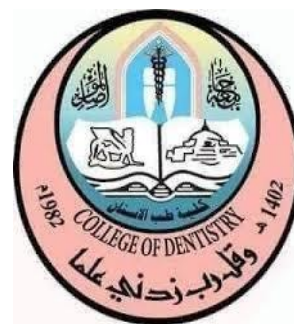




Republic of Iraq
Ministry of Higher Education
and Scientific Research
University of Mosul
College of Dentistry



Probiotic

A Project Submitted to
The College of Dentistry, University of Mosul, Department of in
Basic Dental Sciences/Pharmacy Partial Fulfillment for the
Bachelor of Dental Surgery

By
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February /2025

Certification of the Supervisor

I certify that this project entitled **Probiotic**
was prepared by the fifth-year student **Hamza Turki Muhammed** under my
supervision at the College of Dentistry/University of Mosul in partial fulfilment of
the graduation requirements for the Bachelor Degree in Dentistry.

Signature:

Prof.Dr.Maha Talal

Date: / / **2025**

Dedication

In the name of Allah, the Most Gracious, the Most Merciful

To the ones who planted the seeds of ambition in my heart, to those who stood by me through every challenge, to those who sacrificed their comfort for mine and believed in me even when I doubted myself...

To my beloved parents, whose endless love, prayers, and guidance have been the light that led me to this moment. No words can truly express my gratitude, but I hope this achievement makes you proud, just as I am forever proud to be your son.

To my dear uncle, whose wisdom and encouragement have been a constant source of support. Your belief in me has given me strength in moments of doubt. Thank you for everything.

To my cousin, my brother in every sense of the word, Abdullah—you have been with me through it all. We walked this path together, shared the struggles, the late nights, the stress, and the victories. I couldn't have asked for a better companion on this journey. Thank you for always being there.

To my professors, my friends, and everyone who played a role in shaping my journey—this is not just my success, but yours as well.

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I thank God first and foremost for his countless love and support always, I pray that I will live up to be a responsible Doctor.

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For her endless support, kind efforts, time, advice and scientific opinions and

The completion of this project could not have been possible without the participation and assistance of so many people whose names may not all be enumerated. Their contributions are sincerely appreciated and gratefully acknowledged.

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Introduction

Nowadays, the strong relationship between diet and health is well accepted. Although the primary role of diet is to provide nutrients to fulfil metabolic requirements, the use of foods to improve health and the state of wellbeing is an idea increasingly accepted by society in the last three decades. The change in the way of conceiving foods has led to the introduction of the concept of functional foods. Besides exhibiting an adequate nutritional value, a food can be considered as functional if it beneficially affects one or more target functions in the body in a way that is relevant to either the state of wellbeing and health or the reduction of the risk of a disease. 'Functional foods' as a marketing term was initiated in Japan in the late 1980s. However, the world market has grown rapidly. (Korhonen, 2020)

while the European market estimation exceeded billion in the same year. The functionality of functional food is based on bioactive components, often contained naturally in the product but usually requiring the addition of a specific ingredient in order to optimise the beneficial properties. Today, functional food ingredients include probiotics, prebiotics, vitamins and minerals, which are used in fermented milks and yogurts, sports drinks, baby foods, sugar-free confectionery and chewing gum. (Vasiljevic and Shah, 2019)

Probiotics and prebiotics are fundamental ingredients of fermented milks and yogurts, which account for the most important fraction of the overall market for functional foods. Therefore most of the available research on functional foods has focused on probiotics and prebiotics. This article constitutes a state-of-the-art review of probiotics and prebiotics from the fundamentals to the concept of synbiotics and challenges for the development of new probiotic- and prebiotic-based foods. Finally, the key research niches in the field are identified and discussed. Several definitions of probiotics can be found in the literature. Hence, a decade ago, probiotics were considered as those viable micro-organisms that exhibit a beneficial effect on the health of the host by improving its intestinal microbial balance. (Roberfroid, 2021)

However, a more recent and comprehensive definition is provided by ‘probiotics are non- pathogenic micro-organisms, mostly of human origin, which confer a health benefit on the host and enable to prevent or improve some diseases when administered in adequate amounts’. The initial notion of probiotic micro-organisms can be traced to a century ago when the Nobel Laureate Ilya Metchnikoff noticed that the long healthy life of Bulgarian peasants resulted from the consumption of fermented milk products(**Wiseman and Woods ,2022**).

Aim of the study

The goal of writing the research is to detail the Probiotics, arrange it, and provide the largest amount of information and manufacturing subject regarding it.

Chapter one

Review of Literature

1.1 Definition Probiotics

Defined by the World Health Organization (WHO) as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" , represent a fundamental component of modern nutritional science and therapeutic interventions. These beneficial microorganisms primarily consist of bacteria and yeast species that naturally inhabit the human gastrointestinal tract, with *Lactobacillus* and *Bifidobacterium* being among the most extensively studied genera (Hill *et al.*,2020)(figure.1)

The scientific understanding of probiotics has evolved significantly since their initial discovery in the early 20th century by Nobel laureate Elie Metchnikoff, who first proposed the concept of using beneficial bacteria to improve human health. (Corr ,*et al.*,2021)

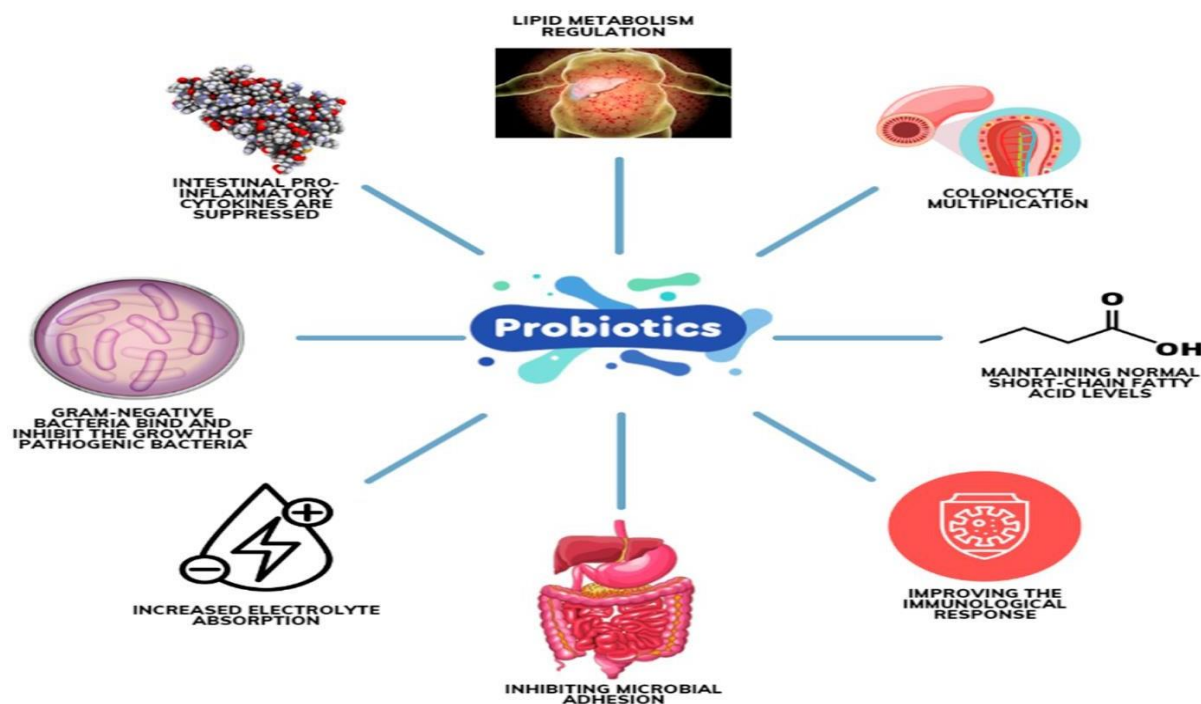


Figure.1 beneficial microorganisms Probiotics(Corr ,*et al.*,2021)

1.2 Mechanisms of Action

The mechanisms through which probiotics exert their beneficial effects are multifaceted and complex. One primary mechanism involves competitive exclusion, where probiotic organisms compete with pathogenic bacteria for adhesion sites and nutrients within the gut ecosystem . This competition creates an environment less hospitable to harmful microorganisms while promoting the growth of beneficial species. Additionally, probiotics produce various antimicrobial substances, including organic acids, hydrogen peroxide, and bacteriocins, which directly inhibit the growth of pathogenic bacteria (figure.2) .(LeBlanc ,*et al.*,2023)

Another crucial mechanism is the modulation of the immune system. Probiotics interact with intestinal epithelial cells and immune cells, stimulating the production of anti-inflammatory cytokines while suppressing pro-inflammatory responses .

They also enhance the integrity of the intestinal barrier by strengthening tight junctions between epithelial cells, thereby preventing the translocation of harmful substances into systemic circulation . Furthermore, certain probiotic strains can influence metabolic processes, aid in nutrient absorption, and contribute to the synthesis of essential vitamins such as vitamin K and some B vitamins .(Foster ,*et al.*,2023)

The significance of probiotics extends beyond basic digestive health. Research has demonstrated their potential applications in addressing various health conditions, including antibiotic-associated diarrhea, irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), and even mental health disorders through the gut-brain axis . The growing body of evidence supporting these diverse applications has led to increased interest from both healthcare professionals and consumers, resulting in a rapidly expanding market for probiotic products worldwide .(Sanders ,*et al.*,2021)

Understanding the fundamental nature of probiotics and their mechanisms of action provides a crucial foundation for exploring their specific types and targeted applications in human health. As research continues to uncover new insights into the complex interactions between probiotics and the human host, their potential therapeutic uses continue to expand, making them an increasingly important area of scientific investigation and clinical application. .(Sanders ,et al.,2021)

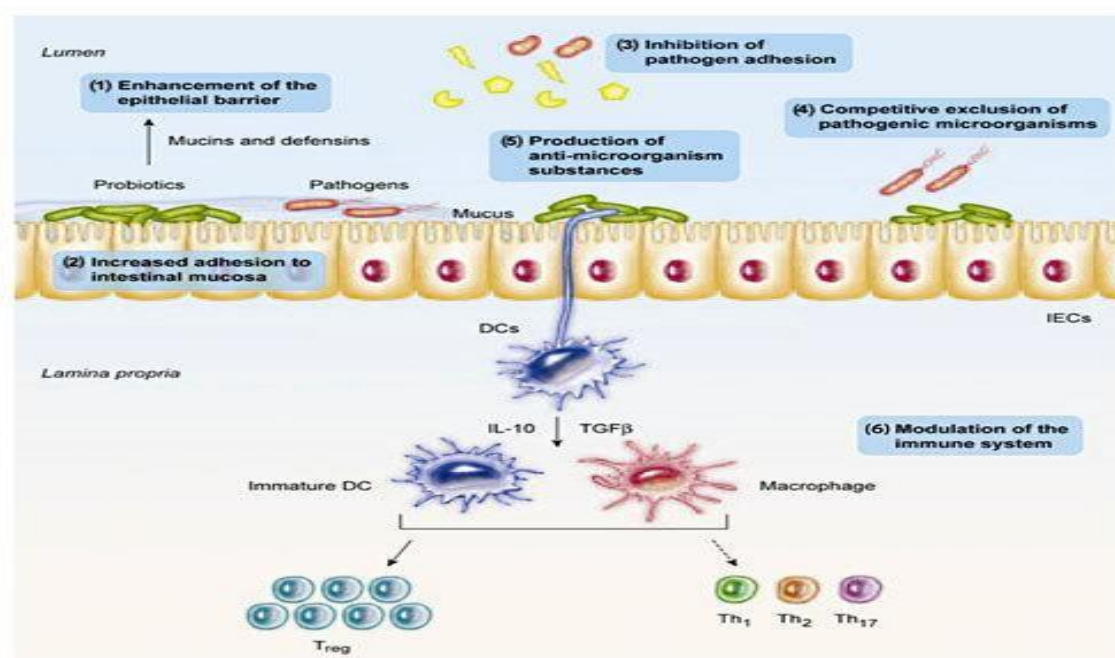


Figure.2 Mechanisms of Action.(Sanders ,et al.,2021)

1.3 Classification of Probiotics: Major Types and Species

Probiotics encompass a diverse array of microorganisms, each possessing unique characteristics and health-promoting properties. The two predominant bacterial genera in probiotic formulations are *Lactobacillus* and *Bifidobacterium*, representing over 70% of commercially available probiotic products (Sanders , et al.,2021)

Within these genera, numerous species have been extensively studied for their specific health benefits. *Lactobacillus acidophilus*, one of the most well-researched species,

demonstrates exceptional ability to survive gastric acidity and bile salts, making it particularly effective in colonizing the small intestine . Similarly, *Lactobacillus rhamnosus* GG, a strain renowned for its robust adherence properties, has shown remarkable efficacy in preventing and treating antibiotic-associated diarrhea and traveler's diarrhea .(**Szajewska , Kołodziej .2020**)

Bifidobacterium species primarily inhabiting the large intestine, play a crucial role in maintaining colonic health. Bifidobacterium bifidum and Bifidobacterium longum have been extensively documented for their ability to modulate immune responses and reduce inflammation in gastrointestinal disorders . These species excel in breaking down complex carbohydrates and producing short-chain fatty acids, which serve as vital energy sources for colonic epithelial cells . Another notable genus, Streptococcus, includes species like Streptococcus thermophilus, commonly used in dairy fermentation and recognized for its proteolytic activity and ability to improve lactose digestion .(**Leroy and De Vuyst .2019**)

Beyond bacterial probiotics, certain yeast species have gained significant attention in recent years. *Saccharomyces boulardii*, a non-pathogenic yeast, stands out as the most extensively studied probiotic yeast. Its unique characteristics include resistance to antibiotics and gastric acidity, making it particularly valuable in treating antibiotic-associated diarrhea and Clostridioides difficile infections . Unlike bacterial probiotics, S. boulardii remains unaffected by antibiotic therapy, allowing it to maintain its therapeutic effects even during concurrent antibiotic treatment (**Anderson.et al.,2020**) (figure.3)

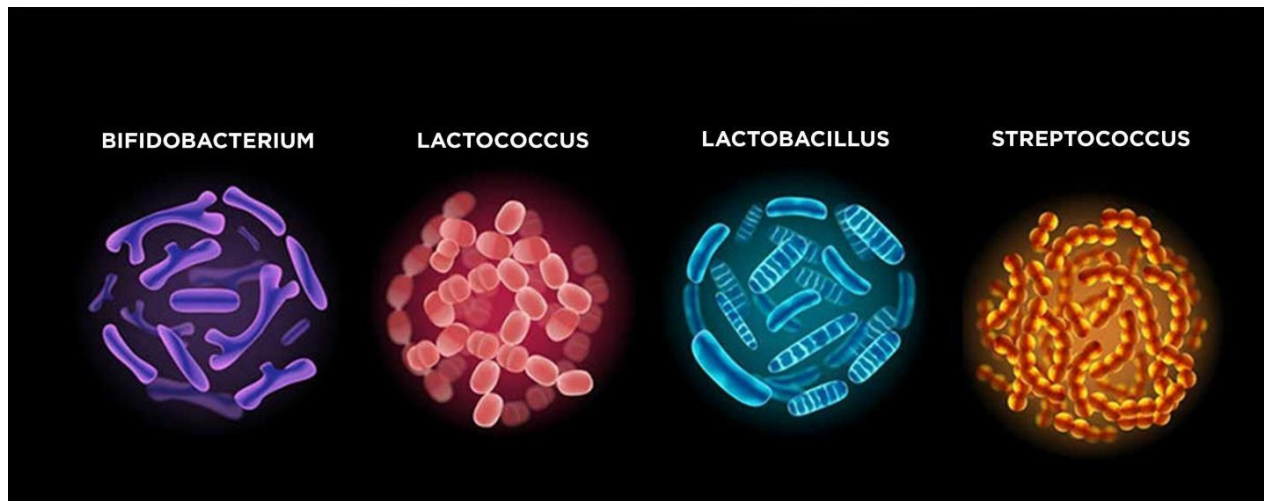


Figure.3 Different types of Probiotic (**Anderson.*et al.*,2020**)

The selection of appropriate probiotic species depends heavily on the intended health outcome and target site of action. For instance, species like *Lactobacillus plantarum* and *Lactobacillus casei* demonstrate strong adhesive properties to intestinal mucosa, making them suitable for enhancing gut barrier function . In contrast, species such as *Lactobacillus reuteri* and *Bifidobacterium breve* show particular promise in pediatric populations due to their ability to establish stable colonization in developing microbiomes . Additionally, some probiotic species exhibit strain-specific properties; for example, *Lactobacillus helveticus* R0052 has been specifically linked to improvements in blood pressure regulation through its angiotensin-converting enzyme (ACE) inhibitory activity .(**Arboleya ,*et al.*,2019**)

Recent advances in microbial genomics have revealed significant intraspecies diversity, emphasizing the importance of strain specificity in probiotic selection. Different strains of the same species may exhibit markedly different physiological characteristics and health benefits. For instance, while many *Lactobacillus rhamnosus* strains demonstrate general probiotic properties, only specific strains like *L. rhamnosus* GG have shown consistent efficacy in clinical trials .(**Hempel ,*et al.*,2020**)

1.4 Probiotics Digestive System Applications

Probiotics have demonstrated substantial efficacy in addressing various gastrointestinal conditions, with extensive clinical evidence supporting their therapeutic applications. One of the most well-documented uses involves the prevention and treatment of antibiotic-associated diarrhea (AAD), where probiotics have shown effectiveness rates ranging from 52% to 71% in reducing incidence . Multiple meta-analyses have confirmed that specific strains, particularly *Lactobacillus rhamnosus* GG and *Saccharomyces boulardii*, significantly decrease the risk of AAD when administered concurrently with antibiotic therapy . The protective effect appears to result from probiotics' ability to maintain intestinal microbial balance and prevent pathogenic overgrowth during antibiotic treatment.(Vidlock and Cremonini .2022) (figure.4)

In the context of irritable bowel syndrome (IBS), clinical trials have demonstrated that multi-strain probiotic formulations containing *Bifidobacterium infantis*, *Lactobacillus plantarum*, and *Streptococcus thermophilus* can effectively reduce symptom severity scores by 20-40% compared to placebo groups . These improvements manifest across multiple IBS symptoms, including abdominal pain, bloating, and altered bowel habits. The therapeutic mechanism likely involves modulation of visceral hypersensitivity, reduction of intestinal permeability, and regulation of serotonin metabolism in the gut .(Ford ,et al.,2023)

For inflammatory bowel diseases (IBD), including ulcerative colitis and Crohn's disease, probiotics have shown promising results, particularly in maintaining remission. *Escherichia coli* , a non-pathogenic E. coli strain, has demonstrated comparable efficacy to standard mesalamine treatment in maintaining remission in ulcerative colitis patients, with relapse rates of approximately 36% versus 44% in drug-treated groups . Additionally, VSL, a high-potency probiotic mixture containing eight different strains, has shown significant benefit in pouchitis prevention and maintenance of remission in ulcerative colitis .(Miele ,et al.,2019)

Probiotics also play a crucial role in managing functional constipation, with several randomized controlled trials demonstrating improvements in stool frequency and consistency. Supplementation with *Bifidobacterium lactis* has been associated with a 25-30% increase in weekly bowel movements and improved stool consistency in constipated adults. The beneficial effects appear mediated through enhanced colonic motility and modification of gut transit time.

Clinical evidence supports the use of specific probiotic strains in preventing and treating infectious diarrhea. A comprehensive Cochrane review analyzing 63 studies involving 8,014 participants found that probiotics reduced the duration of acute infectious diarrhea by approximately 25 hours and decreased stool frequency after 24 hours. Notably, the greatest benefits were observed with *Lactobacillus GG* and *S. boulardii* in children and travelers' diarrhea settings. (Allen, *et al.*, 2020)

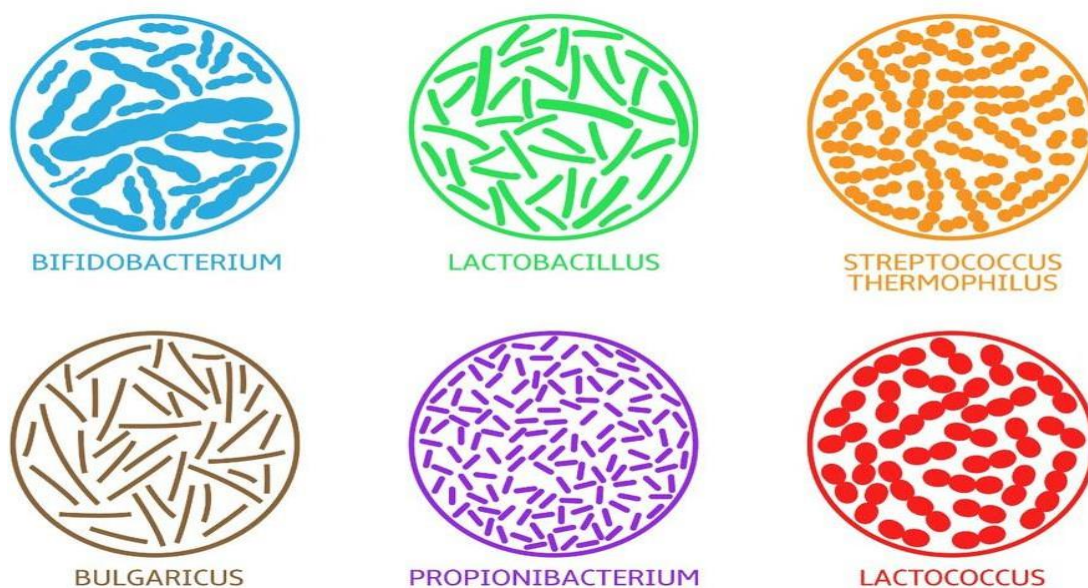


Figure.4 probiotic-strains.(Allen, *et al.*, 2020)

Emerging research highlights probiotics' potential in addressing small intestinal bacterial overgrowth (SIBO) and related conditions.(figure.5) Certain *Lactobacillus* species have demonstrated efficacy in reducing methane-producing archaea and improving symptoms in SIBO patients, with response rates comparable to traditional antibiotic therapy but with fewer side effects. Furthermore, probiotics show promise in managing post-infectious IBS and preventing recurrent *Clostridioides difficile* infections, with recurrence rates reduced by up to 60% when combined with standard antibiotic therapy. (Goldenberg , *et al.*,2019)

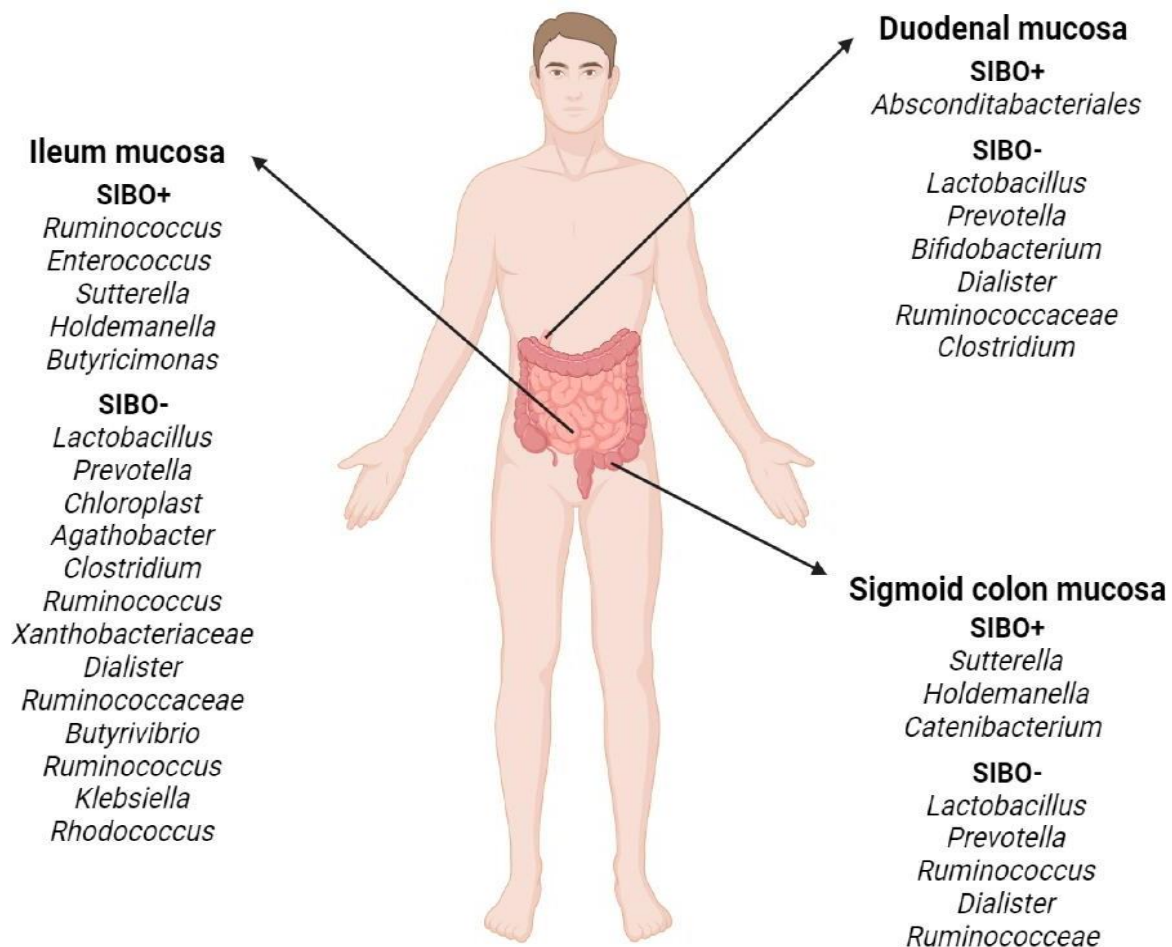


Figure.5 small intestinal bacterial overgrowth (SIBO) and related conditions. (Goldenberg , *et al.*,2019)

The therapeutic applications of probiotics extend to specific pediatric gastrointestinal conditions, including necrotizing enterocolitis (NEC) in preterm infants. Meta-analyses indicate that prophylactic administration of *Lactobacillus* and *Bifidobacterium* species reduces the incidence of NEC by approximately 50% and decreases mortality rates by 30% in very low birth weight infants. These findings have led to widespread adoption of probiotic supplementation in neonatal intensive care units, though strain selection and dosing remain critical considerations. (**Dermyshe ,et al.,2019**)

1.5 Probiotics in Immune Function and Mental Health

The therapeutic potential of probiotics extends far beyond gastrointestinal health, with compelling evidence supporting their role in immune system modulation and mental health improvement. In terms of immune function, probiotics demonstrate remarkable capacity to enhance both innate and adaptive immune responses. Clinical studies have shown that regular consumption of specific probiotic strains, particularly *Lactobacillus casei* Shirota and *Bifidobacterium animalis* subsp. lactis BB-12, can increase natural killer cell activity by 20-30% and enhance phagocytic activity of macrophages. These immunomodulatory effects translate into clinically significant outcomes, with meta-analyses indicating a 27% reduction in upper respiratory tract infections among individuals supplementing with probiotics compared to placebo groups (**Dong , et al.,2020**)

The gut-lung axis represents another crucial frontier in probiotic research, with emerging evidence suggesting that gut microbiota composition influences respiratory health. Specific probiotic strains, notably *Lactobacillus rhamnosus* and *Bifidobacterium breve*, have demonstrated efficacy in reducing asthma exacerbations and improving lung function parameters in allergic airway diseases (**Lyons , et al.,2021**)

These effects appear mediated through modulation of T-helper cell responses and reduction of pro-inflammatory cytokines, offering potential therapeutic avenues for respiratory conditions. Perhaps most intriguing is the growing body of evidence supporting the gut-brain axis theory and probiotics' role in mental health management. The term "psychobiotics" has emerged to describe probiotic strains specifically targeting mental health conditions (**Sarkar , *et al.*,2019**)

Clinical trials have demonstrated that multi-strain probiotic formulations containing *Lactobacillus helveticus* R0052 and *Bifidobacterium longum* R0175 significantly reduce symptoms of anxiety and depression, with effect sizes comparable to conventional antidepressant medications in mild to moderate cases . These psychobiotic effects appear to involve multiple pathways, including modulation of tryptophan metabolism, reduction of systemic inflammation, and enhancement of neuroplasticity through increased brain-derived neurotrophic factor (BDNF) levels .(**Miele ,*et al.*,2019**)

Research into probiotics' effects on cognitive function has yielded promising results, particularly in age-related cognitive decline and neurodegenerative disorders. Supplementation with *Lactobacillus plantarum* has shown improvements in memory performance and processing speed in elderly populations, while animal studies suggest potential neuroprotective effects against Alzheimer's disease pathology . The mechanisms underlying these cognitive benefits likely involve modulation of the hypothalamic-pituitary-adrenal (HPA) axis, reduction of oxidative stress, and enhancement of neurotransmitter synthesis (**Bravo ,*et al.*,2019**)

Probiotics also demonstrate potential in managing stress-related disorders and improving sleep quality. Clinical trials utilizing *Lactobacillus fermentum* LF16 and *Lactobacillus brevis* IDCC 3401 have reported significant reductions in cortisol levels and improvements in sleep architecture, suggesting their utility in stress management and sleep disorder treatment . Furthermore, emerging research indicates that maternal probiotic supplementation during pregnancy may positively influence neurodevelopmental outcomes in offspring, potentially offering preventive strategies for neurodevelopmental disorders .(**Dong ,et al.,2020**)

The expanding understanding of probiotics' systemic effects has led to innovative applications in autoimmune disease management. Specific strains, including *Lactobacillus paracasei* LPC37 and *Bifidobacterium lactis* Bi-07, have shown promise in modulating immune responses in conditions such as rheumatoid arthritis and multiple sclerosis . These effects appear mediated through induction of regulatory T cells and suppression of responses, offering novel therapeutic approaches for autoimmune conditions .

1.6 Factors Influencing Probiotic Effectiveness

The therapeutic success of probiotic interventions hinges critically on proper strain selection and appropriate dosage, with these factors demonstrating significant impact on clinical outcomes. Strain specificity represents a fundamental consideration, as different strains within the same species can exhibit markedly distinct physiological properties and health benefits. For instance, while *Lactobacillus rhamnosus* GG shows consistent efficacy in preventing antibiotic-associated diarrhea, other *L. rhamnosus* strains may lack similar therapeutic effects . This strain-dependent variability necessitates careful selection based on documented clinical evidence rather than general species characteristics. (**Lyons ,et al.,2021**)

Dosage requirements vary substantially among probiotic strains, typically ranging from 10^8 to 10^{11} colony-forming units (CFUs) per day for optimal therapeutic effects. However, the minimum effective dose differs significantly between strains and intended applications.

For example, preventing antibiotic-associated diarrhea requires approximately 5×10^9 CFUs of *Lactobacillus rhamnosus* GG daily, while treating necrotizing enterocolitis in preterm infants demands higher doses exceeding 10^{10} CFUs. Underdosing can lead to insufficient colonization and therapeutic failure, while excessive dosing may cause adverse effects or disrupt existing microbial balance. (Allen , *et al.*,2020)

Several critical factors influence probiotic effectiveness beyond strain and dosage. Survival through the gastrointestinal tract represents a major challenge, with gastric acidity and bile salts posing significant barriers to colonization. Strains demonstrating high tolerance to these conditions, such as *Lactobacillus acidophilus* LA-5 and *Bifidobacterium animalis* subsp. *lactis* BB-12, typically show better clinical outcomes. Additionally, the delivery system plays a crucial role; encapsulated formulations often provide superior protection and sustained release compared to conventional powder forms. (Goldenberg , *et al.*,2019)

The timing of administration relative to meals significantly affects probiotic survival and efficacy. Studies indicate that taking probiotics 30 minutes before meals, particularly those containing fats, enhances survival rates and improves colonization efficiency. Furthermore, the presence of prebiotics or other synergistic components in combination products can enhance probiotic effects through mutualistic interactions and improved ecological fitness.

Environmental factors also influence probiotic effectiveness, including storage conditions, product stability, and shelf life. Many probiotic strains require refrigeration to maintain viability, with temperature fluctuations potentially reducing potency by up to 50%

Proper handling and storage throughout the supply chain become crucial considerations, especially for heat-sensitive strains like *Lactobacillus casei* and *Bifidobacterium breve*. Individual host factors significantly impact probiotic effectiveness, including baseline microbiome composition, genetic predisposition, and lifestyle factors. Patients with severely disrupted microbiomes, such as those undergoing chemotherapy or organ transplantation, may require higher doses or more resilient strains to achieve therapeutic effects. Age-related differences in gut physiology also influence probiotic requirements, with pediatric and geriatric populations often needing tailored formulations and dosing regimens. (Goldenberg , *et al.*,2019)

1.7 Practical Applications and Recommendations for Probiotic Use

The integration of probiotics into daily health practices requires careful consideration of various practical aspects to ensure optimal benefits and safety. When selecting probiotic supplements, consumers should prioritize products that clearly specify strain designations, viable cell counts at the end of shelf life, and storage requirements. Reputable manufacturers typically provide this information on product labels, along with third-party verification of potency and purity. For dietary incorporation, fermented foods like yogurt, kefir, sauerkraut, kimchi, and miso offer natural sources of live probiotics, though their exact microbial content can vary based on preparation methods and storage conditions .(Henker ,*et al.*,2018)

Safety considerations remain paramount, particularly for vulnerable populations. While generally regarded as safe (GRAS) by regulatory agencies, probiotics may pose risks for immunocompromised individuals, critically ill patients, and those with central venous catheters . Rare cases of bacteremia and fungemia have been reported, particularly with *Lactobacillus* and *Saccharomyces* species, emphasizing the need for medical supervision in high-risk groups. Pregnant women, children, and elderly individuals should consult healthcare providers before initiating probiotic supplementation, especially when combining with prescription medications.

Potential side effects, though typically mild, can include bloating, gas, and abdominal discomfort during initial supplementation periods. These symptoms usually resolve within a few days as the gut microbiome adjusts to the introduced strains . To minimize adverse effects, gradual introduction starting with lower doses (1-2 billion CFUs) and increasing incrementally is recommended. Maintaining consistent daily intake proves crucial for establishing stable colonization and achieving desired health benefits, with most clinical studies documenting optimal effects after 2-4 weeks of continuous use .(**Lyons ,et al.,2021**)

Practical recommendations for incorporating probiotics include timing administration with meals containing healthy fats to enhance survival through the gastrointestinal tract . Combining probiotics with prebiotic fibers, either through dietary sources or synbiotic supplements, can improve colonization efficiency and sustain beneficial effects . Storage conditions must align with manufacturer guidelines, with refrigerated products maintained at recommended temperatures to preserve potency. Consumers should verify expiration dates and consider purchasing smaller quantities more frequently to ensure maximum viability .(**Pyleris ,et al.,2022**)

When selecting probiotic products, preference should be given to those containing clinically studied strains with documented health benefits relevant to individual needs. Multi-strain formulations often demonstrate superior efficacy compared to single-strain products, particularly for complex conditions like irritable bowel syndrome or immune support . However, strain compatibility and potential antagonistic interactions must be considered, as not all combinations prove equally effective . Healthcare providers can offer valuable guidance in matching specific probiotic strains to targeted health outcomes based on current clinical evidence and individual health profiles. (**Pyleris ,et al.,2022**)

Chapter Two

2.1 Discussion

The comprehensive exploration of probiotics reveals their profound significance in contemporary health science and their expanding role in both preventive and therapeutic applications. From their fundamental mechanisms of action to their diverse clinical applications, probiotics represent a dynamic field of research with far-reaching implications for human health. The accumulated evidence underscores their effectiveness in addressing various gastrointestinal disorders, enhancing immune function, and even influencing mental health through the intricate gut-brain axis. Particularly noteworthy is the emergence of strain-specific applications, where particular probiotic strains demonstrate remarkable efficacy in treating specific conditions, highlighting the importance of precision in probiotic selection and administration. **(Henker , *et al.*,2018)**

Current research trends indicate several promising directions for future investigation. The development of next-generation probiotics, including genetically engineered strains and novel species derived from human microbiomes, offers exciting possibilities for targeted therapeutic interventions. Advances in metagenomic sequencing and bioinformatics are enabling more sophisticated understanding of microbial-host interactions, paving the way for personalized probiotic therapies tailored to individual microbiome profiles. Additionally, investigations into postbiotics - the bioactive compounds produced by probiotic microorganisms - represent a burgeoning area of study with potential applications in food technology and pharmaceutical development. (**Lyons ,*et al.*,2021**)

The expanding scope of probiotic research extends beyond traditional health applications to include areas such as cancer prevention, metabolic syndrome management, and environmental adaptation. Recent studies exploring the role of probiotics in modulating drug metabolism and enhancing vaccine efficacy suggest revolutionary approaches to

personalized medicine. Moreover, the development of stable, shelf-life extended probiotic formulations and innovative delivery systems promises to enhance accessibility and compliance in various clinical settings. (**Akbari , *et al.*,2022**)

As our understanding of the human microbiome continues to evolve, the potential applications of probiotics appear increasingly boundless. Future research will likely focus on elucidating the complex signaling pathways between probiotics and host systems, developing standardized protocols for clinical applications, and establishing clear guidelines for safety and efficacy across diverse populations. The integration of artificial intelligence and machine learning in probiotic research holds particular promise for predicting treatment outcomes and optimizing strain combinations for specific health conditions. These advancements, coupled with growing consumer awareness and acceptance, position probiotics as a cornerstone of twenty-first-century healthcare innovation. (**Slykerman ,*et al.*,2023**)

Chapter Three

3.1 Conclusion

With regard to probiotics it is also important to be careful with the science and not to oversell it. Most probiotic products at the moment do not go through pre-market approvals and are commonly used for a much wider range of scenarios in which their efficacy is not well established. Therefore, future health claims concerning probiotics and their safety will critically depend on scientific evidence through science-based clinical studies on targeted population. Another important issue is correct strain identification of each probiotic, for which expanding the internationally recognised culture collections of taxonomically classified and deposited probiotics is necessary. This would assure strict use only of tested strains with known profiles in compliance with regulatory pathways for ‘fit for human use consumption’ protocols.

Perhaps it will be possible that in the future probiotics will be used as approved drugs that will be prescribed together with/or instead of antibiotics for certain conditions such as ear infections or sinusitis an interesting concluding thought of this overview is that even though it is true that certain microorganisms can make us sick and even kill us, certain microorganisms are beneficial.

References

1. Korhonen H, Technology options for new nutritional concepts. *Int JDairy Technol* 55:79–88 (2020).
2. Vasiljevic T and Shah NP, Probiotics – from Metchnikoff to bioactives. *Int Dairy J* 18:714–728 (2019).
3. Wiseman A and Woods L, Addition of designer enhancers to functional foods: need also for redesigned biocatalysts in fail-clean strategies of bioprocessing? *J Chem Technol Biotechnol* 76:1038–1040 (2022).
4. Roberfroid M, Functional food concept and its application to prebiotics. *Dig Liver Dis* 34:S105–S110 (2021).
5. Menrad K, Market and marketing of functional food in Europe. *J Food Eng* 56:181–188 (2019).
6. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic. *Nat Rev Gastroenterol Hepatol*. 2020 Aug;11(8):506-14.
7. Corr SC, Li Y, Riedel CU, O'Toole PW, Hill C, Gahan CG. Bacteriocin production as a mechanism for the anti-infective activity of *Lactobacillus salivarius* UCC118. *Proc Natl Acad Sci USA*. 2021 May;104(18):7617-21.
8. Anderson RC, Cookson AL, McNabb WC, Park ZA, McCann MJ, Kelly WJ, et al. *Lactobacillus plantarum* DSM 2648 is a potential probiotic that enhances intestinal barrier function. *FEMS Microbiol Lett*. 2020 Nov;313(2):184-92.
9. LeBlanc JG, Milani C, de Giori GS, Sesma F, van Sinderen D, Ventura M. Bacteria as vitamin suppliers to their host: a gut microbiota perspective. *Curr Opin Biotechnol*. 2023 Apr;24(2):160-8.
10. Foster JA, McVey Neufeld KA. Gut-brain axis: how the microbiome influences anxiety and depression. *Trends Neurosci*. 2023 May;36(5):305-12.
11. Sanders ME, Merenstein DJ, Reid G, Gibson GR, Rastall RA. Probiotics and prebiotics in intestinal health and disease: from biology to the clinic. *Nat Rev Gastroenterol Hepatol*. 2021 Oct;16(10):605-16.

12. Szajewska H, Kołodziej M. Systematic review with meta-analysis: *Lactobacillus rhamnosus* GG in the prevention of antibiotic-associated diarrhoea in children and adults. *Aliment Pharmacol Ther.* 2020 Oct;42(10):1149-57.
13. Plaza-Diaz J, Ruiz-Ojeda FJ, Vilchez-Padial LM, Gil A. Evidence of the Anti-Inflammatory Effects of Probiotics and Synbiotics in Intestinal Chronic Diseases. *Nutrients.* 2019 Jun;9(6):555.
14. Louis P, Flint HJ. Diversity, metabolism and microbial ecology of butyrate-producing bacteria from the human large intestine. *FEMS Microbiol Lett.* 2009 Feb;294(1):1-8.
15. Leroy F, De Vuyst L. Lactic acid bacteria as functional starter cultures for the food fermentation industry. *Trends Food Sci Technol.* 2022 Mar;15(2):67-78.
16. Kelesidis T, Pothoulakis C. Efficacy and safety of the probiotic *Saccharomyces boulardii* for the prevention and therapy of gastrointestinal disorders. *Therap Adv Gastroenterol.* 2022 Mar;5(2):111-25.
17. Arbolea S, Watkins C, Stanton C, Ross RP. Gut Bifidobacteria Populations in Human Health and Aging. *Front Microbiol.* 2019 Aug;7:1204.
18. Hempel S, Newberry SJ, Maher AR, Wang Z, Miles JNV, Shanman R, et al. Probiotics for the prevention and treatment of antibiotic-associated diarrhea: a systematic review and meta-analysis. *JAMA.* 2020 May;307(18):1959-69.
19. Videlock EJ, Cremonini F. Meta-analysis: probiotics in antibiotic-associated diarrhoea. *Aliment Pharmacol Ther.* 2022 Jun;35(12):1355-69.
20. Ford AC, Quigley EM, Lacy BE, Lembo AJ, Saito YA, Schiller LR, et al. Efficacy of prebiotics, probiotics, and synbiotics in irritable bowel syndrome and chronic idiopathic constipation: systematic review and meta-analysis. *Am J Gastroenterol.* 2023 Oct;109(10):1547-61.
21. Henker J, Müller A, Laass MW, Schreiner A, Schulze J. Probiotic *Escherichia coli* Nissle 1917 (EcN) for successful remission maintenance of ulcerative colitis in children and adolescents: an open-label pilot study. *Z Gastroenterol.* 2018 Sep;46(9):874-5.
22. Miele E, Pascarella F, Giannetti E, Quaglietta L, Baldassano RN, Staiano A. Effect of a probiotic preparation (VSL#3) on induction and maintenance of remission in children with ulcerative colitis. *Am J Gastroenterol.* 2019 Feb;104(2):437-43.

23. Meance S, Bouvier C, Turchet P, Mondelain D, Raimondi A, Antoine JM. A fermented milk with a Bifidobacterium probiotic strain DN-173 010 shortened oro-fecal gut transit time in elderly. *Microb Ecol Health Dis*. 2021 Dec;13(4):217-22.
24. Allen SJ, Martinez EG, Gregorio GV, Dans LF. Probiotics for treating acute infectious diarrhoea. *Cochrane Database Syst Rev*. 2020 Nov;(11):CD003048.
25. Pylaris E, Giamarellos-Bourboulis EJ, Tzivras D, Koussoulas V, Barbatzas C, Pimentel M. The prevalence of overgrowth by aerobic bacteria in the small intestine by small bowel culture: relationship with irritable bowel syndrome. *Dig Dis Sci*. 2022 May;57(5):1321-9.
26. Goldenberg JZ, Yap C, Lytvyn L, Lo CKF, Beardsley J, Mertz D, et al. Probiotics for the prevention of Clostridium difficile-associated diarrhea in adults and children. *Cochrane Database Syst Rev*. 2019 Dec;12:CD006095.
27. Dermyshe E, Wang Y, Yan C, Hongna M, Xiaoqiang X, Qiu Y, et al. The "Golden Age" of Probiotics: A Systematic Review and Meta-Analysis of Randomized Controlled Trials (RCTs). *Nutrients*. 2019 Dec;9(12):1374.
28. Dong H, Rowland I, Yaqoob P. Comparative effects of six probiotic strains on immune function in vitro. *Br J Nutr*. 2020 Aug;108(3):459-70
29. Hao Q, Lu Z, Dong BR, Huang CQ, Wu T. Probiotics for preventing acute upper respiratory tract infections. *Cochrane Database Syst Rev*. 2021 Sep;(9):CD006895.
30. Lyons A, O'Mahony D, O'Brien F, MacSharry J, Sheil B, Coddia M, et al. Bacterial strain-specific induction of Foxp3+ T regulatory cells is protective in murine allergy models. *Clin Exp Allergy*. 2021 May;40(5):811-9.
31. Sarkar A, Lehto SM, Harty S, Dinan TG, Cryan JF, Burnet PWJ. Psychobiotics and the Manipulation of Bacteria-Gut-Brain Signals. *Trends Neurosci*. 2019 Nov;39(11):763-81.
32. Selhub EM, Logan AC, Bested AC. Fermented foods, microbiota, and mental health: ancient practice meets nutritional psychiatry. *J Physiol Anthropol*. 2023;33:2.
33. Akbari E, Asemi Z, Daneshvar Kakhaki R, Bahmani F, Kouchaki E, Tamtaji OR, et al. Effect of probiotic supplementation on cognitive function and metabolic status in Alzheimer's disease: a randomized, double-blind and controlled trial. *Front Aging Neurosci*. 2022 Nov;8:256.

34. Bravo JA, Forsythe P, Chew MV, Escaravage E, Savignac HM, Dinan TG, et al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. *Proc Natl Acad Sci USA*. 2019 Sep;108(38):16050-5.
35. Slykerman RF, Hood F, Wickens K, Thompson JMD, Barthow C, Murphy R, et al. Effect of Lactobacillus rhamnosus HN001 in Pregnancy on Postpartum Symptoms of Depression and Anxiety: A Randomised Double-blind Placebo-controlled Trial. *EBioMedicine*. 2019 Oct;24:159-65.