Potential health benefits of probiotics, prebiotics and synbiotics: A review.

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Abstract

The concept of probiotics is the colonization of beneficial bacteria in the intestinal tract, promoting efficient functioning of digestion, helping prevent digestive upsets, and stimulating and maintaining the natural immunity of the body. Probiotic bacteria are normal inhabitants of the intestines and are normally found in the healthy gut of all humans. Probiotics have been in use for as long as people have consumed fermented milks, but their association with health benefits dates only from the turn of the century when Metchnikoff drew attention to the adverse effects of the gut microflora on the host and suggested that ingestion of fermented milks ameliorated this so-called auto-intoxication. The use of the term 'probiotic' to describe food supplements specifically designed to improve health, dates from 1974 when Parker used it to describe growth- promoting animal feed supplements. He defined the term as 'organisms and substance which contribute to intestinal microbial balance. Supplementation with probiotics, prebiotics and synbiotics has shown promising results against various enteric pathogens due to their ability to compete with pathogenic microbiota for adhesion sites, to alienate pathogens or to stimulate, modulate and regulate the host's immune response. Hence, this review aims to study the beneficial impact of probiotics, prebiotics and synbiotics.

Keywords: Gut microflora, Probiotics, Prebiotics, Synbiotics, Human GI tract, Lactose hydrolysis, Fermented dairy products.

Introduction

The term Probiotics is derived from a Greek word meaning “for life” and used to define living non-pathogenic organisms and their derived beneficial effects on hosts. The term “Probiotics” was first introduced by Vergin, when he was studying the detrimental effects of antibiotics and other microbial substances, on the gut microbial population. He observed that “probiotika” was favourable to the gut microflora. Probiotic were then redefined by Lilly and Stillwell as “A product produced by one microorganism stimulating the growth of another microorganism”. Subsequently the term was further defined as “Non-pathogenic microorganisms which when ingested, exert a positive influence on host’s health or physiology” by Fuller. The latest definition put forward by FDA and WHO jointly is “Live microorganisms which when administered in adequate amounts confer a health benefit to the host”.

Some of the popularly used probiotic microorganisms are *Lactobacillus rhamnosus, Lactobacillus reuteri, bifidobacteria* and certain strains of *Lactobacillus casei, Lactobacillus acidophilus*-group, *Bacillus coagulans, Escherichia coli* strain *Nissle* 1917, certain enterococci, especially *Enterococcus faeciumSF68,* and the yeast *Saccharomyces boulardii*. Bacterial spore formers, mostly of the genus Bacillus dominate the scene. These probiotics are added to foods, particularly fermented milk products, either singly or in combinations. New genera and strains of probiotics are continuously emerging with more advanced and focused research efforts.

In recent years, especially since the 1970s, consumers in many developed countries have been particularly interested in the health benefits of foods. There is an increased interest in foods that are harshly processed and preserved, but are natural and fermented foods are considered natural and healthy. Consumers interest in and demand for fermented foods have resulted in a large production increase of many products that had very small markets before. In addition consumer’s interest in the health benefits of some beneficial species has stimulated production of new products containing live cells of these bacteria. These products are generally designated as probiotics. The term has been currently defined as a product containing living microorganisms, which on ingestion in certain numbers exert health benefits beyond inherent general nutrition. In this review the current status of our knowledge on intestinal microbial ecology, beneficial effects of probiotics are briefly presented (Figure 1).

Composition of probiotics

Lactic acid bacteria (*lactobacilli, Streptococci, and bifidobacteria*), constitute the probiotic currently used preparation. These three genera have been shown to be

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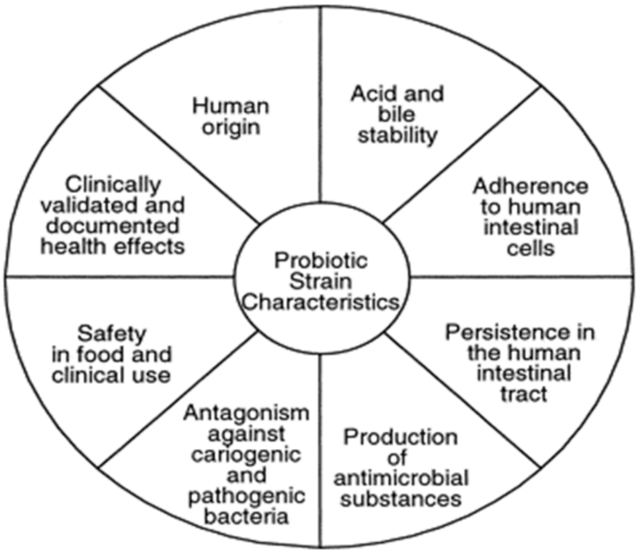

Figure 1. *Characteristics of an ideal probiotics.*

important components of the gastrointestinal microflora, which are all relatively harmless. It has also been shown in recent experiments that administration of *Escherichia coli* to infants can prevent the colonization of the gut by the antibiotic resistant strains of *E. coli*. A probiotic preparation may contain or several of the different strains of bacteria.

Lactobacilli: Fermented foods and dairy products like yogurt contain the species of Lactobacilli. There are three types of Lactobacilli, including *Lactobacillus plantarum, Lactobacillus casei,* and *Lactobacillus sporogenes*. The benefits that Lactobacilli can provide include preventing and treating diarrhea caused by antibiotics, prevention of vaginal and urinary tract infections; prevention of overgrowth of bacteria like *H. pylori*, *Salmonella* and *E. coli*; and help with the digestion of lactose products. In addition to these benefits *L. sporogenes* has also been shown to reduce LDL cholesterol levels, which is the bad cholesterol and raise HDL cholesterol level, making it a supplement for treating high cholesterol levels and heart disease.

Bifidobacterium: The most common kind of intestinal bacteria found in infants include Bifidobacteria. As individual get older, the level of the bacteria decreases, and they can be naturally found occurring in the vagina as well as the intestine. The most commonly seen species of these bacteria in humans include *Bifidobacterium longum, Bifidobacterium infantis, Bifidobacterium breve, Bifidobacterium adolescentis and Bifidobacterium pseudocatenulatum*. The group of bifidobacteria contains several kinds of probiotics, all of which are beneficial. These probiotics are known to help protect the intestinal lining, they produce acids to keep the pH in the intestine balanced, they help to decrease the side effects of antibiotics, ensures regular bowel movements, and helps build B-complex vitamins.

Streptococcus thermophilus: The most important lactic acid bacteria for commercial purposes, typically used as a starter culture for dairy foods other than yogurt, like mozzaeraella cheese is *Streptococcus thermophilus*. This bacterium is known to help an individual with malnutrition. It reduces intestinal atrophy from short term fasting and also possesses anti-oxidant properties. This probiotic prevents nitrates from changing into nitrates that are known to cause cancer and has shown to protect the intestines from mucositis during chemotherapy treatment.

The different strains of lactic acid bacteria used in probiotics are mostly intestinal isolates of importance such as L. acidophilus, *L. casie, Enterococcus faecium* and *Bifidobacterium bifidum*. Starter bacteria for yogurt (*L. bulgaricus* and *Streptococcus thermophilus*) are also included because yogurt has always been associated with health benefits in the past.

The following mechanisms have shown that probiotcs play important role in human health:

Competition for nutrients: Utilization of the same types of nutrients by the beneficial as well as pathogenic microorganisms is seen within the gut. Thus there exists general competition for these nutrients by the groups of microbes to grow and reproduce. Hence if the gut is flooded with beneficial microorganisms, more competition is created between beneficial and pathogenic microorganisms.

Competition for adhesion sites: Most intestinal pathogens rely on adhesion to the gut wall. Adhering to adhesion sites along the gut wall is an important factor in colonization to prevent the pathogenic forms from being swept away by peristaltic movement of the food along the gastro-intestinal tract (Figure 2).

One of the most important functions of these probiotic bacteria is to help prevent or limit the growth and colonization of potentially pathogenic bacteria such *as E. coli, Salmonella, Listeria, Campylobacter* and *Clostridia* within the gut. Major disturbances within the gut are caused by pathogenic bacteria, thus preventing efficient digestion and ineffective nutrient absorption within the gut and may result in diarrhea or

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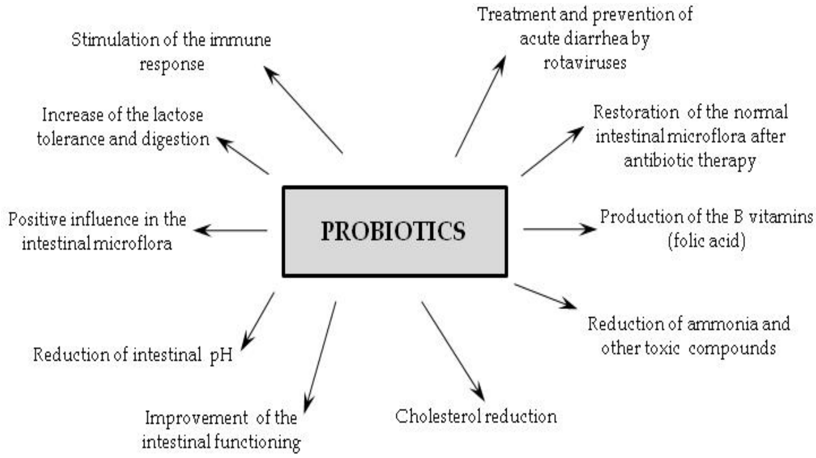

Figure 2. *Properties and beneficial effects of probiotic.*

vomiting. When the gut microflora are well balanced with the beneficial microorganisms, colonizing the gut helps reduce the risk of pathogens.

Stimulation of immunity: An optimum balance of the microflora is maintained by the use of probiotics in order to stimulate and maintain the natural immune system of the host. It has been observed that when probiotics are used regularly, the enhanced immune effects help prevent illness.

Direct antimicrobial effect: Bacteriocins are known to be produced by many species of lactic acid bacteria. Also, the production of organic acids by these organisms can either have a direct effect or operate by reducing the pH of the gut, thus displaying an antimicrobial effect.

Some of the ways in which probiotics can benefit humans are,

Help reduce the effect of stress

Reduce incidences of diarrhea and other digestive upsets

Help improved immunity and impart resistance to disease

Reduce the symptoms of digestive disease such as lactose intolerance and IBS

Help stimulate peristaltic movement of the gut (thus reduce constipation and greatly improve digestion)

Help in the supply of digestive enzymes (breakdown of most food products)

Reduce absorption of cholesterol

Promote the production of B group vitamins (biotin, niacin B2, pyridoxine B6, and folic acid) (Figure 3).

What makes a good probiotics?

Safety: Non-pathogenic and non-toxic microorganisms must be chosen as the component of a probiotic.

Multistrian: A good-quality probiotic must contain several species of beneficial microorganisms in order to have an improved overall spectrum of activity within the gut and with maximum benefit in a wider range of host species.

Viability: Viability of the microorganisms in a probiotic is very important as it can only work if the microorganisms contained within the probiotic remain viable during the storage of the product and when consumed through the gut to ensure proper colonization.

Minimum Dose: The concentration of a probiotic must be such that inclusion rates provide 107 to108 CFU per dose (that is 10 million to100 million beneficial bacteria per dose) (Figure 4).

Properties of probiotics

Qualityassurance: It is essential thata probiotic has not become exposed to contamination with any other microorganism other than the particular probiotic microorganisms chosen at any stage e.g. fermentation of the manufacturing process or during transport and storage.

Intestinal beneficial bacteria

Since the discovery of food fermentation our ancestors recognized that the process yielded products that had not only better shelf life and desirable qualities but also some benefits, especially to combat some intestinal ailments. The belief in the health benefits of fermented foods continued throughout civilization and even today remains of interest among many consumers and researchers. There are differences between early beliefs and the current interest: whereas the early beliefs probably emerged from associated effects without knowing the scientific basis, current interest is based on understanding the microbiology and biochemistry of fermented foods, microbial ecology of the human gastrointestinal tract, and roles of some bacteria in the GI tract and in fermented foods in human health.

Microbiology of the human GI tract

The GI tract of humans contains more than 1014 microorganisms many more than the total number of our body cells. They are metabolically diverse and active; thus it is quite likely that they have a great influence on our wellbeing. It is estimated that the human GI tract harbors ca. 1000 bacterial species, but only 30-40 species constitute 95% of the population. Normally, the microbial level in the small intestine in the jejunum and ilium is ca. 106-7 /g, and in the large

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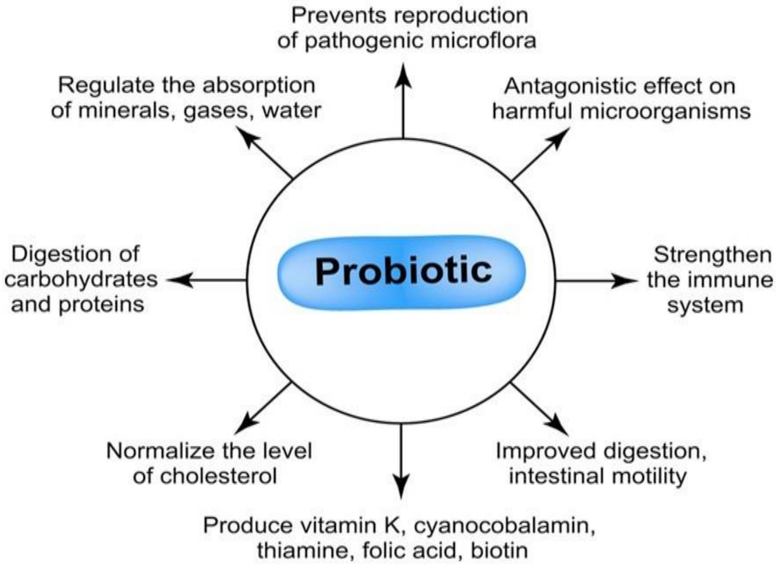

Figure 3. *Functions of probiotics in human health.*

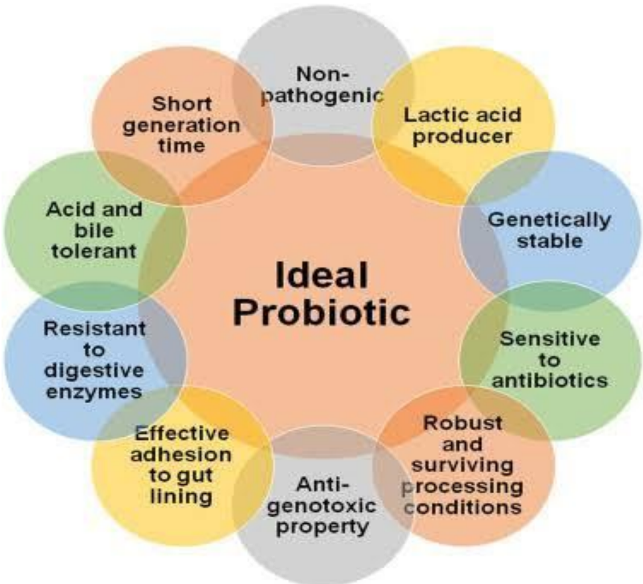

Figure 4. *Characteristic features of probiotics.*

intestine. The most predominant types in the small intestine are several species of Lactobacillus and Enterococcus and in the large intestine are several genera of *Enterobacteriaceae*, different species of *Bacteroides*, *Clostridium*, *Enterococcus*, *Bifidobacterium*, and *Lactobacillus.*

The intestine of a fetus in the uterus is sterile. At birth it is inoculates with vaginal and fecal flora from the mother. Subsequently, a large variety of microorganisms enter in the digestive tract of infants from the environment. From these the normal flora of the GI tract is established. In both breast fed and formula -fed babies during the first couple of days, Escherichia coli and Enterococcus appear in large numbers in the feces. Then in the breast fed babies large numbers of Bifidobacterium species and a lower level of both Esc. coli and Enterococcus species appear. In formula fed babies in contrast Esc. coli and Enterococcus together with Clostridium and Bacteroides, Clostridium and others increase, but Bifidobacterium still remains high. When breast feeding is completely stopped Bacteroides, Bifidobacterium and Lactobacillus species predominate, along with some Esc. coli, Enterococcus, Clostridium and others. By the second year of life the different microflora establish themselves at their specific ecological niche in the GI tract and the population resembles that of adult GI tracts.

The intestinal microflora are divided into indigenous (autochthonous) and transient (allochthonous) types. Many indigenous species can adhere to intestinal cells, which helps maintain them in their specific niche. Whereas the indigenous types are permanent inhabitants, the transient types are either passing through or temporarily colonizing a site from where the specific indigenous type has been removed because of some inherent or environmental factors (such as antibiotic intake) (Figure 5).

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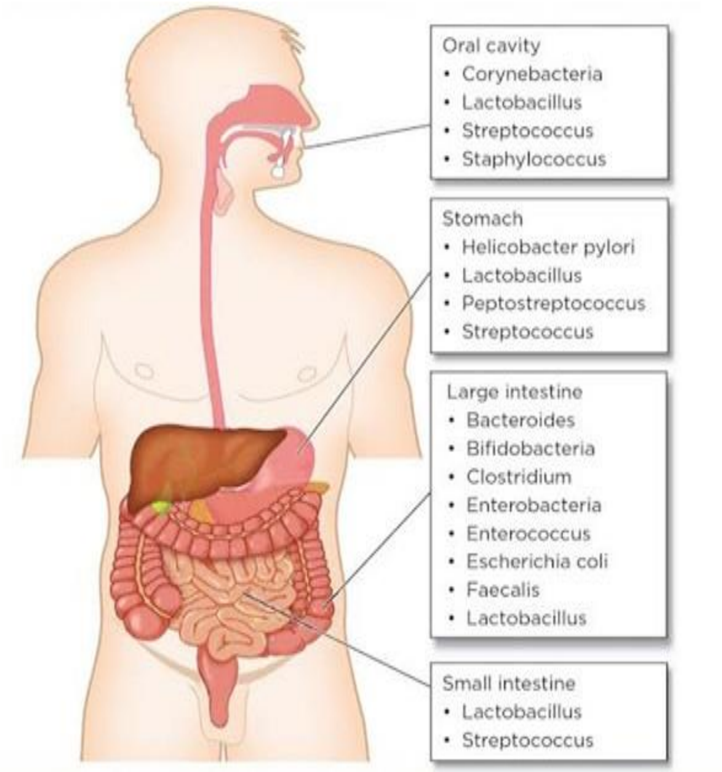

Figure 5. *Distribution of major bacterial groups in the GI tract.*

Among the indigenous microbial flora, several species of *Lactobacillus* in the jejunum and ilium and *Bifidobacterium* in the large intestine are thought to have beneficial effects on the health of the GI tracts of the hosts. From the intestines and intestinal content of humans, *Lactobacillus acidophilus, Lab. fermentum, Lab, rhamonosus, Lab. reuteri, Lab, casei, Lab. lactis, Lab, leichmannii, Lab. plantarum, Bifidobacterium bifidus, Bif. Longum, Bif. adolescentis, Bif. infantis*, and others have been isolated. However, age, food habits, and health conditions greatly influence the species and their levels. There is some belief that a portion of the intestinal Lactobacillus species is transient. Initially it was considered that *Lab. acidophilus, Lab reuteri* and some *Bifidobacterium* are the main indigenous species. At present several other Lactobacillus species such as *Lab. casei* and *Lab. rhamnosus*, have been tested to be beneficial. The presence of high numbers of the indigenous Lactobacillus species in the feces (and content of the large intestine) probably results from their constant removal from the small intestine.

The most common of the numerous bacteria harboured in the oral cavity are streptococci. Bacteria do not colonise the stomach in high numbers because of its low pH and rapid transit; nevertheless, in the healthy adult stomach there may be around 103 bacteria in every millilitre (ml) of stomach contents, the main inhabitants being lactobacilli, enterococci, Helicobacter and bacilli. The duodenum also tends to be acidic with a rapid transit but additionally receives pancreatic secretions and bile that create a hostile environment for microbes. Here, lactobacilli and streptococci predominate, with total numbers of bacteria at 102-104 per ml. along the jejunum and particularly the ileum there is a gradual increase in the numbers and diversity of bacteria present. Finally, the colon contains the majority of GI microbes, with as many as 1011 organisms per ml.

Prior to birth, micro-organisms are absent from the GI tract but quickly colonize it during and after birth. Exactly which microbiota develops is dependent on factors such as the method of delivery and the environment in which birth takes place, the mother's microbiota and the manner of feeding. *Bifidobacteria* dominate the faecal microbiota of healthy breast-fed infants whereas healthy formula-fed infants have a wider range of organisms present, including *bifidobacteria, bacteroidetes, clostridia, enterobacteria* and *streptococci*. At weaning, there are changes in the numbers and diversity of the gut microbiota, which gradually begins to resemble those of the adult. Once the adult microbiota is established, by the age of about 2–3 years, it is relatively stable within an individual but nevertheless subject to influence by diet, disease, use of medication (particularly antibiotics) and ageing.

While the adult microbiota is extremely complex and has a significant contribution to health and disease, the gut of the newborn is essentially sterile. The colonization process commences immediately after birth and successive development in the infant is influenced by a number of factors including early environmental exposure (especially route of delivery vaginal or cesarean section), gestational age, and use of antibiotics especially in the perinatal period in neonatal intensive-care units [1].

The strong influence of the maternal microbiota on neonatal colonization was observed in infants born vaginally who have greater numbers of Bifidobacteria as compared to those born by cesarean section that have increased colonization by Klebsiella, Enterobacter, Clostridia [2], and organisms prevalent in-hospital settings. Delivery route also influences

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immunological function during the first year of life, with babies delivered by cesarean section having lower bacteria cell counts in fecal samples and a higher number of antibody-secreting cells. Infant-feeding patterns greatly affect microbial colonization breast milk contains antimicrobials, antibodies, and lactobacilli (Martin et al., 2003) whereas formula-fed infants have an in- creased prevalence of Clostridia and Bacteroides in the gut [2].

Important characteristics of beneficial bacteria

Some relevant characteristics of *Lab. acidophilus, Lab. reuteri* and *Bifidobacterium* species are briefly discussed. All three are found in the GI tract of humans as well as in animals and birds. They are Gram positive rods and grow under anaerobic conditions. *Lab. acidophilus* is an obligatory homolactic fermentator; *Lab reuteri* is a heterolactic fermentator and produces lactic acid, ethanol and CO2; and *Bifidobacterium* species produce lactic and acetic acids (in 2:3 ratio).

They are less sensitive to stomach acid than many other bacteria under a given condition and highly resistant in bile, lysozyme and pancreatic enzymes present in the GI tract (small intestine). The two Lactobacillus species are present in low numbers in the jejunum but in relatively high numbers in the ilium, especially toward the distal part, whereas *Bifidobacterium* species are present in the proximal part of the colon (near the ilium). All three are able to colonize in their respective niches, but studies with *Lab. acidophilus* reveal that all strains do not adhere to the GI mucosa of the host. Other studies have shown that the ability to adhere to the intestinal epithelial cells by *Lab. acidophilus* strains can be species specific that is a specific strain can adhere to a particular species only and the trait may be lost during prolonged culturing under laboratory conditions (Figure 6) [3].

Under normal conditions these three species are thought to help in maintaining the ecological balance of GI tract microflora by controlling growth rate of undesirable microflora. This effect is produced through their ability to metabolize relatively large amounts of lactic and acetic acids. In addition they can produce specific inhibitory substances, several of which are recognized. Many strains of *Lab. acidophilus* are known to produce bacteriocins, although they are most effective against closely related Gram-positive bacteria. Also because of the sensitivity of bacteriocins to proteolytic enzymes of the GI tract, their actual role in controlling undesirable Gram-positive bacteria in the GI tract is disputable. Some strains of Lab. acidophilus are able to deconjugate bile acids to produce compounds that are inhibitorier than the normal bile acids. Some Lactobacillus strains can also produce H_2O_2, but probably not under anaerobic conditions in the GI tract. Identification of specific antibacterial compounds other than acids in these beneficial bacteria will help in understanding their role in maintaining intestinal health.

Several studies have indicated that beneficial effects of these bacteria are produced when they are present in relatively high numbers in the intestinal tract. Diets rich in foods from plant sources, an opposed to those rich in foods from animal sources, seem to favor their presence in higher numbers. Many other conditions in a host also can reduce bacterial numbers in the GI tract, such as antibiotic intake, mental stress, starvation, improper dietary habits, alcohol abuse, and sickness and surgery of the GI tract. This in turn can allow the undesirable indigenous or transient bacteria to grow to high levels and produce enteric disturbances, including diarrhea, flatulence and infection by enteric pathogens.

Beneficial effects of probiotics

In the last 40 years, studies have been conducted to determine specific health benefits from the consumption of live cells of beneficial bacteria. Live cells have been consumed from three principle sources: (1) as fermented milk products, such as yogurt, which contains live cells of *Lab. delbrueckii ssp. bulgaricus* and *Streptococcus thermophilus* and is supplemented with Lab acidophilus and others, and pasteurized milk which contains Lab acidophilus; (2) as supplementation of foods and drinks with live cells in the form of tablets, capsules and granules. The beneficial effects from consuming these live cells were attributed to their ability to provide protection enteric pathogens, supply enzymes to help metabolize some food nutrients (such as lactase to hydrolyze lactose) and detoxify some harmful food components and metabolites in the intestine, stimulate intestinal immune systems, and improve intestinal peristaltic activity (Figure 7). Some of these are briefly discussed here:

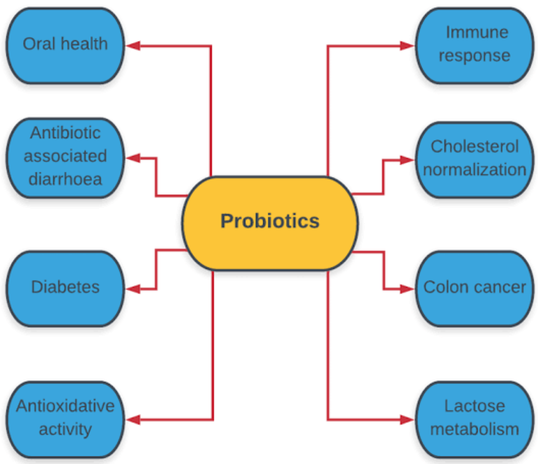

Figure 6. *Role of probiotics in disease prevention and treatment.*

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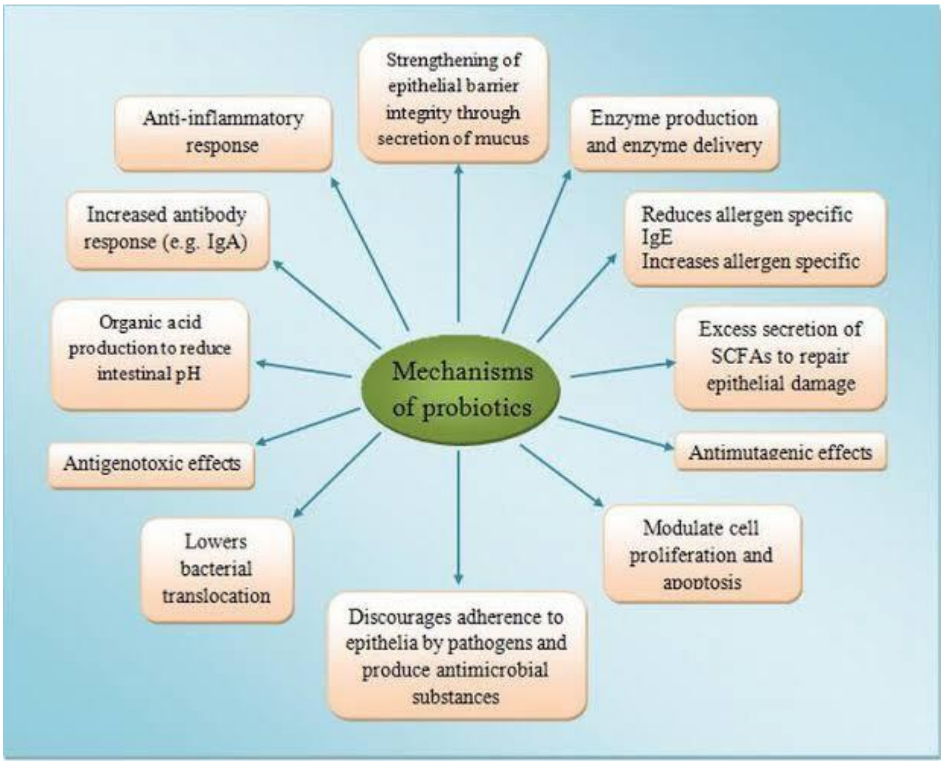

Figure 7. *Probiotic mechanism of action recent advances.*

Lactose hydrolysis

Lactose-intolerant individuals, because of a genetic disorder, are unable to produce lactase in the small intestine. When they consume milk, lactose molecules are not hydrolyzed in or absorbed from the small intestine but passed to the colon. They are then hydrolyzed in the colon by lactase of different bacteria to glucose and galactose and then further metabolized to produce acids and gas, resulting in fluid accumulation, diarrhea and flatulence. Consumption of yogurt, acidophilus milk and live cells of *Lactobacillus*, especially *Lab. acidophilus* in fresh milk and pharmaceutical products reduces the symptoms in lactose-intolerant individuals. This benefit is attributed to the ability of beneficial bacteria to supply the needed lactase in the small intestine. However, as *Lab. delbrueckii ssp. bulgaricus* and *Str. thermophilus* do not survive stomach acidity well and are not normal intestinal bacteria, the benefit of consuming normal yogurt is considered to be due to the reduced amounts of lactose in yogurt as compared to milk and to the supply of lactase from the dead cells. In contrast the intestinal bacteria especially some Lactobacillus species, could under proper conditions, colonize the small intestine and subsequently supply lactase.

Reducing serum cholesterol level

Consumption of fermented dairy products (some containing unknown microorganism) and high numbers of live cells of beneficial Intestinal bacteria has been associated with low levels of serum cholesterol in humans. This is attributed to two possible factors. One is the ability of some intestinal lactobacilli to metabolize dietary cholesterol, thereby reducing amounts absorbed in blood. The other possibility is that some lactobacilli can conjugate bile salts and prevent their reabsorption in the liver. The liver, in turn, uses more serum cholesterol to synthesize bile salts and indirectly helps reduce cholesterol level in serum.

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Reducing colon cancer

Many of the undesirable bacteria in the colon have enzymes that can activate procarcinogens, either present in food or produced through metabolism of undesirable bacteria, to carcinogens that, in turn, can cause colon cancer. Beneficial intestinal bacteria, both *Lactobacillus* and *Bifidobacterium* species, by their ability to control growth of undesirable bacteria in the colon, can reduce the production of these enzymes. Also, beneficial bacteria, by increasing intestinal peristaltic activity, aid in regular removal of fecal materials. This, in turn, lowers the concentrations of the enzymes and carcinogens in the colon and reduces the incidence of colon cancer. Several studies have shown that oral consumption of large numbers of live cells of the beneficial bacteria reduces fecal concentrations of enzymes such as B-glucuronidase, azoreductase, and nitroreductase of undesirable colon bacteria.

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Reducing intestinal disorders

Under certain conditions as indicated before the population of beneficial bacteria can be reduced. The undesirable bacteria in the intestine and some transient pathogens such as enteric pathogenic bacteria and Rotaviruses from the environment can then cause enteric disorders, including infection and inflammatory bowel disease. Ingestion of large numbers of live cells of beneficial intestinal bacteria over a period of time was reported to reduce these problems. Both infants and adults on oral antibiotic therapy can develop diarrhea because of a loss of desirable bacteria in the intestine and an increase in undesirable pathogenic bacteria in the intestine and produce antibacterial compounds (acids, bacteriocins and reuterine) which in turn control the pathogens. Deconjugation of biles by beneficial species also produces compounds that are more antibacterial than the bile salts; this has also been suggested as a mechanism to control the growth of undesirable enteric bacteria. Probiotic bacteria also the specific immunoglobulins, reduce intestinal permeability, and normalize intestinal microflora.

Modulating immune response

Limited studies have shown that intestinal microorganisms act on intestinal defense barriers and help regulate systemic and local immune response. This is more effective at an early age, during the development of lymphoid tissue in the gut. Normal establishment of GI tract flora at an early age helps develop immunity to oral administration of antigens associated with inflammatory reaction in the gut. Oral administration of probiotic gutflora overcomes some immune response caused by the undesirable gut microflora. This beneficial effect is produced possibly by changing intestinal permeability, altering gut microbiology, improving intestinal immunological barrier functions. Specific immune modulation function of probiotics includes the activation of T helper cells to produce cytokines that in turn activate phagocytic cells for clearance of pathogenic bacteria from circulation and activation of macrophages to produce cytokines to induce immune responses. Humoral response includes increased production of mucosal secretory IgA to prevent attachment of pathogens and antiviral IgG to eliminate viral infection such as during rotavirus induced diarrhea.

Reducing allergic diseases

Establishment of normal gut flora, which starts after birth and continues up to 2 years of age, may be important in the development in later life of counter regulatory ability against several specific immune responses. The normal flora of the GI tract enters the body through food, water, air and other environmental sources. Raising infants in an over sanitary environment and feeding semi sterile processed foods may interfere with the establishment of normal microflora in the GI tract. This may cause the immune system of infants to develop inflammatory response to many food antigens. Probiotics containing beneficial gut bacteria can have a suppressive effect to such reaction by stimulating the production of anti-inflammatory cytokines and reducing allergic reaction in sensitive individuals.

Miscellaneous benefits

Many other health benefits of probiotics have been claimed such as prophylaxis against urinogenital infection, increases calcium absorption from the intestine, stimulation of endocrine systems, growth promotion, and prolongation of youth and life.

Prebiotics

The beneficial effect of probiotic bacteria depends on their presence in high numbers in the GI tract. This can be achieved either by consuming a large number of viable cells of probiotic bacteria or by stimulating rapid growth of desirable gut bacteria by supplying appropriate nutrients. Among the beneficial gut bacteria, *Lactobacillus* species are predominant in the small intestine whereas Bifidobacterium species are predominant in the large intestine (colon). An approach has been taken to stimulate growth of *Bifidobacterium* in the colon by supplying one or more selective carbon and energy source that are not metabolized by the bacteria in the small intestine as well as by many bacteria found in the colon. This gives *Bifidobacterium* a selective growth advantage and allows it to reach high numbers. These nutrients are termed prebiotics and defined as nondigestible food ingredients that beneficially affect the host by selectively stimulating the growth or activity or both of one or limited number of bacteria in the colon, which can improve the host's health. Some of the nutrients that have gained importance as prebiotics are lactulose, lactitol, fructooligosaccharides, galactooligosaccharides, lactosucrose and inulin. Their actual effectiveness is currently being studied [4].

Prebiotics pass by the small intestine to the lower gut and become accessible for probiotic bacteria without being utilized by other intestinal bacteria. Lactulose, galactooligosaccharides, fructooligosaccharides, inulin and its hydrolysates, maltooligosaccharides, and resistant starch are prebiotics normally used in the human diet. The essential end components of carbohydrate metabolism are short-chain fatty acids, particularly acetic acid, propionic acid and butyric acid, which are used by the host organism as an energy source. They can also be found in different sources such as chicory, onion, garlic, asparagus, artichoke, leek, bananas, tomatoes and many other plants. Generally, oligosaccharides are combinations of sugars with a different degree of polymerization [5]. Prebiotic oligosaccharides can be manufactured by three different methods: isolation from plant resources, microbiological production or enzymatic synthesis, and enzymatic degradation of polysaccharides [5]. Most of prebiotic oligosaccharides are manufactured and are generally available in the markets. A large number of patents regarding prebiotic oligosaccharides have been filed and their number is growing [6].

The growth and reproduction of probiotics cannot be achieved without the promotion of prebiotics. Prebiotics are ingredients, mostly polysaccharides that cannot be digested and absorbed by the human body, which can contribute to the growth or reproduction of active microorganisms in the host [7]. Prebiotics have the function of improving the regulation of immunity, resisting pathogens, influencing metabolism, increasing mineral absorption, and enhancing health [8]. Prebiotics usually refer to certain polysaccharides, oligosaccharides, microalgae, and natural plants, with a wide range of sources. Emerging prebiotics are mainly found in algae, fruit juice, peels, seeds, traditional Chinese medicine, and microorganism involving polysaccharides, polyphenols, and polypeptide polymers.

Criteria for classifying compounds as prebiotics

Gibson [9] posited the following criteria as being a necessity in the classification of a compound as a prebiotic. These include being resistant to the acidic pH of the stomach, hydrolyzed by mammalian enzymes, absorbed in the gastrointestinal tract, fermentable by intestinal microbiota, and able to selectively stimulate the growth and activity of intestinal bacteria. It is noteworthy to state that not all prebiotics are carbohydrates as some are of fiber origin. Carbohydrate-derived prebiotics can be distinguished from fiber-based prebiotics *via* two criteria: fibers are sugars with a Polymerization Degree (DP) that is higher than or equal to 3 and they cannot be hydrolyzed by the endogenous enzymes in the gastrointestinal tract. It is essential to know that the solubility or fermentation ability of fibers is not outstanding [10]. The sources of the Pectic Oligosaccharides (POS) determine the significant differences in their structures [11].

Synbiotics

The term synbiotics is coined to include both the terms probiotics and prebiotics. It is assumed that instead of using probiotics and prebiotics separately. A product containing both that are beneficial gut bacteria in high numbers as well as nutrient supplement for them will enable them to multiply rapidly in the gut and produce health benefit more effectively. This has to be studied to determine their actual effectiveness.

When Gibson introduced the concept of prebiotics he speculated as to the additional benefits if prebiotics were combined with probiotics to form what he termed as Synbiotics [12]. A synbiotic product beneficially affects the host in improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract by selectively stimulating the growth and/or activating the metabolism of one or a limited number of health-promoting bacteria. Because the word “synbiotics” alludes to synergism, this term should be reserved for products in which the prebiotic compound(s) selectively favor the probiotic organism(s) [13]. Synbiotics were developed to overcome possible survival difficulties for probiotics. It appears that the rationale to use synbiotics is based on observations showing the improvement of survival of the probiotic bacteria during the passage through the upper intestinal tract. A more efficient implantation in the colon as well as a stimulating effect of the growth of probiotics and ubiquitous bacteria contribute to maintain the intestinal homeostasis and a healthy body [14].

Synbiotic combination is considered to have more beneficial effects on human health than probiotics or prebiotics alone. Recent studies established that synbiotics improve the intestinal microbial environment and activate host immune function. Administration of synbiotics as a food supplement is safe, simple and convenient. Therefore, characterizing a new and novel synbiotic combination would find multifaceted use in disease prophylaxis and management for human use.

Biogenics

The health benefit from the consumption of fermented dairy products is attributed to the lactic acid bacteria used in fermentation as well as the by- products of metabolism of milk nutrients by them. The latter aspect becomes important to explain health benefits attributed to fermented products in which nongut bacteria such as *Lactococcus lactis, Str. thermophilus* and *Lab. delbrueckii sp. bulgaricus*, are used in fermentation. These products have recently been termed biogenic and include components in food that are derived through the microbial metabolic activity of food nutrients and have health benefits. One such group is the peptide produced by the exoproteinases of some lactic acid bacteria such as *Lac. lactis* in buttermilk and *Lab. delbrueckii ssp. bulgaricus* in yogurt. Some of the peptides thus produced and present in the fermented milk can reduce blood pressure in individuals with hypertension [15].

Biogenic microbial metabolites produced during fermentation process

During fermentation LAB produce a range of secondary metabolites, some of which have been associated with health promoting properties. The most notable of these are the B vitamins and bioactive peptides released from food proteins, as outlined below [16-19].

The production of vitamins by LAB provides a very attractive approach to improve the nutritional composition of fermentated foods. Folacin (folic acid and related compounds: vitamin B11) is an essential vitamin for growth and reproduction.

References

1. Gareau MG, Sherman PM, Walker WA. Probiotics and the gut microbiota in intestinal health and disease. Nat Rev Gastroenterol Hepatol. 2010;7(9):503-14.

2. Conroy ME, Shi HN, Walker WA. The long-term health effects of neonatal microbial flora. Curr Opin Allergy Clin Immunol. 2009;9(3):197-201.

3. Martín R, Langa S, Reviriego C, et al. Human milk is a source of lactic acid bacteria for the infant gut. J Pediatr. 2003;143:754-8

4. Tannock GW. Probiotics: a critical review. J Antimicrob Chemother. 1999;43(1):849-52.

5. Crittenden RA, Playne M. Production, properties and applications of food-grade oligosaccharides. Trends Food Sci Technol. 1996;7(11):353-61.

6. Grajek W, Olejnik A, Sip A. Probiotics, prebiotics and antioxidants as functional foods. Acta Biochimica Polonica. 2005;52(3):665-71.

7. Li X, Zhang Q, Wang W, et al. A novel inulin-mediated ethanol precipitation method for separating endo-inulinase from inulinases for inulooligosaccharides production from inulin. Front Bioeng Biotechnol. 2021;9:679720.

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8. Peredo-Lovillo A, Romero-Luna HE, Jimenez-Fernandez M. Health promoting microbial metabolites produced by gut microbiota after prebiotics metabolism. Int Food Res J. 2020;136:109473.

9. Gibson GR, Scott KP, Rastall RA, et al. Dietary prebiotics: current status and new definition. Food Sci Technol Bull Funct Foods. 2010;7(1):1-9.

10. Slavin JL. Carbohydrates, dietary fiber, and resistant starch in white vegetables: Links to health outcomes. Adv Nutr. 2013;4(3):351S-5S.

11. Gullón B, Gómez B, Martínez-Sabajanes M, et al. Pectic oligosaccharides: Manufacture and functional properties. Trends Food Sci Technol. 2013;30(2):153-61.

12. De Vrese M, Schrezenmeir AJ. Probiotics, prebiotics, and synbiotics. Food Biotechnol. 2008:1-66.

13. Cencic A, Chingwaru W. The role of functional foods, nutraceuticals, and food supplements in intestinal health. Nutr. 2010;2(6):611-25.

14. Peña AS. Intestinal flora, probiotics, prebiotics, synbiotics and novel foods. Span J Dig Dis. 2007;99(11):653.

15. Takano DT. Anti-hypertensive activity of fermented dairy products containing biogenic peptides. Antonie van Leeuwenhoek. 2002;82:333-40.

16. Howlett J, Betteridge V, Champ M, et al. The definition of dietary fiber-discussions at the Ninth Vahouny Fiber Symposium: Building scientific agreement. Food Nutr Res. 2010;54(1):5750.

17. Gulewicz P, Ciesiołka D, Frias J, et al. Simple method of isolation and purification of α-galactosides from legumes. J Agric Food Chem. 2000;48(8):3120-3.

18. Kaur IP, Chopra K, Saini A. Probiotics: Potential pharmaceutical applications. Eur J Pharm Sci. 2002;15(1):1-9.

19. Crittenden RG. In Probiotics: A critical review, GW. Tannock, ed.; Horizon Scientific Press: Wymondham, UK. 1999:141.

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