International Journal of Environmental Sciences
ISSN: 2229-7359
Vol. 11 No. 20s, 2025
https://theaspd.com/index.php

Probiotics, Encompassing Lactic Acid Bacteria, Are Perpetually Updated In Their Attributes And Significance In Human Health

Rohit Kamal[1], Sudhanshu[2], Gaurav Kothiyal[3], Shrishti Raturi[4], Dr. Deepak Som[5]
[1]Ph.D Scholar (Microbiology), Department of Microbiology, School of Basic and Applied Sciences, Shri Guru Ram Rai University Dehradun India
[2] PhD Scholar (Biotechnology), Department of Biotechnology, School of Basic and Applied Sciences, Shri Guru Ram Rai University Dehradun India
[3]Ph.D Scholar (Microbiology), Department of Microbiology, School of Basic and Applied Sciences, Shri Guru Ram Rai University Dehradun India
[4]Ph.D Scholar (Microbiology), Department of Microbiology, School of Basic and Applied Sciences, Shri Guru Ram Rai University Dehradun India
[5]Associate Professor (Microbiology), Department of Microbiology, School of Basic and Applied Sciences, Shri Guru Ram Rai University Dehradun India

Abstract
The gut contains over 100 trillion microorganisms, including probiotics, which maintain physiological homeostasis. Probiotics must be human-safe, resistant to stomach acid, bile salts, and pancreatic juice, and survive in suitable concentrations to provide health benefits. Bile affects intestinal bacteria's function, suggesting isolated strains of bacteria could be potential probiotic cultures for food industries. Lactobacilli, a crucial group, can inhibit harmful microflora and restore gut flora, with these isolated strains showing excellent potential.

INTRODUCTION

In recent years, many studies have been conducted to gather scientific evidence for the positive effects of fermented foods containing probiotic bacteria (M. succi et al., 2005). Traditionally, probiotics have been utilised in dairy products such as milk or yogurt and it has been hypothesized that milk enhances probiotic efficacy by providing lactose as a substrate (Varcoe et al., 2002).[1] With today's need for health-promoting foods that provide nutrients, disease prevention abilities, and other health advantages, recent biological discoveries have sparked growing commercial interest in introducing probiotic bacteria to fermented dairy products. It has been proposed that diet can influence physiological processes other than feeding.[2] Lactic acid bacteria (LAB) are a crucial microorganism in the dairy, probiotics, and food and beverage sectors due to their generally recognized as safe (GRAS) status and unique features that make them suited for certain uses.[3] Probiotics are used to treat an assortment of health conditions, including inflammation, irritable bowel syndrome, bowel disease, acute diarrhea, antibiotic-associated diarrhea, constipation, high blood pressure, allergy-related diseases, and diabetes; however, their efficacy is dependent on epithelial cell adhesion, cholesterol absorption ability, tolerance to gastrointestinal diseases, bile salt hydrolysis, non-hemolytic activity, and protection against viral genes.[4-5] In recent years, millets have been used as probiotics and products, as well as millet-based beverages. Millets, grains, and legumes are rich in nutrients such as fiber, probiotics, and prebiotics. Probiotic products are developed using these substances since they provide nutrition for probiotic cells and protect them from dangers in the gastrointestinal tract.[6] The International Scientific Association for Probiotics and Prebiotics (ISAPP) defines fermented meals and beverages as “foods made through desired microbial growth and enzymatic conversions of food components” (Marco et al., 2021).[7] It can be an appealing choice for diet as these foods are packed with essential nutrients including B and E vitamins, protein, iron, carbohydrates, fiber, and various trace minerals. Adding grains to your meals could help lower the risk of chronic diseases.[8] Lactic acid bacteria have been used in food and alcoholic fermentation for 6000 years, and their anti-microbial substances, such as alcohol, propionic acid and lactic acid, have excellent anti-fungal, anti-bacterial, and anti-viral properties. Lactose synthesized toxins are antimicrobial substances that prevent the growth of closely related bacteria by lowering pH levels and denaturing membrane proteins, thereby reducing membrane permeability and stopping pathogen growth.[9-10]

CLASSIFICATION

There are many different microorganisms currently used as probiotics. Probiotics are diverse microorganisms with various nomenclature and classification. Bacteria are classified by their genus (Lactobacillus) and species (delbrueckii), based on common characteristics like physical and metabolic needs. Species are more precise, distinguishing them from other species. Strains divide individuals within the same species into smaller groups based on various traits, further dividing them into distinct groups. [11-13]

Lactobacillus spp.	delbrueckii
	plantarum
	reuteri
	fermentum
	delbrueckii

Preliminary research suggests that Lactobacilli probiotics can stabilize the mucosal barrier, decrease intestinal permeability, and potentially reduce the severity of chemotherapy-induced enterocolitis, particularly L. plantarum, by lowering vaginal pH.[14-17] Hormone fluctuations during a woman's menstrual cycle may hinder her capacity to colonize lactobacillus, however addressing low estrogen levels can restore colonization without the need for supplements.[18-19]

Bile Resistance mechanism in lactobacillus:

Bile resistance mechanisms in Lactobacillus represent a captivating area of study within the field of microbiology, shedding light on the intricate ways these bacteria navigate and thrive in the harsh environment of the gastrointestinal tract.[35] Lactobacillus, a genus of Gram-positive, lactic acid-producing bacteria, is a common resident of the gut microbiota and is renowned for its probiotic properties.[36]Lactobacillus, a bacterial species, has developed a unique resistance to bile salts, a component of bile, by altering its cell membrane composition. This modification, known as the cytoplasmic membrane or lipid bilayer, acts as a protective barrier, separating the bacterial cell from its external environment. Bile salts can disrupt this membrane, causing cell damage and lysis. To counteract this, Lactobacillus uses various mechanisms to fortify its cell membrane. One significant modification is the fatty acid composition, which can be adjusted to enhance its stability and integrity in the presence of bile salts. This involves increasing the saturation of fatty acids, which create a more rigid and less permeable membrane. Additionally, the length of fatty acid chains can be adjusted to fine-tune the membrane's physical properties. These modifications are dynamic, allowing Lactobacillus to quickly adjust to changing gastrointestinal conditions.[37]

Probiotics have three modes of action: modulating host defenses, directly affecting other microorganisms, and affecting microbial products like toxins and host products. These actions are crucial for preventing and treating infectious diseases, restoring microbial equilibrium in the gut, and inactivating toxins and detoxifying host and food components in the gut. The action mode depends on metabolic properties, surface molecules, and secreted components.[20] Because probiotics compete with pathogens for adhesion sites, or cellular attachments, they have been shown to have advantageous effects. By acting as "colonization barriers," probiotics can stop pathogens from adhering to the mucosa. For instance, probiotics such as Lactobacillus rhamnosus strain GG and Lactobacillus plantarum 299v have been shown to effectively inhibit pathogens that need to associate with the GI tract epithelium in order to colonize.[21] Probiotics can stimulate the immune response, leading to increased secretion of immunoglobulin-A (IgA), increased natural killer cells, and enhanced phagocytic activity of macrophages. This can decrease pathogenic organisms in the gut, improving the microflora. Probiotics may also fight intestinal and urogenital pathogens, help with conditions like inflammatory bowel disease, pouchitis, food allergy, and as an adjuvant to vaccination. They may also compete for nutrients, as seen with Clostridium difficile, which can be inhibited by probiotics in sufficient numbers.[22]

An overview of bile production and secretion is given at the outset of this review, which is followed by an explanation of the resistance mechanism in lactobacillus actions of bile, an analysis of variations in bile mechanism in various bacterial genera, and an examination of the molecular mechanisms underlying tolerance. Among its primary components are bile acids, cholesterol, phospholipids (mostly phosphatidylcholine), and biliverdin (bili in Latin means bile, verdin in Italian means green).[23-26]

A powerful antimicrobial property of bile also contributes to the body's physicochemical defense system. The ability to survive in the small intestine and, consequently, to develop their probiotic function is largely determined by bile tolerance (Lilley, Razzaq, & Dupree, 2002).[27]

BA toxicity is generally more pronounced in Gram-positive bacteria than in Gram-negative bacteria, as the minimum inhibitory concentrations in the first group are significantly lower than in the second. In some cases, the differences can be explained by the presence of lipopolysaccharide that constitutes the majority of the outer leaflet of outer membranes, as well as proteins that function as efflux pumps and proteins.[28-29] The main proteins whose expression was controlled by bile in bacteria, according to earlier and more recent research, are those involved in carbohydrate metabolism, fatty acid, amino acid, and nitrogenous base biosynthesis, as well as transporters that can extrude bile salts and proteins involved in general stress response.[30-32] The key resistance mechanisms identified in intestinal bacteria include the structure and make-up of the cell membrane, the existence of efflux pumps, the function of the BSH enzyme, and the inherent ability of cells to maintain intracellular homeostasis.[33] Specific proteomic findings revealed the existence of protective mechanisms allowing an adaptive response to low pH exposure that could also provide a cross-protection against other stress conditions such as the presence of bile (Lee et al., 2008).[34]

Mechanisms of Probiotic Action on Viruses:

Probiotic bacteria are irreversibly attached to viruses, limiting their binding effect to the host cell receptor. They can obstruct viral attachment on the epithelial surface through steric hindrance and inhibit virus replication through mucin attachments. Probiotics also produce antimicrobial metabolites and contribute to antiviral processes through dehydrogenase synthesis. Epithelial cells stimulate immune responses, causing macrophages and dendritic cells to stimulate the immune response. Viral cells are destroyed by CD8 T cells and T lymphocytes, leading to Th1 and Th2 helper T cells, and ultimately, Ig producing plasma cells.[38] Studies show lactic acid bacteria's potential for treating viral illnesses and infections, with some showing health-promoting antiviral activities, including anti-influenza properties in mice, demonstrating their potential benefits.[39-40] Lactic acid bacteria are recognized as effective antidotes for various viral illnesses, but developing effective medications like COVID 19 remains a significant challenge due to the potential side effects of traditional antiviral drugs, which are the leading cause of death worldwide.[41] The immune system, especially in high-risk groups such as the elderly and children, is very vulnerable to viral infections due to weak immunological function. To solve these issues, it is critical to use probiotic lactic acid bacteria as a weapon against viral infections. These bacteria and their metabolic products can exhibit antiviral activity through a variety of ways, including direct viral contact, production of antiviral inhibitory chemicals, immune system regulation, and stimulation. According to research, the antiviral properties of probiotic lactic acid bacteria vary by strain. This method is critical for maintaining public health and combatting viral infections.[42]

Hurdles to Overcome during Passage through the GIT:

The FAO/WHO (2002) Expert Group states that strain identification should lead to functional characterization, which includes figuring out whether the strain can survive in the GIT. FAO/WHO (2002) and Kiran et al. (2015) report that strains incapable of surviving in the upper and lower gastrointestinal tracts will not be able to settle there and thus will not be able to fulfill their intended roles in the body. Tolerance to high bile salt concentrations and low stomach pH are the two most crucial factors to take into account when choosing probiotic strains. Probiotic bacteria need to be able to endure in the human digestive system in order to be profitable.[43]Probiotic bacteria in food travel through the esophagus to the stomach, producing 2.5 liters of gastric juice daily. The stomach's pH ranges from 4.0 to 3.0, with food causing it to rise. They break down proteins, rennet curdles milk proteins, and distribute emulsified fats. Food stays in the stomach for two hours before moving to the lower digestive tract. Probiotic bacteria face challenges during the gastric phase. Intestinal juice, produced daily with a pH of 7.0-8.0, is broken down by enzymes like pancreatic amylase, maltase, trypsin, elastase, lipase, and nuclease. The pH of small intestine juice is around 7.0. Intestinal lipase is a enzyme that breaks down emulsified fat on monoacylglycerols, fatty acids, and glycerols. It also breaks down aminopeptidase and carboxypeptidase, disrupting peptide bonds. Bile salts, which have a bactericidal effect, increase bacterial cell membrane permeability and lysis. Bile salt hydrolase (BSH) hydrolyzes bile salts, a natural defense mechanism against their toxic effects. BSH typically cleaves glycine or taurine moieties from conjugated bile salts (Vandenplas et al., 2015).[44]

Lactobacillus as probiotic:

The acronym "probiotic" is Greek in origin and means "for life." Lilley and Stillwell originally implemented the term to describe chemicals released by one microbe that promote the growth of another in 1965.[45-46] The first to provide a scientific justification for the advantages of lactic acid bacteria in

fermented milk was a Russian bacteriologist named Eli Metchnikoff (Pasteur Institute, France) in 1908.[47-48] Since ancient times, the bacteria contained in fermented milk have been used as probiotics for therapeutic purposes. Hippocrates and several other scientists utilised sour milk to treat stomach and bowel disorders since they held the view that fermented milk could serve as both food and medicine.[49] A probiotic is a dietary supplement made up of living bacteria that are common in normal flora and have little to no toxicity.[50-51] Probiotics are currently defined as "live microorganisms which when administered in adequate amounts confer a health benefit to the host" by the Food and Agriculture Organisation of the United Nations (FAO) and the World Health Organisation (WHO).[52-53] Numerous gastrointestinal conditions, such as infectious diarrhea, irritable bowel syndrome, inflammatory bowel disease, etc., have been treated with probiotics. The effectiveness of probiotics, such as Lactobacillus sp., has recently been the subject of much research. Clinical trials comparing Lactobacillus probiotics with placebos or standard remedies have been done for a variety of gastrointestinal diseases, endeavors to control cholesterol, bacterial vaginoses, and even attempts to control the immune system.[54]

Other use of lactobacillus bacteria:

All vertebrate newborns require lactose, a disaccharide that is converted into glucose and galactose, among other essential nutrients. Most the populace see a decline this at the age of five, which results in low lactase levels from that point on.[55] Lactate persistence is an inherited trait in humans which many people manage to maintain throughout their adult life.[56] Abdominal pain, bloating, flatulence, and diarrhoea are some symptoms of lactose intolerance. Probiotic supplements or lactase tablets are highly recommended in cases of poor lactase activity in people.[57-58] Gyawali et al. (2020) have revealed that L. bulgaricus strains could release the highest quantity of galactosidase, bolstering the use of lactic acid bacteria as probiotics in the treatment of lactose intolerance.[59]

Diabetes:

In research-based studies, it has been demonstrated that probiotics can positively affect the gut microbiota and are therefore considered a promising treatment for diabetes.[60] The microbiota of the gastrointestinal tract is crucial in the pathogenesis of resistant insulin action (type 2 diabetes). Moreover, several research on both humans and animals have hypothesized that the gut microbiome promotes body weight gain and heightens resistance to insulin. Also, several research indicates that gut microbiota increases body weight gain and insulin resistance and that these disorders are therefore spread with gut microbiota, as observed in microbiota implantation experiments from obese to normal and germ-free mice.[61-63] In the intestinal microenvironment, Gram-positive firmicutes predominate. These bacteria influence metabolic illnesses such as diabetes in human.[64-65] It has been shown that the amount of Firmicutes species is considerably lower in individuals with type 2 diabetes, which is favorably connected with the glucose concentration in the plasma.[66]

Inflammatory Bowel Diseases and Irritable Bowel Syndrome:

Changes in normal intestinal flora produce inflammatory bowel illnesses such pouchitis and Crohn's disease. Probiotics have been found to be a possible medicinal benefit since they may reduce such ailments through gut microbiota alteration.[67-68] This study analyzed randomized clinical trials published between 1990 and 2014 on dairy products and probiotics in relation to inflammatory bowel disease, Crohn's disease, and ulcerative colitis. The review focused on specific LAB and bifidobacteria results and explored the possible probiotic mechanism of action in IBD. Nutrition is crucial in preventing malnutrition and potential deficiencies in IBD and Crohn's disease. A varied diet rich in fiber and fruits may be protective. Probiotics can improve IBD patients' quality of life by increasing intestinal biodiversity and improving symptoms. However, no specific diet has been proven to prevent or treat IBD. Chronic inflammatory bowel disease (CD) is treated with corticosteroids and maintenance therapy with aminosalicylates and immunomodulators. Probiotics and prebiotics are considered therapeutic strategies for CD patients. 5-aminosalicylic acid (5-ASA) is more effective than placebo in preventing relapses, but negative results have been reported.[69]

Cancer:

Probiotics have been researched in animal tumour models for their capacity to prevent colon cancer and the beginning of various malignancies. Some gut bacteria may create carcinogens such as nitrosamines. Understanding this phenomena is crucial since administration of lactobacilli and bifidobacteria decreases absorption of dangerous mutagens as well as β-glucuronidase and carcinogen levels via gut flora change.[70] According to research, L. casei Shirota and probiotic intestinal infusion may prevent cancer recurrence.[71]

Cardiovascular Diseases:

Recent clinical studies have demonstrated the therapeutic effects of probiotics in the management of cardiovascular diseases, most notably hypertension. Probiotics have been shown to reduce systolic and diastolic blood pressure in hypertensive people.[72] Diabetes, hypercholesterolemia, and other disorders are frequently connected with cardiovascular disease. Changes in the gut microbiota frequently result in elevated levels of trimethylamine N-oxide (TMAO), which is related with an increased risk of significant cardiovascular disease.[73]

Allergy:

A complex probiotic including Bifidobacterium breve, Lactobacillus rhamnosus GG, and Propionibacterium freudenreichii given to pregnant mothers decreased the prevalence of atopic dermatitis in children under the age of two.[74] A research used three strains to avoid allergy illness (Bifidobacterium longum subsp. infantis LA308, Lactobacillus rhamnosus LA305, and Lactobacillus salivarius LA307). [75]There is currently no evidence that probiotics can promote allergy tolerance, according to Tang et al 2015.[76]

Probiotics in asthma:

There have been a few research that look at the usefulness of probiotic supplements in the prevention of asthma. Although there was no statistically significant difference between the intervention and control groups of children with asthma in one study using L. casei containing fermented milk, the probiotic group had fewer rhinitis episodes, which led the authors to draw the conclusion that L. casei may help children with allergic rhinitis but not children with asthma.[77]

Gut–Brain Axis:

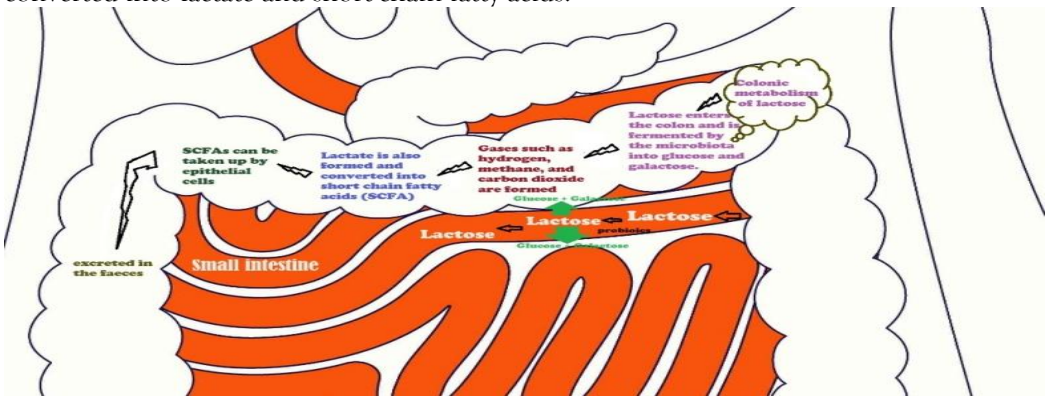
Probiotics have been found to improve human health, notably in the treatment of gastrointestinal problems. They serve an important function in colonizing the gastrointestinal system, which aids in the prevention and treatment of several diseases. However, there is considerable interest in understanding how gut microbes affect the brain and the overall central nervous system. The gut microbiota and the brain communicate bidirectionally, with regulatory signals transferred between the two. Clinical studies have demonstrated that probiotics can improve children's academic performance as well as their eating habits.[78-79]

Acute Diarrheal Disease:

Probiotics can shorten diarrhea by 13 hours and reduce treatment failure by 38%, making them useful for avoiding diarrhea in children. A Cochrane review of 63 randomized and quasi-randomized controlled trials found that probiotics reduced diarrhea duration by 25 hours, reduced the likelihood of diarrhea lasting ≥4 days by 59%, and decreased stool frequency by one bowel movement on day 2. Another meta-analysis found that L. rhamnosus GG was more effective than placebo at reducing diarrhea symptoms in children with rotavirus.[80-83]

Lactose Intolerance:

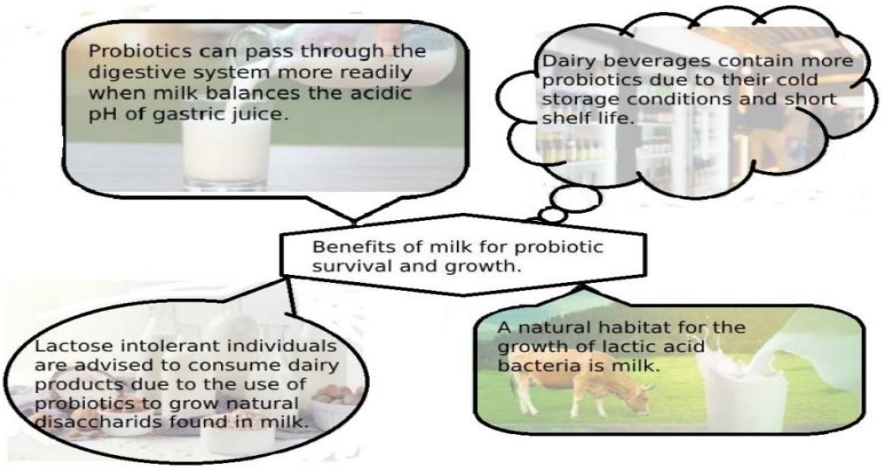
Lactose, a crucial nutrient in all mammals, is broken down into glucose and galactose. Most humans' lactase activity declines during middle childhood, resulting in low lactase levels. However, many people maintain high lactate levels throughout their adult lives. Lactase persistence is a dominant trait, whereas lactase non-persistence is recessive. Lactose intolerance or lactose malabsorption occurs when the small intestine fails to produce adequate lactase after consuming milk. This condition affects small intestinal digestion and colonic fermentation, resulting in clinical symptoms.β-galactosidase, a bacterial enzyme found in the colon, breaks down unabsorbed lactose. This produces glucose and galactose, which are converted into lactate and short-chain fatty acids.



This results in increased osmotic load in the colon, potentially leading to diarrhea due to the formation of microbial biomass, lactose, and intermediate and final products. Lactose intolerance symptoms include abdominal pain, bloating, flatulence, and diarrhea. Probiotic supplements or lactase tablets are recommended for low lactase activity in humans. Overproduced β-galactosidase mutants alleviate lactose malabsorption symptoms. Milk containing L. acidophilus improves lactose absorption. Probiotics can improve colonic microbiota population, potentially treating lactose intolerance.[84-85]

Advantages of Milk as a Primary Ingredient in Probiotic Food Production:

The basis for dairy products that go through fermentation using specific LAB starter cultures is whole milk or reconstituted milk powder with modified fat content. Traditional fermented milk products such as buttermilk, kefir, sour milk, yogurt drinks, and whey beverages fall into the first group; drinks made with carefully chosen probiotic starting cultures go into the second. Dairy products are a common component of probiotic diets due to their high nutritional content and ease of access. Given the current status of the dairy business, creating so-called synbiotic products—made with prebiotics like oligofructose or inulin—is the only method to promote the growth of probiotic strains in fermented meals.[86]



The most widely consumed probiotic dairy products are various types of yogurt and acidophilus milk, whether sweet or sour. According to Mituniewicz-Małek et al. (2013), the probiotic strains that are primarily used to make these beverages are Lactobacillus rhamnosus, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus paracasei, Lactobacillus johnsonii, Bifidobacterium bifidum, Bifidobacterium longum and Lactobacillus plantarum,. Furthermore, LAB isolated from conventional fermented food products is used in products currently in production.[87-88]

CONCLUSION

The COVID-19 pandemic has highlighted the importance of natural remedies like probiotics and lactic acid fermented foods for enhancing the immune system and preventing viral infections. These natural food products can boost immunity and serve as a first line of defense against the virus. Live vaccine prophylaxis could benefit from lactic acid bacteria, which can deliver antigens to the immune system and generate specific antibody responses. Further clinical investigation is needed to fully understand their potential.[89]

REFERENCES

1.Arshad, F. A., Mehmood, R., Hussain, S., Khan, M. A., & Khan, M. S. (2018). Lactobacilli as probiotics and their isolation from different sources. British Journal of Research, 5(3), 43.
2.Umer Khan, S. (2014). Probiotics in dairy foods: a review. Nutrition & Food Science, 44(1), 71-88.
3.Khushboo, Karnwal, A., & Malik, T. (2023). Characterization and selection of probiotic lactic acid bacteria from different dietary sources for development of functional foods. Frontiers in microbiology, 14, 1170725.
4.A'inurrofiqin, M., Rahayu, E. S., Suroto, D. A., Utami, T., & Mayangsari, Y. (2022). Safety assessment of the indigenous probiotic strain Lactiplantibacillus plantarum subsp. plantarum Kita-3 using Sprague–Dawley rats as a model. AIMS microbiology, 8(4), 403.
5.M'hamed, A. C., Ncib, K., Merghni, A., Migaou, M., Lazreg, H., Snoussi, M., ... & Maaroufi, R. M. (2022). Characterization of probiotic properties of Lacticaseibacillus paracasei L2 isolated from a traditional fermented food "Lben". Life, 13(1), 21.
6.Desrouillères, K., Millette, M., Bagheri, L., Maherani, B., Jamshidian, M., & Lacroix, M. (2020). The synergistic effect of cell wall extracted from probiotic biomass containing Lactobacillus acidophilus CL1285, L. casei LBC80R, and L. rhamnosus CLR2 on the anticancer activity of cranberry juice—HPLC fractions. Journal of food biochemistry, 44(5), e13195.

7. Marco, M. L., Sanders, M. E., Gänzle, M., Arrieta, M. C., Cotter, P. D., De Vuyst, L., ... & Hutkins, R. (2021). The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on fermented foods. Nature Reviews Gastroenterology & Hepatology, 18(3), 196-208.
8. Bembem, K., & Agrahar-Murugkar, D. (2020). Development of millet based ready-to-drink beverage for geriatric population. Journal of Food Science and Technology, 57(9), 3278-3283.
9. Mokoena, M. P., Mutanda, T., & Olaniran, A. O. (2016). Perspectives on the probiotic potential of lactic acid bacteria from African traditional fermented foods and beverages. Food & Nutrition Research, 60(1), 29630.
10. Gupta, R., Jeevaratnam, K., & Fatima, A. (2018). 'Lactic Acid Bacteria: Probiotic Characteristic, Selection Criteria, and its Role in Human Health (A Review)'. Rahul Gupta, Kadirvelu Jeevaratnam, Amrin Fatima. Lactic Acid Bacteria: Probiotic Characteristic, Selection Criteria, and its Role in Human Health (A Review), International Journal of Emerging Technologies and Innovative Research (www. jetir. org), 5(10).
11. Khalighi, A., Behdani, R., & Kouhestani, S. (2016). Probiotics: a comprehensive review of their classification, mode of action and role in human nutrition. Probiotics and prebiotics in human nutrition and health, 10, 63646.
12. Goldin, B. R. (1998). Health benefits of probiotics. British Journal of Nutrition, 80(S2), S203-S207.
13. Macfarlane, G. T., & Cummings, J. H. (1999). Probiotics and prebiotics: can regulating the activities of intestinal bacteria benefit health?. Bmj, 318(7189), 999-1003.
14. Shornikova, A. V., Casas, I. A., Isolauri, E., Mykkänen, H., & Vesikari, T. (1997). Lactobacillus reuteri as a therapeutic agent in acute diarrhea in young children. Journal of pediatric gastroenterology and nutrition, 24(4), 399-404.
15. Alander, M., Satokari, R., Korpela, R., Saxelin, M., Vilpponen-Salmela, T., Mattila-Sandholm, T., & von Wright, A. (1999). Persistence of colonization of human colonic mucosa by a probiotic strain, Lactobacillus rhamnosus GG, after oral consumption. Applied and environmental microbiology, 65(1), 351-354.
16. Sullivan, Å., Barkholt, L., & Nord, C. E. (2003). Lactobacillus acidophilus, Bifidobacterium lactis and Lactobacillus F19 prevent antibiotic-associated ecological disturbances of Bacteroides fragilis in the intestine. Journal of Antimicrobial Chemotherapy, 52(2), 308-311.
17. Mao, Y. I. L. E. I., Nobaek, S. O. R. E. N., Kasravi, B. E. H. Z. A. D., Adawi, D. I. Y. A., Stenram, U. N. N. E., Molin, G. O. R. A. N., & Jeppsson, B. E. N. G. T. (1996). The effects of Lactobacillus strains and oat fiber on methotrexate-induced enterocolitis in rats. Gastroenterology, 111(2), 334-344.
18. McGroarty JA. Probiotic use of lactobacilli in the human female urogenital tract. FEMS Immunology and Medical Microbiology. 1993;6(4):251–64.
19. Bruce AW, Reid G. Intravaginal instillation of lactobacilli for prevention of recurrent urinary tract infections. Canadian Journal of Microbiology. 1988;34(3):339–43.
20. Figueroa-González, I., Cruz-Guerrero, A., & Quijano, G. (2011). The benefits of probiotics on human health. J Microbial Biochem Technol S, 1, 1948-5948.
21. Khalighi, A., Behdani, R., & Kouhestani, S. (2016). Probiotics: a comprehensive review of their classification, mode of action and role in human nutrition. Probiotics and prebiotics in human nutrition and health, 10, 63646.
22. Miele, E., Pascarella, F., Giannetti, E., Quaglietta, L., Baldassano, R. N., & Staiano, A. (2009). Effect of a probiotic preparation (VSL# 3) on induction and maintenance of remission in children with ulcerative colitis. Official journal of the American College of Gastroenterology| ACG, 104(2), 437-443.
23. Fausto, N., & Webber, E. M. (1994). The liver: biology and pathobiology. Arias, IM, Boyer, JL, Fausto, N., Jacoby, WB, Schachter, D., Shafritz, DA, Eds, 53-68.
24. Erlinger, S. (1994). Bile flow In: The Liver: Biology and Pathobiology (Arias, IM, Boyer, JL, Fausto, N., Jackoby, DA, Schachter, DA and Shafritz, DA, Eds.).
25. Hofmann, A. F. (1999). Bile acids: the good, the bad, and the ugly. Physiology, 14(1), 24-29.
26. Johnson, L. R. (1998). Bile secretion and gallbladder function. Essential Medical Physiology, 2, 465-471.
27. Lilley, K. S., Razzaq, A., & Dupree, P. (2002). Two-dimensional gel electrophoresis: recent advances in sample preparation, detection and quantitation. Current opinion in chemical biology, 6(1), 46-50.
28. Bustos, A. Y., de Valdez, G. F., Fadda, S., & Taranto, M. P. (2018). New insights into bacterial bile resistance mechanisms: the role of bile salt hydrolase and its impact on human health. Food Research International, 112, 250-262.
29. Horáčková, Š., Plocková, M., & Demnerová, K. (2018). Importance of microbial defence systems to bile salts and mechanisms of serum cholesterol reduction. Biotechnology Advances, 36(3), 682-690.
30. Bustos, M. C., Perez, G. T., & Leon, A. E. (2015). Structure and quality of pasta enriched with functional ingredients. Rsc Advances, 5(39), 30780-30792.
31. Ruiz, J., Olivieri, G., De Vree, J., Bosma, R., Willems, P., Reith, J. H., ... & Barbosa, M. J. (2016). Towards industrial products from microalgae. Energy & Environmental Science, 9(10), 3036-3043.
32. Šárka, E., Sluková, M., & Henke, S. (2021). Changes in phenolics during cooking extrusion: A review. Foods, 10(9), 2100.
33. Liao, Y. S., Chen, B. H., Teng, R. H., Wang, Y. W., Chang, J. H., Liang, S. Y., ... & Chiou, C. S. (2022). Antimicrobial resistance in Campylobacter coli and Campylobacter jejuni from human campylobacteriosis in Taiwan, 2016 to 2019. Antimicrobial Agents and Chemotherapy, 66(1), e01736-21.
34. Wu, R. A., Yuk, H. G., Liu, D., & Ding, T. (2022). Recent advances in understanding the effect of acid-adaptation on the cross-protection to food-related stress of common foodborne pathogens. Critical Reviews in Food Science and Nutrition, 62(26), 7336-7353.
35. Gillor, O., Etzion, A., & Riley, M. A. (2008). The dual role of bacteriocins as anti-and probiotics. Applied microbiology and biotechnology, 81, 591-606.
36. Sanders, M. E., Merenstein, D. J., Ouwehand, A. C., Reid, G., Salminen, S., Cabana, M. D., ... & Leyer, G. (2016). Probiotic use in at-risk populations. Journal of the American Pharmacists Association, 56(6), 680-686.
37. Bron, P. A., Molenaar, D. O. U. W. E., de Vos, W. M., & Kleerebezem, M. I. C. H. I. E. L. (2006). DNA micro-array-based identification of bile-responsive genes in Lactobacillus plantarum. Journal of applied microbiology, 100(4), 728-738.

38. Ayivi, R. D., Gyawali, R., Krastanov, A., Aljaloud, S. O., Worku, M., Tahergorabi, R., ... & Ibrahim, S. A. (2020). Lactic acid bacteria: Food safety and human health applications. Dairy, 1(3), 202-232.
39. Harata, G., He, F., Hiruta, N., Kawase, M., Kubota, A., Hiramatsu, M., & Yausi, H. (2010). Intranasal administration of Lactobacillus rhamnosus GG protects mice from H1N1 influenza virus infection by regulating respiratory immune responses. Letters in applied microbiology, 50(6), 597-602.
40. Kobayashi, N., Saito, T., Uematsu, T., Kishi, K., Toba, M., Kohda, N., & Suzuki, T. (2011). Oral administration of heat-killed Lactobacillus pentosus strain b240 augments protection against influenza virus infection in mice. International immunopharmacology, 11(2), 199-203.
41. Nagai, T., Makino, S., Ikegami, S., Itoh, H., & Yamada, H. (2011). Effects of oral administration of yogurt fermented with Lactobacillus delbrueckii ssp. bulgaricus OLL1073R-1 and its exopolysaccharides against influenza virus infection in mice. International immunopharmacology, 11(12), 2246-2250.
42. Al Kassaa, I., Hober, D., Hamze, M., Chihib, N. E., & Drider, D. (2014). Antiviral potential of lactic acid bacteria and their bacteriocins. Probiotics and antimicrobial proteins, 6, 177-185.
43. Minekus, M., Alminger, M., Alvito, P., Ballance, S., Bohn, T. O. R. S. T. E. N., Bourlieu, C., ... & Brodkorb, A. (2014). A standardised static in vitro digestion method suitable for food–an international consensus. Food & function, 5(6), 1113-1124.
44. Vandenplas, Y., Huys, G., & Daube, G. (2015). Probióticos: informações atualizadas. Jornal de pediatria, 91, 06-21.
45. Khalighi, A., Behdani, R., & Kouhestani, S. (2016). Probiotics: a comprehensive review of their classification, mode of action and role in human nutrition. Probiotics and prebiotics in human nutrition and health, 10, 63646.
46. Lilly, D. M., & Stillwell, R. H. (1965). Probiotics: growth-promoting factors produced by microorganisms. Science, 147(3659), 747-748.
47. Hughes, D. B., & Hoover, D. G. (1991). Bifidobacteria: their potential for use in American dairy products.
48. O'sullivan, M. G., Thornton, G., O'sullivan, G. C., & Collins, J. K. (1992). Probiotic bacteria: myth or reality?.
49. Oberman, H. (1985). Fermented milks.
50. Alvarez-Olmos, M. I., & Oberhelman, R. A. (2001). Probiotic agents and infectious diseases: a modern perspective on a traditional therapy. Clinical infectious diseases, 32(11), 1567-1576.
51. Salminen, S., & Arvilommi, H. (2001). Probiotics demonstrating efficacy in clinical settings. Clinical Infectious Diseases, 32(11), 1577-1578.
52. Chieng, J. Y., & Pan, Y. (2021). The role of probiotics, prebiotics and synbiotics in adult gastrointestinal health. Gastroenterology & Hepatology Letters, 3(2), 5-12.
53. Guarner, F., & Schaafsma, G. J. (1998). Probiotics. International journal of food microbiology, 39(3), 237-238.
54. McFarland, L. V. (2007). Meta-analysis of probiotics for the prevention of traveler's diarrhea. Travel medicine and infectious disease, 5(2), 97-105.
55. Daliri, E. B. M., & Lee, B. H. (2015). New perspectives on probiotics in health and disease. Food Science and Human Wellness, 4(2), 56-65.
56. Rai, V. R., & Bai, J. A. (Eds.). (2015). Beneficial microbes in fermented and functional foods (pp. 551-571). Boca Raton, FL: CRC Press.
57. Daliri, E. B. M., & Lee, B. H. (2015). New perspectives on probiotics in health and disease. Food Science and Human Wellness, 4(2), 56-65.
58. Goh, Y. J., & Klaenhammer, T. R. (2013). A functional glycogen biosynthesis pathway in L actobacillus acidophilus: expression and analysis of the glg operon. Molecular microbiology, 89(6), 1187-1200.
59. Gyawali, R., Oyeniran, A., Zimmerman, T., Aljaloud, S. O., Krastanov, A., & Ibrahim, S. A. (2020). A comparative study of extraction techniques for maximum recovery of β-galactosidase from the yogurt bacterium Lactobacillus delbrueckii ssp. bulgaricus. Journal of Dairy Research, 87(1), 123-126.
60. Nagpal, R., Kumar, A., Kumar, M., Behare, P. V., Jain, S., & Yadav, H. (2012). Probiotics, their health benefits and applications for developing healthier foods: a review. FEMS microbiology letters, 334(1), 1-15.
61. Ley, R. E., Bäckhed, F., Turnbaugh, P., Lozupone, C. A., Knight, R. D., & Gordon, J. I. (2005). Obesity alters gut microbial ecology. Proceedings of the national academy of sciences, 102(31), 11070-11075.
62. Ley, R. E., Turnbaugh, P. J., Klein, S., & Gordon, J. I. (2006). Human gut microbes associated with obesity. nature, 444(7122), 1022-1023.
63. Turnbaugh, P. J., Ley, R. E., Mahowald, M. A., Magrini, V., Mardis, E. R., & Gordon, J. I. (2006). An obesity-associated gut microbiome with increased capacity for energy harvest. nature, 444(7122), 1027-1031.
64. Le Barz, M., Anhê, F. F., Varin, T. V., Desjardins, Y., Levy, E., Roy, D., ... & Marette, A. (2015). Probiotics as complementary treatment for metabolic disorders. Diabetes & metabolism journal, 39(4), 291-303.
65. Kobyliak, N., Conte, C., Cammarota, G., Haley, A. P., Styriak, I., Gaspar, L., ... & Kruzliak, P. (2016). Probiotics in prevention and treatment of obesity: a critical view. Nutrition & metabolism, 13, 1-13.
66. Barrett, H. L., Callaway, L. K., & Nitert, M. D. (2012). Probiotics: a potential role in the prevention of gestational diabetes?. Acta diabetologica, 49, 1-13.
67. Upadhyay, N., & Moudgal, V. (2012). Clinical review-probiotics: A Review. JCOM-Journal of Clinical Outcomes Management, 19(2), 76.
68. Joint, F. A. O. (2002). WHO working group report on drafting guidelines for the evaluation of probiotics in food. London, Ontario, Canada, 30(1), 16-22.
69. Saez-Lara, M. J., Gomez-Llorente, C., Plaza-Diaz, J., & Gil, A. (2015). The role of probiotic lactic acid bacteria and bifidobacteria in the prevention and treatment of inflammatory bowel disease and other related diseases: a systematic review of randomized human clinical trials. BioMed research international, 2015(1), 505878.
70. Mendoza, L. (2019). Potential effect of probiotics in the treatment of breast cancer. Oncology reviews, 13(2).
71. Reid, G., Jass, J., Sebulsky, M. T., & McCormick, J. K. (2003). Potential uses of probiotics in clinical practice. Clinical microbiology reviews, 16(4), 658-672.

72. Antony, S., & de Leon, M. P. (2018). Probiotics and its relationship with the cardiovascular system. Probiotics Curr. Knowl. Future Prospect, 52-68.
73. Yoo, J. Y., & Kim, S. S. (2016). Probiotics and prebiotics: present status and future perspectives on metabolic disorders. Nutrients, 8(3), 173.
74. Kukkonen, K., Savilahti, E., Haahtela, T., Juntunen-Backman, K., Korpela, R., Poussa, T., ... & Kuitunen, M. (2007). Probiotics and prebiotic galacto-oligosaccharides in the prevention of allergic diseases: a randomized, double-blind, placebo-controlled trial. Journal of Allergy and Clinical Immunology, 119(1), 192-198.
75. Neau, E., Delannoy, J., Marion, C., Cottart, C. H., Labellie, C., Holowacz, S., ... & Waligora-Dupriet, A. J. (2016). Three novel candidate probiotic strains with prophylactic properties in a murine model of cow's milk allergy. Applied and environmental microbiology, 82(6), 1722-1733.
76. Tang, R. B., Chang, J. K., & Chen, H. L. (2015). Can probiotics be used to treat allergic diseases?. Journal of the Chinese Medical Association, 78(3), 154-157.
77. Tang, R. B., Chang, J. K., & Chen, H. L. (2015). Can probiotics be used to treat allergic diseases?. Journal of the Chinese Medical Association, 78(3), 154-157.
78. Kerry, R. G., Patra, J. K., Gouda, S., Park, Y., Shin, H. S., & Das, G. (2018). Benefaction of probiotics for human health: A review. Journal of food and drug analysis, 26(3), 927-939.
79. Daliri, E. B. M., Ofosu, F. K., Xiuqin, C., Chelliah, R., & Oh, D. H. (2021). Probiotic effector compounds: Current knowledge and future perspectives. Frontiers in Microbiology, 12, 655705.
80. McFarland, L. V., Elmer, G. W., & McFarland, M. (2006). Meta-analysis of probiotics for the prevention and treatment of acute pediatric diarrhea. International journal of probiotics and prebiotics, 1(1), 63.
81. Urbańska, M., Gieruszczak-Białek, D., & Szajewska, H. (2016). Systematic review with meta-analysis: Lactobacillus reuteri DSM 17938 for diarrhoeal diseases in children. Alimentary pharmacology & therapeutics, 43(10), 1025-1034.
82. Szajewska, H., Skorka, A., Ruszczyński, M., & Gieruszczak-Białek, D. (2013). Meta-analysis: L actobacillus GG for treating acute gastroenteritis in children–updated analysis of randomised controlled trials. Alimentary pharmacology & therapeutics, 38(5), 467-476.
83. Zmora, N., Suez, J., & Elinav, E. (2019). You are what you eat: diet, health and the gut microbiota. Nature reviews Gastroenterology & hepatology, 16(1), 35-56.
84. Umer Khan, S. (2014). Probiotics in dairy foods: a review. Nutrition & Food Science, 44(1), 71-88.
85. Ugidos-Rodríguez, S., Matallana-González, M. C., & Sánchez-Mata, M. C. (2018). Lactose malabsorption and intolerance: a review. Food & function, 9(8), 4056-4068.
86. Heller, K. J. (2001). Probiotic bacteria in fermented foods: product characteristics and starter organisms. The American journal of clinical nutrition, 73(2), 374s-379s.
87. Mituniewicz-Małek, A., Ziarno, M., Dymitrow, I., 2013. Application of frozen goat's milk to production of potentially probiotic fermented drink. Food. Sci. Technol. Qual. 6 (103), 140–149.
88. Zielińska, D., Rzepkowska, A., Radawska, A., & Zieliński, K. (2015). In vitro screening of selected probiotic properties of Lactobacillus strains isolated from traditional fermented cabbage and cucumber. Current microbiology, 70, 183-194.
89. Ibrahim, S. A., Gyawali, R., & Fidan, H. (2020). Self-Defense: A practical approach to combatting COVID-19. Acta Sci. Nutr. Health, 4(7), 33-37.