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Review Article
PROBIOTICS AND PREBIOTICS

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Abstract- Probiotics and prebiotics are a special class of food products as their application in wellness of human beings is well established. Probiotics are living microorganisms that are taken as dietary supplements while prebiotics are non-digestible carbohydrates as dietary components that act as food and promote the growth and proliferation of probiotic microorganisms. There is exponential growth in the commercial exploration of probiotics as food, nutritional supplements, biologics and pharmaceuticals due to their health benefits. Various effects of probiotics and prebiotics on health have been documented.

Keywords- Health benefits, Prebiotics, Probiotics.

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Introduction

Bacteria are normal inhabitants of our gut including different parts of gastrointestinal (GI) tract and a large number (~10^{14} cells per millilitre) are present in colon. The beneficial role of gut microbiota in human health has been realized only three decades ago. They may circumvent the pathological effects of harmful bacteria, modulate the host's GI tract associated processes, smoothen digestion, optimize metabolism and immune system, and even influence the processes beyond the gut [1].

The concept of probiotic emerged in the beginning of the 20th century, when the Russian scientist and Nobel Laureate, Elie Metchnikoff proposed that eating fermented milk products containing lactic acid bacteria (LAB) in good quantity can improve human health and prolong life. He postulated that the LAB prevents the activities of undesirable proteolytic microorganisms such as *Clostridium* and reduces toxic compounds such as ammonia, phenols and indoles from gut. Based on this hypothesis, he developed a fermented milk product using *Bulgarican bacillus* (now *Lactobacillus delbrueckii subsp. bulgaricus*) to manipulate the environment of the gut for improvement of human health [1]. Another incidence of beneficial gut bacteria in maintaining good health comes from a French Pediatrician, Tissier [2], who observed that children suffering from diarrhoea had low number of bacteria and healthy children had high number of these bacteria. Based on these observations he suggested that these bacteria could be given orally to patients suffering from diarrhoea to cure them by reloading the healthy microbes in their gut [3].With these conclusions some awareness about microbes in providing health benefits was created and during First World War commercial yogurts and fermented milk products could find their way as nutraceuticals.

The concept of prebiotics was given by Gibson and Roberfroid [4] as the dietary components that can modulate the gut microbiota in a beneficial way by promoting the growth and proliferation of beneficial bacteria in the gut. Prebiotics are normally non-digestible fibers of some foods such as chicory, garlic, Jerusalem artichokes, onions etc. that passes undigested through the upper part of the GI tract but act as substrate for the advantageous bacteria that colonize in the large intestine and help in increasing their numbers. However, these foods are required to be consumed in large quantities to increase the levels of beneficial bacteria in our gut. Therefore, a combination of probiotic and prebiotic is complimentary to each other to maintain the required level of friendly bacteria in the intestine.

Probiotic bacteria

Probiotics are living microorganisms that can be taken as foods and/or dietary supplements in adequate amounts for health benefit of the host [5]. Good quality curds (yogurts) with live active cultures, fermented milk, kefir, miso and a number of other foods like pickles and other fermented vegetables are also part of probiotics. The sale of probiotic based products begun to grow rapidly during 1980s in Japan and later in 1990s in Europe. Lactic Acid *Lactobacillus, Bifidobacterium*, the yeast *Saccharomyces cerevisiae, Escherichia coli* and *Bacillus* species are the most commonly used probiotics. LAB, can serve dual purpose by acting as food preservatives through fermentation and by imparting health benefits to the consumers [6].

GI tract and its probiotics microbiota

Bifidobacteria and *Lactobacilli* ferment carbohydrates that remain undigested in the upper GI tract and reduce the colon pH [7]. *Bifidobacteria* express β-fructo-furanosidase which helps in the fermentation of fructans [8]. Similarly, high β-galactosidase activity associated with *Lactobacilli* and *Streptococci*, provides advantage in galacto-oligosaccharides (GOS) fermentation [9]. The lower pH in the colon encourages the multiplication and survival of commensal microbes and prevents some pathogens from adhering, growing, and translocating across the intestinal epithelium [10]. In addition, butyrate produced by intestinal microbes enhances the mucosal cell differentiation and may promote the barrier function of the epithelium [11]. Saccharolytic fermentation decreases the harmful protein fermentation and other processes, which give rise to nitrogen and sulphur-containing compounds such as ammonia, *N*-nitroso- and azo- compounds as well as sulphides [12].

Many bacteria produce antimicrobial peptides (bacteriocins) that reduce the survival of competing organisms [13]. Bacteriocins produced by probiotic bacteria

have been observed *in vivo* to decrease the ability of pathogens such as *E. coli* to colonize the intestinal cells in cattle [14]. The effects of prebiotic oligosaccharides and trehalose on growth and production of bacteriocins by lactic acid bacteria has also been reported [15]. This may be one of the mechanisms by which probiotics and prebiotics decrease the infection rate in humans and animals [13].

Probiotics may be responsible for enhancing the production of defensins (antibacterial peptides) in the small intestine by the Paneth cells. Studies reveal that probiotics can stimulate human β-defensin mRNA expression and peptide secretion [16,17]. *In vitro* studies have suggested that probiotics and prebiotics may influence the barrier function of the epithelium by enhancing the resistance of tight junctions, possibly via an effect on tight junction proteins (e.g. occludins and claudins) [18]. Higher expression of genes encoding tight junction proteins has recently been exhibited in human trials, wherein volunteers were administered with a specific *Lactobacillus* strain [6].

Studies conducted on animals revealed that specific probiotics compete with pathogens to occupy the receptor sites on epithelial cells or sites in the mucous layer, resulting in to prevention of pathogens from sticking to or translocation across the GI tract [19]. On the other hand, some probiotics directly binds to the pathogens and reduces their colonization ability in the intestine [20]. Rijkers *et al*. [06] reported that certain probiotic strains can reduce the ability of pathogens such as *S. typhimurium* and *E. coli* to translocate and invade the liver and spleen of mice.

Mechanism of action

The mechanisms by which probiotics and endogenous commensals acts depend on its interaction with the immune system of the GI tract and consequently modulate the immune responses of the host [1]. Gourbeyre et al. [21] reviewed the impact of probiotics on the gut immune system and allergic reactions and reported that it can influence the intestinal microbiota and modulate the immune response and may prevent or alleviate pathogens involved in the gut immune system.

The ingested and endogenous microbes can impact both the innate and the adaptive immune responses of the host through the bacterial epithelial cell cross-talk [22]. and the interaction of commensal, probiotic or pathogen with host cells is mediated through specific receptors (Toll-like receptors), which are associated with cells lining the mammalian GI tract [23]. The activation of these receptors initiates a series of coordinated immune signals leading to different immune responses to potential pathogens and food antigens through T cells and T-regulatory cells [23]. Additionally, activation of the immune pathways may cause differentiation of B cells, production and secretion of protective antibodies into intestine [24]. Probiotics and to some extent prebiotics modulate the activity of phagocytic cells and natural killer (NK) cells in animals and humans [25]. Similarly, the ingestion of specific probiotic strains or prebiotics in human and animal studies has been found to stimulate an increase in the anti-inflammatory cytokines and a decrease in the expression of pro-inflammatory cytokines [26]. It is proposed that these changes in cytokine balance could be a mechanism by which prebiotics and probiotics may be able to mitigate chronic intestinal inflammation [27].

Products and Dosages of Probiotics

A variety of probiotic-containing food products, dietary supplement, meal replacement, nutraceuticals are available in the market and are often being recommended by nutritionists and sometimes by doctors. The more prevalent forms of probiotics are live cultures available in the form of fermented dairy products and probiotic-fortified foods [Table-1]. However, they are also available in the form of capsules, tablets and sachets containing the bacteria in lyophilized form.

Table-1 *List of probiotic strains and their commercial producers.*

Brand name	Producer	Probiotic Strain
LC1	Nestle	*Lactobacillus johnsonii* La1 (Lj1)
Actimel, Dan Active	Danone/Dannon	*Lactobacillus casei* DN-114 001
Yakult	Yakult	*Lactobacillus casei* Shirota
GoodBelly, ProViva	NextFoods Probi	*Lactobacillus plantarum*299V
Reuteri	BioGaia Biologics	*Lactobacillus reuteri* ATTC 55730
Cultura	Arla Foods	*Lactobacillus casei* F19
Valio	Vifit and others	*Lactobacillus rhamnosus* ATCC 53013 (LGG)
Verum	Norrmejerier	*Lactobacillus rhamnosus* LB21
FemDophilus	Chr. Hansen	Tested as mixture: *Lactobacillus rhamnosus* GR-1 & *Lactobacillus reuteri* RC-14
VSL#3	Sigma-Tau Pharmaceuticals, Inc.	Tested as mixture: VSL#3 (mixture of 1 strain of *Streptococcus thermophilus*, four *Lactobacillus* spp., & three *Bifidobacterium* spp. strains
Bio K+	Bio K+ International	Tested as mixture: *Lactobacillus acidophilus* CL1285 & *Lactobacillus casei* Lbc80r
A'Biotica and others	Institut Rosell	Tested as mixture: *Lactobacillus helveticus* R0052 & *Lactobacillus rhamnosus* R0011
Activia	Danone/Dannon	*Bifidobacterium animalis* DN 173 010
Howaru Bifido	Danisco	*Bifidobacterium lactis* HN019 (DR10)
Bifiene	Yakult	*Bifidobacterium breve* Yakult
Align	Procter & Gamble	*Bifidobacterium infantis* 35624
Bioflorin	Cerbios-Pharma	*Enterococcus* LAB SF 68
Mutaflor	Ardeypharm	*Escherichia coli* Nissle 1917
DiarSafe, Ultralevure, and others	Wren Laboratories, Biocodex, and others	*Saccharomyces cerevisiae (boulardii)* lyo
Enterogermina	Sanofi-Aventis	Tested as mixture: *Bacillus clausii* strains O/C, NR, SIN, and T

There is no consensus regarding the dosage of probiotics because it varies greatly depending on the strain and product [28]. The typical dosage used for *Lactobacilli* ranged from 1000–20000 x 10^7 colony-forming units (cfu) per day, whereas, for *Saccharomyces boulardii*, it ranges from 250 to 500 mg [29]. Although many over-the-counter products deliver in the range of 1–10 billion cfu/dose, some products have been shown to be effective at lower levels, while some require substantially more quantity. These typically higher doses are required for adequate and effective gut colonization [30]. The effective dosage for different probiotic strains based on results obtained from human studies is summarized in [Table-2]. The probiotic formulations may have a limited shelf life, and many preparations contain several different species, so dosage may vary depending on the product.

A number of probiotics are available in the market; but, only those products that have been evaluated in controlled human studies should be recommended [Table-1]. Some examples of these commercially available preparations include *S. boulardii* (Florastor, Biocodex, Inc., Beauvais, France), LGG (Culturelle, Amerifit Brands, Fairfield, NJ), *B. infantis* 35624 (Align, JB Laboratories, Holland, MI). Dairy products fermented with probiotics should be labelled with a Live and Active Cultures seal, specifying that the preparation contain a minimum of 100 million viable bacteria per gram at the time of manufacture. An example of such product is Activia yogurt (Dannon /Danone, Paris, France), which contains *B. animalis* DN-173 010, marketed by Dannon/Danone as "Bifidusregularis" [29]. The manufacturing process may deactivate the living microbes and reduces the effectiveness of probiotics [45]. Therefore, different probiotic products and different lots of the same product may have variations in the quality, quantity and purity of the microbes [29, 36, 46].

The probiotics must be alive and ingested on a regular basis to maintain and establish its effective concentration in the gut [29, 47,48]. An analysis comprising of 18 commercially available probiotic products showed that 39% products had differences between the stated and actual concentrations of bacteria [49].

Table-2 *Probiotic Species and Dosing*[a]

Indication and Probiotic	Recommended Dosage Regimen	References
Acute infectious diarrhoea in infants and children		
Lactobacillus reuteri	1010–1011 CFU daily up to 5 days	Van Niel et al., 2002 [31]
Lactobacillus rhamnosus GG (LGG)	At least 1010 CFU in 250 ml of oral rehydration solution; 1010–1011 CFU twice daily for 2–5 days	Guandalini et al., 2000; [32] Van Niel et al., 2002 [31]
Antibiotic-associated diarrhea		
Lactobacillus acidophilus and *Lactobacillus bulgaricus*	2×10^9 CFU daily for 5–10 days	McFarland, 2006[33]
L. acidophilus and *Bifidobacterium longum*	5×10^9 CFU daily for 7 days	McFarland, 2006 [33]
L. acidophilus and *Bifidobacterium lactis*	1×10^{11} CFU daily for 21 days	McFarland, 2006 [33]
LGG	6×10^9–4×10^{10} CFU daily for 1–2 weeks	McFarland, 2006 [33]
Saccharomyces boulardii	4×10^9–2×10^{10} CFU daily for 1–4 weeks	McFarland, 2006 [33]
Clostridium difficile infection		
S. boulardii	2×10^{10} CFU (1 g) daily for 4 weeks plus vancomycin and/or metronidazole	McFarland, 2006 [33]
Travelers'diarrhea		
S. boulardii	5×10^9–2×10^{10} CFU daily starting 5 days before departure and continued throughout trip	McFarland, 2007 [34]
LGG	2×10^9 bacteria daily starting 2 days before departure and continued throughout trip	Hilton et al., 1997 [35]
Irritable bowel syndrome		
Bifidobacterium infantis 35624	10^6–10^{10} CFU daily for 4 weeks	McFarland and Dublin, 2008 [36]
VSL#3[b]	9×10^{11} CFU daily for 8 weeks	McFarland and Dublin, 2008 [36]
Ulcerative colitis (UC)		
Escherichia coli Nissle 1917	Active UC: 5×10^{10} bacteria twice daily until remission (maximum of 12 wk), followed by 5×10^{10} bacteria daily for a maximum of 12 mo39; inactive UC: 5×10^{10} bacteria daily (study duration was 12 weeks)	Kruis et al., 1997 [37]
S. boulardii	Active UC: 250 mg 3 times daily for 4 wk plus mesalamine	Guslandi,et al., 2003 [38]
VSL#3[b]	Active UC: 1.8×10^{12} bacteria (two 3-g sachets) twice daily for 6 weeks plus conventional therapy	Bibiloni et al., 2005 [39]
Atopic disease prevention		
LGG	10^{10} CFU daily for 2–4 wk before expected delivery in pregnant women, followed by infant administration for 6 months	Kalliomaki et al., 2001 [40]
Crohn's disease		
S. boulardii	Maintenance therapy: 1 g daily for 6 mo plus mesalamine	Guslandi et al., 2000 [41]
Pouchitis		
VSL#3[b]	Maintenance therapy: 1.8×10^{12} bacteria daily, given as 3-g sachets twice daily (study duration was 9 mo)46; maintenance therapy: 1.8×10^{12} bacteria daily, given as two 3-g sachets once daily (study duration was 12 months)	Mimura et al., 2004 [42]
Vulvovaginal candidiasis		
LGG	10^9 bacteria per suppository inserted twice daily for 7 days	Hilton, et al., 1995 [43]
L. rhamnosus GR-1 and *Lactobacillus fermentum* RC-14	At least 10^9 bacteria suspended in skim milk given orally twice daily for 14 days	Reid et al., 2001 [44]

[a]CFU = colony-forming units. [b] VSL#3 is a mixture of eight probiotic organisms (*L.casei*, *L. plantarum*, *L. acidophilus*, *L. bulgaricus*, *B. longum*, *Bifidobacterium breve*, *B. infantis*, and *Streptococcus thermophilus*).

Prebiotic bacteria

The prebiotics are food ingredients, which are indigestible in the upper GI tract and beneficially influence the host by selectively promoting the growth and activity of certain bacteria in the colon [4]. Since there are a large number of bacteria present in the GI tract and some of them are non-cultivable, the prebiotics has been revised as a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the GI microflora and confers benefits upon host well-being and health [50,51]. As a functional food component like probiotics and prebiotics are also intermediate between foods and drugs. Prebiotics generally include non-starch polysaccharides and oligosaccharides and promote the growth and proliferation of a selected group of microbes living in the intestine.

Most prebiotics are used as food ingredients such as in biscuits, chocolate, cereal foods, spreads, and dairy products. Commonly known prebiotics are oligofructose, inulin, lactulose, glacto-oligosaccharides, breast milk oligosaccharides, resistant dextrins, polysaccharides such as polydextrose, arabinoxylans and resistant starches as well as some polyols such as lactitol and isomalt [1]. The prebiotics oligofructose is found naturally in many foods, such as wheat, onions, bananas, honey, garlic, leeks and can also be isolated from chicory root or synthesized enzymatically from sucrose [1].

Fermentation of oligofructose by beneficial microbes in the colon results in a large number of physiological effects, such as increase in the numbers of *Bifidobacteria* in the colon, increase in calcium absorption, fecal weight, shortening of GI transit time and possibly, lowering blood lipid levels [51, 52]. The increase in colonic *Bifidobacteria* has been assumed to benefit human health by producing compounds to inhibit potential pathogens, by reducing blood ammonia levels, and by producing vitamins and digestive enzymes [25].

Mechanism of action

Both probiotics and prebiotics are considered to work mainly through modulating the microbiota and environment of the gut and/or the host immune system. In the case of probiotics, live microorganisms are consumed and the high density of microbes has the potential of creating a greater impact in the upper GI tract and at some extent to the colon [51, 52]. Prebiotics, on the other hand enhance the growth of the endogenous microbiota or possibly stimulate the growth of probiotics on simultaneous administration. Thus, probiotics and prebiotics function in complementary to each other for beneficial impact on the host physiology. Probiotics and prebiotics act on and interact with the host by two main modes of action, or a combination of actions i.e., impact of microorganisms or their metabolites/enzymes on the host's GI tract and its microbiota and interaction with the host's cells and immune system.

These mechanisms include competition for dietary ingredients as growth substrates, bioconversion of sugars into fermentation products with inhibitory properties, production of growth substrates viz., EPS or vitamins, direct

antagonism by bacteriocins, competitive exclusion for binding sites, improved barrier function, reduction of inflammation to alter the intestinal properties for colonisation and persistence and stimulation of innate immune response [53].

Effects of Prebiotics and Probiotics

Health Benefits

Probiotics are mainly administered to support the naturally occurring microbiota of the gut in preventing the harmful microbes and also confer the health benefits to the host. Some probiotic preparations are given to the patients on antibiotic therapy to prevent antibiotic associated diarrhoea or as part of the treatment for antibiotic-related dysbiosis [19]. Studies have documented positive effects of probiotic on a variety of gastrointestinal and other disorders, including inflammatory bowel disease (IBD) [27], irritable bowel syndrome (IBS) [54], vaginal infections and immune enhancement [26]. Some probiotics have also been investigated in relation to liver cirrhosis [55], atopic eczema [56] and rheumatoid arthritis [57]. In general, the strongest clinical evidence for probiotics is related to their use in improving gut health and stimulating immune function [1].

Balance of the intestinal microbiota

Normal physiological condition of the host is dependent on the signals given by the intestinal microbes. The gastric acid, digestive enzymes, and IgA present in the intestinal lumen constitute the first line of defence and are lethal to invading and ingested pathogenic bacteria. The indigenous microbes inhibit the pathogenic microbes from adherence and colonization and are necessary for the induction of regulatory T cells [58]. Any changes to the normal intestinal ecosystem could cause an imbalance of the microbiota often associated with various disease states ranging from the most common IBD [26, 27] and IBS [54] to the more unexpected activation of chronic human immunodeficiency virus (HIV) infection [59] and generation of atopy [60, 61, 62].The prebiotics, probiotics and symbiotic have the potential to re-establish the normal microbiota of GI tract and can favourably influence microbial interactions with the immune system and gut epithelium.

Alleviation of lactose intolerance

Lactose intolerance is a condition in which the colonic fermentation of undigested lactose results in gastrointestinal effects such as abdominal pain, bloating, borborygmi or laxation due to decline of lactose. This is due to the down regulation of expression of lactose digesting enzyme in adults [63]. There is evidence that the high-lactose milk products supplemented with starter cultures containing *Lactobacilli* and/or *Bifidobacteria* can be tolerated by lactose-intolerant individuals, possibly because these fermented products contain the microbial β-galactosidase which functions in the small intestine to support lactose hydrolysis [64]. Similarly, *Streptococcus thermophilus* or *Lactobacillus casei* sub sp *defensis* are able to hydrolyze lactate during transit through the gut in mice [65].

Inflammatory Gut Conditions

The inflammatory bowel diseases (IBD) including Crohn's disease (CD) and ulcerative colitis (UC) are serious health ailment [66, 67]. It is associated with a breakdown of the normal barrier function provided by the gut epithelial lining and its associated mucus [68]. Studies conducted on germ-free animals and normal animals showed that germ-free animals are less susceptible to IBD and that the presence of commensal bacteria in normal animals can initiate and/or worsen inflammatory bowel conditions [69]. The CD and UC may result from an improper mucosal immune response to the microbiota of the GI tract in the genetically susceptible individuals [69]. Clinical studies have already shown that the balance of different groups of commensal bacteria might be altered in IBD patients [70].
Administration of both probiotics and prebiotics in animal models, have revealed a positive impact on the prevention or treatment of IBD [71]. In another inflammatory bowel condition known as pouchitis, which can occur after surgery to treat UC, one mixture of probiotic strains (VSL#3) was found effective in maintaining remission [72]. The potential for prebiotics and synbiotics to help the management of IBD has been shown in several studies with fructans, mainly in the reduction of inflammatory markers [71, 73].

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is an abnormal condition that is characterized by symptoms such as abdominal pain, bloating and altered bowel habits that may often alternate between diarrhoea and constipation [54]. IBS affects 5 - 15% of the adult population, with higher rates in women and older people [54]. IBS has been related to inflammatory processes and in a certain cases, it appears that previous gut infections have a role in onset of IBS [74]. Furthermore, lower levels of *Bifidobacteria* have been observed in patients compared with healthy people [75].
Due to the absence of effective therapy for IBS and the detection of abnormal microbiota in IBS patients, both probiotics and prebiotics have been studied for their ability to manage the condition [76]. The studies on the use of probiotics for IBS is complex due to the difficulty of comparisons of the many strains but they have shown positive effects on the variety of symptoms of IBS [77, 54]. Whereas low dosages of some prebiotics led to an improvement in the condition and larger load led to an enhancement of the perceived symptoms [52].

Colon cancer

The relationship between diet and cancer has been supported by many findings and advocates the use probiotics as part of an anti-cancer diet [78]. It may suppress the growth of bacteria that transform procarcinogens into carcinogens [78] by boosting the immune system of the host. An influence of fermented milk containing probiotic strain *L. helveticus* has been reported on the delayed growth of breast tumour. It can inhibit tumour growth of hormone-dependent breast cancer and induced colon cancer by reducing the inflammatory response [79]. Studies revealed that short-lived metabolite mixtures isolated from milk fermented with probiotic strains of *L. bulgaricus* and *Streptococcus thermophilus* are more effective in eliminating the causal factors of colon carcinogenesis [79].

Infant health

Human milk oligosaccharides (HMOs), a group of unconjugated glycans with structural diversity are abundant in the human milk [80] and discovered as a prebiotic that serves as a food with health benefits for the breast-fed infants [81]. Presently, they are known to have much broader role and studies suggests that HMOs are anti adhesive antimicrobials and prevent pathogen attachment to infant mucosal surfaces to lower the risk for viral, bacterial and protozoan infections [82, 83, 84]. In addition, this prebiotic may modulate epithelial and immune cell responses, reduce excessive mucosal leukocyte infiltration, lower the risk of enterocolitis and provide essential nutrients for brain development and cognition of the infant [85, 86]. Studies showed that infant formula augmented with galacto-oligosaccharides (GOS) and/or fructans, helps to stimulate the *Bifidobacteria* that are characteristic of breast-fed infants in a dose-dependent manner and infants fed with infant-foods rich in oligosaccharides have a similar intestinal microbial composition, stool pH and short chain fatty acids (SCFAs) composition to those of breast-fed infants [87]. The use of specific GOS and fructan prebiotics as well as other prebiotic has become widespread practice and accepted as safe.

Mineral absorption

The prebiotics have been considered as the most promising substances for bone-health-promotion in animal models [51]. Nondigestible oligosaccharides (NDO) including inulin, fructo-oligosaccharides, oligofructose, galacto-oligosaccharides, soybean oligosaccharide, sugar alcohols, difructose anhydride and resistant starches assist the mineral absorption, metabolism and bone composition in several animal and human beings [88, 89, 90]. The role of dietary prebiotics is improved by high dietary calcium content. Their efficacy depends on chronological and physiological age, menopausal stage in females and calcium absorption capacity [91]. Multiple mechanisms for prebiotic mediated mineral absorption has been suggested including improved solubility of minerals due to enhanced bacterial production of short-chain fatty acids; increased absorption surface area due to increased number of enterocytes mediated by bacterial fermentation products; higher expression of calcium-binding proteins; degradation of mineral binding phytic acid; improvement of gut health; release of phytoestrogens from foods; stabilization of the intestinal mucus, microbiota and ecology; and impact of modulating growth factors such as polyamines [91].

Gut function

The prebiotics and probiotics can influence gut function in a positive manner. Since the prebiotics is fermented in the colon, results in increased bacterial mass and osmotic water-binding capacity that contribute to increased stool weight, increased stool frequency and softer stools, it takes care of almost all the function of the gut. The SCFA, especially butyrate, have a positive effect on the endothelium and peristalsis of the gut and improves the transit time. In some studies, prebiotics are reported to reduce the intestinal discomfort viz., bloating, abdominal pain and flatulence [53]. The improved transit time may reduce putrefactive activity in the left colon by reducing the levels of polyamines and metabolites such as cresol and indoles [53, 21]

Obesity and related diseases

The adult people suffering with type-2 diabetes showed that they had different gut microbiota compared to non-diabetic adults, and use of probiotics and prebiotics in diabetic patients may potentially improve their health [92]. The natural gut microbiota plays a role in obesity, diabetes and cardiovascular disease study suggests probiotics could prevent obesity and insulin resistance. The patients with diabetes mellitus have lower number of *Faecalibacterium prausnitzii* and increased number of inflammatory markers [93].

Obesity also has close association with changes in the ratios of different bacteria [94]. The population of *Bifidobacteria* and other organisms in the group of Firmicutes is comparatively lower in the individuals with obesity than in thin people [95]. Similar observation was reported for patients with type-2 diabetes mellitus compared to nondiabetic patients [96]. When prebiotics like inulin were fed to mice, the number of *Bifidobacteria* increased significantly, and an inverse correlation was observed between the levels of lipopolysaccharide, glucose tolerance and development of fat mass [97, 98 and 99]. These outcomes suggest that *Bifidobacteria* may play an important role to cure obesity and related problems. The prebiotic approach has also been reported to prevent the over expression of several host genes that are responsible for adiposity and inflammation [99].

The lipoprotein lipase inhibitor increased in mice fed with a high fat diet supplemented with *L.paracasei* and inhibited the uptake of fatty acids from circulating triglyceride-rich lipoproteins [100]. Studies revealed that the obese individuals administered with *L. acidophilus* and *L. gasseri* had lower fat mass and risk of type-2 diabetes mellitus and insulin resistance properties [101, 102]. The clinical trials also have positive results on the patients suffering with diabetic, overweight and obesity treated with prebiotics like arabinoxylan [103,104] and inulin-type fructans [105, 106, 107]

Allergic conditions

With due recognition of the basic role of intestinal microbiota in human health, efforts have been undertaken to evaluate the performance of probiotics in the prevention and/or treatment of allergic conditions in human beings. Children suffering from atopic dermatitis have higher number of *S. aureus* and *Clostridium* in their colon and lower number of *Enterococcus*, *Bifidobacterium,* and *Bacteroides* [108, 109]. The nature of microbiota acquired by the infant in the postnatal period has an important bearing on maturation of the immune system [110, 111, 23]. The studies revealed that when *Lactobacillus* was given to high risk infants, 50% decrease in the atopic eczema was recorded [40]. Similarly, a whey formula with *L. rhamnosus*or, *B. Animalis* sub sp. *lactis* and combination of *L. rhamnosus* plus *L. reuteri* preparations [112] resulted in the improvement of skin condition of the children. The *L. rhamnosus* supplement given to pregnant women and their newborn babies reduced the cumulative occurrence of eczema [59]. A probiotic cocktail of *Bifidobacterium lactis*, *B. bifidum*, and *Lactococcus lactis* reduced eczema in high-risk infants [113, 114].

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