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Probiotics: Nutritional Therapeutic Tool

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Abstract

The advent of various health care policies and digital revolution has fuelled interest in the direction of food supplements, and as preventive or curative drug containing live non-pathogenic bacteria, probiotics. The widespread usage of probiotics by consumers and in clinical practice has emphatically made to understand the benefits associated with these products. The probiotic products are now being marketed worldwide by several multinational companies. Present review attempts to overview the health benefits of probiotics in impeding various lifestyle or metabolic associated disorders, clinical significance, their efficacy and influence on immune system.

Keywords: Probiotics; Gastrointestine; Lactic Acid Bacteria; Health care; Food supplements

Introduction

The term probiotics refers to viable, non-pathogenic microorganisms (bacteria or yests) that, when, ingested, are able to reach the intestine in sufficient numbers to confer health benefits to the host http://probioticindia.com/2011-11-12-13-28-20/probioics-products. Probiotics are naturally occurring microorganisms of ecosystem in different parts of the human body such as oral cavity, skin, vaginal cavity and gastrointestinal tract [1] and have been proved to be safe essentially needed for performing some of our body's vital functions [2,3]. The probiotics play a vital role in keeping the gut healthy. The recommended dose of probiotics is 108-1011 CFU per serving with one to several servings per day. Probiotics have been defined by the Food and Agriculture Organization (FAO)/World Health Organization (WHO) as "live microorganisms which when administered in adequate amount (generally numbering one billion) confer a benefit to host health". They should be resistant to gastric acid, bile and pancreatic juices and reach the target site (small intestine/large intestine) in numbers sufficient enough to elicit the beneficial effect [4]. It should be scientifically validated through well controlled clinical trials (FAO/WHO Expert Consultation Report). The use of probiotics in animal feed is well controlled and is regulated by regulation (EC) no. 183/2003.

In general, probiotic bacteria are categorized amongst the most friendly bacteria belonging to the class of lactic acid bacteria (LAB) [5]. The most prominent members from this category are *Lactobacilli* (cures diarrhea and lactose intolerance in patients) and *Bifidobacteria* (ease the symptoms of irritable bowel syndrome (IBS) [6]. Certain yeasts are also included in this group; *Saccharomyces boulardii* is the common yeast aiding in improving the digestion [7,8]. Probiotic products such as dahi, yogurt or dietary supplements are part of the fermented foods having active live cultures [9].

In the past, there has been an increased interest in probiotic research and in understanding their concepts. Genomic, transcriptomic and proteomic studies unfolded the genes and proteins responsible in probiotic adaptation in host while exerting favourable effects. The on-going clinical research in the field of probiotics and changes in consumer behaviour due to increased health awareness has paved the path for the innovation in probiotics product development. Besides this, the advancement of healthcare polices and digital revolution continues to sustain the development of the specific new probiotic organisms. These live non-pathogenic bacteria, probiotics were identified characterized in lines of food supplements and attempts were made in order to verify their health claims being used as preventive or curative drugs.

Health Claims for Probiotics

The probiotics improve the intestinal microbial balance through lowering of pH to provide a hostile environment for pathogens. Yeasts as probiotic improve nutrient absorption/assimilation from food and digestion. LAB used as probiotic stimulates and balances the immune system [2], prevents vaginal and urinary tract infections [10,11], prevents and treats side effects of antibiotic therapy [12], aids in digestion of lactose and dairy products by reducing lactose intolerance [13,14] helps in the regulation of bowel movements [15], reduces the toxic load of liver [16,17] inhibits the growth of bacteria which produces nitrates in bowel as production of nitrates could in certain cases cause cancer [2], prevents excessive growth of pathogenic microbes such as candida, *E. coli*, *Helicobacter pylori* and *Salmonella* [18-22] reduces the incidence of yeast infections [11], virginities and candidacies [23], calms down the colon irritation following surgery, supports healthy skin in youth, and is the primary bacteria in infants, which helps them to grow and develop their immune system [24,25], therapeutic for upper respiratory complaints [26], act as remedy for bad breath (halitosis) [27], increase ability to synthesize vitamin B, manufactures vitamin B complex [28], increase the ability to absorb calcium [29,30] reduce the occurrence of bladder cancer [31], prevent and manage atopic dermatitis (eczema) in children [32]. Evidences

revealed that all the health claims linked to probiotics are mainly strain specific and the health claim raised by one strain could not be assumed for another strain, even though both comes under the same species [33]. Health benefits associated with probiotics are shown in Figure 1.

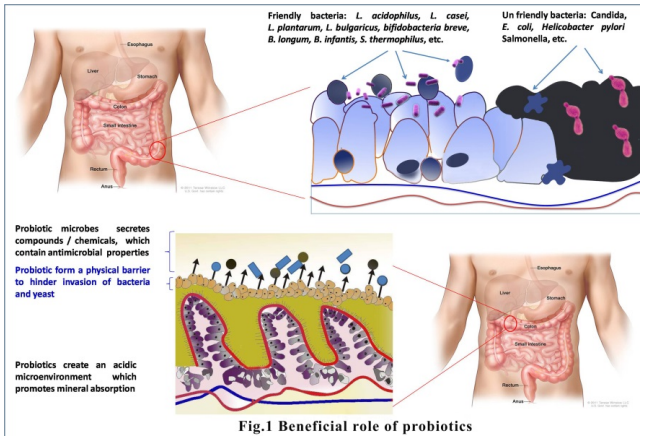

Figure 1: Beneficial role of probiotics.

Lactose Intolerance

The lactose-intolerant, lactase deficiency or hypolactasia individuals could even tolerate lactose to larger extent through the ingestion of certain active strains [34]. About two-third of the world's adult population, mainly in Africa and Asia, suffers from lactose intolerance due to the absence of an enzyme lactase [35,36]. Lactose-intolerant individuals are not able to digest lactose, the sole sugar mainly present in dairy products [37,38]. Yogurt and probiotic lactic acid bacteria promises to be an alternative to milk [13] having high level of the enzyme, lactase (β-galactosidase) [39]. Lactase is produced from bacteria when lysed through bile secretions and is made available to intestinal lumen. The reduced intestinal transit time of yogurt is the alternate reason for the reduction of lactose intolerance thereby allowing slow lactose assimilation. The lactase producing bacteria present in yogurt is *Lactobacillus acidophilus*, which aids in the digestion and lactose absorption [26,40]. Other lactase producing bacteria preventing lactose intolerance are *Lactobacillus bulgaricus* and *Streptococcus thermophiles* [41]. The response of the consumption of fermented milk having *Bifidobacterium longum* was reported to significantly reduce hydrogen production as well as flatulence compared to pasteurized milk [42,43].

Intestinal Disorders

The imbalance in microbial population in gastrointestine leads to disturbance in host microbe interaction in the digestive tract (gastrointestine) due to the harsh conditions and negative environment associated with low stomach pH, bile salts, and digestive enzymes [44]. The consumption of probiotic bacteria in large number ensuring to reach the site of action in the lower GI in adequate number could significantly improves the health of gastrointestine and the benefits are dose dependent [45]. The appropriate number of probiotic bacteria has been set as 107 *bifidobacterial*/g or mL as per the probiotic products such as fermented milk and other lactic acid bacteria containing beverages. It is reported that the gastric inflammation is reduced through administration of probiotics viz. *L. casei*, *L. reuteri*, *L. acidophilus*, *L. plantarum*, *B. infantis*, *B. animalis* and *S. boulardii* [46,47]. Diarrhea is reported to be the major cause of deaths in children and adults in third world countries. Table 1 shows the effective probiotic strains normally employed against gastrointestinal abnormalities.

S.No.	Disease	Effective probiotic strains
1	Diarrhea Antibiotic-associated diarrhea Traveller's diarrhea Rotavirus diarrhea	*L. rehamnosus* GG (LGG), *S. boulardii*
2	Irritable bowel syndrome	VSL#3 (*B. longum*, *B. infantis*, *B. breve*, *L. acidophilus*, *L. casei*, *L. delbrueckii* ssp. bulgaricus, *L. plantarum* and *S. thermophilus*)
3	Inflammatory bowel disease	*Saccharomyces boulardii*
4	Pouchitis	VSL#3
5	*Helicobacter pylori* infection	L. johnsonii La1, *Saccharomyces boulardii*

Table 1: The effective probiotic strains against gastrointestinal abnormalities.

Inflammatory Bowel Diseases (IBD)

The intestinal disorders such as ulcerative colitis and Crohn's disease could finally lead to the surgical removal of colon. The reason for IBD is still unknown but it is believed that both genetic as well as environmental factors contribute to certain extent [48]. The most important factor in the development and recurrence of IBD is believed to be the intestinal flora but the exact mechanism has not yet been explained. The symptoms of IBD could be relieved when probiotic is administered. The mechanism of regulation is either through inflammatory response or through the modulation of the composition of gut microbiota. VSL#3 is a probiotic formulation composed of four *lactobacilli* (*L. acidophilus*, *L. casei*, *L. plantarum*, *L. bulgaricus*), three *bifidobacteria* (*B. breve*, *B. longum*, *B. infantis*) and *S. thermophilus*. The mixture has proven to be quite effective in reducing the recurrence of chronic relapsing pouchitis [48,49]. A probiotic formulation SCM-III developed with a combination of three different strains (*Lactobacillus helveticus*, *L. acidophilus*, and *Bifidobacterium* sp.) was

found to be significantly effective against 68 patients of IBD tested [50].

Allergies

Probiotics found in yogurt are reported to be effective to treat seasonal pollen allergies [51] by altering the bacterial balance in the gut by influencing T-cells [52], or a special type of white blood cell which is involved in our immune response (www.naturalnews.com). Probiotics are also known to induce cytokines or produce secretory IgA for direct modulation of the immune system [53]. The use of probiotics in children suffering from atopic dermatitis resulted in an increased level of IFN-production simultaneously with the decrease level of IgE, antigen-induced TNF-α, IL-5, and IL-10 secretion [53]. It is further reported that stress is a vital component which induces mast cells to release histamine and thereby worsens allergic symptoms [54]. Different probiotic LAB bacteria viz. *L. casei*, *L. paracasei*, *L. acidophilus*, *L. reuteri*, *B. infantis* and *B. animalis* showed variable effects in clinical trials [55]. The probiotic culture of Lactobacillus rhamnosus has been shown to down-regulate the production of IgE and histamine 4 receptor at the same time up-regulate the anti-inflammatory agents like (IL)-8 (http://thelowhistaminechef.com/).

Metabolic Syndrome

Metabolic syndrome (MetS) is a medical problem caused by a group of potential factors that accelerates the risk for cardiovascular diseases (heart disease) and type 2 diabetes. The potential risk factors are overweight/obesity, hypertension and disturbances of lipid and carbohydrate metabolism [47,56]. There is an urgent need to prevent these risk factors by integrating the changes in the diet plan through blending the food products with probiotics in order to employ a practical approach to deal with metabolic syndrome without any side effects [57]. The aforesaid syndrome is determined by genetic, lifestyle and environmental factors (gut microbiota). The gastrointestinal tract (GI) in human contains mixed culture (approx. 1×10^{13} to 1×10^{14}) having collective genome encoding genes which exceeds human genome by a magnitude of 150 [58]. The advancement in metagenomics has paved the path to understand and decipher the diversity of microorganisms in human's gastrointestine tract. Majority of the known bacterial phylotypes (about 90%) belong to the members of *Bacteroidetes* and Firmicutes followed by *Actinobacteria* and *Proteobacteria* [59,60].

Obesity

Studies have shown that VSL#3, probiotic strain formulation, having combination of eight different strains of bacteria, is able to treat obesity and type 2 diabetes [48,49]. There are several other reports also available to prove the potential of probiotics products (containing live microorganisms) against obesity [61]. The individuals suffering from obesity has an altered ratio of *Bacteroidetes*, *Firmicutes* and *Archea* [62]. Yogurt is reported to aid in reducing fat absorption in small intestine with a significant weight loss and an increased level of lipid in faeces in mice [63].

Type 2 Diabetes

The type 2 diabetic patients are reported to have reduced proportion of *Firmicutes* and Clostridia with an increase proportion of *Bacteriodetes* and *Proteobacteria* compared to non-diabetic individuals [64]. The diabetic mice fed with probiotic containing *Bifidobacterium* have significant positive effect in terms of glucose tolerance and low grade inflammation [65]. A probiotic pill having genetically engineered live bacterial strains of normal inhabitants of intestine when administered in mice model, the GLP-1 hormone triggers the release of insulin and blocks the release of glucagon from pancreatic α-cells thereby helping in the reduction of blood glucose level [66,67]. This product is now commercially available for nutritional therapy of Type-2 diabetes treatment.

Cardiovascular Diseases

Cardiovascular diseases fall under the category of metabolic syndrome involving heart or blood vessels. It is mainly attributed to palmitic acid a high-fat diet. The response to heart disease is triggered in obese individuals by action on adipocytes and macrophages of adipose tissue via TLR-4, a LPS receptor. The increased level of adipose TNF-α and IL-6 concentration results to metabolic endotoxaemia having resistance towards insulin and stimulates vascular inflammation thereby leading to hypertension and CVD [68].

Probiotics play a vital role in preventing cardiovascular diseases. *Lactobacillus reuteri* 30242 is reported to lower down the LDL cholesterol level in two distinct ways (a) remove excessive cholesterol from body and/or (b) increase the cholesterol metabolism [66,67]. The bile acids produced from cholesterol in liver is broken down when probiotics are administered; the cholesterol level is depleted, thereby reducing the risk of cardiovascular diseases [69].

Respiratory Infections

Probiotic bacterial strains are also reported to prevent viral respiratory tract infections [70-72]. However, the effectiveness of probiotics is strain and dose dependent with variable results under different clinical studies. Probiotic therapy is based on the mechanism of competition for the adhesion ability to bind the same site of a common receptor by probiotics and pathogenic bacteria. The probiotics are able to displace the pathogen during competition. Probiotics have the potential for epithelial cell surface or mucus adherence through the formation of a protective layer between pathogen and host cells [73]. Strains of *Lactobacillus* such as *L. rhamnosus*, *L. casei*, *L. gasseri*, and *Bifidobacterium B. longum* , *B. bifidum* (verum) have been used to treat respiratory tract infections (otitis media, sinusitis, bronchitis and pneumonia) in children and elderly subjects [74,75]. There is a considerable reduction in nasal colonization with pathogens in healthy adults after administering *Lactobacillus rhamnosus* GG [70]. *Lactobacillus acidophilus* NCFM reduces fever, rhinorrhoea and cough incidence in healthy children [71], *Lactobacillus delbrueckii* subsp. bulgaricus OLL 1073R-1 reduces risk of catching cold or influenza virus in healthy adults and in elderly group [76], *Bifidobacterium animalis* sub sp. lactis Bi-07 and *L. acidophilus* NCFM has the ability to reduce the incidence of fever, cough and sneezing [72].

Urogenital Infections

Lactobacillus rhamnosus, *Lactobacillus acidophilus*, *L. gasseri*, *L. reuteri*, *L. jhonsenii* and *L. crispatus* have been used to cure bacterial vaginosis [77]. The cure for urogenital tract infection, bacterial vaginosis and vulvuvaginal candidasis is interlinked to H_2O_2 and acid production with probiotic concentration used. The vaginal microflora could be modified through the daily intake of *L. fermentum* and *L.*

rhamnosus in combination through oral route [78]. Probiotics reduced the occurrence of both yeast and bacterial pathogens in vagina [78]. Probiotic administration could normalize the flora and opens up the avenues for possible long term therapy especially for pregnant women and for UTI susceptible individuals [79].

Cancer

Clinical studies, on animal models asnd in *in vitro* system have clearly demonstrated that both prebiotics and synbiotics exert anti neoplastic effect [80]. It was reported in a study that the polysaccharide fraction of *Bifidobacterium bifidum* BGN4 inhibits the growth of HCT-116 and HT-29 cells but could not inhibit the growth of Caco-2 cells [81]. The probiotic strains, *Lactobacillus reuteri* ATCC 6475, *L. rhamnoses* and *Bifidobacterium lactis* have been found to be able to activate caspase proteins amongst the cancerous cell line [82]. The probiotic consumption is useful in preventing the onset of cancer and also for therapy [2,3].

Immune System

Several investigations have indicated that each individual may have a unique metagenomic genotype. The gut microbiota is characterised not just at the level of species or phyla but also at the strain level. Probiotics have a great economic value and it has been accepted that they contribute significantly in improving human health by maintaining the health of gastrointestinal tract and also aids in the treatment and/or prevention of specific intestinal infections. The probiotic strains with predictable and measurable beneficial effect require strict attention to strain selection. The mechanism involved behind is still not very clear [2,3,83]. The proposed mechanisms involved are: (a) direct antimicrobial activity through production of bacteriocins or inhibitors of virulence gene expression; (b) competitive exclusion by competition for binding sites or stimulation of epithelial barrier function; (c) stimulation of immune responses via increases of sIgA and anti-inflammatory cytokines and regulation of proinflammatory cytokines; and (d) inhibition of virulence gene or protein expression in gastrointestinal pathogens [84]. Each of these mechanisms is classified further on the basis of functions involved. The prominent among them are epithelial barrier function [85].

Direct antimicrobial activity through production of bacteriocins or inhibitors of virulence gene expression

The probiotics are antimicrobial in nature. It could produce certain active metabolites which are capable of inhibiting or killing potential pathogens. These active metabolites are (i) organic acids such as acetic acid and lactic acid as end products of sugar fermentation. These end products at low pH range possess robust antimicrobial activity [86]. (ii) Acetaldehyde, ethanol, acetoin, reuterin, carbon dioxide, reutericyclin and other germicidal compounds. These are low molecular weight components which are able to inhibit microbial growth or disrupt membrane of the pathogens [86]. (iii) proteinaceous antibiotic like substances designated as bacteriocins which are mainly ribosomally coded short peptides and exert antimicrobial action by interfering with cell wall synthesis and causing pore formation in cell wall of the target organisms [87] (iv) hydrogen peroxide by the action of flavoprotein-containing oxidases, NADH oxidases and superoxide dismutase. Presence of H_2O_2 in lower concentration aids in oxidizing the sulphydryl group of surface proteins and enzymes of target organisms [88].

Competitive exclusion by competition for binding sites or stimulation of epithelial barrier function

The microbial population in the intestinal tract resides as a prior established complex natural resource and is able to maintain themselves in the environment. These colonized organisms prevent other organism to establish and to reduce the impact of pathogenic bacteria [47]. The beneficial organism shares same receptor sites with pathogens whereby the probiotics exclude pathogens from the host intestine, urogenital tract and other host sites. The mechanism described for pathogen exclusion from intestine through probiotics is in the following manner [89] (i) steric hindrance and competitive depletion of essential nutrients (ii) competitive exclusion by adhered probiotics, through competition for receptor sites and by displacement of adhered pathogens (iii) non-competitive exclusion through induction of secretion of antimicrobial components from host cell and by regulation of epithelial barrier function.

Stimulation of immune responses via increases of sIgA and anti-inflammatory cytokines and regulation of pro-inflammatory cytokines

The intestine microflora exerts both harmful and beneficial effects on human health [90]. The interaction between probiotic with epithelial cells and dendritic cells (DC) is believed to be the initiating step in immunomodulation. The effect of probiotic is strain specific, and for each strain the profile of cytokines secreted by lymphocytes, enterocytes or dendritic cells has to be established when it comes in contact. Certain intracellular signalling pathways are activated on interaction of probiotics with the cell surface receptors and induce immune system.

The major encounters with antigens occur at mucosal surface through mucosal immune system, including the surface lining of gastrointestinal, respiratory and genitourinary tracts [91]. The intestinal microbiota influences the mucosal immune system to respond as tolerance or defence. Probiotics are absorbed orally and influence the immune response at the mucosal frontier of gastrointestinal tract [92]. The intestine is protected from pathogens due to mucous membrane covering epithelial layer. The intestinal immune system recognizes the pathogen as a whole by the intestinal epithelial layer or the substances known as antigens released by the pathogen and responds appropriately. The cytokine profile plays an important role in the maintenance of intestinal immune homeostasis that favours tolerance and IgA production. The equilibrium between Th1 and Th2 cytokine production deciphers the direction and outcome of an immune response. It is associated with chronic inflammatory diseases if the deviation is towards Th1. While, on the other hand, an abnormal response of Th2 type have allergic reactions. A slight deviation towards Th2 response over Th1 response was observed in case of chronic inflammatory bowel diseases such as ulcerative colitis. A predominant Th1-mediated cytokine profile was noted in Crohn's disease [93]. The imbalance between Th1 (IL-2, IFNγ, TNF α) and Th2 responses (IL-4, IL-5, IL-10) led to a chronic inflammatory characterized by the production of pro-inflammatory cytokines (IL-1, IL-6, TNFα) from dendritic cells (DC), but regulates the degree of innate immune activation and prevents excessive inflammation. Microbe-associated molecular patterns (MAMPs) from probiotics expressed by major histocompatibility complex molecule (MHC) of DC, interact with *T cell* receptor (TCR) of T cells and shapes the adaptive immunity of host. The consumption of probiotics led to immunomodulatory effect by interfering with helper cell

differentiation and upsetting the equilibrium between the ratios of Th1/Th2. The pro inflammatory effect or anti-inflammatory action is stimulated by different probiotic strains through alteration of Th1/Th2 ratio toward Th1 or towards Th2 respectively [92].

Inhibition of virulence gene or protein expression in gastrointestinal pathogens

Lactobacilli and *Bifidobacteria* play a vital role in maintaining the optimal balance amongst the micro flora present in the healthy gut [94]. Any sort of alteration in the equilibrium of the microbial community may cause change in immune and inflammatory response along with the change in the metabolism of the epithelial cells [95]. The probiotics have the potential to regulate intestinal homeostasis by (a) reducing the adherence and pathogen invasion as it shares different adhesion sites on epithelium with pathogens and/or (b) activating various intracellular signalling pathways by reinforcing tight junctions and intestinal barrier function [84]. The activated proteins produced induce mucin expression, antimicrobial peptides (defensins, cathelicidins) leading to the rearrangement of tight junction proteins [96].

Probiotics modulates the metabolism of short chain fatty acids production (e.g. acetate and butyrate). These SCFAs modulate the gene expression of epithelial cells by influencing epigenetic modulations. These changes stimulate epithelial proliferation and barrier function.

Probiotic Market Segment

The immense importance and progressive interest on these magic bugs, probiotic products are able to establish itself amongst the masses in a short span of time for alternative and "natural" means to promote intestinal health. Probiotics serve as bio therapeutics in restoration of inflammatory metabolic disorders including cardiovascular diseases such as hypertension, atherosclerosis, and stroke etc. In order to combat the imbalance of indigenous micro flora in the intestinal tract, the probiotic therapy has proven to be useful. The specific strains of healthy micro flora are used in this therapy "Nutritional therapy". Probiotics act as both preventive and curative agent in this therapy. The global probiotic demand was $27.9 billion in 2011 and is expected to reach $44.9 billion in 2018 as per CAGR of 6.8% [2,97]. The worldwide demand for probiotics is majorly covered by Asia-Pacific and European region, with Asia-pacific being prominent player with an expected CAGR of 7% from 2013 to 2018. The market revenue for probiotics is mainly dominated by the Asia-pacific region, and the major revenue is generated from China and Japan. India has made a remarkable growth in terms of market revenue in Asia. On the other hand, U.K and Germany amongst the European countries are the most profitable market with an expected CAGR of 6% from 2013 to 2018. It is estimated that amongst the probiotics, the most influential segments are foods and beverages which is expected to be of $37.9 billion by 2018. The aforesaid segments are followed by dietary supplements and animal feed which too witnesses the remarkable growth. The dairy products are the largest application market for probiotics and are estimated to reach US$ 32.2 billion in 2018. While, under the new emerging segment amongst probiotics is animal feed, which is estimated to cross US$ 3 billion by 2018. The major hurdle in terms of market growth is high price, cultivation of culture and lack of product standardization [2]. The market for probiotics, in India, in terms of food applications is larger compared to that for probiotics sold in the form of probiotics sachets, capsules and in other pharmaceutical preparations. Many spurious and ineffective probiotic products with false claims are entering the market due to absence of any regulatory standards which brings the consumers in dilemma about the acceptability of probiotics products in many Asia-pacific countries including India. The probiotic drugs hold a promising market and have been realized by the number of indigenous pharmaceutical companies. Many food companies have taken step forward to extend their existing market profile and to enter into the upcoming probiotic market [80,98]. Some of the probiotic products available in the global market are displayed in Table 2.

Country	Probiotic products					
Japan	Yakult	Meiji bulgaria yogurt and drink	Morinaga bifidus yogurt	Calpis ameal s120, aprobiotic yogurt drink		
Europe	Lifeway kefir	Culturelle probiotic infant formula	France, bravo friscus	Yoplait yogurt	Danone activia	Actimel yogurt drink
USA	Activia creamy yoghurt	Danone gyoplus	Blue bunny-sedona yoghurt ice cream, choclate sweet scoops-frozen yoghurt	Yoyation pierre's probiotic ice cream		
UK	Vita-yo creamy probiotic yoghurt	Yeo valley bioliye yoghurt yeo valley natural fat free yoghurt	Unilever's flora pro activ cholesterol			
Finland	Valio gefilus® and valio kidius gefilus® and evolus® milk drink and yoghurt (lgg)	Yosa yoghurt oat product	Bioferme, valio villis			
Canada	Biobest plant sterols probiotic yoghurt	Kraft liveactive cheddar cheese and chocolate raspberry bars	Liberte yoghurt	Olympic natural no fat probiotic yogurt		
Spain	Kaiku vita, a functional dairy drink from valio	Bio herbal bifidus active green tea yogurt dannone				
Australia	F and n's alive fruitchunk youhurt	Yo-plus digestive yogurt	Wallaby organic yogurt	Bio-life probiotic yogurt	Vaalia probiotic yogurt	Ombar probiotic chocolate
Brazil	Chamyto probiotic drink nestle	Actimel I casei defensis	Danito I. Casei danone	Sofyl yakult		
Czech Republic	Olma revital active yogurt and drink yogurt					
Sweden	Proviva yogurt	Yogenfruz frozen yoghurt	Biogaia products	Liveactive probiotic products		

Germany	Probiotic vitality yogurt	Soyogurt		
Denmark	Klover drinkable yoghurt	Danimal lactobacillus gg	Probio arla cultura	
France	B.aktiy lgg dukat yoghurt and drinks			
Italy	Ganedenbc30® probiotic low fat yogurt	Probiotic dairy drinks latteria sociale merano	Danacol fermented dairy beverage	Yolive frozen yoghurt
New Zealand	Biofarm acidophilus yoghurt			
India	Mother dairy b-activ probiotic dahi/lassi/curd & nutrifit	Amul probiotic dahi (prolife), frozen yoghurt (flaavyo)	Tropilite foods pvt. Ltd. Bioflex probiotic culture (Animal/ Human) Bioflex starter culture (Dahi/ Yoghurt)	

Table 2: List of probiotic products available worldwide.

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Declaration of Interest

The authors report no declaration of interest.

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