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Probiotics: Health implications and future prospective

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Abstract
Probiotics are thelive microorganisms which, when administered inadequate amounts, confer a health benefit on the host. Their benefits to human race have been proven by many scientific researches. The growing awareness about the relationship between diet and health, has led to the advent of functional foods. The Probiotics can be a boon to functional food industry due to its potency in enhancing gastrointestinal health, and thereby an overall health. While probiotics in the form of drugs are widely accepted, probiotic foods are still viewed with scepticism. Acceptance is growing slowly, but it will take a long time while before changing the mindset of Indian consumers. There is still a need for developing various foods with probiotic origin or inclusion.

Keywords: probiotics, functional foods, gastrointestinal health, etc.

Introduction
The name probiotic comes from the Greek word 'pro bios' which means 'for life'. The history of probiotics began with the history of man; cheese and fermented milk were well known to the Greeks and Romans, who recommended their consumption, especially for children and convalescents. Probiotics are defined as the living microorganisms administered in a sufficient number to survive in the intestinal ecosystem. They must pose a positive effect on the host [1]. The term 'probiotic' was first used by Lilly and Stillwell [2] in 1965 to describe the 'substances secreted by one microorganism that stimulate the growth of another'. A powerful evolution of this definition was coined by Parker in 1974 [3], who proposed that probiotics are 'organisms and substances which contribute to intestinal microbial balance' [4]. In today's modern definitions, the concept of an action on the gut microflora, and even that of live microorganisms disappeared. Salminen *et al.* [5] defined probiotics as the 'food which contains live bacteria beneficial to health', whereas Marteau *et al.* [6] defined them as 'microbial cell preparations or components of microbial cells that have a beneficial effect on the health and well-being'. Some modern definitions include more precisely a preventive or therapeutic action of probiotics. Charteris *et al.* [7], for example, defined probiotics as 'microorganisms which, when ingested, may have a positive effect in the prevention and treatment of a specific pathologic condition'. Finally, since probiotics have been found to be effective in the treatment of some gastrointestinal diseases [5], they can be considered as therapeutic agents. It is clear that a number of definitions of the term 'probiotic' have been used over the years but the one derived by the Food and Agriculture Organization of the United Nations/World Health Organization [8] and endorsed by the International Scientific Association for Probiotics and Prebiotics [9] best exemplifies the breadth and scope of probiotics as they are known today: 'live microorganisms which, when administered inadequate amounts, confer a health benefit on the host'. This definition retains historical elements of the use of living organisms for health purposes but does not restrict the application of the term only to oral probiotics with intestinal benefits [10].
Havenaar *et al.* [11], proposed the following parameters to define a probiotic: total safety for the host, resistance to gastric acidity and pancreatic secretions, adhesion to epithelial cells, antimicrobial activity, inhibition of adhesion of pathogenic bacteria, evaluation of resistance to antibiotics, tolerance to food additives and stability in the food matrix. Now a day the only used probiotics are the strains of lactic acid bacteria such as *Lactobacillus*, *Bifidobacterium* and *Streptococcus* (*S. thermophilus*); the first two are known to resist gastric acid, bile salts and pancreatic enzymes, to adhere to colonic mucosa and readily colonize the intestinal tract [4].

History
The origin of cultured dairy products dates back to the dawn of civilization; they are mentioned in the Bible and the sacred books of Hinduism. Climatic conditions for sure favored the development of many of the traditional soured milk or cultured dairy products such as kefir, koumiss, leben and dahi [12]. These products, many of which are still widely consumed, had often been used therapeutically before the existence of bacteria was recognized [13]. At the beginning of the 20th century the main functions of gut flora were completely unknown. Ilya Ilyich Metchnikoff, the Nobel Prize winner in Medicine in 1908, at the Pasteur Institute linked health and longevity to ingestion of bacteria present in yogurt [14, 15]. He believed that the constitution of the human body presented several disharmonies inherited from primitive mammals such as body hair, wisdom teeth, stomach, vermiform appendix, caecum, and large intestine. In 1907, he postulated that the bacteria involved in yogurt fermentation, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*, suppress the putrefactive-type fermentations of the intestinal flora and that consumption of these yogurts played a role in maintaining health. Indeed, he attributed the long life of Bulgarian peasants to their intake of yogurt containing *Lactobacillus* species [15]. In particular, he reported that the large

intestine, useful to mammals in managing rough food composed of bulky vegetables, is useless in humans. Moreover, it is the site of dangerous intestinal putrefaction processes which can be opposed by introducing lactobacilli into the body, displacing toxin-producing bacteria, promoting health, and prolonging life [16]. Tissier's discovery of bifidobacteria in breast-fed infants also played a key role in establishing the concept that specific bacteria take part in maintaining health. In 1906, Tissier reported clinical benefits from modulating the flora in infants with intestinal infections [17]. At the time, many others were dubious about the concept of bacterial therapy and questioned in particular whether the yogurt bacteria (*L. bulgaricus*) were able to survive intestinal transit, colonize and convey benefits [18]. In the early 1920s, *L. acidophilus* milk was documented to have therapeutic effects, in particular, a settling effect on digestion [19]. It was believed that colonization and growth of these microorganisms in the gut were essential for their efficacy, and therefore, the use of intestinal isolates was advocated. In Japan in the early 1930s, Shirota focused his research on selecting the strains of intestinal bacteria that could survive passage through the gut and on the use of such strains to develop fermented milk for distribution in his clinic. His first product containing *L. acidophilus* Shirota (subsequently named *L.casei* Shirota) was the basis for the establishment of the Yakult Honsha Company [20].

Probiotics in Food Products

As it was reported by Chow [21], the notion that food could serve as medicine was first conceived thousands of years ago by the Greek philosopher and Father of medicine, Hippocrates, who once wrote: 'Let food be thy medicine, and let medicine be thy food'**.** However, during recent times, the concept of food having medicinal value has been regained as 'functional foods'. A probiotic may also be a functional food [22].

- Functional foods are defined as: 'foods that contain some health-promoting component(s) beyond traditional nutrients'. Functional foods are also referred to as designer foods, medicinal foods, nutraceuticals, therapeutic foods, super foods, foodiceuticals, and medifoods. In general, the term refers to a food that has been modified in some way to become 'functional'. One way in which foods can be modified to become functional is by the addition of probiotics [23].
- New food products have been formulated with the addition of probiotic cultures. Different types of food matrices have been used such as various types of cheese, ice creams, milk-based desserts, powdered milk for newborn infants, butter, mayonnaise, powder products or capsules and fermented food of vegetable origin [24].
- Dairy products: Food substrate plays an important role in the production of probiotics. Besides buffering the bacteria through the stomach, it may contain functional ingredients that interact with the probiotics, altering their activities. Fat content, type of protein, carbohydrates and pH can affect probiotic growth and survival. Dairy products are especially considered as ideal vehicle for delivering probiotic bacteria to the human gastrointestinal tract. The matrices used most frequently are cheese, yogurt, ice cream and other dairy products.

Commercial Probiotic Products in Indian Market [25]

Worldwide, a diverse array of probiotic products is on the market shelf. Yogurt is perhaps the most common probiotic-carrying food, but the market has expanded beyond yogurt. Cheese, fermented and unfermented milks, juices, smoothies, cereal, nutrition bars, and infant/toddler formula all are food vehicles for probiotic delivery. In addition to being sold as foods, probiotics are sold as dietary supplements, medical foods, and drugs. Often these products are composed of concentrated, dried microbes packaged into capsules, tablets, or sachets. This format is convenient for the delivery of large numbers of microbes that, if manufactured and stored properly, can be quite stable even at room temperature.

Benefits to Human Health and Prevention of Disease

Reviews on the impact of probiotics on human health and disease are numerous and have emphasized different components of the field, such as use of probiotics in medical practice [26; 27], use in pediatric populations [28], immune modulation [29], and intestinal diseases [30; 31].

The following discussion highlights specific areas of probiotic intervention in human health and disease.

Lactose Maldigestion

Lactose is a sugar found in milk, composed of a glucose molecule linked to a galactose molecule. Lactose can be split into glucose and galactose by lactase, an enzyme produced by infants, children, and some adults. Most humans, however, quit producing this enzyme in childhood. If these people consume dairy products with lactose, they can develop gastrointestinal symptoms such as abdominal bloating, pain, flatulence, and diarrhea. This situation is found in 5 to 15% of adults in Northern European and American countries and in 50 to >90% of adults in African, Asian, and South American countries [32]. These people tend to eliminate milk and dairy products from their diet, and consequently, their calcium intake may be compromised. The bacteria used as starter cultures in yogurt (*Streptococcus thermophilus* and *Lactobacillus delbrueckii* subsp. *bulgaricus*) also produce lactase, and when consumed with dairy products can improve lactose digestion and symptoms in these individuals [33]. A number of studies have demonstrated better lactose digestion, as well as a decrease in gastrointestinal symptoms, in people with this condition who consume yogurt with live cultures [31].

Bowel Transit

Daily consumption of one to three servings of fermented milk containing a probiotic strain, *Bifidobacterium animalis* DN-173 010, decreased the amount of time it took food to travel from the mouth to the anus for people who had longer-than-desired transit time [34]. The effect was more pronounced in elderly subjects and in women. A mixture of eight different strains of lactobacilli, bifidobacteria, and *S. thermophilus* (product name, VSL#3) had no effect on gastrointestinal transit time in *irritable bowel syndrome* (IBS) subjects [35]. A recent controlled study showed that *L. rhamnosus* Lcr35 improved symptoms of constipation in children [36].

Irritable Bowel Syndrome (IBS)

Symptoms of abdominal pain, bloating, and flatulence commonly occur in patients with IBS. These symptoms may result in part from fermentations taking place in the colon that generate gas. Certain gut bacteria process leftover food that reaches the colon without producing gas. Other species may

even consume gas, particularly hydrogen. But others produce gas, which is eliminated from the body through flatulence. In a *double-blind, clinical trial* of 48 patients with bloating-predominant IBS, the probiotic mixture VSL#3 decreased flatulence scores [37]. Likewise, two other placebo-controlled trials have shown relief of abdominal bloating in patients with IBS treated with VSL#3 or *Lactobacillus plantarum* 299V [35, 38]. In children, *L. rhamnosus* GG decreased perceived abdominal distension but not abdominal pain [39]. Finally, two large studies in adults showed that either *Bifidobacterium infantis* 35624 or a strain mixture (*L. rhamnosus* GG, *L. rhamnosus* LC705, *Bifidobacterium breve* Bb99, and *Propionibacterium freudenreichii* subsp. *shermanii* JS) can be effective in alleviating symptoms of IBS [40, 41].

Some probiotics seem useful for controlling the symptoms related to intestinal gas in this group of subjects. But the number of studies is small, and further focused research is needed.

Gastrointestinal Infections

A number of clinical trials have tested the efficacy of probiotics in the prevention of acute diarrhea, including antibiotic-associated diarrhea. Both the short- and long-term use of antibiotics can produce diarrhea, particularly when multiple drugs are used. Probiotics given along with antibiotic therapy have been shown to decrease the incidence of antibiotic-associated diarrhea in children and in adults. Different strains have been tested including *L. rhamnosus* GG, the yeast *Saccharomyces cerevisiae* (boulardii) Lyo, and undefined strains of *Lactobacillus acidophilus* and *L. delbrueckii* subsp. *bulgaricus*. *Meta-analysis* of controlled trials concluded that probiotics, particularly *L. rhamnosus* GG and *S. cerevisiae* (boulardii) Lyo, can be used to prevent antibiotic-associated diarrhea [42]. An important complication of antibiotic treatment can be the establishment of *Clostridium difficile* infection resulting in pseudo membranous colitis. Hickson and colleagues (2007) [43] demonstrated that a fermented milk containing *Lactobacillus casei* DN-114 001, *L. delbrueckii* subsp. *bulgaricus*, and *S. thermophilus* can decrease the incidence of antibiotic-associated diarrhea and *C. difficile*-associated diarrhea, providing evidence for the value of this treatment for this potentially refractory condition.

Probiotics are useful as treatment of acute infectious diarrhea in children. Different strains, including *L. reuteri* SD2112, *L. rhamnosus* GG, *L. casei* DN-114 001, and *S. cerevisiae* (boulardii) Lyo, tested in controlled clinical trials decreased the severity and duration of diarrhea. Meta-analysis concludes that these probiotics are safe and effective. Oral administration of probiotics shortens the duration of acute diarrhea in children by approximately 1 day.

Prophylactic use of probiotics has proved useful for the prevention of acute diarrhea in infants admitted to the hospital with chronic disease. Supplementation of an infant formula with *B. animalis* Bb12 and *S. thermophilus* TH4 significantly decreased the incidence of diarrhea in hospitalized infants aged 5 to 24 months (Saavedra *et al.* 1994). A placebo-controlled double-blind study in infants aged 1 to 36 months showed similar results for *L. rhamnosus* GG [44]. In these two studies, control subjects were more than four times more likely to develop diarrhea than those treated with probiotics.

Several studies have investigated probiotics in the prevention of travelers' diarrhea in adults, but methodological deficiencies, such as low compliance with the treatment and problems in the follow-up, limit the validity of their conclusions (Marteau, Seksik, and Jian 2002 [45].

Probiotics have been tested as a strategy for eradication of *H. pylori* infection of the stomach. Some strains of lactic acid bacteria are known to inhibit the growth of *H. pylori* in laboratory experiments. But results in human studies with different probiotics are mixed. Eradication of *H. pylori* was attempted by feeding yogurt containing probiotic strains selected for their ability to inhibit *H. pylori* in laboratory studies. The strategy was not effective in patients not undergoing simultaneous antibiotic therapy [46]. In contrast, other clinical studies have tested the use of probiotics as a supplement to antibiotic therapy for *H. pylori* eradication. In these studies, the use of probiotics decreased the side effects of antibiotics, improved patient compliance with taking the prescribed therapy, and increased the rate at which *H. pylori* was eradicated [47, 48, 49, 50].

Prevention of Systemic Infections

Bacterial translocation is the passage of bacteria through the lining of the intestine, which can lead to infection of organs or the blood. This passage can occur when patients have undergone surgical procedures or are seriously ill with critical conditions, such as severe acute pancreatitis, advanced liver cirrhosis, or multisystem organ failure. Probiotic organisms rarely translocate, even though a disturbed epithelium [51].

In a study of patients with severe acute pancreatitis, treatment with *L. plantarum* 299V significantly decreased the incidence of infection [52]. In another study, liver transplant patients received a synbiotic preparation (including four probiotic strains and four fermentable fibers) or a placebo consisting of the four fibers only. Postoperative infection occurred in only one patient in the treatment group of 33 compared with 17 of 33 in the placebo group [53]. The difference was highly significant. But another clinical study performed with patients who submitted to elective abdominal surgery found no effect of synbiotic treatment (four bacteria strains plus *oligofructose*) on prevention of postoperative infections [54]. In that trial, synbiotic treatment after surgery was delayed until patients were able to tolerate oral nutrition. In contrast, the liver transplant studies introduced synbiotic therapy by naso-gastric tube immediately after surgery.

Necrotizing enterocolitis resulting from immaturity and poor function of the gut mucosal barrier is a severe clinical condition that may occur in low birth weight premature infants. Two controlled studies have demonstrated that the use of probiotic mixtures in these infants significantly decreases the incidence and severity of necrotizing enterocolitis and prevents death [55]. Data from these studies represent one of the few examples of probiotics improving survival rates. Currently, few other strategies have proved effective in decreasing the incidence, morbidity, and mortality of necrotizing enterocolitis in preterm infants.

Allergy

Atopic diseases are caused by exaggerated or imbalanced immune responses to environmental and harmless antigens (allergens). The prevalence of allergic diseases in western societies is increasing at an alarming rate.

The effectiveness of *L. rhamnosus* GG in the prevention of atopic dermatitis has been reported in randomized, controlled trials [56, 57]. In a subsequent study, this same strain was combined

with three other probiotic strains, *L. rhamnosus* LC705, *B. breve* Bb99, and *P. freudenreichii* subsp. *shermanii* JS, and a *prebiotic* to determine the impact on the cumulative incidence of allergic diseases [58]. This large study (925 subjects tracked through the 2-year follow-up) showed no effect on incidence of all allergic diseases, but the treatment did significantly prevent atopic eczema. Furthermore, several well-designed studies have provided evidence that specific strains of probiotics can be somewhat effective in treatment of established atopic dermatitis [59, 60]. Effectiveness in the management of cow's milk allergy in children is associated with the use of probiotics [61].

Colon Cancer

Several experimental animal studies clearly demonstrated a protective effect of prebiotics such as oligofructose, probiotics such as some *Lactobacillus* and *Bifidobacterium* strains, or the combination of prebiotics and probiotics on the establishment, growth, and metastasis of transplantable and chemically induced tumors. Human intervention trials to confirm these animal studies are intrinsically difficult because of the natural history of the disease (difficulty in selecting subjects at high risk and requirement of long-term follow-up). A 4-year study of 398 subjects found that *L. casei* Shirota decreased the recurrence of atypical colonic polyps [62]. The European Union (EU)-sponsored "Synbiotics and Cancer Prevention in Humans" project tested a synbiotic (oligofructose plus *L. rhamnosus* GG and *B. animalis* subsp. *lactis* Bb12) in patients at risk for colonic polyps. Among several intermediate end points that were used as biomarkers of colon cancer risk, the study found that the synbiotic decreased uncontrolled growth of intestinal cells [63].

Vaginal Infection

Vaginal infections are caused mostly by fecal microbes ascending into the vaginal tract and displacing the normal lactobacilli microbiota. The potential of using probiotic lactobacilli to decrease the risk of bacterial or yeast vaginal infections or to improve the clinical outcome during treatment for these infections has captured the interest of researchers for decades [64]. Until recently, most studies have been small and in need of confirmation. After preliminary assessment to document that *L. rhamnosus* GR-1 and *L. reuteri* RC-14 administered in milk could pass through the intestine, ascend to the vagina, and restore a normal lactobacilli microbiota in women prone to infections [65], these strains were delivered in yogurt to African women with bacterial vaginosis and shown to improve therapeutic outcome [66]. These studies have provided the best evidence to date for successful probiotic intervention to improve vaginal health.

Diarrhea in infants and adults

Diarrhea is caused by pathogenic bacterial or viral overgrowth in either the small or large intestine. For example, *Clostridium difficile* induces diarrhea in adults and rotavirus induces diarrhea in children. There are several mechanisms through which these agents cause diarrhea, but the end result in all cases is the accumulation and then expulsion of fluid from the intestinal tract, resulting in loss of body fluid and electrolytes. Some potential causes of diarrhea involving the ecosystems of both the small and large intestines, mechanisms of pathogenic action, and effective Probiotics have also proved to be effective therapeutic agents in cases in which the exact cause of the diarrhea was not identified. Thus, *Lactobacillus* GG, administered in yogurt, was quite effective in controlling erythromycin-induced diarrhea [67].

Keeping People Healthy

Early research evaluating probiotics in humans focused on relieving intestinal distress, frequently with subjects suffering from an intestinal infection or antibiotic-associated complications. As this product concept developed further, the value of probiotics to prevent, rather than treat, disease was appreciated more fully. Toward this end, studies have been conducted in healthy populations, with end points such as decreasing the incidence of colds [68], winter infections [69], or even absences from work [70]. These controlled human studies provide support that certain probiotic strains consumed as part of a daily diet will increase the number of illness-free days. Infants were helped by *Lactobacillus reuteri,* which decreased crying time due to colic [71].

Potential of probiotics in hypercholesterolemia

Sharma *et al* in their study indicate the pooled mean net change for total cholesterol (TC) is −8.40 mg/dl (−13.63, −3.61), for low density lipoprotein (LDL) is −6.63 mg/dl (−10.63, −2.63), for high density lipoprotein cholesterol is 0.59 mg/dl (−0.92, 2.09) and for triglycerides is −1.32 mg/dl (−6.49, 3.85). The result shows that probiotics supplementation does lower serum TC and LDL cholesterol levels significantly and hence a reduction in the risk factor of developing coronary heart disease [72]. The

The effect of probiotics on infectious diseases of the respiratory system with different target populations.

- Children A randomized, double-blind, placebo-controlled trial was performed to determine whether probiotics may reduce the risk of infections in infants. The children involved in the research were younger than 2months of age and were daily provided with milk containing L. rhamnosus GG and Bifidobacterium lactis Bb-12, or placebo milk, administered until 12 months of age. The results suggest that probiotics may represent a mean to reduce the risk of early acute otitis media and the use of antibiotics for recurrent respiratory infections during the first year of life [73]. Similar results have emerged in a study performed on a target population of 326 children aged between 3 and 5 years, showing more than 65% decrease in the incidence of antibiotic use and 25% reduction in school missed days among children treated with probiotics [74].
- Adults A randomized double-blind, placebo-controlled trial assessed whether the consumption for 3 months of Lactobacillus gasser PA16/8, Bifidobacterium longum SP 07/3, B. bifidum MF 20/5, had impacts on symptoms severity, incidence and duration of common cold. For two winter/spring seasons, 479 adults were daily treated with vitamins and minerals enriched or not with probiotics. The results indicate a reduction in the duration of episodes of common cold of at least 2 days and a decrease in the severity of symptoms among subjects receiving probiotics if compared to the randomized placebo-control group [75]. Similar conclusions were obtained in a study that assessed the effect of long-term intake of probiotics on the same pathology [76]. Another, double-blind, randomized, placebo-controlled trial, performed on 237, 234, and 250 healthy adults investigated, in three winter seasons, the efficacy of different probiotics in restoring and maintaining intestinal balance and the potential protection from respiratory tract

infections [77]. The experimental protocol consisted of three phases: (1) in the first phase, an active formulation (A) was tested that contained three types of probiotics (L. plantarum, L. rhamnosus and B. lactis) and fructo-oligosaccharides (FOS), compared to placebo; (2) in the second phase, the same formula was compared to a similar preparation enriched with lactoferrin (B) and to placebo; (3) the third phase compared two symbiotic formulations, each containing probiotics and FOS (C) or galacto-oligosaccharides (GOS, D) with placebo. The average duration of acute respiratory infections improved with respect to ILI (influenza-like illness) and URTI (upper respiratory tract infections) in steps 1 and 2 of the study, while the incidence of cold and cough decreased in phase 3. Similar results emerge from a systematic review of clinical evidence obtained in 14 research trials (RCT) on the use of probiotics in preventing respiratory tract infections (RTI). The reduction in the severity of symptoms related to RTI was recorded in five out of six studies; in three studies out of nine the clinical course was reduced. Probiotics, therefore, have a beneficial effect on the severity and duration of RTI symptoms, although not reducing their incidence [78].

- Elders Two multicentre, randomized, controlled, double-blind studies were conducted in two successive vaccine seasons (pilot study and control). 86 and 222 elderly volunteers consumed, respectively, a fermented milk drink containing L. casei DN-114 001, a fermented yogurt or a control unfermented dairy product, twice a day for a period of 7 or 13 weeks. Vaccination took place after 4 weeks. The study showed that probiotics improve antibody responses to influenza vaccination in individuals over 70 years [79]. L. casei DN-114001 was also evaluated in a multicentre, double-blind, controlled study on 1.072 elderly, to assess the resistance to respiratory infections. The product containing probiotics, well tolerated, induced a reduction in the duration of respiratory infections, especially URTI and nasopharyngitis [80].

Conclusion and Future Prospective

The expectations of probiotic bacteria have become the most demanding for any bacterial group. Probiotics have become a very important element to everyday health food products, and their global market is estimated above US$28.8 billion by 2015 [81]. Consumers are concerned about chemical preservatives and processed foods, even though they provide a grade of safety and food diversity never seen before. However, consumers accept LAB as a natural way to preserve food and promote their health. In the last decade the interest in bacteriocins produced by LAB has increased dramatically [82]. Many bacteriocins inhibit the growth of spoilage and pathogenic bacteria in foods; moreover, bacteriocinogenic LAB are linked and are used as starter cultures in food processing. However, there are many different kinds of pathogens in nature, so the specific use of a particular bacteriocin cannot eliminate all bacterial pathogens. In recent years, the increased numbers of multi-drug resistant pathogens have become a serious problem. The development of a new generation of antimicrobial agents is a difficult task. Biotechnological methods have been applied to create new or multi-functional bacteriocins, so they could be widely used in food, animal husbandry, and medicine. Both traditional cell culture methods, as well as the alternative techniques (direct imaging and visual enumeration, nucleic acid-based enumeration methods, and flow cytometry and cell sorting) offer advantages and limitations for enumerating probiotic microorganisms [83]. The new methods and techniques show considerable promise for quantifying live microorganisms in different metabolic states. But the probiotic efficacy cannot be predicted solely on the basis of viable cells. Salminen [84]. reported that cell wall components from broth dead and living cells contributed to the probiotic efficacy. Very few microorganisms have been subjected to thorough *in vitro* studies confirming their specific health promoting activity, and even fewer have been subsequently subjected to and passed the appropriate human trials [85]. Additionally, probiotics can be dangerous, as they have been linked to an increase in mortality rate if administered to severely immune compromised patients [86]. Subsequent studies are needed to evaluate the health-promoting activity of probiotic bacteria.

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