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Probiotic formulations for human health: Current research and future perspective

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ABSTRACT

Probiotics are living microorganisms known for their beneficial properties and have been extensively researched and utilized in various products worldwide. These microorganisms have essential nutritional needs and exhibit significant functional qualities. Probiotics have been employed to enhance the well-being of both animals and humans by influencing the balance of microorganisms in the intestines. Several probiotic strains, such as *Bifidobacterium* and *Lactobacilli,* became identified and studied for their potential in mitigating the incidence of gastrointestinal (GI) infections or as a therapeutic approach for treating such infections. With the rise of microbiota displaying resistance and tolerance to traditional medications and antibiotics, the effectiveness of drugs has diminished. Several probiotic strains have been identified to possess notable properties, including potent anti-inflammatory and anti-allergic effects. Consequently, introducing beneficial bacterial species into the GI tract offers an appealing approach to restore microbial balance and prevent diseases. Furthermore, probiotics have demonstrated the capacity to inhibiting the action of intestinal bacterial enzymes responsible being synthesizing colonic carcinogens. Probiotics offer a promising preventive and therapeutic advancement, but further research is required to better understand their specific impact on intestinal health. Probiotics can also exert a direct influence on other microorganisms, including pathogens, which is crucial in preventing and treating infections and restoring the balance of microorganisms in the GI tract. The present review deals with probiotic formulations, their mechanisms, and role in human health.

1. INTRODUCTION

In recent times, diets emphasizing health and wellness have gained significant popularity among consumers [1]. As a result, the demand for functional foods has risen substantially. The Japanese government pioneered the concept of functional foods in the mid-1980s [2]. In recent times, there has been a widespread utilization of functional foods, including probiotics, which are produced globally. The term “probiotic,” originating from Greek and meaning “for life,” refers to microorganisms that offer beneficial effects to the host when consumed in suitable quantities [3]. The consumption of probiotic foods positively affects the balance of the intestinal microflora and overall health. According to an expert committee, probiotics refer to “live microorganisms that, while ingested in varying quantities, deliver additional benefits for health along with inherent nutritional value [4].

Probiotics are available in various forms, such as dietary supplements, beverages, food products, and medicinal. Accredited for their health

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benefits, probiotics are known to help alleviate lactose intolerance, stimulating the immune system, provide relief from constipation, lower cholesterol levels, exhibit anti-mutagenic properties, enhance mineral absorption, offer anti-carcinogenic effects, and assist in controlling hypertension [5]. The primary function attributed to probiotics is their ability to combat pathogenic microorganisms [6]. Probiotics achieve by competitively excluding harmful microbes and hindering their overgrowth through nutrient competition and occupying adhesion sites [7]. Probiotics consist of various microbial strains, with the majority of commercially available probiotic strains belonging to the genera and *Bifidobacterium, Lactobacillus* [8]. Furthermore, numerous species of *Bacillus* that exhibit probiotic potential, along with *Bacillus amyloliquefaciens, B. cereus, B. clausii, B. coagulans, B. licheniformis, B. polyfermenticus, B. pumilus,* and *B. subtilis* [9].

Probiotics bacteria offer various health benefits when consumed in sufficient quantities [10]. They are often known as "beneficial" bacteria since they assist in maintaining a harmonious microbial environment within the digestive system [11]. Probiotic microbiome is commonly utilized in dietary supplements and also found naturally as live microflora in a variety of fermented food products that people consume [12]. The ways in which probiotics positively impact on human health involves in multiple molecular mechanisms including enhancing regulating the response of immune, the strength and function of the intestinal barrier, and counteracting infectious agent by producing antimicrobial substances or competing for binding sites against mucosal surface [13]. The human gastrointestinal (GI) system harbors a vast population of bacteria, encompassing both advantageous and potentially detrimental species. Probiotics have significant importance in preserving a harmonious microbial ecosystem by impeding the proliferation of harmful bacteria while fostering the growth of beneficial ones [14]. In addition, they contribute to fortifying the intestinal barrier, facilitating digestion, and aiding in the absorption of nutrients [15]. At present, probiotic research aims to comprehend the composition of typical healthy gut microbiota in individuals. This understanding can then be utilized as a nutritional management strategy for particular ailments of gut and serve a foundation for future developments in bacterioprobiotic bacteriotherapy applications [16].

The use of antibiotics can disturb the natural equilibrium of gut bacteria, resulting in conditions such as antibiotic-associated diarrhea (AAD). However, incorporating probiotics into one's routine during antibiotic treatment and for a duration thereafter can support in restore a fit gut microbiota and mitigating these adverse effects [17]. Probiotics can potentially influence the gut-brain axis, potentially offering benefits in terms of alleviating symptoms associated with anxiety, depression, and stress. However, additional research is necessary to obtain a comprehensive comprehend of the underlying mechanisms involved through this relationship [18]. Probiotics have been the subject of investigation concerning their potential to improve skin health [19]. Their effects on conditions such as acne, eczema, and rosacea are being explored, as they have the ability to modulate inflammation and foster a favorable skin microbiome. Moreover, specific strains of probiotics have shown promise in maintaining a healthy vaginal microbiota, potentially preventing or reducing the occurrence of vaginal infections, including yeast infections and bacterial vaginosis [20]. The effectiveness of probiotics can differ depending on various factors, including specific strains, dosage, and individual variations in gut microbiota. It is important to choose probiotics that have been extensively researched and are relevant to our specific health needs to ensure optimal results. Consulting a healthcare professional or registered dietitian can be helpful in determining the most suitable probiotic product or strain for our specific health goals [21].

2. PROBIOTIC MECHANISMS AND ACTION

Probiotics play a significant role in regulating the immune response to the host. The immune system is comprised of two main components: the adaptive systems and innate [22]. The adaptive immune response is reliant on T and B lymphocytes that possess the ability to bind to specified antigens. This interaction is essential for mounting an effective immune response. The primary mechanism through which probiotics confer their health benefits by positively influencing the regulation of intestinal immune response and intestinal tract of host [23]. This regulation occurs through the stimulation of specific cytokines and the secretion of immunoglobulin A in intestinal mucosa. These actions are essential for sustaining a fit gut environment. The strain used in a probiotic has a pivotal role in immune modulation [24]. The mechanism and action of probiotics involves in several key aspects firstly, probiotics are capable of colonizing and normalizing the microbial communities in the intestine of both children and adults [25]. By doing so, they create a competitive environment for pathogens and produce bacteriocins, these substances are antimicrobial agents that hinder the growth of harmful bacteria. In addition, probiotics have the ability to modulate fecal enzymatic activities that are involved in the metabolism of biliary salts. They can also contribute to the inactivation of carcinogens and other foreign substances, known as xenobiotics, which help to promote a healthier GI environment [Figure 1].

Probiotics exhibit their effects through a range of mechanisms [26]. These activities aid in the generation of branched-chain fatty acids and short-chain contribute to cell adhesion, and stimulate the mucin production, all of which promote a favorable gut environment. In addition, probiotics regulate the immune system, up regulation of anti-inflammatory cytokines, leading to the differentiation of T-regulatory cells and the growth factors [27]. Furthermore, they interact with brain-gut axis, regulating endocrine and neurological functions. These diverse actions demonstrate the various ways in which probiotics positively influence overall health and well-being [28]. Recent research has highlighted the significance of bacteria in the intestine has developed of numerous disorders. Specifically, certain components of commensal organisms, in combination with genetic susceptibility in individuals, have been found to potentially initiate abnormal immune responses [29]. Consequently, this process can contribute to the development of inflammatory bowel disease (IBD). Intestinal microorganisms play a crucial role in protecting against infections and contribute to the development and regulation of the host mucosal immunity [30]. They actively engage in transforming the developmental and regulatory signals, thereby conferring mucosal immune protection [31]. The incidence of bacterial infections has seen a significant rise, surpassing the number of infections caused by *Salmonella* [32]. This increase in infections can be attributed to factors such as consumption of broiler meat, which may account for approximately 20–30% of these cases. Illness or asymptomatic carriers are caused by aggressive production of harmful Bacilli in digestive system, constantly polluting the external environment, by the products which are derived from infected animals by food adulterate by feces of animals, or *Salmonella* or by the contact with infected people or birds, that are responsible for food poisoning. *Salmonella* causes severe dehydration in elders and children, by the electrolyte imbalance [33]. The effective solution for controlling *Campylobacteriosis* and *Salmonella* are antiseptic, and their act was only to eliminate unfavorable bacteria [34].

Disease management in aquaculture is great importance globally, with

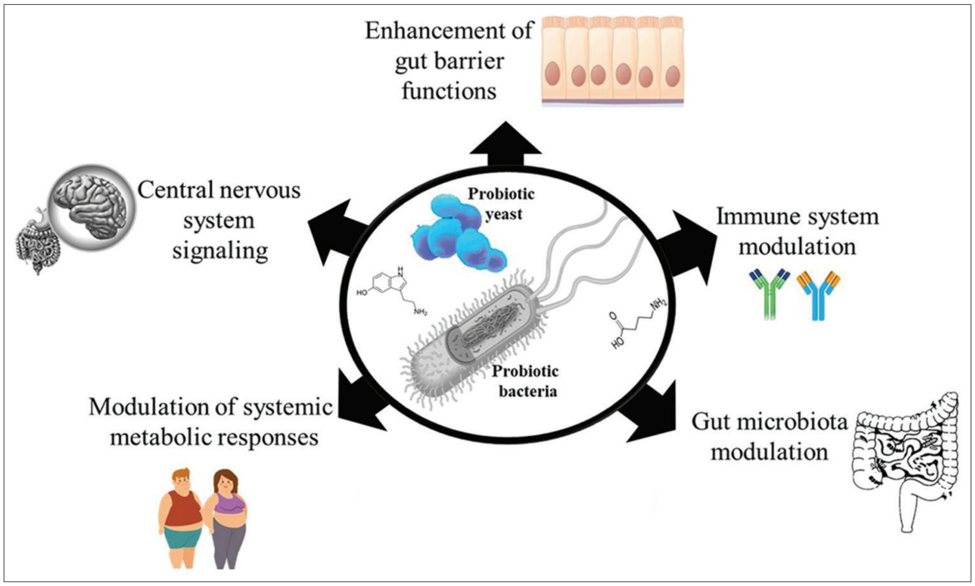

Figure 1: Mode of action of probiotics. Source: Daliri *et al*. [171].

efforts focused on mitigating its impact through various preventative and therapeutic approaches. Scientists have explored different modes of action, particularly in terms of immune modulation. This has raising questions about the potential differentiation between plant-based products, probiotics and other immune stimulants, and oral vaccines. Numerous pieces of evidence indicate that probiotic bacteria in aquatic animals have the ability to inhabit and establish colonies within specific regions of the GI mucosal epithelium and digestive tract. Probiotics function by enhancing the digestibility of feed through synthesis of vital nutrients, such as biotin, fatty acids, and Vitamin B12 [35].

3. PROPERTIES OF PROBIOTIC MICROBES

For probiotic microbes to be effective, they need to demonstrate resilience against the challenging state of GI tract, including exposure to bile salts and stomach acid. In addition, they should have the ability to attach the intestinal lining and successfully the gut colonize, enabling them to exert their beneficial effects [36]. Probiotics have the capability to engage with the immune system, contributing regulation and balance the immune responses. They can enhance the activity of specific immune cells, stimulate antibody production, and modulate inflammatory mediators. This immune modulatory characteristic is crucial for maintenance of a healthy immune system [37]. Probiotics have the capability to produce wide range of beneficial substances for the host. Certain strains of bacteria, for instance, can generate short-chain fatty acids, which are essential for gut health and act as an energy source for colon cells. In addition, probiotics can produce antimicrobial compounds that aid in suppressing inhibit the growth of dangerous microbes in the gut [38].

Probiotics can compete with pathogenic microorganisms for resources and space within the intestines. The probiotic inhibits the colonization of harmful bacteria. Probiotics create an environment in the gut that is less conducive to the growth of pathogens, thus reducing the risk of infections [39]. Probiotic microbes have the ability to metabolize specific nutrients and components of diet, leading to the aid in the breakdown of composite molecules and production of beneficial metabolites. This metabolic activity can influence the overall constitution of gut microbiota and have implications for various aspects of health [40]. Specific probiotics became found to support the integrity of the gut barrier. They assist in reinforcing the tight junctions between cells in the intestinal lining, thereby reducing gut permeability and preventing the passage of harmful substances into the blood stream [41]. Probiotic microbes have the ability to impact the composition and diversity of intestinal microbiome. Probiotics encourage the development of beneficial bacteria while suppressing proliferation of harmful species, resulting in a balanced and healthy gut microbiome [42]. The properties and mechanisms of probiotic microbes can differ significantly based on the specific strain and genus. Each probiotic may possess unique characteristics and exert its effects through distinct mechanisms. Therefore, it is essential to consider the specific strains and their documented properties when evaluating probiotic products for addressing specific health concerns [43] [Figure 2].

4. PROBIOTIC FORMULATION

Over the last few decades, there has been a significant shift in the approach toward health and nutrition. Rather than just providing essential nutrients, food is currently seen as a way to enhance overall well-being. People are more interested than ever before in taking control of their own health. There are multiple factors which are responsible for this trend toward using food as medicine [44]. Probiotic formulation consists of lactic acid bacteria (LAB) that are considered safe for consumption. These microorganisms have been extensively researched and have been associated with various health benefits. Probiotics have the potential to treat several ailments including gastroenteritis, diarrhea, IBD, irritable bowel syndrome, compromised immune function, cancer, lactose intolerance, failure to thrive, infant allergies, liver diseases, *Helicobacter pylori* infection, and hyperlipidaemia [45].

Functional additives are used in other food items and beverages to modulate the human immune system [46]. These functional foods contain specific amounts of probiotic strains to ensure their functionality and viability. For example, Yakult, the first fermented dairy beverage, contains probiotic *Lactobacillus casei* Shirota. *Saccharomyces* strains, including *Saccharomyces cerevisiae*, are used in the production of

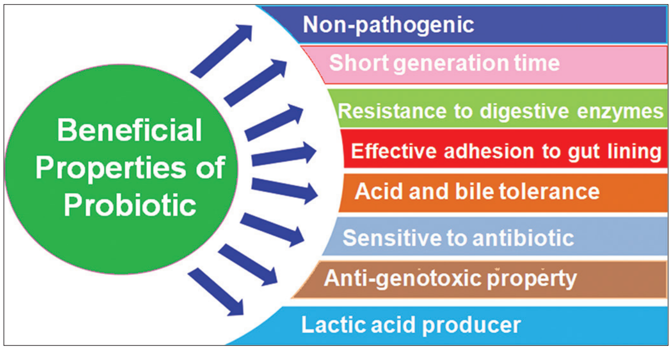

Figure 2: Characteristics of beneficial properties of probiotic.

wine, while kefir is composed of *Saccharomyces* yeasts that often form symbiotic networks with bacteria. These yeasts are also sometimes found in kombucha [46]. Probiotics have become increasingly popular in the pharmaceutical industry as well as in the food industry [47]. There is a rising interest in potential probiotic applications and human microbiome, partly due to the increasing awareness of the need for alternatives to antibiotics [48] [Table 1].

The functional and technological properties of kefir drink make it a source of probiotic microorganisms. A study isolated yeast strains from Malaysia and evaluated their probiotic potential. Nine probiotic yeast strains were identified using their 16S rDNA sequences. The study assessed their properties including antibiotic susceptibility, antimicrobial activity and tolerance GI conditions [49]. Kefir is a fermented dairy beverage with distinctive characteristics, including a yeasty and slightly sour flavor, as well as a creamy, dense, and viscous texture. Traditionally, kefir is produced using unevenly block cauliflower-like grains with a color ranging from white to yellowish [50]. Kefir grains are a notable example of a symbiotic community in which a diverse microbial population coexists. In contrast to pure cultures of microorganisms that do not spontaneously form when combined in a test tube, kefir grains can be encouraged to form and grow through traditional methods under suitable conditions [51].

Yogurt is a fermented food that originates from the Turkish word "yogurmak," that means coagulating, curdling, and thickening [52]. In yogurt making process, milk is acidified to promote the formation of curd. This acidification process relies on the proliferation of native probiotic LAB. This LAB was found to have various health benefits, such as reducing heart rate, blood pressure, cholesterol levels, and having antihypertensive effects [53]. Yogurt is a major contributor to the global probiotic business share, accounting for 78% [54]. A cost-effective probiotic drink was formulated using coconut water, which is lactose-free and fermented by *L. casei* shirota. The study included two types of coconut water products, are using packaged coconut water and the other using fresh coconut water. The optimal cultivation time for both cultures was found to be 12 h at 36°C, despite the total cultivation time being 48 h. The pH, cell concentration, and total acidity were monitored during the fermentation process [55]. The manufacture of goat milk and products of dairy has been expanding in various countries due to the growing demand. This research aimed to develop chocolate-flavored dairy beverages using goat milk and incorporate the probiotic *Bifidobacterium lactis*, while also evaluating the impact of goat cheese whey on sensory and physicochemical resources of the drinks [56]. Ryan *et al*. [57] conducted research the on development of a probiotic dairy drink enriched with mango juice containing *Lactobacillus acidophilus*. In the mentioned study, researchers evaluated the longevity of *L. acidophilus* in mango dairy drinks over a -week storage period at 4°C. They also analyzed the important physicochemical resources, including acidity, pH, titratable, viscosity, and color, along with conducting sensory evaluations of the products.

4.1. Probiotic Diary Based Beverages

Functional dairy products constitute over 40% of the functional foods market, with fermented products being the primary category. This category includes yogurt and yogurt-type products that are either lactose-free or low lactose, and also those enriched with various functional ingredients such as vitamins, conjugated linoleic acid, minerals, probiotics/prebiotics, and sterols/stanols. These products have demonstrated consistent market success [44]. The products of milk, including yoghurts, became widely used as transporter for delivering probiotics to humans for a long time [58]. While these products provide various health benefits such as supplying nutrients and aiding in the treatment and preventing from certain non-communicable and communicable diseases, there have also limitations to their use due to various factors. These include the increased lactose intolerance, allergens presence, hypercholesterolemia effects, the vegetarian probiotic need options, religious beliefs, and cultural food taboos against milk. As a result, the utilization of milk and its products as probiotic carriers is restricted in several regions, including Africa [59]. A probiotic beverage was created using finger millet (*Eleusine coracana*), incorporating the nutritional benefits of both the millet and the probiotic.

To prepare the beverage, cooked finger millet was combined with *L. casei* and incubated at 37°C for different durations (2 h, 4 h, and 6 h). The mixture was supplemented with fresh cow milk, cocoa powder, and sucrose, which were added to the mixture to create the final beverage, which was stored in refrigerated conditions (5 ± 1°C) [60]. In Tanzania, there has been limited production of fermented cereal-based probiotic beverages. However, probiotic cultures such as *Lactobacillus brevis* for Togwa, *Lactobacillus plantarum* for Kimpumu and Mbege, and *Pediococcus pentosaceus* for kindi have been utilized in their production. These beverages are not commonly made, local fermented cereal-based beverages have demonstrated their potential for several decades [61].

4.2. Probiotic Whey-based Beverages

Whey is a green-yellowish translucent liquid fraction that remains after milk clotting and casein removal during cheese or casein manufacturing [62]. The yellowish hue of whey is attributed to significant levels of riboflavin (vitamin B2). Whey constitutes 80–90% of the total volume of milk and contains about 50% of the nutrients present in the original milk, including whey proteins (~10%), lactose (~70% depending on whey acidity), minerals (~12%), vitamins, and some fat. magnesium, calcium, potassium, and sodium salts constitute the majority of these minerals, with over 50% being NaCl and KCl, along with calcium salts. On the other hand, metals like zinc and copper are present in insignificant quantities [63]. The fabrication of whey-based beverages commenced in the 1970s, and numerous types of whey beverages have been developed since that time. These beverages can be made from various types of whey, including acid whey or native sweet whey deproteinized, diluted whey native, whey powder, or through whey fermentation [64]. Whey proteins are a popular choice for ready to drink protein beverages due to their excellent nutritional value, bland flavor, easy digestibility, and unique functionality in beverage systems. Over the past few decades, food and beverage industry has been influenced by five key trends: convenience, pleasure, ethnic fusion, tradition, and health and wellness. A variety of whey-based beverages

Table 1: Details of different probiotics.

S. No.	Products	Bacteria	Country	References
1.	Probiotic yoghurt drink	*L. acidophilus*	Netherlands	Hilton *et al*. [172]
2.	Probiotic yoghurt drink	*Streptococcus*	Netherlands	García-Albiach *et al*. [173]
3.	Probiotic yoghurt drink	*L. bulgaricus*	Netherlands	García-Albiach *et al*. [173]
4.	Amul	*L. acidophilus*	Gujarat	Bafna *et al*. [174]
5.	Amul	*B. lactis*	Gujarat	Sakhare *et al*. [175]
6.	Yakult	*L. casei*	Japan	Kiwaki and Sato [176]
7.	Yakult	*B. breve*	Japan	Shimakawa *et al*. [177]
8.	Nestle	*L. johnsonii*	Switzerland	Marteau *et al*. [178]
9.	Kimchi	*L. plantarum*	Korea	Lee and Lee [179]
10.	Kimchi	*L. brevis*	Korea	Chin *et al*. [180]
11.	Kimchi	*L. mesenteroides*	Korea	Chin *et al*. [180]
12.	Kimchi	*L. citreum*	Korea	Chin *et al*. [180]
13.	Sauerkraut	*L. lactis*	German	Harris *et al*. [181]
14.	Sauerkraut	*L. mesenteroides*	German	Johanningsmeier *et al*. [182]
15.	Brined cucumber	*L. johnsonii*	UK	Zielińska *et al*. [183]
16.	Brined cucumber	*L. rhamnosus*	UK	Zielińska *et al*. [183]
17.	Fermented cassava	*L. jensenii*	Nigeria	Ogunbanwo *et al*. [184]
18.	Fermented cassava	*L. brevis*	Nigeria	Ogunbanwo *et al*. [184]
19.	Fermented cassava	*L. plantarum*	Nigeria	Ogunbanwo *et al*. [184]
20.	Fermented cassava	*L. fermentum*	Nigeria	Ogunbanwo *et al*. [184]
21.	Stinky tofu	*L. plantarum*	China	Liu *et al*. [185]
22.	Fermented rice noodle	*L. fermentum*	Thailand	Techo *et al*. [186]
23.	Fermented rice noodle	*L. plantarum*	Thailand	Lu *et al*. [187]
24.	Fermented rice noodle	*Lactobacillus*	Thailand	Techo *et al*. [186]
25.	Sourdough bread	*L. plantarum*	Europe	Arici and Coskun [188]
26.	Cheddar cheese	*L. salivarius*	England	Gardiner *et al*. [189]
27.	Cheddar cheese	*L. paracasei*	England	Gardiner *et al*. [189]
28.	Cottage cheese	*L. casei*	America	Abadía-García *et al*. [190]
29.	Cottage cheese	*L. rhamnosus*	America	Abadía-García *et al*. [190]
30.	Probiotic ice cream	*B. lactis*	China	Salem *et al*. [191]
31.	Probiotic ice cream	*L. acidophilus*	China	Turgut and Cakmakci [192]
32.	Hardaliye (grape fruit)	*L. paracasei*	Turkey	Arici and Coskun [188]
33.	Hardaliye (grape fruit)	*L. casei*	Turkey	Arici and Coskun [188]
34.	Cashew apple	*L. casei*	Brazil	Pereira *et al*. [193]
35.	Tempeh	*L. plantarum*	*Indonesia*	Ashenafi and Busse [194]
36.	Ogi	*L. plantarum*	West Africa	Odunfa and Adeyele [195]
37.	Ogi	*L. mesenteroides*	West Africa	Ijabadeniyi [196]
38.	Boza	*L. rhamnosus*	Turkey	Todorov *et al*. [197]
39.	Bushera	*Lactobacillus*	Ugandan	Muyanja *et al*. [198]
40.	Bushera	*Streptococcus*	Ugandan	Muyanja *et al*. [198]
41.	Bushera	*L. plantarum*	Ugandan	Muyanja *et al*. [198]
42.	Bushera	*L. paracasei*	Ugandan	Kalui *et al*. [199]
43.	Bushera	*L. fermentum*	Ugandan	Kalui *et al*. [199]
44.	Mahewu	*L. paracasei*	Zimbabwe	Moiseenko *et al*. [200]
45.	Chicha	*Lactiplantibacillus*	America	Rebaza-Cardenas *et al*. [201]

B. breve: Bifidobacterium breve, B. lactis: Bifidobacterium lactis, L. johnsonii: Lactobacillus johnsonii, L. plantarum: Lactiplantibacillus plantarum, L. acidophilus: Lactobacillus acidophilus, L. brevis: Levilactobacillus brevis, L. bulgaricus: Lactobacillus bulgaricus, L. casei: Lacticaseibacillus casei, L. citreum: Leuconostoc citreum, L. fermentum: Limosilactobacillus fermentum, L. jensenii: Lactobacillus jensenii, L. johnsonii: Lactobacillus johnsonii, L. lactis: Lactococcus lactis, L. mesenteroides: Leuconostoc mesenteroides, L. paracasei: Lacticaseibacillus paracasei, L. plantarum: Lactiplantibacillus plantarum, L. rhamnosus: Lacticaseibacillus rhamnosus, L. salivarius: Ligilactobacillus salivarius.

consisting of plain, alcoholic, carbonated, and fruit flavored have been successfully developed and marketed all over the world. Benefits of whey proteins can easily be enhanced by beverages manufactures into different products, that is, pH range of 2–10 is highly soluble, produces stable and logical beverage in the 3.0–3.2 pH range [65].

The growing demand for sheep cheese and goat, driven by its nutritional and health benefits, has resulted in a significant increase in whey by-product [66]. One potential solution for this waste is to produce probiotic functional fermented beverages using diverse types of whey protein concentrates (WPC), which can provide both economic sustainability and reduced environmental pollution. In this study, beverage probiotic containing kiwi powder 1% were manufactured using WPC from sheep, cow, and goat (each at 15% concentration). Fermentation was carried out using *Streptococcus salivarius* subsp. *Thermophilus*, *Bifidobacterium animalis,* and *L. acidophilus* subsp [67]. The study investigated the utilization of WPC and trypsin hydrolysate as components of a probiotic encapsulation matrix affect the antioxidant capacity of a beverage. Results indicate that hydrolysate carrier exhibited spherical factor, antioxidant capacity, and higher encapsulation efficiency in both before and after fermentation, as compared to the carrier with non-hydrolyzed proteins [68]. Fermented whey beverages are known to have lower viscosity, a milder flavor profile, and reduced probiotic viability compared to their milk-based counterparts. This study examined the impact of supplementing whey with 30% milk and cofermenting with the ABY-6 starter culture commercially and added *Lactobacillus rhamnosus* strain on the grade attributes of the end product. The results suggested that formulating the beverage in this manner could produce a fermented product that fulfills the necessary criteria for probiotics [69].

4.3. Buttermilk Whey-based Beverages

Buttermilk is occasionally linked or even mistaken for sour milk, natural (conventional) buttermilk, cultured milk, cultured buttermilk, and cultured skim milk or even at times with fermented milk [70]. It is a liquid that separates during the churning of cream in butter production. In dairy industry, buttermilk is a valuable derivative that is produced during butter production. It contains several highly beneficial constituents, including lecithin, milk fat globule membrane (MFGM), minerals, proteins, and lactose. MFGM is especially noteworthy as it contains bioactive compounds that have been found to have antitumor and cholesterol-lowering effects. In addition, MFGM has been shown to act as an inhibitor on *H. pylori*, which can help to prevent GI infections [63]. Liquid and powdered buttermilk offer significant buffering and antioxidant capabilities, making them valuable ingredients in functional foods and beverages. Buttermilk phospholipid content also has antimicrobial properties that hinder the development of certain pathogens [71]. Furthermore, cultured buttermilk can serve as a method for delivering bioactive or functional components, such as prebiotics, probiotics, dietary fiber, bioactive peptides, and fruit-based functional ingredients [72]. To this end, cultured buttermilk was prepared both with and without the fortification of hydrolyzed guar gum partially which is a source of dietary fiber [73].

The concept of health and nutrition has undergone a significant transformation in the past few decades [74]. Instead of merely serving to meet our fundamental dietary requirements, food is now recognized as a powerful tool to enhance overall well-being [75]. The expansion in this field can be attributed to technological advancements, creation of novel products, and a rising population of health-conscious individuals seeking products that enhance their quality of life. As the global market for functional foods continues to grow each year, the development of food products becomes a critical research priority and presents a significant challenge for both the industry and scientific community [76]. Probiotic beverages are enriched with live useful bacteria that can support gut health and strengthen the immune system. They are often marketed as having various health benefits, but it is important to evaluate these claims to determine their validity [77].

Certain studies indicate that probiotics may have a positive impact on digestive health, potentially alleviating symptoms related to irritable bowel syndrome, diarrhea, and constipation [78]. Nevertheless, the existing evidence on the effectiveness of probiotics for digestive health is inconclusive, emphasizing the need for further research to reach more definitive conclusions [79]. Probiotics have the potential to enhance the immune system by stimulating the production of antibodies and bolstering the activity of immune cells [80]. Certain probiotics have been associated with a potential risk reduction for specific diseases, including respiratory infections, urinary tract infections, and allergies. However, further investigation is necessary to establish their efficacy and determine the most effective strains for these conditions [81]. Overall, while there is some evidence to support the health claims made about probiotic beverages, additional research is required to gain a comprehensive understanding of their overall effectiveness. It is crucial to acknowledge that not all probiotic strains have the same effects, and the amount of live cultures in a probiotic beverage can vary widely. Therefore, it is important to consult with a health-care provider or a registered dietitian before using probiotic beverages for health purposes [82].

At present, consumers are more motivated than ever to take charge of their own health [83]. Numerous factors contribute to this shift, including the growing acceptance of the "food as medicine" concept. For instance, both developed and developing countries have witnessed an increase in an average life expectancy, indicating a desire for better health outcomes and well-being. Functional foods are categorized as whole, fortified, enriched, or enhanced foods, as well as food compounds that have demonstrated beneficial effects on the human body, promoting overall health and well-being [84]. Functional dairy products hold a significant position within the functional foods sector, representing more than 40% of this market [85]. A large majority of functional dairy products fall under the category of fermented products.

The global market for functional dairy beverages is highly dynamic and is projected to reach a market value of 13.9 billion USD by 2021. This forecast excludes traditional dairy beverages such as koumiss, kefir, and buttermilk others [44]. Traditional dairy beverages have been consumed in various regions in worldwide and possess a well-established reputation for promoting health, backed by a solid scientific foundation [86]. As the health benefits of consuming live bacteria become increasingly evident, there is a growing trend of producing foods that incorporate probiotic bacteria. In the current context, functional, healthy, and nutritious foods are essential choices for promoting survival and well-being. They play a crucial role in strengthening the immune system, which is vital for defending against various diseases [87].

4.4. Topical Probiotics

The skin which serves as the outer most layer of the human body, hosts commensal microbiota, and functions as a physical barrier, safeguarding against intrusion of harmful foreign microorganisms [88]. In recent times, there has been a growing fascination with the skin microbiome, extending beyond the previously dominant focus on gut microbiome. This expanded interest centers around understanding the impact of the skin microbiome on the management of various skin conditions. Probiotics also play a pivotal role in upholding human well-being and preventing diseases. Topical probiotics have exhibited positive outcomes in addressing specific inflammatory skin conditions such as acne, rosacea, and psoriasis, among others [89]. In addition, they have shown promise in promoting wound healing [90]. Over the past few years, there has been a remarkable surge in popularity of commercially available topical probiotics. The utilization of topical probiotics for skincare and therapeutic purposes dates back to the early 20th century. In the few years, there has been a significant increase in the availability of commercial topical probiotic products [91]. Unlike topical bacteriotherapy, which involves the transplantation of skin microbiota from one person to another, topical probiotics entail the application of laboratory-cultured bacteria.

The concept of utilizing topical bacteriotherapy as a remedy for cutaneous conditions was initially introduced in 1912. During this time, it was documented that the topical application of *Lactobacillus bulgaricus* showed improvements in acne and seborrhea [92]. After the surge in popularity of oral probiotics, there has been a plethora of suggested topical probiotic formulations aimed at addressing skin dysbiosis and restoring immune balance by stabilizing the skin's microbiota [93]. *Lactobacilli,* in particular, demonstrate antimicrobial effects against skin pathogens, including *Escherichia coli*, *Pseudomonas aeruginosa*, and pathobionts, which are resident microbes with the potential for pathogenicity, such as *Cutibacterium* (formerly known as *Propionibacterium*) acnes [94]. At present, the food and drug administration (FDA) classifies probiotics into various product categories, including foods, food additives, cosmetics, dietary supplements, medical devices, or drugs, as determined on a case-by-case basis. However, the FDA lacks a specific regulatory definition or agency dedicated to addressing topical probiotics [95]. The FDA does not mandate pre-market approval for cosmetic products and their ingredients [96]. As a result, manufacturers have the freedom to include unverified therapeutic claims on probiotic labels, and the increasing consumer usage in pursuit of these unproven benefits is becoming a notable concern.

4.5. Cosmetic Probiotics

As per the definition provided by the US FDA, a cosmetic is described as a product (with the exception of pure soap) that is meant for application to the human body with the purposes of cleansing, enhancing beauty, promoting attractiveness, or modifying appearance [97]. This definition encompasses products intended for use on skin, hair, and oral care. It is crucial to emphasize that this description does not encompass any claims related to health. The use of probiotics varies greatly in terms of type, breadth, and purpose. This extends to cosmetic applications, where the probiotics market is forecasted to experience a 12% of growth rate over the next decade, primarily driven by North America [98]. Many cosmetic and personal care products are designed to offer nourishment and safeguarding for the skin, its microbiota, and associated cells. Their aim also to enhance barrier functions, prevent pathogenic growth, cleanse, and moisturize the skin surface, collectively contributing to the overall health of the skin [99].

Cosmetic and personal care products are thus created to supply nutrients and shield the skin, enhance its barrier functions, deter pathogenic growth, and moisturize the skin surface [99]. A search conducted on the websites of two prominent cosmetics retailers in North America uncovered a minimum of 50 products currently available in the market, each claiming to contain probiotics. Probiotic-infused cosmetic products often incorporate particular bacterial strains, such as *Lactobacillus*, *Bifidobacterium*, or other probiotic species renowned for their positive impact on the skin. These strains have the potential to support the skins inherent barrier function, decrease inflammation, and potentially alleviate skin concerns such as acne or rosacea [100].

4.6. Bakery Based Probiotics

Bakery items are widely regarded as essential food items globally, frequently enjoyed during breakfast, afternoon tea, and evening snacks [101]. Nevertheless, these products often carry a reputation for being less healthy due to their high levels of refined sugars and fats, combined with a limited supply of dietary fiber [102]. Efforts have been undertaken to enhance the unfavorable perception of bakery items, such as the integration of probiotics into these products. In the usual process of adding probiotics to bakery items, where probiotics are mixed into the dough, a substantial reduction in viable probiotics within the bakery products occurs due to the high temperatures employed during the baking process. While it is possible to reduce the loss of probiotic viability by directly adding them to cream filling or spreading them on the surface of the baked bakery product, this approach may not be suitable for all bakery items, especially those that are not cream filled [103]. After the baking process, microcapsules containing *Saccharomyces boulardii*, *L. acidophilus*, and *Bifidobacterium bifidum* were introduced into three distinct types of cakes: Cream filled, marmalade filled, and chocolate coated. These microcapsules were produced through spray drying and chilling, and they were applied as both single-layered and double-layered versions during the cake production process [103].

4.7. Vaginal Probiotics

A distinct microbiome found in the female reproductive system also has a significant impact on women's overall health and balance [104]. The microbiome of the vagina constitutes a portion of the reproductive tract, is primarily made up of *Lactobacillus*, that assists the host through a symbiotic connection [105]. Probiotics are being studied more and more in relation to their potential to prevent vaginal disorders, and as a result, an efficient administration method is receiving greater attention [106]. A unique approach that was successful in topical drug administration was the introduction of probiotics to the vaginal mucosa using electrospun nanofibers. For instance, probiotics have recently been successfully delivered by including them in biohybrid nanowebs made of polyvinyl pyrrolidone (PVP) K30, PVP K90, and PVA to treat bacterial vaginosis. Pliszczak *et al*. [107] developed a bioadhesive probiotic delivery system. The system is a microparticle composed of pectin and hyaluronic acid that is used to encapsulate probiotics and prebiotics. The system was continually released for the first 10 h and concluded at 16 h. After that, the probiotics started to grow, which is an intriguing aspect of this study. This probiotic controlled and continuous release method was extremely important in delivering local medications to the vagina [108].

4.8. Dental Caries Probiotics

One of the common health problems that people encounter worldwide is dental disease [109]. An infectious condition known as dental caries is brought on by cariogenic bacteria, which ferment carbohydrates to generate organic acids [110]. The mineral crystals in the enamel, dentin, and cementum are partially dissolved by these acids when they penetrate into these tissues. Minerals then begin to diffuse out of the tooth, which, if the process remains unchecked, will eventually result in cavity (creating a hole in the tooth) [111]. Today, the prevalence of dental caries has increased in developing nations due to, among other things, a high consumption of refined sugar, insufficient fluoride exposure, and expensive oral health-care services. The effectiveness of probiotics in preventing dental caries has been assessed in a number of research [112]. Children's dental caries and *Streptococcus mutans* concentrations are both reduced by 6% when milk is supplemented with *L. rhamnosus* GG [113]. Another study concluded that short-term ingestion of cheese containing the probiotic strains *L. rhamnosus* and *L. rhamnosus* could reduce the oral cariogenic microbial flora in young adults [114].

4.9. Otic Probitics

Probiotics are associated with intestinal health, and the majority of clinical investigations are focused on preventing or treating GI infections and illnesses [115]. This is demonstrated by the higher occurrence of middle ear effusion in kids with underlying anatomical conditions that affect the function of the muscles that open the eustachian tube, such as those with cleft palate or Down syndrome [116]. However, during the past 10 years, an increasing number of studies have looked into the potential benefits of probiotic bacteria for treating and/or preventing respiratory and urogenital infections, as well as for preventing allergies and atopic illnesses in young children. Otitis media is one of the biggest problem that pediatricians facing. At least one episode of acute otitis media (AOM) affects about 80% of children while between 80% and 90% of preschoolers experience secretory otitis media (SOM) [117]. One of the main symptoms of SOM, or asymptomatic persistence of effusion in the middle ear cavity, which is a probable response to AOM, is persistent fluid in the middle ear cavity [118]. The most common bacterial infections that cause AOM, including *Streptococcus pyogenes*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*, ascend through the eustachian tube from the nasopharynx to the middle ear, inducing an inflammatory response [119]. In a study concluded that, *S. salivarius* K12 when administered to children with a clear presence of a middle ear exudate, second to establish the potential protective effect in terms of reducing AOM recurrences, and third to track the progression of SOM using tone audiometry, tympanome, and other methods [118].

5. STABILITY ASPECTS OF PROBIOTIC FORMULATIONS

Stability is indeed a critical aspect of probiotic formulations, as it directly affects the viability and effectiveness of probiotic bacteria over the products shelf life [95]. It is essential for manufacturers to consistently monitor and enhance their formulations and storage guidelines to ensure consumers derive the utmost benefits from probiotic products. Ensuring stability remains a continuous priority for manufacturers. They must regularly assess and enhance their formulations and storage guidelines to maximize the benefits consumers receive from probiotic products [120].

The technology used for formulating probiotics is often proprietary within the industry. However, a fundamental requirement is that probiotic product should maintain stability in a powdered form, typically with a spore concentration of around 1×10^9 spores per gram [121]. Formulation technology for probiotics is frequently proprietary in the industry. Nonetheless, a crucial criterion is that the probiotic product should remain stable in a powdered form, typically containing a spore concentration of approximately 1×10^9 spores per gram [122]. Hence, maintaining the stability of probiotic product during formulation process and industry relevant storage conditions is a crucial requirement for its successful commercial application. Ideally, the shelf life of such a product should be no <2 years [123].

6. COMMERCIALIZATION OF PROBIOTICS

There has been a growing interest in the impact of probiotic functional foods and drugs on human health, particularly concerning the gut microbiota [23]. Research and commercial attention are actively exploring various aspects of these products. When it comes to selecting strains for probiotic products, ensuring proper process and storage conditions, probiotics requires a careful considered for functionality and cell viability ensuring successful carriage of probiotics at the targeted site. Encapsulation and many technologies are explored for the reorganization of probiotics are being made to stabilize probiotics in their dried form [124]. Probiotics are available in the market as pharmaceuticals, nutritional supplements, or functional foods. However, marketing a pharmaceutical product requires substantial time, intricate and costly research, as well as specific therapeutic targets for regulatory approval and clinical use [125].

In food service settings, several aspects come into play when working with microbial preparations containing probiotics [6]. This includes handling the probiotic cultures carefully to maintain their viability, implementing stringent quality control measures, seeking regulatory approval for the products, educating consumers about their benefits, and promoting them through marketing strategies to increase their adoption and usage. The second application is extension of shelf life of food service systems in large scale. Probiotic LAB are widely employed in therapeutic preparations and add on foods [126].

At present, probiotics are primarily utilized for GI applications, but they can be readily extended to improve skin, vaginal health, and oral as well [127]. As per the global industry analysis report in 2012, the latest global probiotic market was estimated to experience a 7% annual growth rate, primarily driven by European and Asian consumers. The market is expected to reach approximately 48 billion dollars over the next 5 years [128]. During the COVID-19 pandemic, over time, people have recognized the advantages of consuming fermented products such as kombucha, milk, and water kefir [129]. Water kefir has specifically garnered significant interest from individuals who follow plant-based and vegan diets or those who have allergies to milk proteins or are lactose intolerant. This fermented beverage offers an appealing and nutritious alternative to dairy-based products, water kefir is an ancient fermented beverage, characterized by its acidic, fruity, moderately carbonated, and sour taste [130]. It contains high lactic acid content, typically up to 2%, and low alcohol content, usually <1%. The production of water kefir involves fermenting sugary water with water kefir grains (starters), and dried fruits are often added to enhance the flavor. The resulting beverage is then fermented, filtered, and free from grains, commonly referred to as water kefir [131].

There are various verities of probiotic foods which is available in the market, probiotic dairy products stand out due to their traditional association with LAB. Cheese serves as a remarkable carrier of probiotic microbes, providing a protective environment that shields these microorganisms during their journey through the GI tract. A popular Brazilian soft and semi-fat cheese known as 'minas frescal' is renowned for its high moisture content, making it ideal for fresh consumption [132]. This cheese is produced through enzymatic coagulation of milk using rennet or other appropriate coagulating enzymes, aided by specific LAB [133]. In the latest study, probiotic-enhanced nutritional malt beverage has been prepared from kodo millet grains collected from different districts of Himachal Pradesh, India. Malt beverage was produced in four sets by adding different combinations of in house probiotic cultures [134].

Researchers have explored microbial polysaccharides for their potential as nutraceuticals, as well as their bioactive properties [135]. In food industry, there is a growing demand for live microbes or the polysaccharides, they produce due to their claimed health benefits beyond basic nutritional values. The properties and applications of polysaccharides produced by probiotic strains, as well as future plans aimed at enhancing the understanding of the process, are under exploration [136]. A novel strain of *B. coagulans* CGMCC 9551, obtained from the feces of healthy piglets, exhibited a wide spectrum of antibacterial activities against six major pathogenic bacteria, namely *Staphylococcus aureus*, *E. coli*, *Listeria monocytogenes*, *Streptococcus suis*, *Pasteurella multocida* and *Salmonella enterica* [137].

Probiotics offer potential benefits for treating conditions related to old age, as well as antibiotic use and immunocompromised states. Choosing dietary interventions over pharmaceutical drugs has clear advantages, including cost-effectiveness, reduced side effects, and the ability to reach a larger population easily [138]. Probiotics encompass a diverse array of bacterial genera, species, and strains. Different strains possess different actions in different clinical situations [139]. Probiotics are subject to extensive global research, innovative product design, regulatory scrutiny, effective marketing, and significant consumer interest and usage advocated by healthcare professionals. Products are produced in accordance with applicable good manufacturing practices to ensure safety, purity, and stability [140].

LAB serves as beneficial microorganisms for humans, animals, and dairy products. Their effects are correction for GI tract, lactose intolerance, anti-diarrheal activity, for the maintaining normal blood insulin levels, exhibiting antineoplastic activity in clones, and displaying anti-inflammatory properties [141]. Yogurt, a widely consumed probiotic functional food globally, allows customers to conveniently access probiotics in sufficient quantities. Regular consumption of probiotic yogurt is associated with various health benefits, such as preventing respiratory and GI infections, reducing blood cholesterol, slowing down HIV progression, enhancing glucose metabolism, and manage Type 2 diabetes and obesity [142].

7. APPLICATIONS OF PROBIOTICS IN HUMAN HEALTH

Probiotics find extensive applications across multiple sectors, including medicine, veterinary care, technology, and food industries. They are utilized for the production of drugs and nutraceuticals and various models of probiotic bacteria are isolated from different sources [6]. Probiotic microbes are used in poultry as substitute sources of antibiotics agent against pathogens, to support microbiota and developing animal growth and productive performance [6]. A lot of attention is taken by probiotic supplements and revealed an extraordinary growth in this field. LABs are essential for the fermentation process in dairy products and beverages. These bacteria are responsible for the production of lactic acid, which acts as end product of fermentation [143].

Probiotics are utilized in treatment of chronic inflammatory GI disorders and various other medical conditions. They are used in the development of novel formulations categorized as functional foods, specifically designed to address and manage specific diseases [144]. The collection of probiotics present in our intestines can be viewed as a microbial colony functioning as a metabolic organ. These beneficial microorganisms exert substantial effects on human health, such as influencing metabolism and immunological functions [145]. Probiotic bacteria synthesize vitamins, immune-modulatory proteins, and peptides with restraint activities. The antimicrobial compounds produced by these probiotic strains are widely utilized in the food industry as effective preservatives. Certain fermented foods, including milk, are acknowledged as beneficial functional foods because they contain probiotic bacteria such as *Lactobacillus helveticus*. These probiotics are present during milk fermentation, are known to produce factors that promote the activation of the enzyme calcineurin [6]. Paraprobiotics, a novel product, has been discovered as an alternative to live probiotics. It involves the use of inactivated or heat-killed probiotic cells to achieve similar benefits. Its application is to treatment of various diseases including viral infections. Probiotics offer numerous benefits to human health across various aspects, including their antimicrobial properties, alleviation of lactose intolerance, management of diarrheal diseases, treatment of ulcers, stimulation of immunity, preservation of food, and potential role in colon cancer prevention [146].

7.1. Infectious Diarrhea and AAD

Diarrhea often occurs as a common side effect of antibiotics. Diarrhea is characterized by loose or watery stools, with a stool weight exceeding 200 g/day or a frequency of more than three bowel movements per day. However, AAD has been recommended to be clinically remarkable when an individual experiences three mushy or loose watery stools per day [147]. AAD affect the patients, and specially used with broad-spectrum antibiotics. At times, AAD can be severe to the point of prematurely discontinuing antibiotics, leading to suboptimal treatment of the infection. AAD has been shown to extend hospital stays, raising risk of other infections, and result in higher overall healthcare expenses. AAD is characterized by the development of diarrhea from a few hours after starting antibiotic therapy to 6–8 weeks after discontinuing antibiotics. AAD can result from direct intestinal toxicity of antibiotics, changes in digestive function that decrease the concentration of beneficial gut microbes, or overgrowth of pathogens [148].

Probiotics, such as *S. boulardii* and *Lactobacillus*, are employed to prevent antibiotic associated diarrhea. The overgrowth of toxigenic bacteria, such as *Clostridioides difficile*, which is resistant to the prescribed antibiotic, is the underlying cause of AAD. *C. difficile* infection is rising in contemporary hospital settings, especially among elderly patients, where 10–20% of these cases are observed [149]. *C. difficile* is a Gram-positive, spore-forming, anaerobic *Bacillus* that produces toxins. It can colonize the gut of around 70% of neonates and infants exists as a commensal part of the intestinal flora in asymptomatic adults, and widespread in the natural environment. *C. difficile* infection is the primary cause of healthcare-associated diarrhea [150].

Antibiotics, including co-amoxiclav, fluorquinolones, and cephalosporins, can disturb the natural balance of gut bacteria, leading to pathogen colonization and overgrowth, which can trigger AAD. The older population faces additional challenges due to an aging immune system (immunosenescence) and alterations in intestinal microbial diversity [151]. Probiotics are extensively studied for various clinical applications, including preventing AAD and supporting treatments for conditions like *H. pylori* infection the prevention of allergies; irritable bowel disease, vaginitis, and necrotizing enter colitis in newborns. Antibiotic usage can lead to side effects, including the development of AAD, which affects up to 30% of patients. The specific strain trials of probiotic are *Saccharomyces* and *Lactobacillus* have demonstrated positive results in addressing AAD, as supported by meta-analyses [152]. Patients with COVID-19 often require extensive antibiotic therapy, which can increase their risk of developing AAD. In COVID-19, diarrhea can be categorized into two types: Early viral diarrhea and late diarrhea. It is crucial to differentiate between these types because viral diarrhea is typically mild and resolves on its own without specific treatment. However, antibiotic-associated diarrhea, if left untreated, can lead to severe consequences, potentially even death, or aggravate the course of COVID-19 [153]. Probiotics are cure- all to AAD and very attractive solution for problems with significant morbidity. Probiotics can temporarily colonize the gut, where they produce bactericidal acids and peptides, compete for nutrients, and adhere to the gut's epithelial cells [154].

7.2. Lactose Intolerance

Lactose intolerance is a clinical syndrome that exhibits with characteristic signs and symptoms of consuming food substances containing lactose, a disaccharide. Lactose is the small intestinal brush border [155]. Lactose intolerance has a syndrome characterized by pain, loose stools, flatulence, nausea, abdominal distention, and diarrhea after the utilization of lactose [156]. It is primary carbohydrate found in milk, serving as a significant source of energy during the breastfeeding period in mammals. To benefit from milk lactose, mammals need to hydrolyze it into glucose and galactose, which are monosaccharides that can be readily absorbed by the intestinal tract. In humans, the digestion of milk lactose is facilitated by an enzyme called lactase phlorizin hydrolase (LPH) or commonly known as lactase [157].

Lactose intolerance ranges between 57% and 65%, the activity of the intestinal enzyme is caused by LPH, which is responsible for the digestion of lactose [158]. In mammalian milk, lactose is broken down by the intestinal enzyme lactase, which splits it into glucose and galactose, facilitating absorption [159]. Lactose intolerance is widespread food sensitivity, not uncommon in regions with dairy farming, and often linked to the prevalence of lactase non-persistence. In addition, secondary causes related to mucosal integrity can also contribute to lactose intolerance. Small intestine epithelium cannot absorb the lactose without first being broken down by lactase [160]. The pathophysiologic mechanisms leading to deficient lactose absorption in the intestine can be primary, secondary to other enteropathies, or concurrent with other intestinal diseases presenting similar symptoms. Conditions such as irritable bowel syndrome, bacterial overgrowth syndrome, or celiac disease may coexist, causing diagnostic and treatment challenges due to their overlapping symptoms.

In cases of GI diseases with lactose intolerance, patients often need to eliminate dairy products from their diet to manage the symptoms effectively [161]. The activity of enzyme lactase can be influenced by several factors, including integrity of the small intestinal membrane, race, age, and small intestinal transit time. LI is treated currently with the supplements and symptom management medications, and probiotics gained high interest in the prospective compensation for lactase insufficiency. Probiotics improve lactose digestion in LI by boosting the overall hydrolytic capacity in the small intestine and encouraging colonic fermentation [162].

7.3. GI Diseases

Numerous clinical trials are conducted to assess the preventive and therapeutic impacts on GI diseases triggered by pathogenic microorganisms or disruptions to the natural gut microbiota. GI infections can be attributed to various factors, including traveler's diarrhea, *C. difficile* related diarrhea, antibiotic-associated diarrhea, rotavirus-induced diarrhea, and *H. pylori*, [163]. GI symptoms pose a significant health-care concern globally, comprising 6% of all outpatient consultations and accounting for 31% of cases related to gastroenterological disorders [164]. GI diseases rank among the most prevalent disorders observed in pet rabbits. Maintaining a consistent and appropriate diet is essential for ensuring the healthy functioning of a rabbit's GI. The primary cause of GI disease in rabbits is the absence of sufficient fiber in their diet, which can result from dietary deficiencies or conditions leading to anorexia [165]. The coronavirus effects on the respiratory system, however, their impacts on the digestive system receive considerably less attention. Coronaviruses have been known to infect mammals and can exhibit GI pathogenicity, resulting in symptoms like diarrhea and vomiting. Some coronaviruses causing GI disorders in both mammals and humans might play a role in facilitating the coping mechanisms during SARS-CoV-2 infection [166].

Eosinophilic GI diseases (EGIDs) represent a diverse set of conditions marked by GI symptoms and elevated eosinophil levels in the intestinal mucosa [167]. EGIDs are classified into two main types: Eosinophilic esophagitis and eosinophilic gastroenteritis (EGE), depending on the affected regions within the GI tract. These allergic diseases are caused by food or environmental allergens [168]. The GI tract harbors the most abundant microbiota in the body, and it plays a crucial role in microbe host interactions. IBD encompass a group of chronic autoimmune conditions, which include ulcerative colitis and Crohn's disease. These conditions are distinguished by persistent and recurrent inflammation in different segments of the GI tract [169]. Abdominal pain and spasms are common symptoms found in organic GI diseases such as IBD and biliary diseases. Antispasmodic agents have shown effectiveness in certain patients with IBD, particularly those experiencing remission with mild chronic pain [170].

8. CONCLUSIONS

Probiotics have demonstrated potential in enhancing human health through diverse mechanisms. These beneficial microorganisms can play a beneficial role in gut health and contribute to the enhancement of immune system, potentially influence mental well-being, and women's health. The effectiveness of probiotics can vary depending on the specific strains used and the individuals' unique microbiota composition. While probiotics have demonstrated benefits in certain areas, their effectiveness and specific applications are still being researched. It is important to exercise caution when considering probiotic supplementation and to seek guidance from healthcare professionals. Different strains of probiotics possess distinct characteristics and may offer varying health benefits. Hence, it is advisable to adopt a diverse and balanced approach to incorporating probiotics into one's diet to maximize their potential benefits. Probiotic formulations have garnered considerable attention for their potential health benefits, as they involve the intentional selection and combination of specific beneficial microorganisms. Probiotic formulations have shown effectiveness in enhancing different aspects of human health. These formulations typically contain well-researched specific strains of bacteria or yeast known for their beneficial effects on gut microbiota and overall well-being. In the future, probiotics holds potential to serve as a valuable tool for promoting and sustaining human health.

9. AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

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This study does not involve experiments on animals or human subjects.

13. DATA AVAILABILITY

All the data is available with the authors and shall be provided upon request.

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