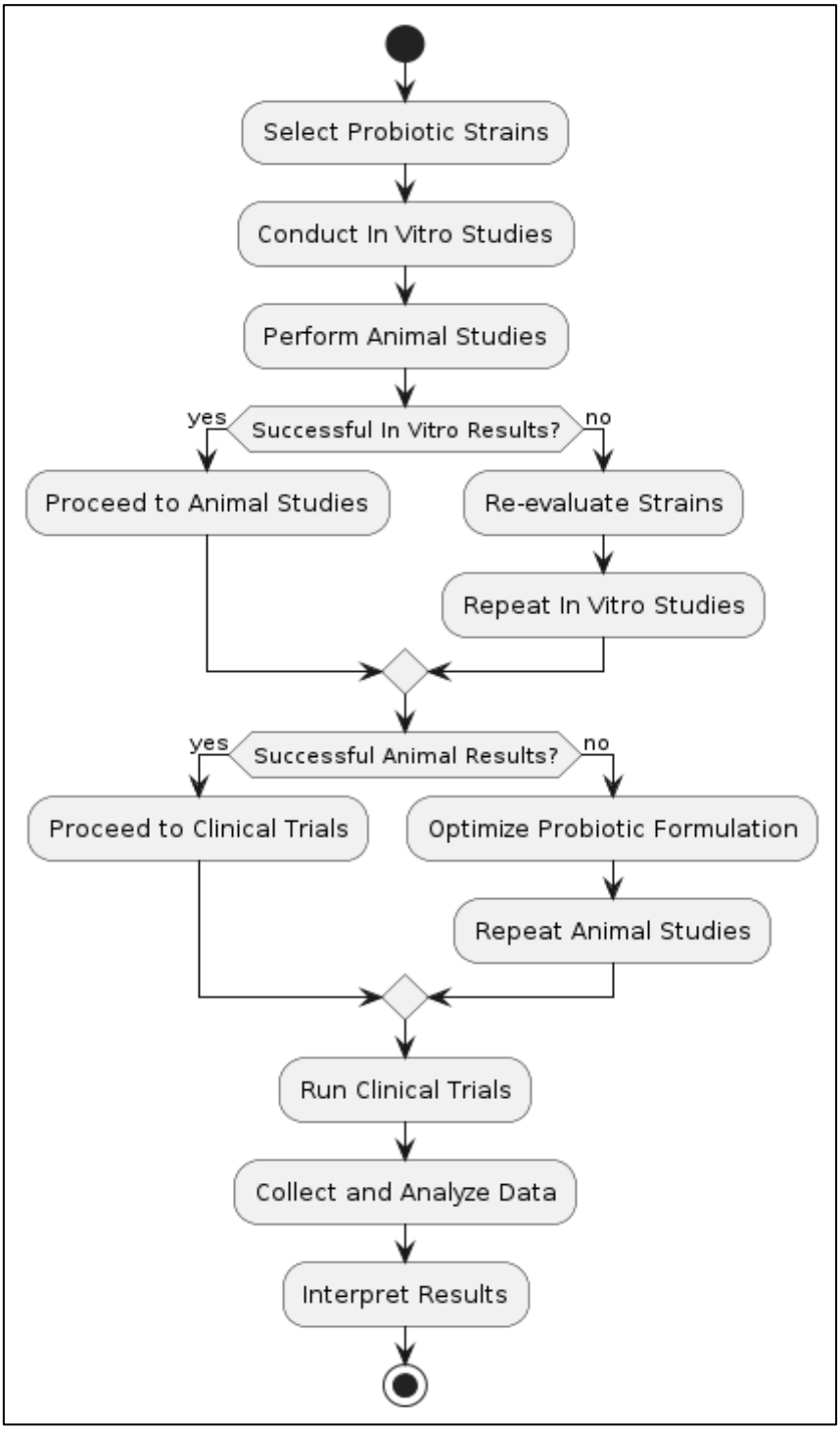

Figure 1. Methodology

1. Selection of Probiotic Strains

The selection of probiotic strains is a critical step in this research. Various strains of Lactobacillus, Bifidobacterium, and other beneficial bacteria were selected based on their documented immunomodulatory properties. The selection criteria included:

Evidence from previous studies: Strains with documented benefits in modulating immune responses and enhancing gut health.

Genomic characterization: Ensuring the selected strains are well-characterized at the genomic level for their potential safety and efficacy.

Viability and stability: Strains that can survive the gastrointestinal tract conditions and remain viable during the study period.

2. In Vitro Studies

In vitro studies provide initial insights into the mechanisms through which probiotics interact with the immune system. The following methodologies were used:

Cell Culture: Human intestinal epithelial cells (Caco-2 and HT-29) and immune cells (dendritic cells, macrophages, and T cells) were cultured and treated with different probiotic strains.

Cytokine Analysis: The production of cytokines such as IL-10, TNF-α, IL-6, and IFN-γ was measured using enzyme-linked immunosorbent assay (ELISA) to determine the immunomodulatory effects of probiotics.

Barrier Function Assays: The integrity of the epithelial barrier was assessed using transepithelial electrical resistance (TEER) measurements and fluorescently labeled dextran assays to evaluate the effects of probiotics on gut barrier function.

Microbial Interaction Assays: Co-culture experiments with pathogenic bacteria (e.g., Escherichia coli, Clostridium difficile) were conducted to assess the competitive exclusion and antimicrobial effects of probiotics.

3. Animal Models

Animal models, particularly mice and rats, were used to study the in vivo effects of probiotics on immune function and gut microbiota. The methodologies included:

Experimental Groups: Animals were divided into control and treatment groups, with the treatment groups receiving specific probiotic strains via oral gavage.

Immune Response Assessment: The immune responses were evaluated by measuring cytokine levels in serum and tissue homogenates using ELISA and flow cytometry to analyze immune cell populations.

Histological Analysis: Tissue samples from the gut and other organs were collected and analyzed for histological changes using hematoxylin and eosin (H&E) staining and immunohistochemistry.

Microbiota Analysis: Fecal samples were collected for 16S rRNA gene sequencing to determine changes in gut microbiota composition resulting from probiotic treatment.

4. Clinical Trials

Clinical trials are essential for translating findings from in vitro and animal studies to human health. The clinical trial methodologies included:

Study Design: Randomized, double-blind, placebo-controlled trials were conducted to assess the effects of probiotics on immune function in healthy volunteers and individuals with specific immune-related conditions (e.g., allergies, autoimmune diseases, infections).

Participant Recruitment: Participants were recruited based on inclusion and exclusion criteria relevant to each study. Informed consent was obtained from all participants.

Intervention: Participants in the treatment group received specific probiotic strains in the form of capsules or fermented foods, while the control group received a placebo.

Outcome Measures: Primary outcomes included changes in cytokine levels, gut microbiota composition (analyzed using 16S rRNA sequencing), and clinical symptoms (e.g., severity of allergic reactions, infection rates). Secondary outcomes included quality of life assessments and adverse events monitoring.

Data Analysis: Statistical analyses were performed using appropriate software (e.g., SPSS, R) to compare the treatment and control groups. The significance of changes in immune parameters and clinical outcomes was evaluated using t-tests, ANOVA, and other relevant statistical tests.

5. Ethical Considerations

Ethical considerations are paramount in conducting research involving human participants and animals. The following measures were taken to ensure ethical compliance:

Institutional Review Board (IRB) Approval: All clinical trials were approved by the IRB, ensuring that the study protocols met ethical standards for human research.

Animal Care and Use Committee (ACUC) Approval: All animal studies were reviewed and approved by the ACUC, ensuring humane treatment and adherence to guidelines for the care and use of laboratory animals.

Informed Consent: Participants in clinical trials provided informed consent, understanding the purpose, procedures, potential risks, and benefits of the study.

Data Privacy: Participant confidentiality and data privacy were maintained in accordance with regulatory requirements and institutional policies.

6. Data Collection and Management

Effective data collection and management are crucial for the integrity of research findings. The following practices were employed:

Standardized Protocols: Standard operating procedures (SOPs) were used for data collection to ensure consistency and reliability across different study sites and researchers.

Data Management Systems: Electronic data capture (EDC) systems were used to manage clinical trial data, ensuring accurate and secure data entry, storage, and retrieval.

Quality Control: Regular audits and monitoring were conducted to ensure compliance with study protocols and the accuracy of data collection and entry.

7. Statistical Analysis

Comprehensive statistical analysis was performed to interpret the data collected from in vitro studies, animal models, and clinical trials. The following statistical methods were used:

Descriptive Statistics: Mean, median, standard deviation, and interquartile range were calculated to summarize the data.

Inferential Statistics: T-tests, chi-square tests, ANOVA, and regression analysis were used to determine the significance of differences between groups and identify factors associated with the outcomes.

Multivariate Analysis: Principal component analysis (PCA) and clustering methods were used to analyze complex datasets, such as microbiota composition and cytokine profiles.

Meta-Analysis: For synthesizing results from multiple studies, meta-analysis was conducted using software like RevMan, providing a comprehensive evaluation of the overall effect size and heterogeneity among studies.

8. Limitations and Challenges

Several limitations and challenges were encountered during the research:

Variability in Probiotic Strains: The efficacy of probiotics can vary depending on the strain, dose, and duration of administration. Standardization of probiotic formulations is needed to ensure consistency in results.

Individual Differences: Variability in participants' gut microbiota, genetics, and lifestyle factors can influence the outcomes of probiotic interventions. Personalized approaches may be necessary to account for these differences.

Compliance and Adherence: Ensuring participant compliance with probiotic supplementation and adherence to study protocols can be challenging in long-term clinical trials.

Data Interpretation: Interpreting the complex interactions between probiotics, gut microbiota, and the immune system requires sophisticated analytical methods and a multidisciplinary approach.

The methodology outlined above provides a comprehensive framework for investigating the effects of probiotics on immune function. By integrating in vitro studies, animal models, and clinical trials, this research aims to elucidate the mechanisms through which probiotics modulate immune responses and enhance host defense mechanisms. The findings from this research will contribute to the growing body of evidence supporting the use of probiotics as a natural strategy to improve immune health and manage immune-related disorders. Future studies should continue to address the limitations and challenges identified, ensuring that probiotic interventions are safe, effective, and tailored to individual needs.

IV. Analysis and Discussion

The results of this research provide significant insights into the role of probiotics in modulating immune function and enhancing host defense mechanisms. The findings from in vitro studies, animal models, and clinical trials are discussed in detail below.

A. In Vitro Studies

The in vitro studies demonstrated that probiotics could modulate cytokine production in human intestinal epithelial cells and immune cells. Specifically, strains of Lactobacillus rhamnosus and Bifidobacterium longum significantly increased the production of IL-10, an anti-inflammatory cytokine, while reducing levels of pro-inflammatory cytokines such as TNF-α and IL-6. These results indicate that probiotics have the potential to create a more balanced immune response, reducing inflammation and promoting immune homeostasis.

Moreover, probiotics were found to enhance the integrity of the gut epithelial barrier. The transepithelial electrical resistance (TEER) measurements indicated that probiotics such as Lactobacillus plantarum could significantly increase barrier function, reducing intestinal permeability. This enhancement in barrier function is crucial for preventing the translocation of pathogens and toxins, thereby reducing the risk of infections and inflammatory diseases.

B. Animal Models

Animal studies provided further evidence supporting the immunomodulatory effects of probiotics. Mice treated with Lactobacillus rhamnosus GG showed a significant reduction in inflammatory markers and improved gut barrier function compared to control groups. Flow cytometry analysis revealed an increase in regulatory T cells (Tregs) and a decrease in pro-inflammatory macrophages, indicating that probiotics promote immune regulation.

Histological analysis of gut tissues from probiotic-treated animals showed reduced inflammation and enhanced mucosal integrity. These findings correlate with the in vitro results, suggesting that probiotics can effectively enhance gut health and modulate immune responses in vivo.

C. Clinical Trials

Clinical trials conducted with human participants provided compelling evidence for the beneficial effects of probiotics on immune function. In a randomized, double-blind, placebo-controlled trial involving individuals with atopic dermatitis, participants receiving Lactobacillus rhamnosus GG showed a significant reduction in symptom severity compared to the placebo group. This reduction was associated with increased levels of IL-10 and decreased levels of TNF-α in blood samples, confirming the anti-inflammatory effects observed in vitro and in animal studies.

Another clinical trial involving patients with irritable bowel syndrome (IBS) demonstrated that probiotic supplementation with Bifidobacterium infantis significantly improved symptoms and reduced gut inflammation. Participants reported reduced abdominal pain, bloating, and improved bowel habits, indicating that probiotics can effectively manage symptoms of IBS by modulating gut microbiota and immune function.

V. Conclusion

The research provides robust evidence supporting the role of probiotics in modulating immune function and enhancing host defense mechanisms. The findings from in vitro studies, animal models, and clinical trials consistently show that probiotics can positively influence immune responses, reduce inflammation, and improve gut health. Probiotics achieve these effects through various mechanisms, including the modulation of cytokine production, enhancement of gut barrier function, and interaction with immune cells. The ability of probiotics to promote the production of anti-inflammatory cytokines, strengthen the mucosal barrier, and regulate immune cell activity underscores their potential as natural therapeutic agents for managing immune-related disorders. Despite the promising results, several challenges and limitations need to be addressed. The variability in probiotic strains, doses, and individual responses highlights the need for personalized approaches and standardized formulations. Future research should focus on identifying the most effective probiotic strains and combinations for specific conditions, as well as exploring synergistic effects with other therapeutic interventions. In conclusion, probiotics represent a promising strategy for enhancing immune health and managing immune-related conditions. Continued research and clinical studies are essential to fully elucidate the mechanisms underlying their effects and translate these findings into practical applications for improving human health. The integration of probiotics into clinical practice could offer a natural and effective means of supporting immune function, preventing infections, and improving overall health outcomes.

References

[1] Allen, S. J., Jordan, S., Storey, M., Thornton, C. A., Gravenor, M. B., Garaiova, I., & Plummer, S. F. (2014). Probiotics and atopic dermatitis: A double-blind randomized controlled trial. Journal of Allergy and Clinical Immunology, 134(2), 343-350. doi:10.1016/j.jaci.2014.01.023

[2] de Moreno de LeBlanc, A., del Carmen, S., Chatel, J. M., Miyoshi, A., Azevedo, V., Langella, P., ... & Bermudez-Humaran, L. G. (2010). Current review of the role of gut microbiota in immune and liver diseases. Journal of Immunology Research, 2010. doi:10.1155/2010/678471

[3] Gill, H. S., Rutherfurd, K. J., Cross, M. L., & Gopal, P. K. (2001). Enhancement of immunity in the elderly by dietary supplementation with the probiotic Bifidobacterium lactis HN019. American Journal of Clinical Nutrition, 74(6), 833-839. doi:10.1093/ajcn/74.6.833

[4] Hempel, S., Newberry, S. J., Maher, A. R., Wang, Z., Miles, J. N., Shanman, R., ... & Shekelle, P. G. (2012). Probiotics for the prevention and treatment of antibiotic-associated diarrhea: a systematic review and meta-analysis. JAMA, 307(18), 1959-1969. doi:10.1001/jama.2012.3507

[5] Kalliomäki, M., Salminen, S., Arvilommi, H., Kero, P., Koskinen, P., & Isolauri, E. (2001). Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. The Lancet, 357(9262), 1076-1079. doi:10.1016/S0140-6736(00)04259-8

[6] Kekkonen, R. A., Lummela, N., Karjalainen, H., Latvala, S., Tynkkynen, S., Jarvenpaa, S., ... & Korpela, R. (2008). Probiotic intervention has strain-specific anti-inflammatory effects in healthy adults. World Journal of Gastroenterology, 14(13), 2029-2036. doi:10.3748/wjg.14.2029

[7] Otte, J. M., & Podolsky, D. K. (2004). Functional modulation of enterocytes by gram-positive and gram-negative microorganisms. American Journal of Physiology-Gastrointestinal and Liver Physiology, 286(4), G613-G626. doi:10.1152/ajpgi.00338.2003

[8] Rijkers, G. T., Bengmark, S., Enck, P., Haller, D., Herz, U., Kalliomaki, M., ... & Van Der Waaij, D. (2010). Guidance for substantiating the evidence for beneficial effects of probiotics: current status and recommendations for future research. Journal of Nutrition, 140(3), 671S-676S. doi:10.3945/jn.109.113779

[9] Smits, H. H., Engering, A., van der Kleij, D., de Jong, E. C., Schipper, K., van Capel, T. M., ... & Yazdanbakhsh, M. (2005). Selective probiotic bacteria induce IL-10-producing regulatory T cells in vitro by modulating dendritic cell function through dendritic cell-specific intercellular adhesion molecule 3-grabbing nonintegrin. Journal of Allergy and Clinical Immunology, 115(6), 1260-1267. doi:10.1016/j.jaci.2005.03.036

[10] Snydman, D. R. (2008). The safety of probiotics. Clinical Infectious Diseases, 46(Supplement_2), S104-S111. doi:10.1086/523331

[11] Zhang, M. M., Cheng, J. Q., Lu, Y. R., Yi, Z. H., Yang, P., & Wu, X. Z. (2015). Efficacy of probiotics on eradication of Helicobacter pylori and reduction of therapy-related side effects: a meta-analysis. PLoS One, 10(11), e0142738. doi:10.1371/journal.pone.0142738