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Review Article

Probiotics and the physiological & biological aspects of probiotic microorganisms

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Abstract

Since ancient times, food fermentation has been practiced and evolved via changes in substrates, procedures, and technology. Microbial culture is performed using techniques such as enrichment and back-slopping to improve the organoleptic quality, nutrient availability, and storage life of food. In many cases, this also adds healthy microorganisms to the consumer's diet. Lactic acid bacteria (LAB), many of which are known to have probiotic properties, are among the principal groups of microbes employed in conventional and industrial cereal fermentation, followed by yeast and mold. The end products of Probiotic products must contain viable cells 10^8 to 10^9 cfu/ml. Probiotic products may be used to increase the health of plants, animals, humans, and also soils at certain limits. LAB converts cholesterol to coprostanol. They help to remove aflatoxins from foods and reform the antinutritional elements' bioavailability. They become a good indicator before disease development. Here, we scrutinized all the general possible probiotic microflora presence, their compositions, and possible concentrations for use in various applications.

Abbreviations

LAB: Lactic Acid Bacteria; FBDs: Food-Borne Diseases; FAO/WHO: Food and Agriculture Organization/World Health Organization; cfu: Colony Forming Unit; β-GOS: β-Glucooligosaccharides; MTDR: Multidrug-Resistant; CLA: Conjugated Linoleic Acids; NGPs: Next-Generation Probiotics; CVD: Cardiovascular Disease; T2DM: Type 2 Diabetes; CPSs: Capsular Polysaccharides; EPS: Exopolysaccharides; FOS: Fructooligosaccharides

Introduction

Many fermented food products are produced worldwide and constitute an important component of the diets of many people. An unusual class of food products known as fermented food products experiences various forms of carbohydrate breakdowns in the presence of probiotic microorganisms, albeit seldom is the carbohydrate the only component impacted. Foods that provide a functional or probiotic purpose in addition to providing nourishment are growing in popularity. In addition to having nutritional value, many foods also have health advantages or protection from food-borne illnesses. Human-beneficial living microorganisms (probiotics) are necessary for the prevention and control of food-borne diseases (FBDs), which are complex problems. These infections and the accompanying health risks must be eliminated [1].

In his article "Anti-und Probiotika," Ferdinand Vergin (1954) coined the term "probiotics" for the first time. The phrase "probiotic" was first used in 1965 by Lilly and Stillwell to describe a substance produced by one bacterium that aids in the development of another. The most widely used definition of probiotics comes from Fuller (1989), who defined them as "living microbial feed additions that benefit the host animal by boosting their gut microbial balance." Havenaar and Huis In't Veld (1992) expanded the definition of the term to include both food and non-food use as well as the blending of mono- and mixed-cultural usage. Probiotics should not enter host cells (Tang, et al. 1993). Furthermore, "viable microorganisms"

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(lactic acids and other bacteria or yeast given as dried cells or as a fermented product) have a beneficial effect on the host's health after consumption by enhancing its native microflora. Probiotics, according to the FAO/WHO, are living microbial meals that are advantageous to the host (Hotel and Cordoba, 2001). Probiotics are defined as "live microorganisms which, when administered in adequate amounts, confer health benefits on the host". Many fermented foods are sources of probiotic strains, and a variety of factors, including interactions between probiotic bacteria and the host's microbiome, affect how effective probiotics are [2]. Probiotic bacteria are frequently found in fermented non-dairy substrates, but they can also be found in animals. These bacteria are selected based on a variety of factors, including technical qualities, including raw material growth, stability, and viability; sensory qualities that are acceptable; post-consumption survival in the gastrointestinal tract; and functional qualities, such as adhesion, antigenotoxicity, antimicrobial production, colonization, immune stimulation, safety, and pathogen prevention. Gibson and Roberfroid [3] defined prebiotics as "non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacterial species already resident in the colon and thus attempting to improve host health" [4]. Regarding the importance of the digestive tract for human health, Hippocrates said in the 25th century that "all diseases originate in the stomach." Current research on the human microbiome suggests that fermented foods should be a part of a balanced diet to temporarily improve the abundance of live bacteria in the human gut. The gut microbiota is a massive and diverse community of microbes. Nearly 10 times as many cells make up a human body as are found in the large intestine; these cells are home to 10^{13}–10^{14} microorganisms, the majority of which belong to the bacterial phyla Firmicutes and Bacteroidetes. They significantly contribute to the host's health by affecting the regulation of energy metabolism and the growth of the immune system [5]. Probiotic products that enhance gut health have one of the largest and fastest-growing markets. Probiotics are defined as "live microorganisms that, when provided in a proper dose, exhibit a favorable influence on the host health" [6]. Probiotics are microorganisms that, when given in sufficient proportions, help the host's health, mostly through repopulating or introducing healthy bacteria to the gastrointestinal tract. Currently, probiotic food production relies heavily on lactic acid bacteria (LAB), primarily from the genera *Lactobacillus, Bifidobacterium, Streptococcus,* and *Enterococcus*. Although there is no clear agreement on the minimum quantity of probiotic bacteria required to have any positive effects on the host's health, it is generally agreed that the final product must include at least 10^6 to 10^7 cfu/mL or g of viable probiotic cells at the time of consumption. These cells must reach through the digestive tract after being swallowed (10^9 cfu/day), enter the colon, and then cling to and colonize the gut epithelium [7].

Fewer studies have examined the health benefits of resident bacteria throughout the history of microbiology, with the majority of human studies concentrating on disease-causing organisms found on or in humans. The endogenous flora of the human body is poorly understood, as has been mentioned in various reviews. The gut microbiota changes in composition from birth through adulthood. The host and the gut bacteria have a symbiotic relationship. The primarily commensal gut microbiota contributes to the production of specific nutrients, including vitamins, short-chain fatty acids, and other low-molecular-mass compounds, as well as to the differentiation of the host immune system and the enhancement of resistance to infections [8]. Probiotics from the *Bifidobacterium* and *Lactobacillus* genera and microalgae have been linked to positive effects on humans. Microalgae were obtained from a river in Mexico and identified using molecular techniques. The prebiotic activity of *Bifidobacterium longum* and *Lactobacillus plantarum* after inclusion in the food matrix was assessed. Additionally, after being infected with rotavirus, HT-29 cells were exposed to 1 x 10^9 CFU/mL *L. plantarum* and *B. longum* metabolites alone or in combination with 1x10^9 cells/mL *Chlorella sorokiniana* [9].

As a supplement to green feed, probiotics can regulate the gut flora, stop the spread of infectious agents, outcompete pathogenic bacteria for nutrients and attachment sites in the intestine, provide host metabolic energy through the production of volatile fatty acids, and enhance host production and the immune response. Broiler chickens can benefit from *in-vivo* injections of *Bifidobacteria* as a growth stimulator, which has advantages such as improved growth performance, intestinal development, and thyroid hormone metabolism as well as increased counts of some beneficial bacteria and decreased counts of harmful bacteria in the gut [10]. Lactic acid bacteria are often encountered in acidic environments, and they have developed various mechanisms to improve their acid resistance. The emergence of high-throughput techniques has improved the acid resistance of LAB. LAB with high acid resistance were generated by these approaches. It is important to fully understand the mechanisms of acid resistance in LAB, as this understanding will accentuate the benefits of probiotics for humankind [11].

A notion with many faces is food that enhances human life and heals illnesses. One of the most complex loops involves nutrients (prebiotic), which are handled by particular bacteria (probiotic), and physiologically active products (postbiotic). Clinicians, microbiologists, dieticians, nutritionists, food technologists, and those working in agriculture are all paying close attention to probiotics, their nutrient prebiotics, and the postbiotics that are formed from the latter. Problems with probiotics and prebiotics in generally healthy, functional foods and beverages, effects of processing on some sources, consumer preferences, mathematical models for probiotic fermentation, and treating viral diarrhea are just a few of the more recent topics covered [12]. The original definition of a prebiotic was "a non-digestible food element that benefits the host by specifically promoting the growth and/or activity of one or a restricted number of bacteria in the colon, and so enhances human health" [3] (Figure 1).

Currently, probiotic cosmetic products are promoted. The percentages represent the various product categories that are currently promoted as "probiotic cosmetics." Probiotic cosmetics come in a variety of forms, including deodorants, primers, balms, soap bars, foundations, cleaners, exfoliants, gels, masks, serums, and creams. Not all skincare products

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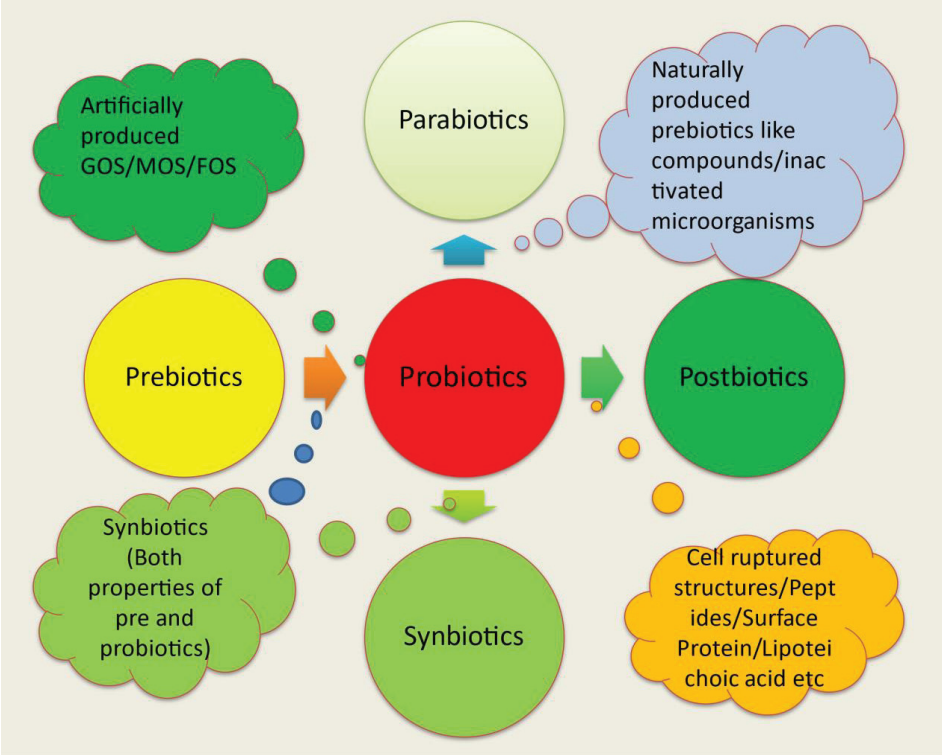

Figure 1: Diagrammatic representation of Interrelationship of Pre-, Pro-, Post-, Para- and Syn-biotics.

for men or women need to be applied locally. Probiotics taken orally have been shown to alter the gut flora, perhaps improving skin diseases, including atopic dermatitis, acne, and rosacea. Early research revealed that probiotic administration throughout pregnancy and during the first few years of life may be necessary to decrease the prevalence and adverse effects of atopic dermatitis, suggesting immune regulation and strengthening of gut barrier function. Probiotic strains are commonly freeze-dried. However, the final viability can differ depending on the drying protectant applied. Skim milk, serum, trehalose, glycerol, betaine, adonitol, sucrose, glucose, lactose, and polyethylene glycol are the most commonly utilized protectants; however, they cannot be compatible with the product's intended usage or physicochemical properties. When utilizing this technique, the strains should not be exposed to water because doing so will cause them to rehydrate too soon [13].

Supplementing probiotics enhanced aerobic capacity and reduced stress and anxiety. To ascertain the mechanisms by which probiotic ingestion causes these outcomes, however, additional research must be performed. Long-term, strenuous athletic training can increase the risk of depression, upper respiratory infections, gastrointestinal pain, and other mental health issues. Stress is defined as the process by which a person senses risk and reacts with a combination of psychological and physiological changes, which may include increased anticipation and anxiety. The phrases "anxiety," "anticipation," and "stress" are connected [14].

The genera Bifidobacteria and other Lactobacillus spp. (*L. acidophilus, L. johnsonii, L. casei, L. rhamnosus,* and *L. reuteri*) are the most prevalent probiotic LAB species (*B. bifidum, B. animalis subsp. lactis, B. longum subsp. longum,* and *B. longum subsp. infantis*). The use of Lactobacillus Acid Bacteria (LAB) in the treatment of various illnesses brought on by pathogenic germs that are drug-resistant is also beneficial. Probiotic bacteria can create enzymes, suppress infections, promote immunological responses, provide nutrients and promote growth [1].

Growth surroundings of lactic acid bacteria

The generic name for intestinal lactobacilli is *Bacillus acidophilus*, which was used to characterize the species *Lactobacillus* spp., facultative straight rods isolated from the feces of breastfed newborns (Moro 1990). The genus is distinguished by rods or coccobacilli that are gram-positive, exclusively fermentative, non-spore-forming, non-flagellated, and low in G+C content (32 - 51 mol%), aerotolerant or aerobic. The genus Lactobacillus contains 56 species, although only a handful of them, including *Lactobacillus crispatus, L. gallinarum, L. gasseri, L. amylovorus,* and *L. johnsonii*, have been extensively studied. The ideal temperature range for Lactobacillus spp. to flourish is between 5.5 and 6.0 °C, with a maximum temperature tolerance of 45 °C. Its acid tolerance ranges from 0.3 to 1.9%. The majority of the species of Lactobacilli and bifidobacteria tested in this study, as well as all of the cocci, were able to use β-glucooligosaccharides (β-GOS) as their primary carbon source. Additionally, the probiotic utilizing the β-GOS metabolism pathway has been demonstrated by the fact that several pathogens do not significantly develop on β-GOS when compared to prebiotic fructo-oligosaccharide (FOS) and inulin substrates. When cultivated in media using β-GOS as the only carbon source instead of glucose, *Lactococcus lactis subsp. lactis*,

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Lactobacillus reuteri, and *Pediococcus acidilactici* showed increased antimicrobial activity. In comparison to glucose, *L. lactis subsp. lactis* was able to grow exponentially with the help of β-GOS, which increased nisin Z synthesis by approximately 25%. These findings imply that β-GOS can selectively modify the development of probiotics, specifically cocci, and antibacterial activity, which has significant ramifications for both industrial uses and future nutritional research [15,16].

Bifidobacterium's growth medium is a semi-synthetic medium that contains lactose, three free amino acids, cysteine, glycine, and tryptophan, as well as several vitamins. In contrast to milk, bifidobacterium generally grows better in rich synthetic media, such as tryptophan and MRS broth. FOS (fructooligosaccharide) accelerates plant growth approximately 10-fold. A just-right amount is the *therapeutic* dose, just enough to provide the intended effect without problems. The therapeutic dose suggests that 10^6 - 10^7 live cells per millilitre are present in a 100-gram fermented bioproduct. Commercially available bifidobacterium culture products include those sold under the trade names A-38, Mil-Mil, Acidophilus buttermilk, Bifigurt, etc. There are also several combinations of bifidobacterium and Lactobacillus available [17].

The mechanism and biological processing of probiotics

There are various types of food products, such as beverages, biscuits, cakes, canned (tinned) foods, chips, crisps, corn snacks, nuts, seeds, and condiments, available on the market. These products may be fortified with probiotic microorganisms to enhance their quality. The following are some details of the probiotic microorganisms and their underlying mechanisms and biological aspects.

Health benefits of probiotics

According to the WHO (1948), health is defined as a state of complete physical, mental, and social well-being. Physical, mental, and social welfare are interconnected. Mental and social welfare is enhanced by heartfulness meditation, simplicity, love, etc., whereas physical health is related to our regular exercise, yoga, etc. Food product quality is enhanced by the use of probiotic microorganisms. Some health-related concerns are described here.

Control of intestinal infection

On earth, there are approximately 4-6 × 10^{30} prokaryotic cells. They are common, varied, and plentiful. There are 3.5 × 10^{30}, 0.25 - 2.5 × 10^{30}, and 2.6 × 10^{30} prokaryotic cells in the ocean, terrestrial, and soil, respectively. Only 1% of bacteria are treated with culture-dependent molecular technologies; the remaining 99% are treated with culture-independent molecular techniques. More than 10 million prokaryotic cells are believed to be unknown, unlike the 14300 prokaryotic cells that are known. Extreme temperatures, pH, hydrostatic pressure, and salinity are significant environmental influences [18]. Several examples of intestinal disorders include diarrhea, antibiotic-induced travelers, infantile, constipation, colitis, lactose intolerance, Salmonella, Shigella infection, and flatulence. Dysbiosis of the microbial community in the gastrointestinal tract is the primary cause of this illness. In humans, there are 10^{11} - 10^{12} bacteria per gram of feces and fewer than 10^{11} bacteria per square millimeter of skin and mouth. An organism must have the capacity to endure a harsh environment, establish itself, and spread throughout the human digestive system to play a positive role. Inhibitors to an organism's survival and growth in the digestive tract include lysozymes, low pH, low surface tension, immune systems, gastric fluids with bactericidal effects, and competition with other organisms [19].

Non-culture-based approaches and culture-based phenotypic methods for the identification of microorganisms both utilize a variety of cell targets. To define new bacterial species, a polyphasic combination of phenotypic (morphology, environmental and culture conditions, pathogenesis, enzymology, phage and bacteriocin typing, and serotyping); chemotaxonomic (chemical makeup of cellular components such as exopolysaccharides, fatty acid methyl ester, lipopolysaccharides, mycolic acids, polar lipids, and quinines); genotypic (16S rRNA sequencing similarity, G-C content, and DNA-DNA hybridization) characteristics; and comparisons with the phylogenetically closest species that have to stand in nomenclature [20]. The need for new alternative antibacterial medicines is greater due to the increase in the MTDR, or bacteria that become resistant to antibiotics after repeated use. A new alternative with some restrictions is "phage therapy," which can be used alone or in combination. Instead of those viruses that perform lysogenic cycles, phage therapy that uses viruses with the ability to enter the lytic cycle and no pathogenicity is preferable [21].

It has been demonstrated that a lactic acid bacterium increases the folic acid content in yogurt, buttermilk, and kefir as well as the amounts of niacin and riboflavin, vitamin B12, and vitamin B6 in cheese. To improve nutrient digestion, probiotics can be coupled with enzymes that aid in dissolving complex dietary components into simpler components. According to animal and *in vitro* studies, probiotic bacteria may lessen the risk of colon cancer by reducing the occurrence and quantity of tumors. Probiotics are used to treat Candida infections in older patients because they are more vulnerable to Candida infections due to poor dental hygiene, medicines, chronic illnesses, decreased salivary flow, and immune system impairment. The intestinal effects of probiotics include pain relief, diarrhea recovery (from rotavirus, traveler's disease, and antibiotic-induced diarrhea), lactase production, lactose intolerance and malabsorption symptoms, constipation relief, colitis treatment, and gastrointestinal immunity enhancement. Probiotic microorganisms can generally be used to treat conditions such as hypertension, halosis, lactose intolerance, allergies, and candidiasis as well as to improve soil fertility and intestinal tract health [22].

The gut microflora of humans and boilers

Following Hippocrates' proverbs, "Let food be your medicine and medicine be your food, and "All diseases originate in the gut", recent studies have suggested that healthy diets should include fermented foods to temporarily improve live microbes

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in our stomachs. To examine the advantages of various fermented non-dairy drinks (legume, cereal, pseudocereal, fruit, and vegetable) as potential carriers of bioactive compounds (produced during the fermentation process), prebiotics, and various probiotic bacteria, protecting to ensure that their viability is in the range of 10^6 - 10^7 CFU/mL at the time of consumption to reach the intestine in large amounts and improve human health through modulation of the gut [23]. Any disturbance to the gut's 10^{13} - 10^{14} microflora, which contains more than 1000 species, is referred to as dysbiosis. The host's health could be harmed by this modification. Cell-surface proteins that detect host targets, such as the mucus layer and extracellular matrix, are the major agents that mediate the adherence of pathogens and commensals to the gut. The contact of pathogenic or non-pathogenic bacteria with host tissue is facilitated by adhesins, which are adherence factors. The fimbriae, glycocalyx or capsule, pili, S layer, slime layer, teichoic and lipoteichoic acids, and slime layer are adhesion agents [24]. According to reports, several adhesins participate in interactions between lactobacilli and hosts. Mucus-binding proteins, collagen/fibronectin-binding proteins, and moonlighting-binding proteins are three different categories of adhesins. *Lactobacillus acidophilus* S-layer protein A (SlpA) prevents bacterial infection by obstructing the activity of the murein hydrolase and the cellular receptor DC-SIGN. Others that are of Lactobacillus origin include adhesins such as MapA, MUB, CmbA, 32-Mmubp, LAF 0673, Msa, Ip 1643, Cnb, CbsA, SlpB, LCABL 01820, FbpA, FbpB, Ef-Tu, GroEL, Eno (enolase), and glutamine synthetase [25].

Based on 16S rRNA gene sequencing, Naumova, et al. [26] reported that multiple phyla were detected in fecal samples during research on obesity-related health issues. Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Verrucomicrobia, Unclassified Bacteria, and Others were included in this group. With Firmicutes and Bacteroidetes predominating, a bioinformatic study revealed that the bacteria were distributed throughout 14 phyla, 21 classes, and 125 genera. Human obesity is thought to be significantly influenced by the gut microbiota. After brief (2-week) treatment of obese patients with a probiotic preparation that included Bifidobacterium longum, the probiotic treatment altered the composition of the gut microbiome in obese patients. The probiotic treatment increased the relative abundance of Actinobacteria (Bifidobacteriaceae and Coriobacteriaceae), Firmicutes, and Bacteroidetes (Prevotellaceae and Bacteroidaceae) (Negativicutes: Veillonellaceae and Clostridia: Peptostreptococcaceae). Probiotic therapy reduced the patients' overall blood sugar levels and improved their perception of their physical and emotional well-being.

The gut microbiome is crucial for individuals with cognitive behavior, mood, and neuropsychiatric disorders such as schizophrenia, depression, and autism. More than 20 hormones directly interact with distinct central nervous system receptors in the gut (CNS). Butyrate, propionate, and acetate work together to fix microglial dysfunction. Butyric, propionic, and acetic acids all serve similar purposes, whereas acetic acid serves a different purpose since it may cross the blood-brain barrier and accumulate in the hypothalamus, where it regulates hunger [27]. Through persistent oxidative stress and inflammation, excessive training may prevent physiological muscle adaptation. Overtraining and a poor diet can also disturb intestinal homeostasis, which increases inflammation. Probiotic supplementation may improve anaerobic and aerobic performance in some way. It is important to continue researching the gut-muscle axis phenomenon to maintain function, not just in athletes [28].

Broiler diets that include DL-methionine, L-lysine, L-threonine, and probiotics (*Bacillus subtilis*) can be supplemented with blue lupine (*Lupinus angustifolius*) seeds at a rate of 30% without having any negative effects on the ability of the broilers to grow, the appearance of their carcasses or immune systems, or their gut morphology. Additionally, probiotics support the immune system, gastrointestinal health, and growth of broilers fed diets containing 20 and 30% blue lupine [29]. To lower the risk of gastrointestinal sickness, accelerate growth, improve antioxidant and immunological status, and promote profitability in the production of chickens, ovo inoculation with bifidobacterial strains is favored [10].

The hypocholesterolemic potential of probiotic microorganisms

The greatest cholesterol elimination benefits were shown in the growth phase of the LAB cells. Growing cells may be able to absorb and assimilate cholesterol as fatty acids to build cell membranes and convert cholesterol to coprostanol, according to certain theories [30]. Cholesterol assimilation, bile salt deconjugation, cholesterol coprecipitation, cholesterol adhesion to the probiotic cell wall, and micellar sequestration of cholesterol were all investigated as ways to lower cholesterol in a group of potential probiotic LAB, including *Lacticaseibacillus paracasei* M3, *Lacticaseibacillus casei* M5, *Lacticaseibacillus paracasei* M7, and a few others. The bile salt hydrolase (BSH) activity of *Lacticaseibacillus casei* M5 peaked, releasing 57.63 nmol of glycine per minute. The LAB isolate M9 generated 52.12 nmol of glycine per minute. *Lacticaseibacillus casei* M5 deconjugated sodium glycocholate to yield 27.77 mol/mL cholic acid, whereas 20–26 mol/mL cholic acid was generated by other isolates. Isolates M6 (82.15%) and *Lacticaseibacillus casei* M5 extensively absorbed cholesterol (76.51%). The cholesterol coprecipitation ability of *Lacticaseibacillus casei* M5 was greater (50.16 g/mL) than that of the other LAB isolates (33 - 44 g/mL). The LAB isolate M8 (a reduction of 87.5%) reduced the micellar cholesterol levels the most, followed by the isolates M5 (a reduction of 84.75%), M9 (a reduction of 84%), M10 (a reduction of 84%), and M37 (79%). *Lacticaseibacillus casei* M5 achieved a greater level of cell wall adhesion to cholesterol (42.48 g/mL) than did the other LAB isolates (30 - 40 g/mL). The probiotic bacteria selected for this study can produce short-chain fatty acids (acetate, propionate, and butyrate), which is yet another method by which probiotics can decrease cholesterol levels [31].

The impact of putative functional stresses on the expression of genes involved in signalling and cholesterol metabolism was investigated. Six strains may control Niemann–Pick C1-like 1

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(NPC1L1) expression via the liver X receptor (LXR)/farnesoid X receptor (FXR) pathway. Four of these agents have been shown to treat atherosclerosis by decreasing lipid accumulation in ox-LDL-treated macrophages. *Bifidobacterium animalis* subsp. *lactis* F1-7 and *Lactobacillus vaginalis* FN3 could be considered prospective probiotic candidates for additional *in vivo* investigations based on their lipid-lowering properties and common characteristics. They may also have economic utility [32]. Through several mechanisms, including bile salt hydrolase activity, deconjugation of bile salts, cholesterol assimilation, adsorption of cholesterol onto cell walls, inhibition of micelle formation, and micellar sequestration of cholesterol, LAB probiotics were able to lower cholesterol levels. To determine the economic potential of LAB isolates such as *Lacticaseibacillus paracasei M3, Lacticaseibacillus caseiM5*, and *Lacticaseibacillus paracasei M7*, which have promising hypocholesterolemic potential. Additionally, research into the molecular mechanisms governing the role of probiotics in decreasing cholesterol may help us comprehend these procedures [31]. In their subchronic toxicity test, Thumu and Halami [33] reported that feeding animals (all groups) a high-fat diet for the duration of the test period caused the *Lactobacillus fermentum* strain to have lower cholesterol levels in the liver (90 days). Liver samples from the control and low-dose (10^7 CFU/ml) animals exhibited hepatic steatosis, hepatocyte ballooning, and severe macrovesicular steatosis, while those from the animals treated with medium (10^8 CFU/ml) or high (10^{10} CFU/ml) dosages exhibited significant improvement with decreased steatosis. *Pediococcus acidilactis*, *Bifidiobacterium adolescentis*, *Lacticaseibacillus rhamnosus*, and *L. acidophilus* had higher BSH activity and bile-salt deconjugation capacity than did the other probiotic strains. Within 24 hours, the cholesterol concentration in cholesterol micelles decreases [34]. Two powerful LAB strains, *Enterococcus faecalis*, and *Lactococcus lactis* were found in the intestine of *Channa argus*, a freshwater carnivorous fish that is significant to the economy, has a good taste, grows quickly, and has the powerful ability to decrease cholesterol [35].

Anticarcinogenic properties of probiotic microorganisms

One of the leading causes of death worldwide is cancer. The complexity of cancer cells and their capacity to infiltrate the immune system make treating cancer difficult, despite considerable advancements in the field. By increasing the epithelial barrier and anticarcinogenic and anti-inflammatory responses, probiotics change cellular and immunological responses. Probiotics are popular because they can control cancer signals. These changes may be caused by mechanisms involving the activation of tumor suppressors, induction of apoptosis, inhibition of kinases, inhibition of mutagenesis activity, downregulation of oncogenes, induction of autophagy, and downregulation of oncogenes [36]. The development of certain malignancies can be stopped or delayed by probiotic microbes. Since nitrosamines and other carcinogens can be produced by gut bacteria, this is the result of that knowledge. As a result, administering lactobacilli and bifidobacteria could alter the flora, resulting in lower levels of glucuronidase and carcinogens [37]. An interferon-stimulated gene called cholesterol 25-Hydroxylase (CH25H) transforms cholesterol into oxysterol 25-Hydroxy cholesterol (25HC). Dysregulation of CH25H may play a role in cancer and chronic inflammatory diseases. The enzyme CH25H is found in the endoplasmic reticulum and hydroxylates the iso-octyl side chain of cholesterol. To effectively suppress *Listeria monocytogenes* and *Shigella flexneri*, 25HC molecules play a key role [38].

Aflatoxins, a class of mycotoxins generated by *Aspergillus spp.*, such as *Aspergillus flavus*, *A. parasiticus*, and *A. nominus*, are diverse secondary metabolites. These plants may grow in raw foods and agricultural goods, particularly figs, nuts, cereals, chilies, nuts, maize, dry fruits, and others. Aflatoxicosis negatively affects these metabolites. Aflatoxins are also widely known for causing cancer, being a component of mutations, and suppressing the immune system. There are still 18 known aflatoxin compounds. The B1, B2, G1, G2, and M1 categories are particularly significant in terms of toxicity and the number of impacted foods. The most potent and common kind of mycotoxin is aflatoxin B1 (AFB1). Both humans and animals are affected by this mycotoxin. The cytochrome P450 (CYP450) detoxification system in the liver serves as the primary mechanism by which the harmful effects of mycotoxins are initiated. The maximum amount for overall consumption was set at 20 µg/kg by the United States Food and Drug Administration (USFDA). The biological removal or reduction of aflatoxins from food and feed employing probiotic bacteria through absorption or degradation methods. Such toxins can be reduced by adsorption or an enzyme degradation process by *Lacticaseibacillus casei* and *L. acidophilus*. After more than 4 hours of challenge (acid, bile salts, enzymes, etc.), there was a 13.86–70% decrease in the AFM1 concentration, which was maintained at the therapeutic level (>10^7 log CFU/ml) [39].

Optimization of food-grade media for the coproduction of bioactive substances

A functional food has a food component, whether or not it is a nutrient, that positively influences one or more targeted bodily functions. Foods that have had a potentially dangerous component (or components) eliminated using technology fall under this category as well [40]. Numerous techniques can be applied to increase product yield, lower cost, and increase fermentation process efficiency. Analytical technologies such as real-time monitoring systems for measuring processing factors such as dissolved oxygen, pressure, temperature, pH, etc., automated fermenters with improved built-up controls to guide the fermentation process, and developing technologies to simplify fermentation along with the development of new, more robust and successful cultures through traditional and modern "omic" practices have been proposed [41,42]. A processing technique called fermentation uses microorganisms and their enzymes to carry out basic biochemical alterations in the food matrix. The shelf -life and organoleptic qualities of food products are enhanced through fermentation, which also boosts the bioavailability and bioaccessibility of nutrients [43]. Probiotic organisms can be bacteria, molds, or yeasts, although bacteria make up the majority of them. Lactic Acid

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Bacteria (LAB) are among the bacteria that are employed in probiotic production. *Enterococcus faecalis*, *Enterococcus faecium*, *Bifidobacterium species*, *Lactiplantibacillus plantarum*, *L. bulgaricus*, *Streptococcus thermophilous*, and *E. coli* were found [22]. Probiotic lactic acid bacteria appear to suppress the growth of foodborne pathogenic microorganisms according to several in vitro investigations [1]. Therefore, the use of bacterial probiotic cultures and cultures that could improve the usability and safety of fermented products is an emerging trend [44].

Probiotics are considered viable biological alternatives for inclusion in fish diets as growth promoters because they stabilize fish health status through their actions and effects on the intestinal microbiota, which leads to improved use of nutrients and enhances physiological performance and systemic immunity. The addition of a probiotic containing *Bacillus subtilis* and *Bacillus cereus* at a rate of 0.60 g/kg feed is advised since it increases *the* growth and health of *Rhamdia quelenioides* throughout the growth stage [45].

Rhizogenic biostimulant effect

Excessive chemical fertilizer use can cause severe environmental damage. In recent decades, the use of biostimulants to promote soil composition and plant development has made a substantial contribution to environmental conservation. During the growth of turfgrass (a narrow-leaved grass species that forms a uniform, long-lived ground cover that can tolerate traffic and low mowing heights), rhizogenic biostimulant application increased microbial activity, organic matter, and enzymatic activity in both kinds of soil. With the application of the biostimulant, the calcium, potassium, magnesium, and phosphorus contents of the soil increased, while its pH and electrical conductivity decreased. The most significant improvements were a 77% increase in calcium and a 38% increase in potassium for sandy soil and sandy loam soil, respectively. Turf root length significantly increased after the application of a biostimulant. With increases of 43% for sandy soil and 34% for sandy loam soil, respectively, compared to those of the control, this increase was greater for sandy soil. The application of the biostimulant increased the biological community, enzymatic activity, and root accessibility to soil nutrients in sandy loam and sandy soils as well as the physical and chemical composition of the plants [46]. The prebiotic molecules produced by the fermentation of humic acids and the probiotic molecules produced by a *Bacillus sublitis* bacterium strain both contributed to the enhancement of microbial activity. The soil pH and EC were reduced using a biostimulant. The uptake and availability of the plant nutrients Ca2+, Mg2+, K+, and P were made possible by the decrease in soil pH [47].

Crop cultivation necessitates the use of expensive, environmentally damaging nutrient additives. Additionally, to boost output and more efficiently use resources such as nutrients, crop production must meet global demands. Some entomopathogenic fungi can help plants grow, although research on these benefits has been conducted only in ideal situations with plenty of nutrients available. When nutrients are plentiful, *Beauveria bassiana* seed treatment could be utilized to boost maize development, but when nutrients are low, the fungus does not affect growth [48]. Vitamins and important micronutrients are abundant in plant diets. The right amounts of trace minerals (such as iron, zinc, magnesium, and manganese) are necessary for the human body to function properly and for its critical role. The main sources of these trace minerals are cereals and pulses. Despite these minerals, a sufficient diet of plant foods cannot supply all the nutrients needed by the organism. Phytate, tannins, phenols, oxalates, and other antinutritional elements are abundant in plant diets. These elements may reduce the bioavailability of some vital micronutrients in plant-based meals. However, studies in the literature suggest that processing techniques such as fermentation can increase the bioavailability of nutrients and minerals in plant diets [49].

Improvement in the self-life of probiotic microorganisms

Probiotic viability during fermentation and storage can be increased by using specific probiotic carrier techniques, such as microencapsulation and spray drying. The most prevalent probiotic bacteria employed in the creation of these products are *Lactobacillus* and *Bifidobacterium*. Understanding the types of hostile environments that food is exposed to both before and after consumption is necessary for the design of an efficient probiotic delivery system. The ability of probiotics to survive during the production, storage, transportation, and gastrointestinal transit of food is influenced by a variety of physicochemical variables, such as mechanical stressors; light, oxygen, gastric acid, digestive enzyme, and bile acid availability. The tolerance of probiotics to unfavorable circumstances can be improved by microencapsulation. To increase the amount of probiotics that can enter the colon, a variety of oral delivery strategies, including coating and embedding techniques, have been created. To maximize the survival of probiotics during storage and within the human gut, as well as their capacity to colonize the colon, encapsulation technologies are necessary. These technologies function by enhancing probiotic mucoadhesive qualities and shielding them from harsh environmental conditions. Typically, food-grade substances such as lipids or biopolymers are used to coat or encapsulate probiotics. To increase survival, additional components, such as nutrients or protective chemicals, may occasionally be coencapsulated [50]. According to Lee and Salminen [51], the "therapeutic minimum" for probiotics is 1 x 10^5 colony-forming units per gram or millilitre of the finished product. For any positive effects to manifest in people, viable cells ranging from 1 x 10^6 to 1 x 10^9 CFU must be consumed every day. Even during cold storage, *Lactobacillus acidophilus* and *Bifidobacterium bifidium* exhibit a brief stationary phase followed by rapid cell viability loss. As a result, the short self-life of these probiotic microbes poses logistical difficulties for researchers and manufacturers alike. Compared to *Lactobacillus acidophilus* and *Bacillus spp.*, *Lactobacillus casei* and *L. plantarum* have longer self-lives. Lactic acid concentrations range from 0.5 to 1.5 w/v in typical cultured milk, which has an acidic pH ranging from 3.5 to 4.5) These include both high-temperature processes such as spray drying and low-temperature processes

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such as spray chilling, freeze drying, emulsification, extrusion, coacervation, gelation, and electrohydrodynamic atomization [4].

Due to the demand for poultry products, broiler chicken farming is one of the most lucrative food production sectors worldwide. *Bacillus* spp. are easily isolated from their surroundings and can survive tough conditions in the digestive tract for up to 100% of the time. In addition to these significant factors, the main benefit of using Bacilli as feed probiotics is their robustness concerning industrial production due to the high density of spores produced, as spores can produce more than 1x 10^{11} spores/mL. In addition, spores can maintain approximately 90% of their vitality during the probiotic harvesting procedure. Additionally, these spores have a potential shelf life of five years when made into probiotic products at a concentration of 1 x 10^{9} spores/mL [52].

Role of their primary/secondary metabolites, such as EPSs, bacteriocins, conjugated linoleic acids (CLA, C18:2), and free linoleic acid (FLA)

Next-generation probiotics (NGPs) are gaining popularity as live bacterial treatments for treating diseases as a result of the advancement of high-throughput DNA sequencing and molecular analysis technology. More research is required to fully understand the interactions between prebiotics and NGPs inside and outside of hosts to improve their nutritional status. NGPs and prebiotic substrates. Next-generation probiotics include *Akkermansia* (aerotolerant anaerobe), *Faecalibacterium* (strict anaerobe), *Eubacterium* (strict anaerobe), *Bacteroides fragilis* (obligate anaerobe), *Clostridium* (obligate anaerobe), *Propionibacterium* (facultative anaerobe) and *Roseburia*. Traditional probiotic species include *Lactobacillus spp.*, an obligate anaerobe [53]. The nutritional status of the host is significantly influenced by the gut microbiota. By increasing the effectiveness of nutrient extraction, gut microbiota modification may enhance overall health, end malnutrition, and fight disease. One-size-fits-all techniques are scarce due to the high uniqueness of the gut microbiota composition and function; hence, personalization will be needed. Combining well-established techniques such as pro/pre/synbiotics and recently emerging methodologies with microbiome screening and subsequent personalization can result in personalized gut microbiota modification for nutritional purposes. While some techniques are simple to implement, others require additional research and testing to determine their viability and security. Safety is of the utmost importance in the creation and use of customized microbiome therapies because of the possible detrimental effects on individuals and/or entire communities [54]. Depending on the type of iron present, multiple pathways for iron absorption in the intestine are used. It is only partially understood how heme iron (Fe^{2+}), which is mostly contained in meat diets, is absorbed by enterocytes. Hemoxygenase-1 (Hem-1) in cells releases iron from heme (HO-1). Before being delivered into intestinal absorptive cells, non-heme iron (Fe^{3+}), which is found primarily in vegetarian diets, is reduced to Fe^{2+} by the ferric reductase CYBRD1 (DCYTB) enzyme. A protein known as the divalent metal transporter transports heme iron into intestinal enterocytes after non-heme iron is converted to it in the intestinal lumen (DMT 1). Iron inside enterocytes can either be stored as ferritin or transferred into the bloodstream via ferroportin (FPN1), also known as the iron exporter, across the basolateral membrane. Hepcidin controls the expression of FPN1. By joining iron to apo-transferrin and merging two Fe^{3+} ions into a single transferrin molecule (Tf), hephaestin regulates the metabolism and homeostasis of iron absorption. There are numerous options for treating iron deficiency, including oral iron derivatives, which can efficiently absorb iron in the intestine, mostly in the duodenum, given that the stomach and other regions of the gut are less engaged in the absorption process [55]. In hospitalized and immunocompromised patients, superficial and lethal invasive Candida infections represent severe clinical problems. The restricted availability of antifungals and their corresponding adverse effects worsen emerging treatment resistance among Candida species. Numerous probiotic yeasts, including *Candida albicans*, *Candida tropicalis*, *Candida glabrata*, *Candida parapsilosis*, *Candida krusei*, and *Candida auris*, have been found in preclinical trials to successfully reduce the virulence of Candida species. However, the only probiotic yeast that is marketed is *Saccharomyces cerevisiae* var. *boulardii*. Probiotics employ many defense strategies, such as creating a physical barrier, aggregating pathogens, and neutralizing virulence. Secreted metabolites such as short-chain fatty acids efficiently inhibit the adherence and morphological changes of Candida species. Overall, probiotic yeasts show promise as a viable substitute or part of combination therapy for treating Candida infections [56].

The principal byproducts of SCFA-producing bacteria are propionate, butyrate, and acetate, which increase the activation of FFAR2 and FFAR3. These improvements in FFAR2 and FFAR3 increase heart rate and energy expenditure for energy homeostasis in addition to promoting noradrenalin secretion [57]. Increased leptin production and adipogenesis and the suppression of lipolysis in adipose tissues are influenced by SCFAs. Type 2 diabetes (T2DM) and cardiovascular disease (CVD) are two metabolic illnesses that are a growing public health concern and have major negative impacts on people's quality of life. People with T2DM have a relative risk of CVD that is two to four times greater than that of nondiabetic people. CVD is the leading cause of death in T2DM patients. In recent decades, dynamic changes in dietary macronutrient intake and lifestyle modifications have been linked to the development of metabolic diseases. Increased obesity, cell dysfunction, metabolic endotoxemia, systemic inflammation, and oxidative stress are all strongly facilitated by changes in the gut microbiota composition. The improvement in the gut microbiota caused by probiotics and prebiotics can reduce the risk of T2DM and CVD by stimulating insulin signaling and decreasing cholesterol [58]. According to some research studies, diarrhea, gastroenteritis, irritable bowel syndrome, Inflammatory Bowel Disease (IBD) (Crohn's disease and ulcerative colitis), cancer, impaired lactase digestion, infant allergies, failure to thrive, hyperlipidemia, hepatic diseases, *Helicobacter pylori* infections, genitourinary tract infections, and others may all benefit from the use of probiotics. For

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patients with these and possibly additional medical disorders, the potential benefits of probiotics should be further examined. Additionally, the potential of probiotics for harmful side effects should be investigated. The nature and number of interrelated factors dictate the proper composition and concentration of the gut microflora. Trying to "optimize" nature's finely regulated gastrointestinal environment by changing one aspect, such as concentration, may very well be changing a condition that nature never intended to change. Given the complexity of the gastrointestinal environment, it may be challenging to assess the short- and long-term implications of this shift [59]. Probiotics can reduce Necrotizing Enterocolitis (NEC) in preterm newborns according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) standards. In comparison to feeding infants (alone or with human milk), *Lactobacillus acidophilus* has been shown to have the most promising effect on lowering the risk of NEC [60].

Amiri, et al. [61] used a statistical approach and the Box–Behnken design to maximize the co-production of conjugated linoleic acid (C18:2), exopolysaccharides, and bacteriocins. A temperature of 42 °C, a fermentation temperature of 12 hours, and a yeast extract concentration of 2% were the best conditions for the coproduction of *Lactobacillus acidophilus* LA-5 in cheese whey medium. Exopolysaccharides, conjugated linoleic acids, viable cell number, and inhibition zone had optimal values of 2.26×10^8 CFU/ml, 348.24 mg/ml, 51.46 g/ml, and 12.46 mm, respectively. Exopolysaccharides are bioactive substances that have the potential to function as anti-inflammatory, anticancer, and anticholesterolemic agents. Numerous polysaccharides can be produced by bacteria, some of which are tightly bound to the cell surface and known as Capsular Polysaccharides (CPSs) or are released as exopolysaccharides. Exopolysaccharides can be produced by lactic acid bacteria (LAB), which are employed in the food sector, primarily for the manufacturing of dairy products (EPSs). Since they favorably affect the texture and organoleptic features of dairy products, evaluating the rheological and sensory attributes of EPS is crucial. Additionally, due to their biocompatibility, non-toxicity, and biodegradability, EPSs have attracted significant interest for pharmaceutical and nutraceutical uses. These bioactive substances could have anti-inflammatory, prebiotic, antibacterial, and antioxidant effects [62].

A good indicator of future disease development

In the human intestine, Actinobacteria and Firmicutes dominate (>90% of the total microbial population) and are crucial for nutrient uptake, mucosal barrier reinforcement, xenobiotic metabolism, angiogenesis, and postnatal intestinal maturation. Diet regulates the makeup of these bacteria, which is important for the emergence of metabolic diseases [63-67]. According to Ramezani and Raj [68], the human gut contains more than 100 trillion bacteria that are important for digestion, metabolism, nutrition, illness prevention, and sustaining overall health [26]. Dysentery, diarrhea, or inflammatory reactions such as rheumatoid arthritis originate from disturbances in gastrointestinal homeostasis, particularly when the makeup of the gut microbiota is drastically altered (rheumatoid arthritis). *Provotella* spp. are typical anaerobic, non-spore-forming gut flora of humans. Its role is to digest polysaccharides, consume carbohydrates and high-fiber diets, and be used as a biomarker of diet and a precursor to the development of rheumatoid arthritis [69]. At the beginning of rheumatoid arthritis, *Provotell copri* is the causative bacterium that disturbs the normal gut flora. Additionally, long-term use of antibiotics, NSAIDs, stress, and inflammatory conditions leads to an imbalance in the microbiota in the human stomach, which can lead to dysbiosis. *Collinsella aerofaciens, Eggerthella lenta, Faecalibacterium* spp., *Haemophilus* spp., *Prevotella* spp., and *Streptococcus* spp. are known to cause abnormalities in the normal gut microbiota and, therefore, loss of integrity of the inner epithelium of the gut and the emergence of rheumatoid arthritis [70]. Increased fluid retention, neural migration, and inflammatory cell release (IL-1, IL-8, IL-12, IL-15, IL-17, IL-29, IL-18, and TNF-α) are all symptoms of RA. TNF-α and IL-6 inhibitors are efficient at treating RA according to previous studies. Therefore, preclinical trial treatment with *Lactobacillus acidophilus* or *Lacticaseibacillus casei* over 28 days reportedly prevented the development of arthritis by reducing arthritis symptoms and the levels of proinflammatory cytokines, such as IL-17, IL-1, IL-6, and TNF-α; releasing anti-inflammatory cytokines, such as IL-4 and IL-10; and helping to ameliorate rheumatoid arthritis [71].

Osteoblast differentiation is crucial for both bone growth and bone density maintenance. In Korea, raw milk from a local farm was obtained without Pasteurization, and *Propionibacterium freudenreichii* MJ2 was identified from this farm. The raw milk was serially diluted and cultivated on a YEL agar plate. A single CFU on the plate was subcultured in Reinforced Clostridial Medium (RCM) and identified by 16S rRNA sequencing following incubation at 30°C under anaerobic conditions for 7 days. Osteoblast mineralization was significantly increased in cells treated with heat-killed *Propionibacterium freudenreichii* MJ2 (hkMJ2) via an increase in the Osteoprotegerin (OPG)/receptor activator of nuclear factor-ligand (RANKL) ratio as well as by promoting the expression of bone morphogenetic protein 2 and runt-related transcription factor 2 compared with hkMJ2, live MJ2 is ineffective [72].

To identify the microbial profile in tumor tissues from patients with colorectal cancer in North India. To determine the prevalence of particular germs, next-generation sequencing of bacterial 16S rRNA V3–V4 hypervariable regions taken from the tumor and surrounding tissue was carried out. At the phylum level, Proteobacteria were differentially expressed in colorectal cancer tissues compared to nearby normal tissues, indicating that the expression profile analysis revealed a lower diversity among the tumor-associated microbial communities. Additionally, in only colorectal cancer, *Bacteroides massiliensis, Alistipes onderdonkii, Bifidobacterium pseudocatenulatum,* and *Corynebacterium appendicis* could DESeq2 normalization identify 4 out of 79 unique species ($p < 0.005$). Therefore, our results point to the potential use of these microbial signatures as putative biomarkers that can separate colorectal cancer tissues from their surrounding normal tissues, which may provide insight into the pathogenesis of colorectal cancer [73].

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The shortcomings of probiotics

The sensitivity of several NGPs to oxygen and other environmental factors in the human digestive tract may be limited. The ability of probiotics to regulate human intestinal function through interactions with the microbiota is improved by the administration of prebiotics, such as FOS and GOS, and bioactive substances or biopolymers, such as vitamins and plant polyphenols, in hostile environments [53]. This strategy requires an understanding of how probiotics can act as transporters for iron, transform inaccessible iron into its available form, or produce metabolites that indirectly boost the absorption of iron in the gut [74]. To demonstrate that probiotics are successful at delivering bacteria to the human colon using microencapsulation techniques, *in vivo* human feeding experiments are needed. There are several types of microgel, including coating technology, nutrient-doped microgels, gastric-resistant microgels, core-shell microgels, and biopolymer complex microgels [50]. Because it affects body weight, proinflammatory behavior, and insulin resistance, intestinal microbiota may be a significant factor in the development of type 2 diabetes(T2DM) and Cardiovascular Disease (CVD). The makeup and operation of the gut microbiota can be influenced by probiotics and prebiotics, as is generally accepted by the scientific community. Probiotics and prebiotics are believed to have an impact on T2DM and CVD by altering the gut flora, controlling insulin signaling, and reducing cholesterol. However, understanding how probiotics taken orally interact with the gut microbiota is difficult [58].

Further perspective

Legumes, cereals, pseudocereals, fruits, and vegetables—non-dairy matrices—represent potential probiotic, prebiotic, and bioactive chemical transporters. Due to the organic acids produced during fermentation, their nutritional and functional makeup, and their digestibility, these vegetable matrices are good substitutes for dairy matrices in terms of shelf life and safety. Additionally, all of the matrices under investigation had probiotic concentrations greater than the minimum advised concentration (>7 Log CFU/mL). As a result, they are good substitutes for dairy goods on the market for individuals who are hypercholesterolemic, allergic to or intolerant to milk proteins, vegetarians, or those who are intolerant to dairy. However, additional *in vivo* research, such as human clinical studies addressing matrix combinations and doses in different populations, is needed to support the health advantages of consuming fermented non-dairy beverages [23]. It is crucial to this strategy to comprehend how probiotics can transport iron, transform inaccessible iron into its usable form, or produce metabolites that subsequently boost the intestinal absorption of iron. Further research must concentrate on these formulations because the few available trials to date have already produced encouraging findings. Iron absorption can be influenced by consuming probiotics and prebiotics, but the type of iron consumed is crucial. To effectively cure iron deficiency, the cytotoxicity of unabsorbed iron to gut cells (enterocytes) must be thoroughly addressed, and specialized meals can do this [74]. Due to its ease of use and low cost, fermentation is still the most popular biotechnological technique employed in cereal-based beverages. Fermented drinks have a long history and are well known for their flavor and health benefits. The market for functional, natural, and non-alcoholic beverages is continuously growing worldwide due to their appealing sensory qualities and growing consumer awareness of the value of a balanced diet. This essay describes the recent technological advances made to improve the nutritional value and quality of non-alcoholic fermented grain beverages (NFCBs). NFCBs are developing as a new research topic. As mentioned, NFCBs have functional advantages for one's health. To address certain health issues, new studies should be conducted to create NFCBs that combine probiotic-fermented beverages with items such as fruit juices, vegetables, and cereals. Future fermented cereal drinks must strike a balance between their sensory qualities, nutritional content, alcohol level, and resource commitments if they are to become even more alluring, nutritious, and affordable [75]. Non-dairy items did not receive enough attention in modern pre- and pro-bios. Cereals in particular present fresh, fascinating possibilities. Because of their accessibility and nutritional value, these plants are frequently consumed worldwide. These prebiotics were tested in a recent study. Prebiotics of non-dairy origin, among other things, are effective at reducing excessive blood sugar and improving the course of several metabolic diseases. Moreover, they effectively prevent intestinal ailments, including cancer, atherosclerotic disease, and cardiac occurrences. The vast potential of this aspect of nutrition is provided by a range of cereals, particular bacteria employed for fermentation, and hundreds of intermediate and final biologically active compounds known as postbiotics. This will encourage further scientific study in this field [12]. Deficiencies in micronutrients are a global public health issue. According to emerging research, probiotics may improve micronutrient status, which could help prevent malnutrition linked to non-communicable diseases. the impact of probiotic supplementation on nutritional status and pinpointed specific future lines of inquiry. Despite the variety of related research, probiotic consumption in healthy individuals may increase vitamin B12, folate, calcium, zinc, and iron intake [76]. To identify any potential negative effects, each probiotic and prebiotic should be carefully assessed. Future research is necessary to better understand how the ingested and intestinal flora interact [58]. The probiotic challenge is to maintain their self-life and viable counts. They are lived via lyophilization of probiotic inoculum or gel coating. Then our research goes to surroundings, prebiotics that are non-living things that provide the growth of probiotics to increase their activity. Therefore, the attention is to synbiotics, parabiotics, and postbiotics.

Conclusion

The majority of the species of Lactobacilli and bifidobacteria can use β-glucooligosaccharides (β-GOS) as their primary carbon source. For MTDR organisms, a new alternative may be "phage therapy," which can be used alone or in combination. To determine the economic potential of LAB isolates such as *Lacticaseibacillus paracasei M3*, *LacticaseibacillusM5*, and *Lacticaseibacillus paracasei M7*, which have promising

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hypocholesterolemic potential. *Lactobacillus acidophilus* has been shown to have the most promising effect on lowering the risk of NEC. To demonstrate that probiotics are successful at delivering bacteria to the human colon using microencapsulation techniques, *in vivo* human feeding experiments are needed. There are several types of microgel, including coating technology, nutrient-doped microgels, gastric-resistant microgels, core-shell microgels, and biopolymer complex microgels. probiotics may improve micronutrient status, which could help prevent malnutrition linked to non-communicable diseases. Despite the variety of related research, probiotic consumption in healthy individuals may increase vitamin B12, folate, calcium, zinc, and iron intake. Probiotics can control cancer signals. These changes may be caused by mechanisms involving the activation of tumor suppressors, induction of apoptosis, inhibition of kinases, inhibition of mutagenesis activity, downregulation of oncogenes, induction of autophagy, and downregulation of oncogenes. They become also good indicators of disease development. Probiotic Microorganisms are used for a large number of areas such as regulation of oncogenes, indicator before the development of disease obesity, arthritis, anal cancer, etc., as reforms the dysbiosis, may be used as energy drinks, industrial uses, fortified drinks with vitamins, etc. Dairy products are now shifted towards non-dairy products. After that functional foods and fermented foods, Alcoholic products are now shifted to Non- alcoholic fermented grain beverages [77].

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Author contributions

Triyugi Narain Kushwaha and Shweta Maurya were responsible for the study design. Data was acquired, analyzed, and interpreted by Triyugi Narain Kushwaha and Shweta Maurya. The manuscript was prepared by Triyugi Narain Kushwaha. Both authors contributed to the editing and reviewing of the manuscript.

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