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2. Benefits of Probiotics and Prebiotics to Control Diseases

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Abstract:

Probiotics are beneficial bacteria, and Prebiotics provide nourishment to these bacteria. Consuming both in foods or supplements can assist in balancing your intestinal flora. In recent years and in the forthcoming decades, significant advancements in technologies and related approaches will continue to play a crucial role in the prebiotic and probiotic fields. This review provides current perspective on the probiotics and prebiotics concept, sources of probiotics and prebiotics, as well as the current insight into their effect on human health. The mechanism of beneficial effects is described, and proven study findings demonstrating their efficiency in human nutrition are discussed.

Keywords:

Probiotics, Prebiotics, Bacteria, Health, Supplements, Beneficial.

2.1 Introduction:

According to the World Health Organization (WHO), probiotics are defined as the live microorganisms that "when administered in adequate amounts, confer a health benefit on the host" [1]. Most common species of probiotics belong in the families of Lactobacillus, Bifidobacterium and Streptococcus [2] with the first two families being mostly used in studies related to human health [3]. As these microorganisms are naturally found in the gut microbiota, most studies are focused on their effects in the context of the natural function in the gut and as preventive or therapeutic agents against disease development [4–11]. They play an important role in creating a healthier gut environment by inhibiting undesirable microbes and by crossfeeding other beneficial gut microbes, resulting in production of butyrate, which fuels intestinal epithelial cells [12]. Thus, organic acids commonly produced by many different probiotic strains and species contribute to general gut health benefits [13]. Thus, probiotics have been used for the study and treatment of intestinal diseases such as gastroenteritis [14], intestinal hyperpermeability [15], urinary tract infection [16], intestinal dysbiosis [17], irritable bowel syndrome [18], Crohn's disease [19], colon cancer [20,21], ulcerative colitis [22,23] and peptic ulcer [18]. Identifying and establishing precise mechanisms responsible for any given health benefit remain active areas of research. Probiotics are poised as a valuable means of influencing the function of the gut ecosystem to improve nutritional status and health. [24]

On the other hand, Prebiotics are the substances which reach the colon in the intact form are given to the animals and beneficial for microbial growth in the intestine and normal digestion process. They act as fertilizer for probiotics for example: insulin, fructooligosaccharides. [26] Gibson and Roberfroid [27] in 1995 defined prebiotics as "a non-digestive food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon that can improve the host health." Later, these authors revised the concept and proposed a new definition for prebiotic as "a selectively fermented ingredient that allows specific changes; both in the composition and/or activity in the gastrointestinal microbiota that beneficially affects the host health." [27,28]. The Food and Agriculture Organization of the United Nations defines prebiotics as "a nonviable food component that confers a health benefit on the host associated with modulation of the microbiota." [29]

2.2 Probiotics:

The word probiotics derives from the Latin word pro means for and the Greek bios means life. Probiotics are the community of microbes living in our intestines and are considered a metabolic 'organ' due to their positive impact on human wellbeing, including our metabolism and immune function. Our gut microbiome has actually evolved as humans have undergone evolution and have shaped and interacted with our body over thousands of years, influencing our physiology [30].

2.2.1 Common Microbes Used as Probiotics:

Human microbiota is composed of different types of bacteria, yeasts, fungi used as probiotics. New studies indicate that our microbiome can change incredibly fast in the human gut—within three or four days of a big shift in what we eat. Eating a mainly plant based diet supports health giving probiotics [31]. Specific probiotic strains have mostly been shown to provide health advantages.

- **Bacterial microbes**: (i) Lactobacillus Species: acidophilus, sporogenes, plantarum, delbrueck, reuteri, brevis, fermentum, lactus, cellobiosus, , casei, farciminis, rhamnosum paracasei, gasseri, crispatus; (ii) Bifidobacterium Species: bifidum, adolescentis, longum, thermophilum, infantis, breve, lactis, animalis;(iii) Streptococcus: lactis, cremoris, alivarius, thermophilis, intermedius, diacetylactis; (iv) Leuconostoc mesenteroides; (v) Enterococcus; (vi) Propionibacterium; (vii) Bacillus; (viii) Pediococcus; (ix) Enterococcus faecium
- **Yeast and molds:** Saccharomyces bourlardii, Saccharomyces cerevisiae, Candida pintolopesii, Aspergillus niger, Aspergillus oryzue, Sacaromyces boulardii
- **Viruses:** Our guts are home to several plant-derived viruses, and it has been hypothesised that these viruses may alter the local bacterial flora. [32,33]

2.2.2 Characteristics of A Good Probiotics [34-36]:

- The probiotic ought to have a beneficial effect on the host. It ought to be resistant to bile, acid, and at least 30 109 CFU per Gram.
- The probiotic must have a high survival rate and rapidly multiply.
- The probiotic's adhesive ability must be firm and swift.

- Reduce or eliminate pathogenic adhesion.
- Make acids, peroxide, and bacteriocins that stop pathogens from growing.
- Safe, non-invasive, non-pathogenic, and free of cancer
- Collect into a normal, well-balanced flora.
- In order to reach the intestine alive, probiotics need to be durable enough to withstand commercial manufacturing, processing, packaging, and distribution.

2.2.3 Mechanism of Action:

The following are some suggested ways that probiotic microorganisms may exert their beneficial effects on health: **[37-42]**

a. Production of inhibitory agents that prevent pathogenic bacteria from adhering to the intestinal epithelium;
b. Suppression of pathogenic bacteria's growth by directly binding to gram-negative bacteria
c. Maintenance of normal levels of short-chain fatty acids (SCFAs)
d. Suppression of intestinal pro-inflammatory cytokine production.
e. Regulate lipid metabolism.
f. Enhance the intestinal immune response
g. Repair of intestinal permeability by colonocyte multiplication
h. Inhibits the growth of pathogenic enteric bacteria by decreasing luminal pH
i. intestinal electrolyte absorption is increased
j. Improves the barrier function and changes the form and function of the intestinal epithelium.

2.2.4 Sources of Probiotics:

Probiotics supplements are not necessary for normal, healthy individuals. For healthy adults, daily consumption of probiotics-rich foods, like yoghurt and cultured milk drinks, and fiber rich diets (prebiotics) should adequately supply the amount of probiotics required to maintain a healthy digestive system and overall wellbeing [43].

Probiotics in our Diet: The bacteria in fermented foods increase its levels of vitamins B, C, and K, deactivate harmful nutrients such as the protein inhibitors and phytic acid, and release nutrients from food that would otherwise have passed through the intestines undigested.

Yogurt is a dairy product made from milk that has undergone bacterial fermentation. Streptococcus salivarius subsp. and Lactobacillus bulgaricus are used in the culture used to make dairy yoghurt.

Live cheeses contain probiotics such as Live Active natural cheese snacks and yogurt Cheese (prepared with the probiotic live cultures Lactobacillus acidophilus and bifidobacterium).

Buttermilk Commercial cultured buttermilk is produced from cow's milk using either Streptococcus lactis or Lactobacillus bulgaricus.

Kefir is a fermented milk beverage that also contains yeasts such Candida humilis, Kazachstania unispora, and Kluyveromyces lactis as well as bacteria like Lactobacillus acidophilus, brevis, casei, and delbrueckii subsp. Bulgaricus.

Kombucha is a Chinese tangy/sweet "mushroom tea." The yeast component of kombucha may contain Saccharomyces cerevisiae, Brettanomyces bruxellensis, or Candida stellata.

Sauerkraut, Tempeh, Miso, Soya sauce, Natto are some other sources of probiotics

Probiotic supplements: They come in tablet, powder, capsule, and liquid forms. They do not provide the nutrition like probiotic foods, but they are an option to promote healthy gut bacteria. [44]

2.2.5 Probiotics Effects on Human Health:

A. Irritable Bowel Syndrome and Probiotics

Probiotics were somewhat effective in children and adults with irritable bowel syndrome (IBS) and in children with functional abdominal pain, in clinical trials.

Pain and flatulence in patients with irritable bowel syndrome is decreased by administration of a L plantarum strain in a double blind clinical trial. [45]

B. Allergy and Probiotics

Probiotics associated with disappearance of food allergy manifestation with decrease in concentration of IgE in the serum and with a lower frequency of allergies was reported by Loskutova et al and Trapp et al in two different studies [46,47].

C. Skin and Probiotics:

Lactobacilli and Bifidobacterium are the most commonly used probiotics and thought to mediate skin inflammation, treat atopic dermatitis (AD) and prevent allergic contact dermatitis (ACD). [48]

D. Oral Health and Probiotics:

Probiotics can help to destroy the harmful microbes in the oral cavity by fighting against them and helps in maintaining healthy gums and teeth. Since probiotics is an all-natural treatment it should not have any side effects [49,50].

Both *lactobacillus acidophilus* and *bifidobacterium lactis* have well known antifungal property [51].

Table 2.1: Role of Probiotics in Health Improvement and Disease Treatment

Disease	Probiotic Strains	References
Atopic eczema	Escherichia coli Bifidobacterium bifidum Bifidobacterium lactis	[52,53]
Food allergy	Escherichia coli	[54]
Immunity Modulation	Bacillus circulans PB7 Lactobacillus plantarum DSMZ 12028	[55,56]
Removal of Antibiotic effect	Enterococcus mundtii ST4SA Lactobacillus plantarum 423 Lactobacillus brevis KB290 Lactobacillus strains Bifidobacterium strains	[57,58,59]
Gastroenteritis	Lactobacillus casei	**[60]**
Intestinal hyperpermeability	Lactobacillus plantarum species 299 (LP299)	**[61,62,63]**
Vaginal candidiasis	Lactobacillus rhamnosus GR-1 Lactobacillus reuteri RC-14	**[64]**
Urinary tract infection	Lactobacillus rhamnosus GR-1 Lactobacillus reuteri RC-14	**[65]**
Lactose intolerance	Lactobacillus acidophulus	**[66]**
Non-steroidal anti-inflammatory drug	Escherichia coli strain Nissle 1917	**[67]**
Intestinal dysbiosis	Lactobacillus johnsonii La1 Lactobacillus strain	**[66,68,69]**

Disease	Probiotic Strains	References
	Lactobacillus GG	
Irritable bowel syndrome	Bifidobacterium infantis 35624 Escherichia coli DSM17252 Bifidobacterium infantis 35624	**[70-72]**
Traveler's diarrhea	Lactobacillus GG Lactobacillus plantarum	**[66,73]**
Crohn's disease	Escherichia coli strain Nissle 1917	**[74]**
Prevention of colon cancer	Enterococcus faecium M-74 lactic acid bacteria	**[75,76]**
Ulcerative colitis	Lactobacillus acidophilus Escherichia coli Nissle 1917 Bifidobacterium	**[77-79]**
Peptic ulcer disease	Lactobacillus acidophulus	**[80]**
Hypercholesterolemia and cardiovascular diseases	Enterococcus faecium M-74 Lactobacillus plantarum Propionibacterium freudenreichii Lactobacillus plantarum PH04	**[81,82]**
Oral Health and dental caries	Actobacillus acidophilus Bifidobacterium lactis	**[83]**
Caries gingivitis	Lactobacillus reuteri	**[84]**

2.3 Prebiotics:

Prebiotics are "a nonviable food component that imparts a health benefit on the host associated with regulation of the microbiota," according to the Food and Agriculture Organization of the United Nations [85]. Prebiotics promote particular microbial genera and species' growth or activities in the gut microbiota in order to boost the host's health.

Table 2.2: Criteria for Characterization of an Ingredient as A Prebiotic [87]

Characterization of Prebiotics
• Counteract gastric acidity, hydrolysis by mammalian enzymes, and absorption in the upper GI tract • Fermented by the intestinal microbiota • Selectively promotes the growth and/or activity of intestinal bacteria potentially associated with health and well-being

2.3.1 Sources of Prebiotics:

Prebiotics	Source	References
Inulin	Present in a range of natural foods, including chicory, onion, garlic, Jerusalem artichokes, tomatoes, and bananas	[87]
Fructooligosaccharides (FOS)	Occur naturally in fruits and vegetables (asparagus, endive, sugar beet, garlic, chicory, onion, Jerusalem artichokes, bananas, tomatoes). FOS is prepared commercially from chicory in a hydrolysis reaction using inulinase and may also be derived in an enzymatic synthetic reaction via transfer of fructosyl units from sucrose molecules. Other sources: cereals, wheat, barley, rye, and honey	[88-90]
Galactooligosaccharides	Legumes, nuts, soy beans and soy products, peas, rapeseed meal, lentils, Chickpeas/hummus, green peas, lima beans, kidney beans	[91,92]
Fructans	Naturally occurring oligosaccharides found in onions, bananas, wheat, artichokes, garlic, and other whole foods. They are also extracted from chicory or manufactured from sucrose for use in the food industry	[93,94]
Resistant starch granules	Raw potatoes, bananas	[95]
Pectins	Apple, sugar beet pulp	[95]
β-Glucans	Oats and barley	[96,97]
Psyllium	Psyllium husk (plant)	[97]
Isomaltooligosaccharides	Produced commercially from the enzymatic action of α-amylase, pullulanase, and α-glucosidase on cornstarch	[98]
Lactulose	Galactofructose isomerization product derived from lactose	[99,100]

Prebiotics	Source	References
Milk oligosaccharides	Human and cow's milk. They may also produce synthetically from lactose syrup using β-galactosidase	[101-103]

2.3.2 Mechanism of Action of Prebiotics:

The molecular structure of prebiotics determines their physiological effects and the types of microorganisms that are able to use them as a source of carbon and energy in the bowel [103].

The mechanism of a beneficial effect of prebiotics on immunological functions remains unclear. Several possible models have been proposed [104, 105]:

a. Prebiotics are able to regulate the action of hepatic lipogenic enzymes by influencing the increased production of short-chain fatty acids (SCFAs), such as propionic acid.
b. The production of SCFAs (especially of butyric acid) as a result of fermentation was identified as a modulator of histone acetylation, thus increasing the availability of numerous genes for transcription factors.
c. The modulation of mucin production.
d. It was demonstrated that FOS and several other prebiotics cause an increased count of lymphocytes and/or leukocytes in gut-associated lymphoid tissues (GALTs) and in peripheral blood.
e. The increased secretion of IgA by GALTs may stimulate the phagocytic function of
f. intra-inflammatory macrophages.

The main aim of prebiotics is to stimulate the growth and activity of beneficial bacteria in the gastrointestinal tract, which confers a health benefit on the host.

Through mechanisms including antagonism (the production of antimicrobial substances) and competition for epithelial adhesion and for nutrients, the intestinal microbiota acts as a barrier for pathogens.

2.3.3 Prebiotics Mechanisms for Health Maintenance and Protection against Disorders:

A. Irritable Bowel Syndrome and Crohn's Disease:

IBS is a gastrointestinal syndrome characterized by chronic abdominal pain and altered bowel habits in the absence of any organic cause. IBDs like Crohn's disease, which can affect any portion of the digestive system from the mouth to the anus, are chronic, relapsing conditions. According to reports, the populations of Bifidobacteria and Faecalibacterium prausnitzii as well as the Bacteroides to Firmicutes ratio were lower in people with IBS and Crohn's disease [106, 107]. It has been reported that supplementation with 15 g/day FOS for 3 weeks elevated Bifidobacteria population in the feces and improved Crohn's disease [108].

B. Colorectal Cancer:

Normal cell replication is aided by butyrate, which also has an anticarcinogenic effect by reducing altered or mutant cells through apoptosis.109]. Butyrate also functions as an HDAC inhibitor, which increases the accessibility of transcriptional factors to nucleosomal DNA and modifies the expression of oncogenes by hyperacetylating histones. Butyrate's capacity to regulate cell cycle and gene expression is due to these outcomes. Butyrate enhances the activity of glutathione S-transferase, an enzyme that detoxifies xenobiotics, according to studies on colonic cancer cells. Butyrate has the ability to mediate the growth and proliferation of tumour cells by blocking the decay-accelerating factor. [110]

C. Necrotizing Enterocolitis:

Necrotizing enterocolitis (NEC) is a gastrointestinal emergency disorder which is most common in premature neonates, causes portions of the bowel undergo necrosis. It can lead to high morbidity and mortality rates [111]. Prebiotics like FOS and GOS, which can increase the proliferation of gut microbiota (such Bifidobacteria) and decrease pathogenic bacteria in preterm newborns, are thought to be able to prevent NEC [112-114].

D. Cardiovascular Disease:

Unhealthy diets that are low in complex carbohydrates, fruits, and vegetables and heavy in fats, salt, and free sugar can raise the risk of CVDs. Low-density lipoprotein (LDL) levels have been closely linked to the risk of CVD. The microbial population in the gut uses prebiotics to make SCFAs (acetate, butyrate, and propionate), which may lower the risk of CVDs and enhance lipid profiles. [115-117]

E. Type II Diabetes and Glycemic Control (T2D):

By 2030, diabetes will, unfortunately, rank as the sixth largest cause of mortality. [118] T2D prevention and management depend on understanding how food affects the regulation of glycemia and metabolic diseases. According to some reports, consuming fibre regularly may decrease the pace at which glucose is absorbed, prevent weight gain, raise levels of healthy nutrients and antioxidants, and so aid in the prevention of diabetes. [119]. People who ingested more than 15 g of fibre per day had a considerably decreased probability of developing diabetes, indicating an antagonistic link between dietary fibre intake and the onset of T2D. [120]

F. Weight Management:

By altering the GI tract, gut microbiota is crucial in the regulation of weight. The effects of FOS supplementation on body weight were assessed in overweight and obese people during a 12-week, randomised, double-blind, placebo-controlled experiment. According to the study's findings, FOS caused a decrease in body weight, whereas the control groups had an increase. [119]

G. Immune Function:

It is possible to stimulate the immune system by enhancing gastrointestinal microbiota, increasing the growth of probiotics, and/or limiting the growth of harmful microbes. [121]. This can be accomplished by regularly consuming specific prebiotic kinds that support gut-associated modulation of immune and microbial activity.

H. Prebiotics and The Nervous System:

For instance, prebiotics are given to piglets to reduce grey matter and enhance neural pruning [122]. Prebiotics' effects on human brain regulation, however, are still not well understood. There are three ways that the gut microbiota might affect the brain: neurological, endocrine, and immunological pathways. Prebiotics like FOS and GOS can regulate synaptic proteins including synaptophysin and N-Methyl-D-aspartate or NMDA receptor subunits as well as brain-derived neurotrophic factors, neurotransmitters, and d-serine [123,124].

Mood: Stress hormones have the power to influence behaviours linked to anxiety [125,126]. Adrenocorticotropic hormone (ACTH) and corticosterone levels were shown to rise in germ-free mice after exposure to controlled stress, according to research. Corticosterone and ACTH levels returned to normal after taking Bifidobacterium infantis [127].

Learning, focus, and memory The relationship between memory and the administration of fermentable chemicals in both animals and humans has recently been demonstrated in a number of studies [128]. Prebiotics that can improve general cognition and slow the formation of dementia-related glial fibrillary acidic protein in mice include arabinoxylan and arabinose [129].

Hepatic encephalopathy: When the liver is not functioning properly, it can cause hepatic encephalopathy. The main cause of hepatic encephalopathy is a rise in blood ammonia levels. It was established in 1966 that lactulose might successfully cure hepatic encephalopathy by lowering the amount of ammonia in the gut. People with hepatic encephalopathy can live better lives because to lactulose. [130-132]

I. Prebiotics and Skin:

Prebiotics (such fructo-oligosaccharides, galacto-oligosaccharides, and konjac glucomannan hydrolysates) help probiotics proliferate, which helps treat disorders like atopic dermatitis, acne, and photo ageing. [48]

2.4 Conclusion:

Throughout the coming decades, the use of probiotics and prebiotics in food and medicine will grow significantly. Medical practitioners should take into account their use in the prevention and treatment of various illnesses, and the food sector should promote it. Before being marketed, newly created probiotic strains should undergo a rigorous safety assessment.

Although there is still much to understand about the ways in which probiotic strains work and how best to administer them, it is obvious that different strains can have very diverse impacts. Additionally, their impacts may differ in terms of health and disease, as well as in different disease states and age groups. To better understand mechanistic difficulties and interactions, more research is required. Clinicians need to be aware of the dangers and advantages of these treatments given the growing use of probiotics and prebiotics as dietary supplements and medicinal agents.

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