

PROBIOTICS: A BENEFICIAL HEALTH OPTION

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A paradigm shift in health care is ensuing and the concept of functional foods (foods which provide health benefits beyond their contributions to nutritional requirements) is fast gaining popularity in our modern society obsessed with search for self-care methods and complementary medicine. Probiotics fall within the category of functional foods. They are food products containing live microorganisms that exert beneficial health effects in the host by improving microbial balance in the intestine.

INTRODUCTION

A healthy human gastrointestinal tract (GIT) contains about 1.2 Kg of bacteria and large number of yeasts¹. There are several hundred species, and the total microbial numbers are estimated at about 10-fold the number of cells comprising the human body. Only a few of these microbes have been identified or characterized till now. These indigenous microbes in the GIT play an important role in the health and well being of the host. Some of these are beneficial to health while others are harmful. The beneficial effects may comprise inhibition of pathogens, stimulation of immune system, aiding in digestion, synthesis of vitamins, metabolising drugs and others². However, this protective effect of helpful microbial flora lasts as long as a proper balance is maintained among the different microbes residing in the intestine. Many factors tend to affect the microbial flora of the intestine, which cause an imbalance, resulting in the overgrowth of potentially harmful microbes. These factors include the age of the host, nutritional and immunological status, viral or bacterial infections, diet, antibiotic use, stress,

alcohol consumption and several others. The common symptoms of this imbalance include constipation, diarrhea, flatulence, liver damage and cancer². These are clearly the result of a probiotic deficiency or a shortage of beneficial bacteria. If left untreated, the symptoms may become chronic as in irritable bowel syndrome, and can compromise the immune system leading to other serious illnesses. Thus the human gut microbiota plays a very important role in maintaining the health of an individual.

Although microbes have been used over thousands of years in food and alcoholic fermentations, only recently they have been scrutinized scientifically for their purported health benefits. This has kindled a renewed interest in the study of 'PROBIOTICS' Probiotics (from the Greek 'for life') are live microbial food supplements that beneficially affect the host by improving its intestinal microbial balance. The concept of probiotics evolved around 1900, when the Nobel Prize recipient Elie Metchnikoff hypothesized that the long, healthy lives of Bulgarian peasants were the result of their consumption of fermented milk products³. However, the term was only coined in 1965 by Lilly and Stillwell to refer to the stimulation of

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the growth of one microbe by another⁴ (the opposite of antibiotics). Later a British scientist, Roy Fuller popularized its definition. Conventional medicine has turned its attention to the scientific study of these friendly bacteria only in the last few decades. The rise in antibiotic-resistant bacteria has awakened the scientific community to the prophylactic and therapeutic uses of probiotics, and to reconsider them as alternatives to antibiotics⁵.

MICROORGANISMS USED AS PROBIOTICS

To be defined as a probiotic, a microbe must meet a set of the following criteria :

- I Exert a beneficial effect on the host.
- I Survive transit through the intestinal tract such as exposure to stomach and bile acids.
- I Adhere to the intestinal epithelial cell lining.
- I Produce antimicrobial substances towards pathogens.
- I Stabilize the intestinal microflora.
- I Accepted by the host's immune response.
- I Non-pathogenic and non-toxic.
- I Good shelf life in food and other preparations.

The most frequently used probiotics found in dairy-based food products are Lactobacilli and Bifidobacteria. Since these belong to the indigenous human microflora, they have a long history of safe use and there are evidences to support their positive roles, some of these have been designated as GRAS (generally regarded as safe) by the FDA (Food and Drug Administration) due to their long history of use in food fermentations⁶. *Lactobacillus*, first identified by Pasteur, was the first genus of bacteria suspected to have health benefits, rather

than to be agents of disease. Metchnikoff had introduced his intoxication theory, which stated that the main cause of ageing are 'toxicants' formed by intestinal putrefaction and fermentation, and proposed a diet containing milk fermented by lactic acid bacteria. Thus Lactobacilli suddenly attracted attention of the scientific community as well as common man. *Lactobacillus acidophilus*, found in yogurt, was believed to be responsible for the longevity of some eastern Europeans who traditionally consumed it as a staple food. In the 1920's and 1930's, *Lactobacillus acidophilus* was used in the form of acidophilus milk to treat constipation and diarrhea in the USA. Although *L. acidophilus* is the most popular species among the Lactobacilli group of probiotic bacteria, other *Lactobacillus* sp. have been found to be beneficial as well e.g. *L. rhamnosus*, *L. plantarum*, *L. casei*. Among *Bifidobacterium* species, the important ones are *B. bifidum*, *B. breve* and *B. lactis*.

There are three major guardians that live and work inside the human intestinal tract. *Lactobacillus acidophilus* guards the small intestine, Bifidobacteria protect the large intestine, whereas *Lactobacillus bulgaricus* is a traveling transient bacterium that aids the other two as it passes through the body.

The interest in the use of strains other than the traditional lactic acid bacteria (Lactobacilli and Bifidobacteria) is increasing. For Example, the yeast *Saccharomyces boulardii*, non-pathogenic *Escherichia coli*, *Streptococcus thermophilus* and complex mixture of intestinal microbes have been studied for their use as probiotics.²

BENEFICIAL EFFECTS OF PROBIOTICS

Probiotics are purported to impart numerous nutritional and therapeutic benefits to the host^{2,3}. In some instance, the probiotic microbes function for the benefit of the host, such as antimicrobial mechanisms. While in other cases, the probiotic microbes may trigger the indigenous microbes or the host physiology to induce the action. One probiotic preparation maybe, but need not be, multi-functional. The beneficial attributes of probiotics, presented in Table 1, can be broadly grouped as : antimicrobial, biochemical, physiological and immunological.

ANTIMICROBIAL MECHANISMS

These refer to the action of the probiotic preparation on another microbe or group of microbes. This may be helpful directly for enhanced resistance against intestinal pathogens and in the prevention of diarrhea. The interactions may include competitive colonization (the probiotic strain can successfully out compete the pathogen for either nutrients or the site of colonization) as well as adhesion and growth inhibition. As the first step in infection by most gastrointestinal pathogens is attachment to the intestinal mucosa, the inhibition of adhesion would be beneficial to the host. During growth of the probiotic, various compounds may be produced which are inhibitory to the pathogen's growth. These include organic acids such as lactic and acetic acids, bacteriocins and reuterin. The organic acids not only lower the pH, thereby affecting the growth of the pathogen, but they can also be toxic to the microbes. Reuterin, produced by *Lactobacillus reuteri*, is inhibitory to a broad range of cells. Lactobacilli are known to produce many types of bacteriocins like

acidophilin, acidolin, lactocidin, bulgarican, lactolin, lactobacillin and lactobrevin. They can either have a broad range of activity or may specifically inhibit the growth of a very limited range of closely related microbes.

Probiotic microbes also affect urinogenital health in women, since urinary and genital tract infections are often associated with colonic bacteria. The consumption of probiotics has been linked to a reduced recurrence of *Candida* infections and bacterial vaginitis.

BIOCHEMICAL EFFECTS

These include (i) the reduction of faecal enzymes that can convert pro-carcinogens to carcinogens in the digestive tract, (ii) decrease of lactose intolerance, (iii) reduction of serum cholesterol, (iv) relieve constipation and (v) improve the quantity, availability and digestibility of some dietary nutrients.

The ingestion of Lactobacilli is known to result in the reduction of faecal enzymes such as β -glucuronidase, azoreductase and nitroreductase in humans, which are capable of converting pro-carcinogens to carcinogens in the digestive tract. Thus they lower the chances for tumor development.

Lactose intolerance is seen in persons lacking the enzyme lactase (β -galactosidase). The symptoms include abdominal pain and osmotic diarrhea after eating foods high in lactose, since the lactose is not degraded and absorbed in the upper regions of the small intestine and thus used by the indigenous microbiota, resulting in production of gases and organic acids responsible for the characteristic symptoms of lactose-intolerance. Probiotic microbes containing lactase

(*S. thermophilus*, *L. bulgaricus*, etc.) can degrade lactose before it reaches the indigenous microbes in the lower part of the small intestine.

Probiotic microbes can also be useful in the treatment of hypercholesterolemia. There are reports that probiotics like Lactobacilli can assimilate cholesterol and deconjugate bile acids, leading to a reduction in the serum cholesterol levels. There is also some preliminary evidence on antihypertensive effects of probiotics, and thus documenting their role in blood pressure control. Fermented milk containing *Saccharomyces cerevisiae* and *Lactobacillus helveticus* has been found to be effective. Thus, regular consumption of probiotics may provide a modest prophylactic effect against heart disease. There is an evidence to support the role of lactic acid bacteria in improving intestinal mobility and treating constipation, possibly through a reduction in gut pH.

Microbial fermentations tend to increase the content of various nutrients in the food. Termed as bio-enrichment, it involves enrichment of food value by supplementation with proteins, essential amino acids, minerals and vitamins. For example, lactic acid bacteria increase folic acid in yogurt, bifidus milk and kefir, niacin and riboflavin levels in yogurt, vitamin B₁₂ in cottage cheese, and vitamin B₆ in Cheddar cheese. Probiotic microbes may release various enzymes into the intestinal lumen, thus aiding the digestion process.

PHYSIOLOGICAL MECHANISMS

These refer to the influence of probiotic microbes on the host response, including stimulation of immune system and reduction of risk of colon cancer. Probiotics can enhance

both specific and nonspecific immune responses, without eliciting a harmful inflammatory response. Their effects are mediated through activation of macrophages by increasing levels of cytokines, natural killer cell activity and/or levels of immunoglobulins. The cell components of *Lactobacillus* are known to stimulate the immune response, which tends to protect the host from infection as well as from conditions involving the immune response, such as irritable bowel syndrome and colon cancer. The binding of probiotic microbe may trigger receptors to initiate signals that result in the synthesis of cytokines (proinflammatory proteins released by immune cells), and thus enhancing immune function. As extensively studied probiotic bacterium, *Lactobacillus* GG (LGG) colonises the GIT in 1-3 days after consumption, and thus, reduces infections like *Clostridium difficile*, pediatric diarrhea, traveler's diarrhea and antibiotic-associated diarrhea. The intestinal immunity is also enhanced by LGG due to increase in the number of immunoglobulin cells in the mucosa. This might be useful against the causative agents of inflammatory bowel disease and ulcerative colities.

Probiotic microbes might even serve as efficient delivery vehicles to deliver drugs, vitamins or vaccines. *Lactobacillus lactis* has been genetically modified to secrete the anti-inflammatory molecule interleukin-10 to reduce colitis in mice¹.

SOME PROBIOTIC FOODS

The best known example of a probiotic food is yogurt. Some other foods that are commonly known for their probiotic properties are acidophilus milk, bifidus milk, kefir, koumiss and tempeh (fermented soy). Various fermented

milk products like sour cream, cheese and fermented vegetables like sauerkraut are also considered as potential sources of probiotics. Probiotics are also available in the form of tablets, capsules or powder¹. The shelf life for refrigerated products containing probiotics range between 3 and 6 weeks, whereas the shelf life for dried supplements is about 12 months. Consumption of the product in the beginning of the shelf life ensures the highest levels of viable probiotics.

PREBIOTIC SUBSTANCES

Prebiotics are non-digestible dietary supplements that are beneficial to the consumer because they selectively stimulate the growth and/or activity of one or a limited number of probiotic microbes or of favorable intestinal microbes^{7,8}. These include lactic acid, lactulose, inulin, tagatose and variety of oligosaccharides. Presently, oligosaccharides are the largest group of prebiotics in the market. Among these, fructooligosaccharides (FOS) have been known as prebiotics for some time. They are naturally found in foods like Jerusalem artichoke tubers, onions, leeks, some grains and honey. Galactooligosaccharides (GOS) and other digestion resistant carbohydrates have been added to these. Prebiotics are either not digested or only partially digested by humans and are, therefore, low in calories. They may also increase the absorption of minerals from mineral-containing food.

Synbiotics, on the other hand, are products that contain probiotics as well as prebiotics^{7,8}. The term should be used for products in which the prebiotic selectively favours the probiotic included in the symbiotic. A yogurt has recently

been introduced in the market that contains both the live bacteria and FOS.

Table 1. The Beneficial Attributes of Probiotics

- I Enhancement of resistance against pathogens.
- I Stimulation of immune system.
- I Improve lactose absorption in lactose intolerant.
- I Prevention and treatment of diarrhea (traveller's, pediatric, antibiotic-associated and diarrhea secondary to *Clostridium difficile*).
- I Prevention or reduction of constipation.
- I Reduction of irritable bowel syndrome.
- I Regression of tumors and reduction in carcinogen and mutagen production.
- I Reduction in recurrence rate of female urinary tract and vaginal infections.
- I Production of nutraceuticals and vitamins.
- I Reduction in serum cholesterol, blood pressure, management of diabetes and prevention of osteoporosis.
- I Probiotics are considered good pharmaceutical delivery systems. For example, the use to *Lactobacillus* sp. as live vectors in oral vaccination.

FUTURE PERSPECTIVES

There is an enough evidence to support the beneficial effects of probiotics on hosts over a wide range of clinical conditions. However, some issues like dosage and viability of probiotic strains, industrial standardization and safety aspects need to be dealt with. At present, cholesterol, cancer and immunology are the three major areas of research on probiotics. Genetic engineering and other approaches are

being used to enhance the beneficial effects of probiotic microbes.

The introduction of food with the added probiotics could play a significant role in national health care programmes especially in developing countries where diarrhea and gastrointestinal problems are very common. Moreover, probiotics can be very easily introduced into the diet just by sprinkling them onto the food. Over time, new food products containing probiotics such as energy bars, juices, cereals as well as disease-specific medicinal foods continue to emerge. Despite an impressive list of therapeutic and prophylactic attributes, probiotics don't form a part of the medical practitioner's list of prescribed drugs, but are available without prescription from the retail outlets like supermarkets and health food stores⁵.

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DO YOU KNOW?

- Q 4. Is there a theoretical limit of weight for an animal walking on land?
- Q 5. It is believed that elephants have phenomenal memory. Is this really true?