Journal of Current Biomedical Reports
Volume 0, Number 0, 2024
jcbior.com
eISSN: 2717-1906

Review

The Unknown of probiotics: The role of good bacteria in infant health

Seyedeh Zohreh Jalali[1, 2,*]

[1]Department of Paediatric, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[2]Pediatric Diseases Research Center, Guilan University of Medical Sciences, Rasht, Iran

Abstract

Probiotics are live strains of bacteria that are beneficial to health, especially the digestive system. Intestinal microflora plays an essential role in creating a barrier against colonization of pathogens, facilitating important metabolic functions, stimulating the development of the immune system, and maintaining intestinal motility. Probiotics can be prescribed to supplement intestinal flora and help with digestion, prevention of infectious diseases and even weight maintenance. Some studies showed probiotics help children with digestive problems such as constipation, inflammatory bowel disease, irritable bowel syndrome, and infectious diarrhea. However, other studies show that probiotics do not have such an effect. Because every child has its own individual microbiome. Each person's microbiome is unique, like a fingerprint. Most probiotics contain strains of *Lactobacillus*, but other types may also be present in the gut. Probiotics can only help a child's health if they contain the right bacteria strains for the child's gut. Otherwise, they may have no effect. Probiotics may help relieve acute constipation, colic, and reflux in healthy infants and children. They may also help prevent secondary infections and diarrhea in children taking antibiotics and help prevent eczema and allergies in some children. Currently, despite the extensive studies on children, there is little information about the effects of probiotics on the physiology of infants or their effectiveness in the face of infant diseases. In addition, there is insufficient safety information about probiotics for infants and this area requires additional studies to clarify the unknowns. Considering these issues, the main objective of this study is to introduce the importance and necessity of conducting additional research regarding the role of probiotics and their related products in the health of infants.

Keywords: Infants, Microbiome, Probiotics

1. Introduction

In the intricate ecosystem of the human body, trillions of microorganisms coexist, contributing to various physiological functions. Among these, the spotlight increasingly shines on probiotics, the beneficial bacteria believed to play a pivotal role in maintaining health, particularly in infants [1]. The journey through infancy marks a critical period of growth and development, where every factor, from nutrition to environment, profoundly affects an infant's well-being (Figure 1).

In recent years, research has underscored the significance of probiotics in shaping infant health, offering insights into their potential to safeguard against ailments and foster robust immunity [2]. Delving into the realm of these microscopic allies

*Corresponding author:
Seyedeh Zohreh Jalali, MD
Pediatric Diseases Research Center,
Guilan University of Medical Sciences, Rasht, Iran
Tel/Fax: +98 13 33690099
Email: z_jalali@gums.ac.ir
http://orcid.org/0000-0002-5897-9982

Received: August, 21, 2024
Accepted: September, 24, 2024

unveils a realm of promise and possibility, yet also poses questions about their optimal usage and the mysteries that still surround their efficacy. Considering these issues, the main objective of this study is to introduce the importance and necessity of conducting additional research regarding the role of probiotics and their related products in the health of infants.

2.1 Role of probiotics in infant health

The emerging body of research sheds light on the multifaceted roles of probiotics in promoting infant health. One of the primary benefits attributed to probiotic supplementation is the prevention and management of gastrointestinal disorders, including colic, diarrhea, and infantile reflux. Studies have suggested that certain probiotic strains, such as *Lactobacillus reuteri* and *Bifidobacterium infantis*, can alleviate symptoms associated with these conditions by modulating gut motility, reducing inflammation, and restoring microbial balance [4, 5].

Furthermore, probiotics have been implicated in reducing the risk of allergic diseases, such as eczema and food allergies, in high-risk infants [6]. By modulating immune responses and strengthening the gut barrier function, probiotics may help mitigate inflammatory reactions to allergens, thus offering a potential avenue for allergy prevention strategies [6, 7].

Beyond gastrointestinal and immune health, probiotics exert systemic effects that extend beyond the confines of the gut. Emerging evidence suggests

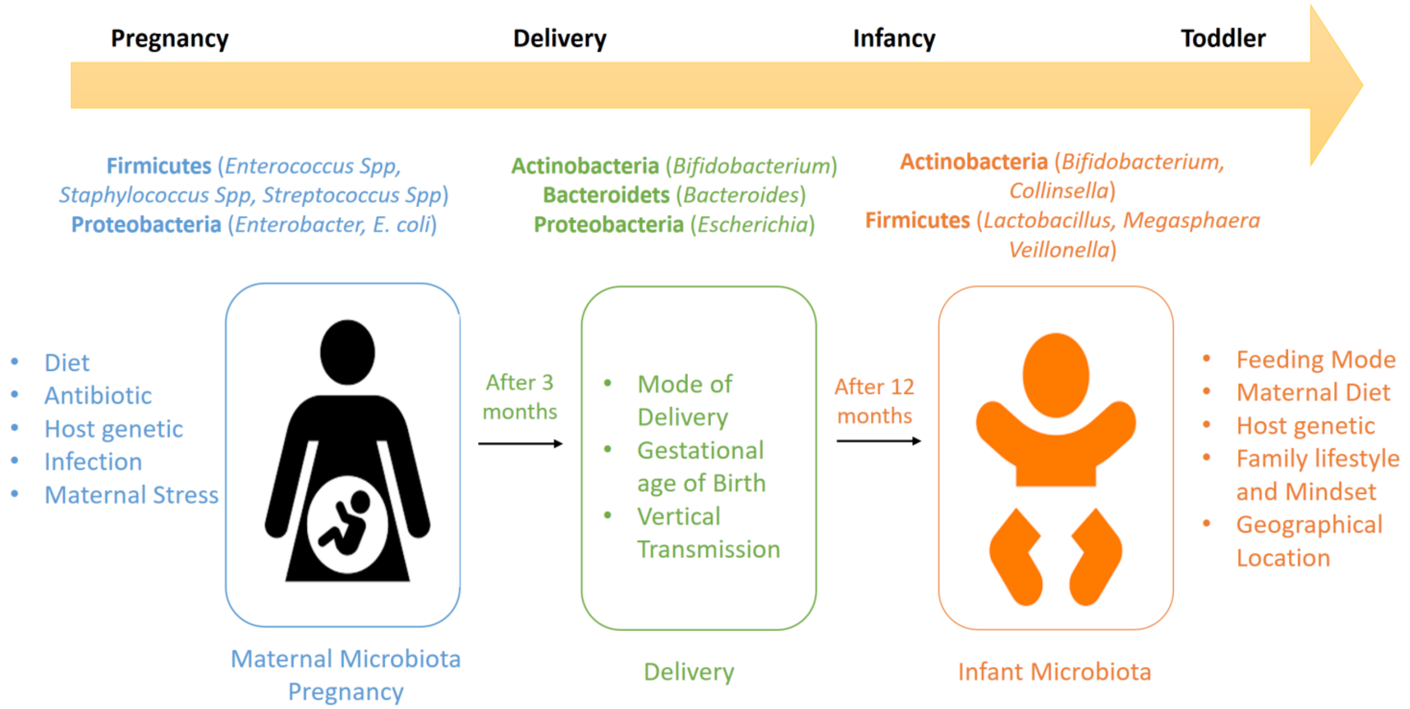

Figure 1. Window of opportunity for microbiota modulation. Different microbiome types as well as how microbiome composition can be influenced by natural competitors or various interventions.

2. Understanding Probiotics

The human gastrointestinal tract serves as the primary residence for these beneficial bacteria, where they aid in nutrient absorption, regulate immune responses, and maintain a balanced microbial environment. In infants, the gut microbiota undergoes dynamic changes during the early stages of life, influenced by factors such as mode of delivery, feeding practices, and antibiotic exposure. This period of microbial colonization lays the foundation for the infant's lifelong health, making it a critical window for interventions aimed at shaping the gut microbiome [3].

their role in neurodevelopment, with certain probiotic strains demonstrating the ability to influence cognitive function and behavior through the gut-brain axis [8]. Moreover, probiotics have been investigated for their potential to mitigate the risk of metabolic disorders, such as obesity and diabetes, by modulating energy metabolism and promoting insulin sensitivity [9, 10].

2.2 Challenges and controversies

Despite the promising findings surrounding probiotics, challenges and controversies abound, particularly concerning their efficacy, safety, and optimal dosing regimens for human populations especially for infants [11]. The heterogeneity of probiotic strains, coupled with variations in study designs and patient populations, has contributed to conflicting results across clinical trials. Additionally, the regulatory landscape governing probiotic products remains relatively lax, raising concerns about quality control, standardization, and the potential for microbial contamination.

Moreover, the safety of probiotics in vulnerable populations, such as preterm infants and immunocompromised individuals, remains a subject of debate. While the majority of studies have reported favorable safety profiles, rare cases of adverse events, including infections and sepsis, have been documented, prompting cautious consideration of their use in certain patient cohorts [12, 13].

Furthermore, questions persist regarding the optimal timing and duration of probiotic supplementation during infancy [14]. The transient nature of the infant gut microbiota, coupled with the influence of external factors, complicates efforts to establish clear guidelines for probiotic use. Further research is warranted to elucidate the long-term effects of early-life probiotic interventions and their implications for overall health outcomes [14, 15].

2.3 Future directions and concluding remarks

As our understanding of the gut microbiome continues to evolve, so too does our appreciation for the role of probiotics in shaping infant health. While much remains to be elucidated, the potential of these beneficial bacteria to modulate immune function, mitigate gastrointestinal disorders, and influence systemic health outcomes holds immense promise for improving the well-being of infants worldwide [16, 17].

Moving forward, concerted efforts are needed to address the existing gaps in knowledge surrounding probiotics, from elucidating their mechanisms of action to optimizing their therapeutic potential. Collaborative endeavors between researchers, clinicians, and regulatory agencies are essential to ensure rigorous evaluation, standardization, and responsible use of probiotic interventions in clinical practice [18].

3. Optimizing Probiotic Formulations

At the forefront of probiotic research is the quest to identify the most effective strains and formulations for targeting specific health outcomes in infants. While certain strains, such as *Lactobacillus rhamnosus* GG and *Bifidobacterium breve*, have shown promise in alleviating gastrointestinal symptoms, the optimal dosage, duration, and mode of administration remain areas of ongoing investigation. Additionally, the potential synergistic effects of combining multiple probiotic strains, known as synbiotics, warrant further exploration to enhance their therapeutic efficacy [18].

Moreover, advancements in probiotic technology hold the promise of overcoming the challenges associated with stability and viability, particularly in formulations intended for infants. Microencapsulation techniques, such as freeze-drying and spray-drying, offer innovative solutions for preserving probiotic viability during storage and transit, ensuring their efficacy upon consumption. Furthermore, the development of genetically engineered probiotics, equipped with enhanced functionalities and tailored for specific health targets, represents a frontier of biotechnological innovation with vast implications for infant health [19].

3.1 Unraveling mechanisms of action

While the beneficial effects of probiotics on infant health are well-documented, the underlying mechanisms through which they exert their therapeutic effects remain incompletely understood. Elucidating these intricate pathways is essential for optimizing probiotic interventions and uncovering new therapeutic targets.

At the forefront of probiotic research is the exploration of their interactions with the host immune system, particularly in the context of early-life immune development [20]. Probiotics have been shown to modulate immune responses through various mechanisms, including the production of anti-inflammatory cytokines, the enhancement of mucosal barrier function [21, 22], and the induction of regulatory T cells [23]. Understanding how probiotics shape the developing immune system holds promise for developing novel strategies for preventing immune-mediated diseases in infancy and beyond.

Furthermore, the gut-brain axis has emerged as a key interface through which probiotics exert their effects on neurodevelopment and behavior. Communication between the gut microbiota and the central nervous system occurs via a complex network of neural [24], endocrine , and immune signaling pathways [21, 25], influencing mood, cognition, and social behavior [26]. Probiotics have been shown to modulate neurotransmitter production, reduce neuroinflammation [27], and promote the synthesis of neurotrophic factors [28], highlighting their potential for supporting optimal brain development and mental health in infancy [29].

3.2 Navigating regulatory challenges

The regulatory landscape surrounding probiotic products remains a complex and evolving terrain, with implications for both industry stakeholders and healthcare practitioners. In many jurisdictions, probiotics are classified as dietary supplements rather than pharmaceuticals, resulting in less stringent oversight and regulation. While this facilitates accessibility and innovation, it also raises concerns about product quality, consistency, and safety [30].

To address these challenges, regulatory agencies must establish clear guidelines for the evaluation, approval, and labeling of probiotic products, ensuring transparency and accountability throughout the supply chain. This includes stringent criteria for strain identification, potency verification, and quality control, as well as post-market surveillance to monitor adverse events and ensure product safety [31].

Moreover, healthcare professionals play a crucial role in navigating the complex landscape of probiotic products, providing evidence-based recommendations and guidance to parents and caregivers. Continuing education and training programs are essential for equipping healthcare practitioners with the knowledge and skills needed to critically evaluate probiotic products, interpret clinical evidence, and make informed decisions about their use in clinical practice.

4. Charting the Course Ahead

As we embark on this journey into the unknown of probiotics in infant health, collaboration and cooperation among stakeholders are paramount. From researchers and clinicians to industry partners and regulatory agencies, each plays a crucial role in advancing our understanding of probiotics and harnessing their therapeutic potential for the benefit of infants worldwide.

Investment in research infrastructure and funding initiatives is essential for supporting innovative research projects, fostering interdisciplinary collaborations, and translating scientific discoveries into clinical applications. Furthermore, public education and awareness campaigns are needed to empower parents and caregivers with accurate information about probiotics, dispelling myths and misconceptions and promoting evidence-based practices.

4.1 *Exploring the microbiome: A gateway to personalized medicine*

Central to the burgeoning field of probiotic research is the recognition of the gut microbiome as a dynamic ecosystem with profound implications for human health. Comprising trillions of microorganisms, including bacteria, viruses, fungi, and archaea, the gut microbiome plays a pivotal role in regulating host metabolism, immune function, and neurological processes. Disruptions in the microbial balance, known as dysbiosis, have been linked to a myriad of health conditions, ranging from inflammatory bowel diseases to neurodevelopmental disorders.

In the context of infant health, the establishment of a diverse and resilient gut microbiome during the early stages of life is critical for immune development, nutrient metabolism, and disease prevention. Factors such as mode of delivery, feeding practices, antibiotic exposure, and environmental exposures shape the composition and functionality of the infant gut microbiome, laying the foundation for lifelong health trajectories [32].

Probiotics offer a promising avenue for modulating the infant gut microbiome and promoting microbial balance, thereby safeguarding against adverse health outcomes. By delivering beneficial bacteria directly to the gastrointestinal tract, probiotics can augment the diversity and stability of the gut microbiome, enhance immune function, and mitigate the risk of gastrointestinal disorders and allergic diseases. Furthermore, probiotics have been shown to interact with the gut microbiome in a bidirectional manner, exerting effects on microbial composition and metabolic activity [33]. Through mechanisms such as competitive exclusion, production of antimicrobial compounds, and modulation of host immune responses, probiotics can shape the ecological dynamics of the gut microbiome, fostering an environment conducive to health and well-being.

4.2 Harnessing the power of precision medicine

As our understanding of the gut microbiome continues to evolve, so too does our appreciation for the concept of precision medicine—a paradigm that seeks to tailor medical interventions to the individual characteristics of each patient. By integrating data from genomics, metabolomics, and microbiomics, precision medicine holds the promise of personalized probiotic interventions tailored to the unique needs of infants based on their genetic makeup, microbial profile, and environmental exposures [34].

Through advanced technologies such as next-generation sequencing and metagenomic analysis, researchers can characterize the composition and functional potential of the gut microbiome with unprecedented resolution. This allows for the identification of microbial signatures associated with health and disease, as well as the discovery of novel probiotic strains with specific therapeutic properties [35].

Moreover, advances in artificial intelligence and machine learning hold the potential to revolutionize our ability to predict, prevent, and treat health conditions in infants through probiotic interventions. By analyzing large-scale datasets encompassing clinical, genomic, and microbiomic information, machine learning algorithms can identify patterns and associations that elude traditional statistical approaches, informing the development of personalized probiotic regimens tailored to individual infants (Figure 2) [36].

4.3 Looking Ahead: A roadmap for infant's probiotic research

As we chart the course ahead in infant's probiotic research, several key priorities emerge to guide our efforts in unlocking the full potential of these beneficial bacteria in infant health:

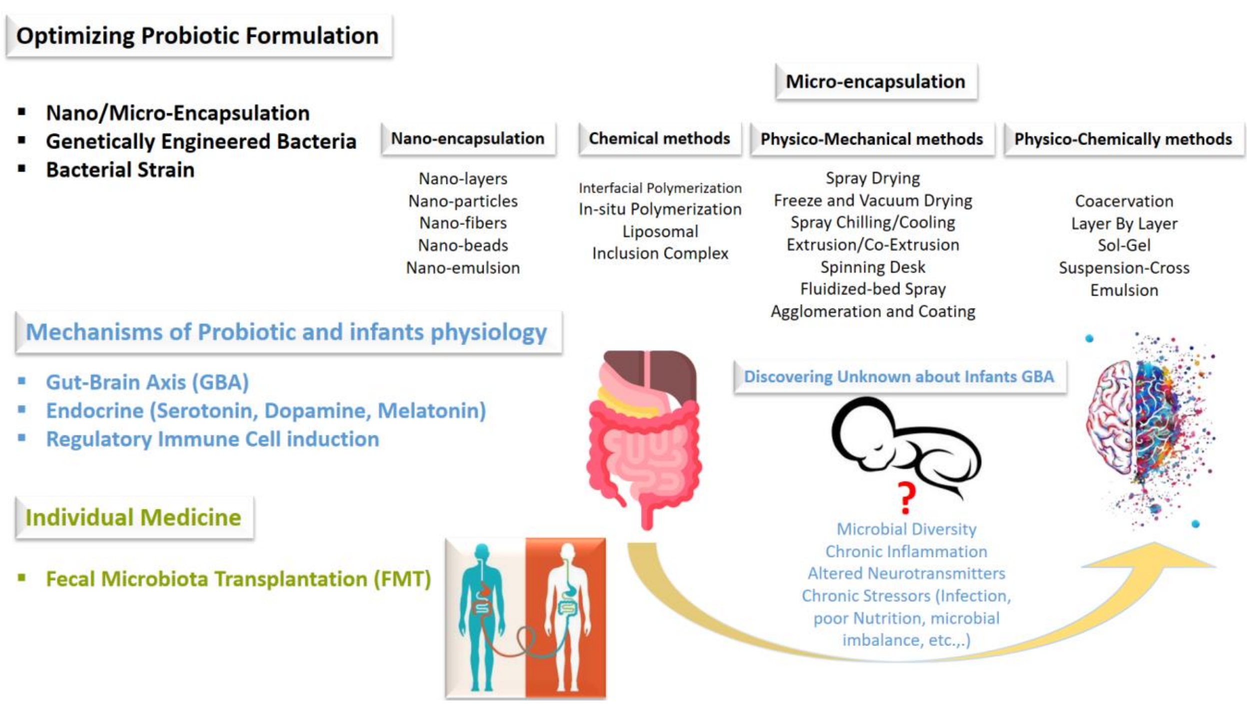

Figure 2. Methods and advances made in relation to infants and probiotic science.

Enhancing Our Understanding of Microbial Ecology: Continued research is needed to elucidate the complex interactions between probiotics, the gut microbiome, and infant's physiology. By unraveling the underlying mechanisms governing these interactions, we can develop more targeted and effective probiotic interventions tailored to the unique needs of infants.

Optimizing Formulations and Delivery Systems: Advances in probiotic technology offer opportunities to improve the stability, viability, and efficacy of probiotic formulations, particularly for use in infants. Microencapsulation techniques, genetic engineering, and innovative delivery systems hold promise for enhancing the therapeutic potential of probiotics while ensuring safety and tolerability.

Integrating Precision Medicine Approaches: Precision medicine holds the key to unlocking personalized probiotic interventions tailored to the individual characteristics of each infant. By integrating data from genomics, metabolomics, and microbiomics, we can identify microbial signatures associated with health and disease, enabling the development of targeted probiotic regimens optimized for efficacy and safety.

Fostering Collaboration and Partnerships: Collaboration among researchers, clinicians, industry partners, and regulatory agencies is essential for advancing probiotic research and translating scientific discoveries into clinical practice. By fostering interdisciplinary partnerships and sharing resources, expertise, and best practices, we can accelerate progress towards harnessing the full potential of probiotics in promoting infant health.

While the spotlight on probiotics in infant health continues to shine brightly, there is a vast expanse of uncharted territory waiting to be explored. Beyond the established benefits and challenges lie untapped potential and unanswered questions that beckon researchers and clinicians alike to delve deeper into the mysteries of these microscopic allies.

5. Conclusion

In conclusion, the unknown of probiotics in infant health represents a frontier ripe for exploration and discovery, offering the promise of improved health outcomes and enhanced well-being for the youngest members of our society. By embracing precision medicine approaches, leveraging advanced technologies, and fostering collaboration and partnerships, we can unlock the transformative potential of probiotics and shape the future of infant health for generations to come.

Authors' contributions

Author confirm the sole responsibility for the conception of the study, presented results and manuscript preparation.

Conflict of interests

None to declare.

Ethical declarations

Not applicable.

Financial support

Self-funded.

References

1. Jalali SZ, Mojtabaei SH, Heidarzadeh A, Aghamahdi F, Ahmad-Soltani M. The influence of lateral and supine position on bacterial colonization of endotracheal tube in neonates admitted to neonatal intensive care unit. Iran J Pediatr. 2012; 22(4):499-504.
2. Jalali S, Enteshari M, Saadat F. Reciprocal assessment of urinary beta-2-microglobulin and BUN levels in renal dysfunction of neonates with birth asphyxia. J Matern Fetal Neonatal Med. 2022; 35(25):6624-30.
3. Jalali SZ, Shirazi MG. Effect of probiotics on full intestinal feeding in premature infants: a double blind, Clinical Trial. Iran J Pediatr. 2020; 30(3): e100139.
4. Hakimzadeh M, Arefian A, Ahmadi M, Javaherizadeh H. Therapeutic Effect of Synbiotics (Lactobacillus reuteri, Lactobacillus rhamnosus, Bifidobacterium infantis, and Fructooligosaccharides (FOS)) on Acute non-Bloody Diarrheal Episodes in Hospitalized Children Aged Between 6-24 Months: Randomized Double-Blind Placebo-Controlled Trial. Jundishapur J Nat Pharm Prod. 2024; 19(2): e144123.
5. Papagaroufalis K, Fotiou A, Egli D, Tran L-A, Steenhout P. A randomized double blind controlled safety trial evaluating d-lactic acid production in healthy infants fed a Lactobacillus reuteri-containing formula. Nutr metab insights. 2014; 7:19-27.
6. Di Costanzo M, Vella A, Infantino C, Morini R, Bruni S, Esposito S, Biasucci G. Probiotics in Infancy and Childhood for Food Allergy Prevention and Treatment. Nutrients. 2024; 16(2):297.
7. Simpson MR, Dotterud CK, Storrø O, Johnsen R, Øien T. Perinatal probiotic supplementation in the prevention of allergy related disease: 6 year follow up of a randomised controlled trial. BMC Dermatol. 2015; 15:1-8.
8. Tian P, Zou R, Wang L, Chen Y, Qian X, Zhao J, et al. Multi-Probiotics ameliorate Major depressive disorder and accompanying gastrointestinal syndromes via serotonergic system regulation. J Adv Res. 2023; 45:117-25.
9. Wang C-C, Tung Y-T, Chang H-C, Lin C-H, Chen Y-C. Effect of probiotic supplementation on newborn birth weight for mother

with gestational diabetes mellitus or overweight/obesity: A systematic review and meta-analysis. Nutrients. 2020; 12(11):3477.

10. Rasaei N, Heidari M, Esmaeili F, Khosravi S, Baeeri M, Tabatabaei-Malazy O, Emamgholipour S. The effects of prebiotic, probiotic or synbiotic supplementation on overweight/obesity indicators: an umbrella review of the trials' meta-analyses. Front Endocrinol. 2024; 15:1277921.

11. Oh JH, Jang YS, Kang D, Chang DK, Min YW. Efficacy and safety of new lactobacilli probiotics for unconstipated irritable bowel syndrome: A randomized, double-blind, placebo-controlled trial. Nutrients. 2019; 11(12):2887.

12. Khailova L, Frank DN, Dominguez JA, Wischmeyer PE. Probiotic administration reduces mortality and improves intestinal epithelial homeostasis in experimental sepsis. Anesthesiology. 2013; 119(1):166-77.

13. Costa RL, Moreira J, Lorenzo A, Lamas CC. Infectious complications following probiotic ingestion: a potentially underestimated problem? A systematic review of reports and case series. BMC Complement Altern Med. 2018; 18:1-8.

14. Saavedra JM, Abi-Hanna A, Moore N, Yolken RH. Long-term consumption of infant formulas containing live probiotic bacteria: tolerance and safety. Am J Clin Nutr. 2004; 79(2):261-7.

15. Lundelin K, Poussa T, Salminen S, Isolauri E. Long-term safety and efficacy of perinatal probiotic intervention: Evidence from a follow-up study of four randomized, double-blind, placebo-controlled trials. Pediatr Allergy Immunol. 2017; 28(2):170-5.

16. Miniello VL, Miniello A, Ficele L, Skublewska-D'Elia A, Dargenio VN, Cristofori F, Francavilla R. Gut Immunobiosis and Biomodulators. Nutrients. 2023; 15(9):2114.

17. Bezirtzoglou E, Stavropoulou E. Immunology and probiotic impact of the newborn and young children intestinal microflora. Anaerobe. 2011; 17(6):369-74.

18. Szajewska H, Canani RB, Domellöf M, Guarino A, Hojsak I, Indrio F, et al. Probiotics for the management of pediatric gastrointestinal disorders: position paper of the ESPGHAN Special Interest Group on Gut Microbiota and Modifications. J Pediatr Gastroenterol Nutr. 2023; 76(2):232-47.

19. Boontun C, Vatanyoopaisarn S, Phalakornkule C, Domrongpokkaphan V, Thitisak P, Thaveetheptaikul P, Bamrungchue N. Influence of protectant for encapsulation by freeze-drying and spray-drying techniques, and packaging environments on the stability of the probiotic Bifidobacterium animalis subsp. lactis strain KMP-H9-01 during storage. Dry Technol. 2024:1-13.

20. Xiang Q, Wu X, Pan Y, Wang L, Cui C, Guo Y, et al. Early-life intervention using fecal microbiota combined with probiotics promotes gut microbiota maturation, regulates immune system development, and alleviates weaning stress in piglets. Int J Mol Sci. 2020; 21(2):503.

21. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics mechanism of action on immune cells and beneficial effects on human health. Cells. 2023; 12(1):184.

22. Yang J, Kuang H, Li N, Hamdy AM, Song J. The modulation and mechanism of probiotic-derived polysaccharide capsules on the immune response in allergic diseases. Crit Rev Food Sci Nutr. 2023; 63(27):8768-80.

23. Fiyouzi T, Pelaez-Prestel HF, Reyes-Manzanas R, Lafuente EM, Reche PA. Enhancing regulatory T cells to treat inflammatory and autoimmune diseases. Int J Mol Sci. 2023; 24(9):7797.

24. Feng P, Zhao S, Zhang Y, Li E. A review of probiotics in the treatment of autism spectrum disorders: Perspectives from the gut–brain axis. Front Microbiol. 2023; 14:1123462.

25. Nemati M, Ebrahimi B, Montazeri-Najafabady N. Probiotics ameliorate endocrine disorders via modulating inflammatory pathways: a systematic review. Genes Nutr. 2024; 19(1):7.

26. Walden KE, Moon JM, Hagele AM, Allen LE, Gaige CJ, Krieger JM, et al. A randomized controlled trial to examine the impact of a multi-strain probiotic on self-reported indicators of depression, anxiety, mood, and associated biomarkers. Front Nutr. 2023; 10:1219313.

27. Mudaliar SB, Poojary SS, Bharath Prasad AS, Mazumder N. Probiotics and Paraprobiotics: Effects on Microbiota-Gut-Brain Axis and Their Consequent Potential in Neuropsychiatric Therapy. Probiotics Antimicrob Proteins. 2024; 16(4):1440-1464.

28. Dehghani F, Abdollahi S, Shidfar F, Clark CC, Soltani S. Probiotics supplementation and brain-derived neurotrophic factor (BDNF): A systematic review and meta-analysis of randomized controlled trials. Nutr Neurosci. 2023; 26(10):942-52.

29. Johnson D, Letchumanan V, Thum CC, Thurairajasingam S, Lee L-H. A microbial-based approach to mental health: the potential of probiotics in the treatment of depression. Nutrients. 2023; 15(6):1382.

30. Chugh P, Misra S, Dhar MS, Raghuwanshi S. Regulatory Aspects Relevant to Probiotic Products. Probiotics, Prebiotics, Synbiotics, and Postbiotics: Human Microbiome and Human Health: Springer; 2023. p. 513-34.

31. Freedman SB, Schnadower D, Tarr PI. The probiotic conundrum: regulatory confusion, conflicting studies, and safety concerns. Jama. 2020; 323(9):823-4.

32. Qi Q, Wang L, Gebremedhin MA, Li S, Wang X, Shen J, et al. The impact of early-life antibiotics and probiotics on gut microbial ecology and infant health outcomes: a Pregnancy and Birth Cohort in Northwest China (PBCC) study protocol. BMC pediatrics. 2022; 22(1):738.

33. Rosa LS, Santos ML, Abreu JP, Rocha RS, Esmerino EA, Freitas MQ, et al. Probiotic fermented whey-milk beverages: Effect of different probiotic strains on the physicochemical characteristics, biological activity, and bioactive peptides. Food Res Int. 2023; 164:112396.

34. Yang J, Shang P, Zhang B, Wang J, Du Z, Wang S, et al. Genomic and metabonomic methods reveal the probiotic functions of swine-derived Ligilactobacillus salivarius. BMC microbiology. 2023; 23(1):242.

35. Suez J, Zmora N, Elinav E. Probiotics in the next-generation sequencing era. Gut microbes. 2020; 11(1):77-93.

36. Bubnov RV, Babenko LP, Lazarenko LM, Mokrozub VV, Spivak M. In Vitro Study of Specific Properties of Probiotic Strains for Effective and Personalized Probiotic Therapy. Microbiome in 3P Medicine Strategies: The First Exploitation Guide: Springer; 2023. p. 355-70.