



The Impact of Probiotics Co-administration with Antibiotics on Health: A Comprehensive Review

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Abstract

Antibiotics have updated modern medicinal practices by improving outcomes in infectious diseases. Broad-spectrum action of antibiotics can cause disruption in the balance of beneficial gut bacteria that eventually leads to adverse effects such as antibiotic-associated diarrhea (AAD) and an increased susceptibility to sudden infections. Probiotics or live microorganisms are administered in proper amounts, they can benefit our health. Using probiotics is a potential solution to mitigate these adverse effects. This review aims to provide a comprehensive analysis of the impact of probiotics co-administered with antibiotics on various aspects of health, including the prevention of AAD, modulation of gut microbiota, and enhancement of immune function. This research uses a literature review method, namely a series of activities related to collection methods of library data. the co-administration of probiotics with antibiotics represents a promising approach to mitigating the adverse effects of antibiotic therapy on gut health and overall well-being. Additionally, the potential mechanisms underlying these effects and highlighting the challenges and future directions in this field have also been discussed.

Keywords: Probiotics, antibiotics, gut microbiota, Antibiotic-associated diarrhea (AAD), immune modulation, microbiome, dysbiosis, gut barrier function.

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Introduction

Antibiotics have revolutionized modern medicine, playing a pivotal role in the treatment of bacterial infections and significantly reducing morbidity and mortality rates. However, their widespread use has unintended consequences, particularly on the complex ecosystem of the human gut microbiota. The gut microbiota, composed of trillions of microorganisms, plays a crucial role in maintaining host health by contributing to digestion, nutrient absorption, immune regulation, and protection against pathogens (Hou et al., 2022); (Zhao et al., 2023); (Rinninella et al., 2019). Antibiotics, by their nature, are non-selective in their action, targeting both harmful bacteria causing infections and beneficial bacteria residing in the gut. This indiscriminate killing of microbes can disrupt the delicate balance of the gut microbiota, leading to dysbiosis—a state characterized by altered microbial composition and function. Dysbiosis has been associated with various adverse health outcomes, including antibiotic-associated diarrhea (AAD), gastrointestinal infections, and susceptibility to chronic diseases such as obesity, diabetes, and inflammatory bowel disease (IBD) (Chang & Lin, 2016); (Dahiya & Nigam, 2023). In recent years, there has been growing interest in the potential of probiotics to mitigate the adverse effects of antibiotics on gut microbiota and overall health.

Probiotics, defined as live microorganisms that confer health benefits when administered in adequate amounts, have been proposed as a complementary strategy to antibiotics to restore microbial balance and prevent or alleviate antibiotic-induced complications (Maftei et al., 2024). Probiotics exert their effects through diverse mechanisms, including competitive exclusion of pathogens, production of antimicrobial substances, modulation of immune responses, and enhancement of gut barrier function. These mechanisms contribute to maintaining a resilient and diverse gut microbiota, which is essential for optimal health and resilience against infections (Ma et al., 2023); (Rabetafika et al., 2023). Given the rising concerns over antibiotic resistance and the importance of preserving gut microbiota integrity, there is a compelling need to explore the potential synergy between antibiotics and probiotics in clinical practice. However, the effectiveness of probiotics in conjunction with antibiotics remains a subject of debate, with conflicting findings from various studies and clinical trials (Kothari et al., 2019); (Suez et al., 2020). This review aims to provide a comprehensive analysis of the impact of probiotics co-administered with antibiotics on various aspects of health, including the prevention of AAD, modulation of gut microbiota, and enhancement of immune function. By synthesizing evidence from preclinical and clinical studies, we seek to elucidate the potential benefits, mechanisms of action, and challenges associated with this approach. Ultimately, a deeper understanding of the interplay between antibiotics, probiotics, and the gut microbiota will inform strategies to optimize therapeutic outcomes and promote health in antibiotic-treated individuals.

Methodology

This research uses a literature review method, namely a series of activities related to collection methods library data, and information by exploring knowledge or knowledge from sources such as books, written works, lecture notes, and other sources that are related to the research object. The data source for this research using the literature review method came from several sources, both national and international journals using published articles from Google Scholar, PubMed, and Elsevier.

Results

Prevention of Antibiotic-Associated Diarrhea (AAD)

Antibiotic-associated diarrhea (AAD) is one of the most common adverse effects of antibiotic therapy, affecting up to 30% of individuals receiving antibiotics. AAD is characterized by loose or watery stools, abdominal cramping, and discomfort, and it can range in severity from mild to life-threatening. The disruption of the gut microbiota by antibiotics, particularly the depletion of beneficial bacteria such as Lactobacilli and Bifidobacteria, is thought to play a central role in the development of AAD. Probiotics have been extensively studied for their potential to prevent or alleviate AAD by restoring microbial balance and enhancing gut barrier function. Numerous clinical trials and meta-analyses have evaluated the efficacy of various probiotic strains, alone or in combination, in reducing the incidence and severity of AAD across different patient populations and antibiotic regimens.

Studies have shown that certain probiotic strains, such as *Lactobacillus rhamnosus* GG, *Saccharomyces boulardii*, and a combination of *Lactobacillus acidophilus* and *Bifidobacterium bifidum*, are effective in reducing the risk of AAD when administered concomitantly with antibiotics. These probiotics may exert their protective effects through multiple mechanisms, including competitive inhibition of pathogen colonization, production of antimicrobial substances (e.g., bacteriocins), and modulation of mucosal immune responses.

Meta-analyses of randomized controlled trials have consistently demonstrated a significant reduction in the incidence of AAD with probiotic supplementation compared to placebo or no intervention (Rajkumar et al., 2020). Moreover, probiotics have been shown to shorten the duration of diarrhea episodes and decrease the risk of complications such as *Clostridioides difficile* infection, a severe form of AAD associated with high morbidity and mortality. Despite the overall positive findings, the efficacy of probiotics in preventing AAD appears to be strain-specific, with variations in effectiveness observed among different probiotic formulations. Additionally, factors such as the timing, duration, and dosage of probiotic administration, as well as the underlying health status of patients, may influence outcomes.

Modulation of Gut Microbiota

The gut microbiota represents a diverse community of microorganisms inhabiting the gastrointestinal tract, playing a crucial role in host metabolism, immune regulation, and overall health. Antibiotics, while effective in treating bacterial infections, can indiscriminately disrupt the composition and function of the gut microbiota, leading to dysbiosis—a state characterized by a decrease in microbial diversity and alterations in microbial community structure. Probiotics have emerged as a potential strategy to mitigate antibiotic-induced dysbiosis by promoting the restoration of a healthy and diverse gut microbiota. Through various mechanisms, probiotics can modulate the composition and function of the gut microbiota, thereby contributing to the maintenance of gut homeostasis and host health (Ferenc et al., 2024). Studies have demonstrated that probiotic supplementation during antibiotic therapy can help preserve microbial diversity and prevent the overgrowth of opportunistic pathogens, such as *Clostridioides difficile*, which can cause severe gastrointestinal infections. Probiotics may exert their beneficial effects by competing with pathogens for nutrients and adhesion sites in the gut, producing antimicrobial compounds that inhibit pathogen growth, and modulating host immune responses to enhance resistance against infections.

Furthermore, probiotics have been shown to stimulate the growth and activity of beneficial bacteria, such as Bifidobacteria and Lactobacilli, which play a crucial role in maintaining gut barrier integrity and producing short-chain fatty acids (SCFAs) that provide energy for colonocytes and exert anti-inflammatory effects. Clinical studies utilizing advanced

sequencing techniques, such as metagenomic and metatranscriptomic analysis, have provided insights into the dynamic changes in gut microbiota composition and function in response to probiotic supplementation during antibiotic therapy. These studies have highlighted the strain-specific effects of probiotics on gut microbial communities, with certain probiotic strains demonstrating greater efficacy in modulating specific bacterial taxa and metabolic pathways. Moreover, emerging evidence suggests that the timing and duration of probiotic administration relative to antibiotic therapy may influence the magnitude and persistence of probiotic-mediated effects on gut microbiota composition. Strategies such as staggered dosing, where probiotics are administered at intervals between antibiotic doses, have been proposed to maximize the beneficial effects of probiotics on gut microbiota restoration (Éliás et al., 2023).

Immune Modulation

The gut microbiota plays a critical role in shaping host immune responses and maintaining immune homeostasis. Disruption of the gut microbiota composition, as observed during antibiotic therapy, can have profound effects on immune function, increasing susceptibility to infections and inflammatory disorders. Probiotics have been investigated for their potential to modulate host immune responses, both locally in the gut and systemically, thereby enhancing immune defense mechanisms and reducing the risk of antibiotic-associated complications. Several mechanisms have been proposed to explain the immunomodulatory effects of probiotics. Firstly, probiotics can interact with immune cells in the gut-associated lymphoid tissue (GALT), including dendritic cells, macrophages, and T cells, to regulate the production of pro-inflammatory and anti-inflammatory cytokines. By promoting a balanced immune response, probiotics help maintain gut barrier integrity and prevent excessive inflammation.

Secondly, probiotics can enhance the production of antimicrobial peptides (AMPs) by intestinal epithelial cells, which play a crucial role in innate immune defense against pathogens. AMPs exhibit broad-spectrum antimicrobial activity and contribute to the maintenance of microbial homeostasis in the gut. Furthermore, probiotics have been shown to stimulate the production of secretory immunoglobulin A (sIgA), an important component of mucosal immunity that acts as a first line of defense against pathogens by neutralizing and preventing their attachment to the intestinal epithelium. By enhancing sIgA production, probiotics strengthen mucosal barrier function and reduce the risk of gastrointestinal infections. Clinical studies investigating the immunomodulatory effects of probiotics during antibiotic therapy have yielded promising results. Probiotic supplementation has been shown to reduce the incidence and severity of antibiotic-associated complications, such as *Clostridioides difficile* infection and opportunistic infections, by enhancing host immune defenses and restoring gut microbiota homeostasis (Nabavi-Rad et al., 2022).

Moreover, probiotics may have systemic effects on immune function, influencing immune cells and cytokine production in peripheral blood. By modulating systemic immune responses, probiotics can potentially enhance host resistance to infections at distant sites and promote overall health and well-being. However, the immunomodulatory effects of probiotics are complex and may vary depending on factors such as probiotic strain, dosage, and host immune status. Additionally, the optimal timing and duration of probiotic supplementation relative to antibiotic therapy warrant further investigation to maximize therapeutic efficacy (Purdell et al., 2023).

Mechanisms of Action

The interactions between probiotics and antibiotics within the gastrointestinal tract involve complex and dynamic processes that influence gut microbiota composition, host immune

responses and overall health outcomes (Zheng et al., 2020); (Hong et al., 2023). Understanding the mechanisms underlying the effects of probiotics co-administered with antibiotics is essential for optimizing therapeutic strategies and elucidating their potential benefits in clinical practice.

1. **Competitive Exclusion:** Probiotics compete with pathogenic bacteria for adhesion sites and nutrients within the gut, thereby reducing the colonization and growth of harmful microorganisms. By out-competing pathogens, probiotics help maintain microbial balance and prevent the overgrowth of opportunistic pathogens, such as *Clostridioides difficile*, which can cause severe gastrointestinal infections.
2. **Production of Antimicrobial Substances:** Probiotic strains produce a variety of antimicrobial compounds, including bacteriocins, organic acids, and hydrogen peroxide, which inhibit the growth of pathogenic bacteria. These antimicrobial substances exert broad-spectrum activity against a range of bacterial pathogens, contributing to the suppression of infection and the maintenance of gut health.
3. **Modulation of Gut Barrier Function:** Probiotics enhance gut barrier integrity by promoting the expression of tight junction proteins and mucin production, which help strengthen the physical barrier between the intestinal epithelial cells and prevent the translocation of pathogens and toxins into the systemic circulation. By maintaining gut barrier function, probiotics reduce the risk of bacterial translocation and systemic inflammation associated with antibiotic-induced dysbiosis.
4. **Immunomodulation:** Probiotics interact with immune cells in the gut-associated lymphoid tissue (GALT) and peripheral circulation, modulating immune responses to promote a balanced and appropriate reaction to microbial challenges. Probiotics stimulate the production of anti-inflammatory cytokines (e.g., interleukin-10) while suppressing the secretion of pro-inflammatory cytokines (e.g., tumor necrosis factor- α), thereby attenuating inflammation and promoting immune tolerance.
5. **Metabolic Interactions:** Probiotics can metabolize dietary components and produce metabolites, such as short-chain fatty acids (SCFAs), which serve as an energy source for colonocytes and exert anti-inflammatory effects. By modulating host metabolism and immune function, probiotics contribute to the maintenance of gut homeostasis and overall health.
6. **Direct Interaction with Antibiotics:** Probiotics may interact directly with antibiotics, altering their pharmacokinetics and pharmacodynamics within the gastrointestinal tract. These interactions can affect antibiotic absorption, distribution, metabolism, and excretion, potentially enhancing or attenuating antibiotic efficacy and side effects.

Challenges and Future Directions

While probiotics co-administered with antibiotics hold promise for mitigating the adverse effects of antibiotic therapy on gut microbiota and overall health, several challenges need to be addressed to optimize their therapeutic efficacy and safety.

1. **Strain-Specific Effects:** The effectiveness of probiotics in preventing antibiotic-associated complications may vary depending on the specific probiotic strain used. Identifying the most efficacious strains for different clinical indications and patient populations remains a challenge, as probiotic strains exhibit considerable variability in their mechanisms of action and clinical outcomes.

2. **Standardization of Formulations:** There is a lack of standardization in probiotic formulations, including variations in strain selection, dosage, viability, and delivery systems. Standardized protocols for probiotic manufacturing and quality control are needed to ensure product consistency and efficacy across different studies and commercial products.
3. **Dosing Regimens:** Optimal dosing regimens for probiotics co-administered with antibiotics have not been well-defined. Factors such as the timing, duration, and frequency of probiotic administration relative to antibiotic therapy may influence therapeutic outcomes and should be systematically investigated in clinical trials.
4. **Patient Heterogeneity:** The response to probiotic supplementation during antibiotic therapy may vary among individuals due to differences in baseline gut microbiota composition, host immune status, underlying health conditions, and antibiotic regimens. Personalized approaches based on host factors and microbial profiling may help identify individuals who are most likely to benefit from probiotic therapy.
5. **Safety Concerns:** While probiotics are generally considered safe for most individuals, there have been rare reports of adverse events, particularly in immunocompromised patients or those with pre-existing medical conditions. Long-term safety data on probiotic use, especially in vulnerable populations, are lacking, highlighting the need for rigorous safety assessments in clinical trials and post-marketing surveillance.
6. **Regulatory Oversight:** The regulation of probiotics varies between countries, with differences in labeling requirements, quality standards, and health claims. Harmonization of regulatory frameworks and evidence-based guidelines for probiotic use are essential to ensure product safety, efficacy, and transparency for healthcare practitioners and consumers.

Future directions in probiotic research include the development of next-generation probiotics with enhanced therapeutic properties, such as genetically engineered strains, synbiotics (combinations of probiotics and prebiotics), and microbiome-based therapies tailored to individual microbial profiles (Abouelela & Helmy, 2024); (Al-Fakhrany & Elekhrawy, 2024). Advances in omics technologies, such as metagenomics, metatranscriptomics, and metabolomics, will facilitate a deeper understanding of the complex interactions between probiotics, antibiotics, and the gut microbiota (Puig-Castellví et al., 2023).

Conclusion

In conclusion, the co-administration of probiotics with antibiotics represents a promising approach to mitigating the adverse effects of antibiotic therapy on gut health and overall well-being. Through their diverse mechanisms of action, including competitive exclusion of pathogens, production of antimicrobial substances, modulation of immune responses, and enhancement of gut barrier function, probiotics contribute to the restoration of microbial balance and maintenance of gut homeostasis during antibiotic treatment. Clinical evidence supports the efficacy of certain probiotic strains, such as *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*, in reducing the incidence and severity of antibiotic-associated complications, including diarrhea and *Clostridioides difficile* infection. Meta-analyses of randomized controlled trials have demonstrated significant reductions in the risk of antibiotic-associated diarrhea with probiotic supplementation, highlighting the potential clinical benefits of probiotics in

conjunction with antibiotics. However, several challenges remain to be addressed to optimize the therapeutic use of probiotics co-administered with antibiotics. These challenges include the strain-specific effects of probiotics, standardization of formulations and dosing regimens, patient heterogeneity, safety concerns, regulatory oversight, and the need for personalized approaches based on individual microbial profiles. Future research directions include the development of next-generation probiotics with enhanced therapeutic properties, such as genetically engineered strains and synbiotics, as well as the application of omics technologies to better understand the complex interactions between probiotics, antibiotics, and gut microbiota.

Conflict of Interest

No conflict of interest

References:

- Abouelela, M. E., & Helmy, Y. A. (2024). Next-Generation Probiotics as Novel Therapeutics for Improving Human Health: Current Trends and Future Perspectives. *Microorganisms*, 12(3), 430. <https://doi.org/10.3390/microorganisms12030430>
- Al-Fakhrany, O. M., & Elekhrawy, E. (2024). Next-generation probiotics: The upcoming biotherapeutics. *Molecular Biology Reports*, 51(1), 505. <https://doi.org/10.1007/s11033-024-09398-5>
- Chang, C., & Lin, H. (2016). Dysbiosis in gastrointestinal disorders. *Best Practice & Research Clinical Gastroenterology*, 30(1), 3–15. <https://doi.org/10.1016/j.bpg.2016.02.001>
- Dahiya, D., & Nigam, P. S. (2023). Antibiotic-Therapy-Induced Gut Dysbiosis Affecting Gut Microbiota—Brain Axis and Cognition: Restoration by Intake of Probiotics and Synbiotics. *International Journal of Molecular Sciences*, 24(4), 3074. <https://doi.org/10.3390/ijms24043074>
- Éliás, A. J., Barna, V., Patoni, C., Demeter, D., Veres, D. S., Bunduc, S., Eróss, B., Hegyi, P., Földvári-Nagy, L., & Lenti, K. (2023). Probiotic supplementation during antibiotic treatment is unjustified in maintaining the gut microbiome diversity: A systematic review and meta-analysis. *BMC Medicine*, 21(1), 262. <https://doi.org/10.1186/s12916-023-02961-0>
- Ferenc, K., Sokal-Dembowska, A., Helma, K., Motyka, E., Jarmakiewicz-Czaja, S., & Filip, R. (2024). Modulation of the Gut Microbiota by Nutrition and Its Relationship to Epigenetics. *International Journal of Molecular Sciences*, 25(2), 1228. <https://doi.org/10.3390/ijms25021228>
- Hong, M., Lan, T., Li, Q., Li, B., Yuan, Y., Xu, F., & Wang, W. (2023). A comprehensive perspective on the interaction between gut microbiota and COVID-19 vaccines. *Gut Microbes*, 15(1), 2233146. <https://doi.org/10.1080/19490976.2023.2233146>
- Hou, K., Wu, Z.-X., Chen, X.-Y., Wang, J.-Q., Zhang, D., Xiao, C., Zhu, D., Koya, J. B., Wei, L., Li, J., & Chen, Z.-S. (2022). Microbiota in health and diseases. *Signal Transduction and Targeted Therapy*, 7(1), 135. <https://doi.org/10.1038/s41392-022-00974-4>
- Kothari, D., Patel, S., & Kim, S.-K. (2019). Probiotic supplements might not be universally effective and safe: A review. *Biomedicine & Pharmacotherapy*, 111, 537–547. <https://doi.org/10.1016/j.biopha.2018.12.104>
- Ma, T., Shen, X., Shi, X., Sakandar, H. A., Quan, K., Li, Y., Jin, H., Kwok, L.-Y., Zhang, H., & Sun, Z. (2023). Targeting gut microbiota and metabolism as the major probiotic mechanism—An evidence-based review. *Trends in Food Science & Technology*, 138, 178–198. <https://doi.org/10.1016/j.tifs.2023.06.013>

- Maftai, N.-M., Raileanu, C. R., Balta, A. A., Ambrose, L., Boev, M., Marin, D. B., & Lisa, E. L. (2024). The Potential Impact of Probiotics on Human Health: An Update on Their Health-Promoting Properties. *Microorganisms*, 12(2), 234. <https://doi.org/10.3390/microorganisms12020234>
- Nabavi-Rad, A., Sadeghi, A., Asadzadeh Aghdaei, H., Yadegar, A., Smith, S. M., & Zali, M. R. (2022). The double-edged sword of probiotic supplementation on gut microbiota structure in *Helicobacter pylori* management. *Gut Microbes*, 14(1), 2108655. <https://doi.org/10.1080/19490976.2022.2108655>
- Puig-Castellví, F., Pacheco-Tapia, R., Deslande, M., Jia, M., Andrikopoulos, P., Chechi, K., Bonnefond, A., Froguel, P., & Dumas, M.-E. (2023). Advances in the integration of metabolomics and metagenomics for human gut microbiome and their clinical applications. *TrAC Trends in Analytical Chemistry*, 167, 117248. <https://doi.org/10.1016/j.trac.2023.117248>
- Purdell, C., Ungurianu, A., Adam-Dima, I., & Margina, D. (2023). Exploring the potential impact of probiotic use on drug metabolism and efficacy. *Biomedicine & Pharmacotherapy*, 161, 114468. <https://doi.org/10.1016/j.biopha.2023.114468>
- Rabetafika, H. N., Razafindralambo, A., Ebenso, B., & Razafindralambo, H. L. (2023). Probiotics as Antibiotic Alternatives for Human and Animal Applications. *Encyclopedia*, 3(2), 561–581. <https://doi.org/10.3390/encyclopedia3020040>
- Rajkumar, C., Wilks, M., Islam, J., Ali, K., Raftery, J., Davies, K. A., Timeyin, J., Cheek, E., Cohen, J., Wright, J., Natarajan, U., Nicholl, C., Dewhurst, G., Fonseka, M., Slovick, D., Maskell, P., Mukherjee, S., Ali, K., Nari, R., ... Aldulami, D. (2020). Do probiotics prevent antibiotic-associated diarrhea? Results of a multicentre randomized placebo-controlled trial. *Journal of Hospital Infection*, 105(2), 280–288. <https://doi.org/10.1016/j.jhin.2020.01.018>
- Rinninella, E., Raoul, P., Cintoni, M., Franceschi, F., Miggiano, G., Gasbarrini, A., & Mele, M. (2019). What is the Healthy Gut Microbiota Composition? A Changing Ecosystem across Age, Environment, Diet, and Diseases. *Microorganisms*, 7(1), 14. <https://doi.org/10.3390/microorganisms7010014>
- Suez, J., Zmora, N., & Elinav, E. (2020). Probiotics in the next-generation sequencing era. *Gut Microbes*, 11(1), 77–93. <https://doi.org/10.1080/19490976.2019.1586039>
- Zhao, M., Chu, J., Feng, S., Guo, C., Xue, B., He, K., & Li, L. (2023). Immunological mechanisms of inflammatory diseases caused by gut microbiota dysbiosis: A review. *Biomedicine & Pharmacotherapy*, 164, 114985. <https://doi.org/10.1016/j.biopha.2023.114985>
- Zheng, D., Liwinski, T., & Elinav, E. (2020). Interaction between microbiota and immunity in health and disease. *Cell Research*, 30(6), 492–506. <https://doi.org/10.1038/s41422-020-0332-7>

