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Review Article

Advances in the probiotic production, innovation, and therapeutic applications in health and nutrition

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Abstract

Microorganisms have long been used to produce primary and secondary metabolites essential for human health and environmental sustainability. Due to their rapid growth and reproduction rates, as well as their ability to undergo genetic modifications, microorganisms play a critical role in the manufacturing industry. Probiotics, which are non-pathogenic microorganisms, have gained significant interest due to their various health benefits, including treating vitamin deficiencies, alleviating digestive disorders, enhancing immunity, and detoxifying harmful substances. Probiotics are commonly used to address gastrointestinal issues such as inflammatory bowel disease, as well as conditions like obesity, diabetes, constipation, and colon cancer. Despite these applications, recent advancements in understanding the role of probiotics in managing these diseases have been limited. This review presents the latest insights into probiotics' role in health management. With the growing global population, researchers are focusing on strategies to meet the increasing demand for probiotics. Using advanced techniques, scientists are exploring probiotic strains that can be produced industrially and utilized to treat various medical conditions. This review compiles essential information for probiotic researchers, covering strain selection, production, and applications.

Keywords: Probiotics, disease assessment, strain factors, health benefits, microbiome, lactic acid bacteria

Introduction

Microorganisms are important in our daily lives (Horve et al., 2020). The total number of microorganisms that live in the human body is about 38 trillion (Gupta, 2021; Hoffmann et al., 2016). These microbes are vital for strengthening the immune system, detoxifying any harmful substances from the human body, and generating substances that are needed for the metabolic functions of cells (Abdel-Megeed, 2021; Ashaolu, 2020; Oves et al., 2016). The genera *Eubacterium*, *Bacteroidetes, Actinobacteria*, *Bacteroides, Fusobacterium*, *Clostridium*, the lactic acid bacteria, *Escherichia coli*, Peptococcus*,* and *Fusobacterium* are mainly responsible for preserving metabolic equilibrium in humans (Middleton et al., 2024; Nazzaro et al., 2015; Wilson, 2018). Antibiotics and statins are treatment agents that substantially decrease the diversity and richness of the human gut microbiome (ChenLi, 2023; Weersma et al., 2020). When these microbial flora get eliminated or reduced, the accumulation of potentially dangerous products can occur, leading to disruptions in the synthesis of vitamins, cell functions, and anabolic and catabolic responses of the host system, all of which are important for the maintenance of the biological system. As a result, probiotic-containing foods and supplements are becoming more and more varied on the market (Dysin et al., 2023; Leghari et al., 2021).

Probiotics have gained significant attention in the medical profession (Singh and Natraj, 2021; Stavropoulou and Bezirtzoglou, 2020). Probiotic research concentrates on studying the characteristics of different probiotic strains (Liu et al., 2020; Shruthi et al., 2022). The incorporation of bacteria that produce lactic acid into dairy products has been shown to enhance the immune response of the host system while generating a more effective therapeutic effect (Hati and Prajapati, 2022; Khaneghah et al., 2020). Different probiotic species, such as *Aerococcus*, the lactic acid bacteria *Tetragenococcus*, *Lactococcus*, *Lactobacillus*, and *Atopobium* grow well in the African continent, North America and Central Asian countries (Waziri et al., 2022; Zaghloul, 2024). Probiotic researchers performed investigations on human and animal models utilizing the tools and technologies currently available to show the therapeutic potential and efficacy of different probiotic strains against a broad range of medical diseases (Abouelela and Helmy, 2024; Sharma et al., 2021). Prospective studies and reports from clinical trials have shown that probiotic strains show promise in the management of lactose intolerance, diarrhoea, antibiotic therapy, and colon cancer (Khoruts et al., 2020; Kvakova et al., 2022).

While previous evaluations have focused on individual probiotics and their specific applications (Roe et al., 2022; Zommiti et al., 2020), this review explores various probiotics and their applications, beginning with an overview of screening, characterization, production, and research on their use. Additionally, we summarize the latest studies on selecting probiotic strains, assessing their production processes, survivability, and potential applications. These factors are crucial for probiotic researchers who are seeking to discover new therapeutic strains.

Selection criteria and requirements for probiotic strains

Probiotic researchers follow mandatory guidelines in order to meet clinical requirements (Liang et al., 2024). In order to follow these guidelines, the strains had to meet safety and functionality requirements (Hazards et al., 2023; Merenstein et al., 2023). These requirements are very important for patient safety and include how the strains were chosen, how they behaved in the digestive tract, how long they lasted, and how well they kept working during production, processing, and storage (Calvigioni et al., 2023; Forsyth et al., 2023). When probiotics are first being screened and chosen, several important factors are evaluated: how well they stick to intestinal epithelial cells; how stable the phenotypes and genotypes are, including the stability of plasmids; how well they can handle bile and acid, as well as their ability to survive and grow; and how well they make antimicrobial compounds (Dell'Anno et al., 2021; Echers et al., 2021). Antibiotic resistance patterns can be attributed to immunogenicity, spoilage organisms, or both (GuptaSharma, 2022; Sharma et al., 2018).

Probiotics with the best health characteristics

The majority of culturable bacteria are highlighted in fermented food products for their health-promoting properties prior to being labelled as probiotics (Kaur et al., 2022; Sharifi-Rad et al., 2020). Lactic acid bacteria, which are found in yogurt, have become the best probiotic supplement of all the culturable microorganisms as they do not contain lipopolysaccharides or dangerous extracellular proteases (AyiviIbrahim, 2022; Moh et al., 2021). This is because of their unique qualities, as noted by the Food and Agriculture Organization (Organization, 2010). Researchers are now becoming more interested in understanding the molecular processes underlying these strains' ability to treat intestinal disorders due to their mutually beneficial relationship (StavropoulouBezirtzoglou, 2020; Zhao et al., 2023). By liberating both primary and secondary metabolites outside of cells and not restricting them in the periplasm, these strains of bacteria colonized the intestinal tract for a brief period, according to a study that used cutting-edge technology (Chen et al., 2024; PeleCimpeanu, 2012). The investigators used standard strains of *Lactobacillus* and were inspired by this natural characteristic to design therapeutic probiotics that could deliver molecules to the mucosa directly and would not have any negative impacts on systemic distribution or cause side effects (Shi et al., 2016).

Elements that affect probiotic viability

When developing the therapeutic formulation, attention must also be paid to the physiochemical properties. These include the sugar content, as well as the effects of external factors, such as chemical characteristics and fermentation conditions (LiszkowskaBerlowska, 2021; Tse et al., 2021). Probiotics present a number of technological, financial, and microbiological challenges when added to food on an industrial basis (KoiralaAnal, 2021). Previous research indicates that probiotic encapsulation increased the viability of yogurt sample cells (Mahmoodi Pour et al., 2022; Romero-Chapol et al., 2022). Multilayer emulsion also proved to be beneficial in maintaining bacterial viability at the suggested level of efficacy (Mahmoodi Pour et al., 2022). Probiotic bacteria encapsulation is an innovative technique that makes it easier to include and safeguard effective probiotic strains in functional foods to satisfy therapeutic needs (Terpou et al., 2019). However, several methods that improve the viability of probiotics, such as microencapsulation, raise the cost of food production (Martín et al., 2015; Yao et al., 2020). Investigating low-cost technologies is critical to keeping product costs within reachable limits while meeting the expectations of the globalized market for functional items (KnizkovArlinghaus, 2020). More work is required on a number of important issues, including the selection of suitable bacterial strains and the preparation and use of microencapsulation materials (RokkaRantamäki, 2010). The microencapsulation techniques used must be ecologically acceptable, long-lasting, and effective. A proper deployment of various microencapsulation technologies in actual food matrices would require additional testing because they have not yet been fully utilized. The microencapsulation industries are facing challenges in meeting the technical demands of producing more useful and positive products from being used on an industrial basis (Bakry et al., 2016; Boh Podgornik et al., 2021). Given the current circumstances, the food business will require more tools and expertise to successfully introduce the most cutting-edge technology and create the upcoming line of good foods (Galanakis, 2021). More research needs to be done to find the best technologies for screening microbial strains and making encapsulation matrixes that protect probiotics in gastric conditions (Martín et al., 2015).

Physician advice

In microbiome research, the discovery rate of novel microbes with therapeutic potential for human hosts is increasing rapidly(BelizárioNapolitano, 2015). New ways to look into some microbial strains that have systemic immunomodulatory functions include diagnosing and treating food allergies, controlling the gastrointestinal-liver axis, making neuroactive metabolites, and fighting microbes in the gut, skin, and urogenital tract (Dash et al., 2022; Kreft et al., 2020). Moreover, the importance of microbes for several metabolic processes is becoming more widely acknowledged (Figure 1) (Geiger et al., 2023; Yan et al., 2023). These findings will lead to the development of new microbial-based treatments. However, before adopting these strains for therapeutic purposes, further research and validation are required (Sawant et al., 2020).

However, research on the human microbiome indicates that many basic metabolic processes are preserved among members of a community (Shafquat et al., 2014). Within species, there is significant interpersonal variety, but within a population, individuals perform many vital metabolic functions (Del Giudice, 2020). As the field of personalized medicine gains traction, advocates of personalized therapies must clearly state the rationale for group division and substantiate the suggested advanced treatment's effectiveness within the targeted subgroup (Topol, 2011; Tzenios, 2022). A more all-encompassing approach would be the identification and confirmation of microorganisms with notable and recurring effects in a diverse population

(VelegrakiZerva, 2020). Probiotic recommendations should align with therapies in a stratified and heterogeneous population (McFarland et al., 2016).

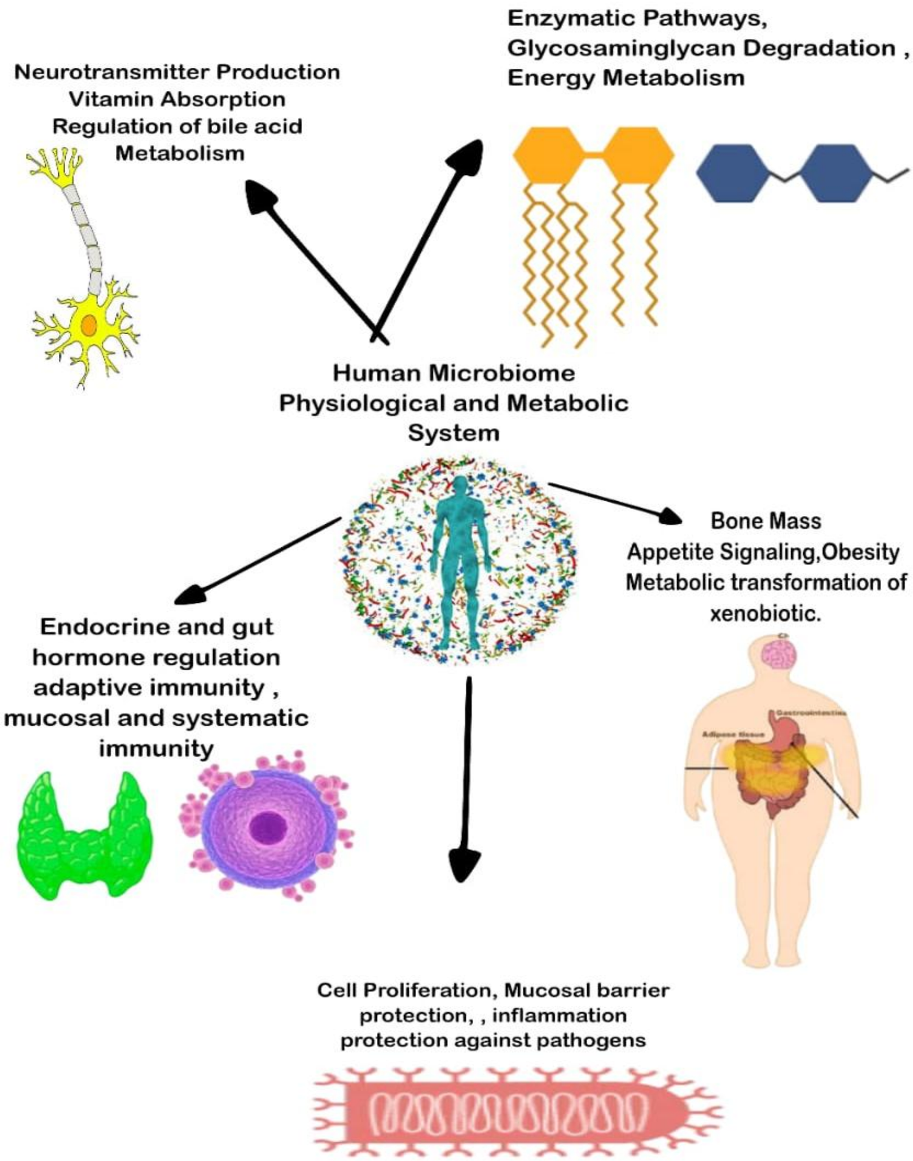

Figure 1. Metabolic and physiological role of human microbiome in health and diseases.

Probiotic starter cultures for dairy production

With increasing knowledge of how to treat any microbial-related illness, consumers look for dairy and food products that have probiotic supplements (N Kumar et al., 2017). Yogurt is one of a classic dairy product (N Kumar et al., 2017). It is widely accepted that yogurt cultures were classified as probiotics due to their beneficial effects on human health (Ghosh et al., 2019). We know that strains BGKMJ1-36 and BGVLJ1-21 can break down αs1-, β-, and κ-casein (Popović et al., 2020; Venkatesh et al., 2024). They can also make curd at 42 °C for five hours and kill Listeria monocytogenes bacteria (Sandulachi et al., 2020; Sun et al., 2021). Exopolysaccharides produced by the strain BGKMJ1-36 are essential to yogurt's rheological properties (Popović et al., 2020).

The BGVLJ1-21 and BGKMJ1-36 colony strains were able to pass through the gastrointestinal system-simulation. Targeted probiotic-supplemented products should be manufactured with viable, effective cells that can withstand harsh conditions, remain stable, and perform consistently across a range of therapies (Puebla-BarraganReid, 2019). Customers want a product to have a high count and to be viable for an extended period in a variety of ambient humidity and temperature ranges, therefore, clinical research should consider this when testing stretches on premium functional food supplements (AramouniDeschenes, 2014). Customers prefer quick and effective strains that can quickly acidify milk and milk products in order to provide additional medicinal benefits (González-González et al., 2022; Sudhakaran VMinj, 2020). During the production process, we briefly describe the processing techniques and emphasize important issues related to manufacturing and achieving consistent product performance (Sartal et al., 2020).

Development of strains and production

Prior to advancing to economical assembly, it is necessary to often examine freeze-drying processes before formulation advances from phenotypic to industrial manufacturing (Matejtschuk et al., 2016). Probiotic dosage levels that have been shown in human studies should serve as the foundation for the finished product. Additionally, the number of units that establish colonies per gram of product is an extra consideration (Fenster et al., 2019).

Although the minimum effective concentrations are still unknown, it is generally accepted that probiotic products should have a minimum concentration of 10^6 colony-forming units (CFU)/g and that 10^8 to 10^9 probiotic microorganisms should be consumed daily for the probiotic effect to be transferred to the consumer (Huys et al., 2013). In addition, the strains ought to be viable during storage and able to grow under typical commercial and production conditions. It is critical to maintain ideal freeze-drying intervals for producing the probiotic product (Luangthongkam et al., 2021). The methods used to achieve this include monitoring pressure, temperature, water content, thickness of the pellet bed, cell quality, quantity, and viability stability (L Kumar et al., 2017). It is possible to alter the dosage or composition of cry protectants in order to preserve cell viability during processing (Rockinger et al., 2021). Determining whether the manufacturing unit's freeze-drying system can be scaled up to an industrial level is crucial (González-González et al., 2022; Sudhakaran VMinj, 2020). The characteristics of a strain's development also differ slightly among strains (He et al., 2022; Wu et al., 2022), for example *L. acidophilus* is eosinophilic and has a high tolerance for bile and acids. During the development phase, it is important to understand the commercial production of probiotics and assess the strains' efficacy in the lab under the same conditions (Gao et al., 2022). The cells' survival during manufacturing and processing, as well as the identification of strain-dependent sensitivity, are critical because each step of the process is dependent on the previous one. In the first downstream lab, scale centrifugation is an important tool for separating small quantities. Furthermore, many of the activities that involve pumping cells during commercial-scale production are not often carried out during counter-scale research and development (Özdemir, 2010).

Dietary requirements of the strains

Probiotic strains require specific nutrition for growth and development; carbon and nitrogen supplies, particularly amino acids, will support the lactic acid bacteria and *Bifidobacteria* strains' metabolic processes (Mendonça et al., 2022; Saeed ASalam A, 2013). Changes made to the raw materials can have a big effect on production and growth (Wrigley, 2017). People frequently utilize simpler carbon sources such as salts, simple carbs, and protein sources like milk and yeast extract (Anastassiadis, 2016). The nutritional microorganisms are environment-adaptable, and the complexity of these autotrophic and nutrient requirements is usually correlated with the source from which they originated (Li et al., 2020). Because *Lactobacillus plantarum* is derived from plant material, it has fewer autotrophs. When isolated from a human's upper gastrointestinal tract, *Lactobacillus johnsonii* exhibits more biosynthetic self-sufficiency and thrives in environments rich in resources, including small peptides, amino acids, and polysaccharides(KumariTaku, 2020). Producing a high-performing final product is easier by developing a special fermentation medium for microbiological requirements (Pirato, 2013). Furthermore, cane and beet molasses are widely accessible worldwide, providing excellent quality and performance that can be used in fermentations with yeast extracts and peptones to yield durable outcomes (Cunha, 2022; Kanwugu et al., 2020).

Production of raw materials

Because Lactic acid bacteria and *Bifidobacteria* production depends on the fermentation medium, changes in the uncommon components can have a significant impact on growth and development(Prasanna et al., 2014). The supplier may alter the raw ingredients because of changing the source of an ingredient, improving procedures at a lower cost, or altering the production process (Weiss et al., 2010). Differences in composition are more noticeable in complex substances like milk, yeast extract, and so on, as well as in small, complicated elements like salts and sugars (Sethi et al., 2022; Tao et al., 2023). Some strains yield consistent results, however, a significant degree of diversity in complex critical elements may go unnoticed due to the strains' differing nutritional requirements and sensitivities (Dwivedi et al., 2017). On the other hand, certain strains can either hurt or help their effectiveness (Koopman et al., 2020). More complex materials, such as yeast extract, alter strain performance more than variations in the distribution of peptide sizes, amino acids, nucleotides, carbohydrates, vitamins, and salt concentrations (Jacob et al., 2019). Beet is commonly used to create baker's yeast, and cane molasses were separated to produce yeast extract and peptone for use in food (Khan et al., 2020; RagauskaiteCizeikiene, 2019). The ingredients used to cultivate and produce the yeast extract and peptone during manufacture have no effect on the strain's ability to function. Moreover, cane and beet molasses are widely available, both of which have been shown to function well and possess a characteristic that can have enduring effects when mixed with peptones and yeast extracts in fermentation processes (Sarker, 2024). Once studies have established that some strains of bacteria are probiotics, the next line of inquiry is to find out if these strains can be grown in large quantities and successfully incorporated into consumer products (Katz, 2012).

In order to prevent studying a commercialized strain, this stage of probiotic commercialization should take place in tandem with clinical trials. Compared to laboratory culturing, industrial production and pilot-scale culturing require considerably different strain requirements. The needs of the media are also influenced by the cost of production. This calls for meticulous documentation of all actions conducted and outcomes attained (Forssten et al., 2020). Once they have generated a significant probiotic bulk, the probiotic strains need to be added to consumer food products. These things have various requirements during the process, from maintaining shelf life to the product's storage circumstances (Allai et al., 2023; dos Santos FormigaJúnior, 2024). It is essential that consumer should still receive a dose that is just marginally effective at the end of the shelf life (Adewoyin, 2023).

Applications of probiotics

Probiotics enhance the formation of short-chain fatty acids (SCFA), affect the microbiota within the gut, and decrease the risk of disease (Markowiak-KopećŚliżewska, 2020). Probiotics lessen the risk of obesity, type 2 diabetes mellitus (T2DM), colon cancer, and constipation as well as treat several gastrointestinal diseases, including a condition called inflammatory bowel disease (IBD) (Khani et al., 2012; Sanders et al., 2019).

Role of probiotics in colorectal cancer

Probiotics are well-known bioactive substances that have a broad range of therapeutic applications. Probiotic-based research revealed that altering the gut microbiome can slow the spread of cancer. In a similar way, probiotic supplements protect colorectal cancer patients from the adverse effects of their treatment. The results show that multiple factors, such as strain, host physiology, dosage, duration of the intervention, and other dietary supplements, help in assessing the therapeutic efficacy of probiotic supplementation(Uccello et al., 2012). Probiotic-treated patients with colorectal cancer have improved intestinal permeability, tight junction function, and enzyme activity. Carcinogens are also reduced, the microbiota is increased, and antimicrobials and anti-carcinogenic chemicals are produced. It has been discovered that a wide range of probiotic species, their metabolites, and other prebiotic elements affect gut immunity and colon cancer prevalence. It has been shown that probiotics have anti-inflammatory, antioxidant, and immune system-regulating qualities helping to minimize inflammation, stop diarrhoea, and lessen lactose intolerance (Chong, 2014).

Research has linked probiotics to colorectal cancer, and data from numerous trials suggests that patients with colorectal cancer may benefit from an additional therapeutic option that includes both single-genus and multi-strain probiotics (Azcárate-Peril et al., 2011). Experiments have demonstrated the effectiveness effect of probiotics in the inhibition of colorectal cancer. Probiotic therapy enhances CD8 cell activation while slowing down the growth of CT26 tumours (Wierzbicka et al., 2021).

Furthermore, studies on the Wnt/β-catenin signalling pathways showed that catenin degradation further lowering the transcriptional activity of cancerous cells (Shang et al., 2017). Probiotics will be critical in preventing cancer and reducing its side effects when more detailed accounts of gut biodiversity and accurate evaluations of alterations in response to anticancer medication become available (Conti et al., 2022). There are also many commercially available probiotic strains that are used to treat colon cancer (Dubey et al., 2016).

Role of probiotics in obesity and type 2 diabetes mellitus (T2DM)

Patients diagnosed with T2DM who had not taken medication for a period of 12 to 13 weeks were given probiotic supplements containing several strains (Sabico et al., 2017). Consequently, the homeostasis model assessment of insulin resistance (HOMA-IR) increased significantly while abdominal fat decreased (Hirose et al., 2016). In type 2 diabetes, probiotics marginally reduce levels of glycated haemoglobin (HbA1c) and fasting insulin. By altering hormone and protein levels linked to hunger and fat storage, as well as by lowering the number of calories intake from meals, probiotics may lower inflammation and the risk of obesity. According to research, probiotics have an impact on three important T2DM indicators. Probiotics will need to be widely used in clinical settings to treat HbA1c, the T2DM homeostatic model assessment of insulin resistance, and fasting blood glucose (FBG). To fully understand the impact of probiotics in individuals with type 2 diabetes, several markers are required (Zhang et al., 2022).

Tao et al. conducted a meta-analysis to investigate the effectiveness of probiotics in T2DM. According to the meta-analysis's findings, probiotic therapy may help T2DM patients' levels of insulin resistance, FBG, and HbA1c. However, to fully understand the role of probiotics in type 2 diabetes, more investigation into the probiotic mechanism and clinical data are required. Kheirkhah et al. examined the impact of a specific probiotic supplement affected the glycaemic outcomes (HbA1c, fasting plasma glucose, fasting plasma insulin, and HOMA-IR) in individuals with type 2 diabetes. These glycaemic indicators seem to be most altered by multi-strain probiotics containing *Lactobacillus acidophilus*, *Streptococcus thermophilus*, *Lactobacillus bulgaricus*, and *Bifidobacterium lactis* (Tao et al., 2020). These supplements contain probiotics that are taken once daily for six to twelve weeks, with dosages ranging from seven million to over 100 billion colony-forming units (CFU) each day. To regulate T2DM, a few other strains were employed, including *Bacteroides*, *Faecalibacterium*, *Akkermansia*, *Roseburia*, *Ruminococcus*, *Fusobacterium*, and *Blautia* (Cunningham et al., 2021; Yang et al., 2021). Even though probiotic supplements are becoming a more popular and viable type 2 diabetes treatment option, further in vivo and in vitro studies are needed to fully comprehend the probiotics' overall effects on glucose regulation (Rizvi et al.).

Role of probiotics in inflammatory bowel disease (IBD)

Clinical data further support the use of probiotics in the treatment of IBD. It is generally established that rerouting the stool stream usually leads to mucosal healing in individuals with Crohn's disease (Atreya et al., 2024; Bernardi et al., 2024). However, faeces return to the healing gut after intestinal integrity is restored, and inflammation ensues. For patients with inflammatory bowel illness, *Saccharomyces boulardii* can be taken as prescribed to provide extra support in addition to its strong anti-inflammatory properties. Inflammatory bowel illness can be effectively treated with chemical therapy using the customized probiotics ECN-pE(C/E)2 (Li et al., 2024). The oral medication increases the expression of tight junction-associated proteins, which protects colon epithelial cells from inflammation-induced death. Furthermore, it increases anti-inflammatory cytokines and helps remove reactive oxygen species in IBD. This indicates that probiotics can be used as a drug to treat long-term illnesses like IBD. Gut microbiota has a role in IBD pathogenesis. Dysbiosis is the term used to describe any imbalance in the gut flora that weakens the gut barrier and triggers inflammatory reactions (Genua et al., 2021).

In individuals with chronic illness, dangerous microbes steadily proliferate while good bacteria gradually decline. Short chain-generating bacteria, such *Faecalibacterium prausnitzii*, have been found to be reduced in these patients, which exacerbates gut inflammation and immune system dysfunction (FinlayFinlay, 2019). Certain probiotics, such *Lactobacillus* sp., have been shown to generate antimicrobial compounds that attach and activate aryl hydrocarbon receptors associated with IBD. It has been demonstrated in recent research that TNF-α overexpression and other pro-inflammatory substances promote the development of IBD. In order to modulate the hyperactive signaling pathways, whole gut restoration (TGR) has been introduced. TGR is a probiotic blend that improves the IL-6 and TNF-α signaling pathways. It consists of five different strains (RoyDhaneshwar, 2023; Wang et al., 2021). Therapeutic effects of probiotics in various gastrointestinal disorders are summarised in Table 1.

Probiotics and metabolism of cholesterol

Unhealthy food consumption is contributing to the rise in neurological illnesses, liver-related diseases, and multifactorial diseases in today's culture (Mansoor et al., 2022). Most diseases are inhibited by metabolic dysfunction, With disturbances in lipid metabolism are the main cause of obesity, hypertension, and heart disease. Probiotics, or living microorganisms, offer additional health benefits. It is also present in dietary supplements intended for use in maintaining a healthy weight. Studies involving multi-strain probiotic supplements show a prominent decrease in TNF-α and LDL cholesterol levels in obese children, simultaneously increasing HDL cholesterol levels. Lipid oxidation in the liver can be triggered by the most commonly utilized probiotics, which include *Lactobacillus*, *Bifidobacterium* spp., *Saccharomyces*, *Bacillus*, *Clostridium*, *Candida*, and *Streptococcus*. These probiotics alter the composition of the gut microbiome (Arora et al., 2013). Additionally, they decrease the body's capacity to accumulate fat. In a recent research, functional foods like probiotics dramatically improve the hydrolase enzyme, which in turn causes the bile salts to hydrolyse and increases the amount of cholesterol absorbed via the digestive system. Its effect on lipid metabolism in metabolic illnesses is important, even if it is not as effective as anti-obesity drugs. Probiotics regulate important enzymes involved in the synthesis and metabolism of cholesterol. Fat accumulation in the liver is regulated by the oxidation of lipids and de novo lipogenesis. Probiotics stimulate lipid oxidation and de novo lipogenesis by increasing the synthesis of SREBP1 and PPAR alpha (Wang et al., 2017).

Probiotics in lactose metabolism

More than 60% of people worldwide have been reported to be lactose intolerant because of decreased lactose disaccharide synthesis (Silanikove et al., 2015). When the enzyme lactase is present, glucose and galactose mix in the gut to form lactose. However, abnormal lactose production can lead to bloating, discomfort in the intestines, nausea, diarrhoea, and other symptoms. Probiotics are an excellent supplier of lactase, an exogenous enzyme that is administered to enhance lactose fermentation and increase the population of beneficial gut microbiota in the intestine. Galactosidase helps in the hydrolysis and transgalactosylation of lactose in the absence of lactase, thereby sustaining glycolysis and promoting the uptake of glucose and galactose by tissues. Additionally, it has been demonstrated that probiotics activate β-galactosidase in the digestive tract (SinghSambyal, 2023).

Probiotics and immune system

Probiotics affect T-cells, B-cells, dendritic cells, and macrophages (Maldonado Galdeano et al., 2019). They are also therapeutically pertinent in immune cell regulation, that has led to many studies examining the use of probiotics as additional treatment for immune system disorders. Probiotics have a major impact on Toll-like receptors (TLRs), and their adaptors can differentiate between intrinsic and extrinsic molecules (Le Noci et al., 2021). In addition, they cover numerous aspects of pathogen identification. Two fish-derived probiotics, *Lactobacillus* and *Saccharomyces*, along with *Bifidobacterium breve*, *Bifidobacterium bifidum*, and *Lactococcus lactis*, have been shown to make crayfish more resistant to infections and start an innate immune response (Wei et al., 2021).

Additionally, they improve the gut flora by upregulating immunogen expression. Prebiotics, the fermented by-product of probiotics, aid in the exopolysaccharide's energy-binding (Mohammadian et al., 2021). Probiotics inhibit the synthesis of Bacteriocins pathogens and short-chain fatty acids while stimulating macrophages to change the way they produce cytokines. Probiotics help B-cells produce more antibodies (IgA), while also increasing the release of TNF-β and IL-10, which stimulate the host immunological response (AshrafShah, 2014).

Probiotics antagonistic properties

Numerous multifactorial and neurodegenerative disorders are linked to oxidative stress (Jomova et al., 2010). At high levels of oxidative stress, GAPDH activity is repressed, which inhibits the glycolysis process and reduces the amount of ATP that cells produce. Calcium pumps and Na/K-ATPase cannot do their job when ATP synthesis is low. This makes metabolic stress in cells even worse and leads to cell death. As a result, techniques to lower ROS remain a significant challenge to all medical researchers. Natural antioxidants have recently been added to probiotics, boosting their acceptability and safety among populations (MullarkyCantley, 2015).

Table 1. Therapeutic effects of probiotics in various gastrointestinal disorder

Gastrointestinal disorder	Probiotic strains	Therapeutic effect	Reference
Irritable bowel syndrome (IBS)	*Lactobacillus rhamnosus GG*, *Bifidobacterium infantis*	Reduce bloating, abdominal pain, and bowel movement irregularities	(KorpelaNiittynen, 2012; SzajewskaHojsak, 2020)
Inflammatory bowel disease (IBD)	*Bifidobacterium breve*, *Lactobacillus casei*	Reduces inflammation, promotes remission, improves gut barrier function	(Saez-Lara et al., 2015; Sireswar et al., 2019)
Clostridium difficile Infection (CDI)	*Saccharomyces boulardii*, *Lactobacillus rhamnosus GG*	Reduces recurrence, supports gut microbiota balance	(Goldstein et al., 2017; Valdés-Varela et al., 2018)
Ulcerative colitis	*Bifidobacterium longum*, *Lactobacillus reuteri*	Induces and maintains remission, reduces inflammation	(Huang et al., 2023; Zhang et al., 2021)
Crohn's Disease	*Escherichia coli Nissle 1917*	Maintains remission, modulates immune response	(Gronbach et al., 2010)
Helicobacter pylori Infection	*Lactobacillus reuteri*, *Lactobacillus acidophilus*	Enhances eradication rates, reduces side effects of antibiotic treatment	(Dore et al., 2014; WangHuang, 2014)
Antibiotic-associated diarrhea (AAD)	*Saccharomyces boulardii*, *Lactobacillus rhamnosus GG*	Prevents onset, reduces severity and duration	(Blaabjerg et al., 2017; Mantegazza et al., 2018)
Constipation	*Bifidobacterium lactis*, *Lactobacillus rhamnosus*	Improves bowel movement frequency, softens stool consistency	(Dimidi et al., 2014; Mitelmão et al., 2022)
Traveler's diarrhea	*Saccharomyces boulardii*, *Lactobacillus rhamnosus GG*	Reduces incidence, shortens duration, alleviates symptoms	(McFarlandGoh, 2019)
Necrotizing enterocolitis (NEC) in Infants	*Bifidobacterium bifidum*, *Lactobacillus acidophilus*	Reduces incidence and severity, improves survival rates	(Bi et al., 2019; Repa et al., 2015)
Lactose intolerance	*L. acidophilus*	Abdominal pain, Abdominal cramping, Vomiting	(Masoumi et al., 2021)
Hypercholesterolemia	*L. fermentum* MJM60397	cholesterol and low-density lipoprotein (LDL) cholesterol levels, LDLR gene	(Palaniyandi et al., 2020)
Cancer	*Pediococcus acidilactici* TMAB26	Significant toxicity on cancer cells, Activation of intrinsic apoptosis	(BarigelaBhukya, 2021)
Allergic reactions	*Lactobacillus* multiple strains, *L. plantarum*	Interferon-γ and IL-2 IL-4, IL-6 Promoted Tregs Interleukin-10 Interferon-γ	(Özdemir, 2010; Snel et al., 2011)

Phenolic antioxidants prevent the initiation of radical chain reactions by donating a hydrogen atom to free radicals, thereby reducing the impact of oxidative stress. Research has indicated that flavonoid extracts have the ability to effectively reduce lipid peroxidation, a significant risk factor for a number of malignancies and cardiovascular illnesses. Numerous studies have demonstrated that adding *Lactobacillus acidophilus* to *Rosa roxburghii* through fermentation has effectively raised the plant's antioxidant content. Additionally, probiotics contribute to eliminating unwanted components like aldehydes (Sadeghi et al., 2022).

Probiotics and oral health

The World Health Organization (WHO) Global Programme states that there is a close relationship between overall quality of life and oral health (Moszka et al., 2023). By 2023, the WHO estimates that 3.5 billion people would have had an oral health issue globally. Probiotics are beneficial when taken in enough amounts orally. Over the last ten years, studies have demonstrated that probiotics can also treat oral diseases, lower the risk of respiratory tract infections, and enhance adaptive immune responses (Lehtoranta et al., 2020). They have historically been used to address conditions pertaining to intestinal health. Certain probiotic bacteria that mothers carry may have an impact on the composition of breast milk. Studies have shown that certain oral microorganisms, including *Lactobacillus*, *Bifidobacterium*, *Streptococcus* strains and many others may be advantageous for maintaining dental health. It is known that their antagonistic action on other commensal oral microorganisms protect against infections in oral cavities. Moreover, IgA, which prevents bacteria from adhering to dental surfaces, is not altered by probiotic consumption. Probiotics also help maintain the equilibrium of the oral microbiota, which protect against oral infections (Luo et al., 2024). Even though the clinical evidence on probiotics' real efficiency in maintaining optimal oral health is still lacking, they have been shown to lessen the signs of halitosis, periodontitis, and gingivitis, helping to preserve the balanced environment of optimal oral health. Probiotics are an efficient preventive measure when used in conjunction with traditional oral care procedures. Probiotics have been approved for use in oral treatments due to their positive impact on oral health (AllakerStephen, 2017).

Conclusion

The study highlights that the advantages of medicinal bacterial strains, increasing the possibility for future therapeutic applications. Probiotic bacteria have been shown to use an assortment of strategies, such as immune system modulation and competing for few resources in the gut, to avoid pathogen colonization and promote gut cleansing. The necessity of probiotic strains in therapeutic applications for curing a wide range of disorders has been the subject of more research in recent years. Numerous in vitro and in vivo studies have demonstrated a strong relationship between these beneficial microbes and adaptive immune responses, further validating their role in disease prevention and treatment.

Authors' contributions

Conceptualization: HMS, MF, BUR, TS, MR, FM, SH and SAI; Data curation: HMS, MF, BUR, TS, MR, FM, SH and SAI; Formal analysis: HMS, MF, BUR, TS, MR, FM, SH and SAI; Investigation: HMS, MF, BUR, TS, MR, FM, SH and SAI; Methodology: HMS, MF, BUR, TS, MR, FM, SH and SAI; Project administration: HMS, MF, BUR, TS, MR, FM, SH and SAI; Resources: HMS, MF, BUR, TS, MR, FM, SH and SAI; Supervision: HMS, MF, BUR, TS, MR, FM, SH and SAI; Validation: HMS, MF, BUR, TS, MR, FM, SH and SAI; Writing-original draft preparation: HMS, MF, BUR, TS, MR, FM, SH and SAI; Writing-review and editing: HMS, MF, BUR, TS, MR, FM, SH and SAI.

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Ethical approval

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Conflict of interest

There is no conflict of interest reported by the authors.

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