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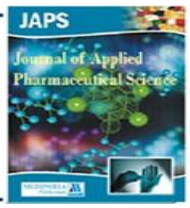

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Probiotics: The Emissaries of Health from Microbial World

Sheel Sharma, Nidhi Agarwal and Preeti Verma

Sheel Sharma, Nidhi Agarwal and Preeti Verma
Department of Food Science and Nutrition, Banasthali University, Rajsthan, India.

For Correspondence
Sheel Sharma
Professor and Head, Food Science and Nutrition, Banasthali University
P.O. – Banasthali Vidyapith, Rajasthan-304022, India
Mobile no. 09352141492
Fax no. - 01438- 228365

ABSTRACT

Probiotics have a long history of human use and are traditionally consumed in several parts of the world. These are live microbes that can be formulated into many different types of products, including foods, drugs, and dietary supplements. Examples of foods containing probiotics are yogurt, fermented and unfermented milk, miso, tempeh, and some juices and soy beverages. Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics; but certain yeasts and bacilli may also fit the bill. Probiotics are also called "friendly bacteria" or "good bacteria". They are gaining importance because of the innumerable benefits, e.g. treating lactose intolerance, hypercholesterolemia and managing cardiac problems like atherosclerosis and arteriosclerosis. With the current focus on disease prevention and the quest for optimal health at all ages, the probiotics potential could reign high. Health professionals and pharmaceutical companies need to objectively help and guide their clients and consumers toward appropriate prophylactic and therapeutic uses of probiotics that deliver the desired beneficial health effects, shunning type and instant benefits.

Keywords: Probiotics, Lactic acid bacteria (LAB), Friendly bacteria, Health benefits, Therapeutic uses.

INTRODUCTION

The term probiotic is a relatively new word meaning “for life” and it is currently used to name bacteria associated with beneficial effects for humans and animals. Probiotics are viable microbial dietary supplements that, when introduced in sufficient quantities, positively influence our health mainly by improving the composition of intestinal microbiota. For this reason, they are called probiotics. There are a large number of probiotics currently used and available in dairy fermented foods, especially in yogurts. Some selected strains of *Lactobacillus, Bifidobacterium, Streptococcus, Lactococcus* and *Saccharomyces* have been promoted in food products because of their reputed health benefits. Probiotics, especially *Lactobacillus* and *Bifidobacterium* have been suggested to be associated with alleviation of lactose intolerance (Ouwehand 1999); prevention and cure of viral, bacterial and antibiotic or radiotherapy induced diarrhoeas (Parvez *et al*., 2006); immunomodulation (Forsythe and Bienenstock, 2010); antimutagenic (Chalova *et al.,* 2008) and anticarcinogenic effects (Liong, 2008); and even blood cholesterol reduction (Ooi and Liong, 2010). The optimism associated with probiotics is, however, counter-balanced by skepticism as many “probiotic” products in the market are unreliable in content and unproven clinically (Hughes and Hillier, 1990; Mackay *et al.*, 1999; Zhong *et al*., 1998).

Also, *Lactobacilli* and *Bifidobacteria* have been rarely associated with human clinical infections which are likely to be a result of opportunistic infections especially in immunocompromised individuals (Mackay *et al.,* 1999; Rautio *et al*., 1999). The possible benefit in other gastrointestinal infections, prevention of postoperative bacterial translocation, irritable bowel syndrome and inflammatory bowel disease continues to emerge. The physiological effects related to probiotic bacteria include the reduction of gut pH, production of some digestive enzymes and vitamins, production of antibacterial substances, e.g., organic acids, bacteriocins, hydrogen peroxide, diacetyl, acetaldehyde, lactoperoxidase system, lactones and other unidentified substances, reconstruction of normal intestinal microflora disorders caused by diarrhoeas, antibiotic therapy and radiotherapy, , stimulation of immune functions, suppression of bacterial infections, removal of carcinogens, improvement of calcium absorption as well as the reduction of faecal enzyme activity (Ouwehand *et al.,* 1999; Zubillaga *et al.,* 2001; Holzapfel & Schilling 2002).

DEFINITION OF PROBIOTICS

Probiotics are defined as live microbial food ingredients that have a beneficial effect on human health (Salminen *et al.,* 1998). The FAO/WHO defines probiotics as 'Live microorganisms which when administered in adequate amounts confer a health benefit on the host' (FAO/WHO, 2001). Symbiosis between microbiota and the host can be optimized by pharmacological or nutritional interventions in the gut microbial ecosystem using probiotics or prebiotics. Given here under; in the tabular form the definitions of probiotics and other related terms along with the benefits that accrue from probiotics. It also gives the ways and means through which the effects can be synergized.

Table. 1: Mechanisms of probiotic/host interaction**.**

(Definitions)

Probiotics	• Live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.
Prebiotics	• Nondigestible substances that provide a beneficial physiological effect for the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria.
Synbiotics	• Products that contain both probiotics and prebiotics.

(Benefits)

	Probiotics
Immunologic benefits	• Activate local macrophages to increase antigen presentation to B lymphocytes and increase secretory immunoglobin A (IgA) production both locally and systemically. • Modulate cytokine profile. • Induce hyporesponsiveness to blood antigens.
Non immunologic benefits	• Digest food and compete for nutrients with pathogens. • Alter local pH to create an unfabourable local environment for pathogens. • Produce bacteriocins to inhibit pathogens. • Scavenge superoxide radicals. • Stimulate epithelial mucin production. • Enhance intestinal barrier function. • Complete for adhesion with pathogens. • Modify pathogen-derived toxins.

PREREQUISITES TO ATTAIN PROBIOTIC STATUS

To achieve a probiotic status, microorganisms must fulfill a number of criteria related to safety, functional effects and technological properties (FAO/ WHO, 2001). From the safety point of view, the probiotic microorganisms should not be pathogenic, have no connection with diarrhoeagenic bacteria and no ability to transfer antibiotic resistance genes, as well as be able to maintain genetic stability. To be recognized as functional food components, they should demonstrate the following properties: acid- and bile-stability, resistance to digestive enzymes, adhesion to intestine surface, antagonistic activity against human pathogens, anti-carcinogenic and anti-mutagenic activity, cholesterol-lowering effects, stimulation of the immune system without inflammatory effects, enhancement of bowel motility, maintenance of mucosal integrity, improvement of bioavailability of food compounds and production of vitamins and enzymes (Ouwehand *et al*., 1999).

ACTION OF PROBIOTICS

Mechanisms for the benefits of probiotics are incompletely understood. However, as a general rule, include (Sartor, 2004)

- Adherence and colonization of the gut
- Suppression of growth or epithelial binding/invasion by pathogenic bacteria and production of antimicrobial substances
- Improvement of intestinal barrier function
- Controlled transfer of dietary antigens
- Stimulation of mucosal and systemic host immunity

Prebiotics act as an alternative for probiotics or their cofactors. Complex carbohydrates pass through the small intestine to the lower gut where they become available for some colonic bacteria but are not utilized by the majority of the bacteria present in the colon. Lactulose, galactooligosaccharides, fructooligosaccharides, inulin and its hydrolysates, maltooligosaccharides, and resistant starch are prebiotics commonly used in human nutrition. The main end products of carbohydrate metabolism are short-chained fatty acids, namely acetate, butyrate and propionate, which are further used by the host organism as an energy source.

HEALTH BENEFITS OF PROBIOTICS

Diarrhea

Diarrhea is a major world health problem, responsible for several million deaths each year. While the majority of deaths occur amongst children in developing countries, it is estimated that up to 30% of the population even in developed countries are affected by food-borne diarrhea each year. Probiotics can potentially provide an important means to reduce these problems. The ability of probiotics to decrease the incidence or duration of certain diarrheal illnesses is perhaps the most substantiated health effect of probiotics. Probiotics can prevent or ameliorate diarrhea through their effects on the immune system.

Moreover, probiotics might prevent infection because they compete with pathogenic viruses or bacteria for binding sites on epithelial cells (Suri, 2006; Parvez *et al.*, 2006).

A new development for probiotic applications is activity against Helicobacter pylori, a Gram negative pathogen responsible for type B gastritis, peptic ulcers and gastric cancer. In vitro and animal data indicate that lactic acid bacteria can inhibit the growth of the pathogen and decrease urease enzyme activity necessary for the pathogen to remain in the acidic environment of the stomach (Midolo *et al.*, 1995; Kabir *et al.*, 1997; Aiba *et al.*, 1998; Coconnier *et al.*, 1998). Various probiotic species have shown promise in the treatment of ulcerative colitis in small studies. All four studies in ulcerative colitis with Escherichia coli (Nissle), bifidobacteria plus L acidophilus and VSL#3 had reported positive results (Harish and Varghese, 2006).

Irritable Bowel Syndrome (IBS)

IBS, as defined by the Rome II criteria, is a syndrome lasting for more than 3 months and may present with either constipation or diarrhea associated with abdominal pain. Several controlled trials of probiotics in irritable bowel syndrome (IBS) have been published (Nobaek et al., 2000; Sen *et al.*, 2002; Niedzielin *et al.*, 2001; O'Sullivan and O'Morain, 2000; Kim *et al.*, 2003). The literature reveals five randomized or blinded controlled studies of which three reported a definite decrease in symptoms (Harish and Varghese, 2006)

Hypercholesterolemia and Cardiovascular Diseases

Cholesterol is essential for many functions in the human body. It acts as a precursor to certain hormones and vitamins and is a component of cell membranes and nerve cells. However, elevated levels of total blood cholesterol or other blood lipids are considered risk factors for developing coronary heart disease (http://en.wikipedia.org/wiki/Cholesterol).

Although humans synthesize cholesterol to maintain minimum levels for biological functioning, diet is also known to play a role in serum cholesterol levels. The extent of influence varies significantly from person to person. Probiotic cultures have been evaluated for their effect on serum cholesterol levels. Some human studies suggest that elevated blood cholesterol levels can be reduced by consumption of probiotic-containing dairy foods.

The dietary cholesterol absorption is reduced in three ways: assimilating, binding, or degradation. Probiotic strains assimilate the cholesterol for their own metabolism. Probiotic strains can get to the cholesterol molecule, and can degrade cholesterol to its catabolic products.

The cholesterol level can be reduced indirectly by deconjugating the cholesterol to the bile acids, thereby reducing the total body pool (Survarna and Boby, 2005). There is preliminary evidence that use of probiotic lactobacilli and metabolic by-products potentially confer benefits to the heart, including prevention and therapy of various ischemic heart syndromes (Oxman *et al.*, 2001) and lowering serum cholesterol (De Roos and Katan, 2000).

Hypertension

Antihypertensive effects have been documented in animal models and in mildly hypertensive adults for three compounds derived from the growth of certain lactobacilli: i) fermented milk containing two tripeptides derived from the proteolytic action of L. helveticus on casein in milk; ii) bacterial cell wall components from cell extracts of lactobacilli; and iii) fermented milk containing fermentation-derived gamma amino butyric acid. Systolic blood pressure was decreased on the order of 10-20 mm Hg. These results suggest that consumption of certain lactobacilli, or products made from them, may reduce blood pressure in mildly hypertensive people **(**Sanders, 2007).

Cancer

In general, cancer is caused by mutation or abnormal activation of genes that control cell growth and division. Many processes or exposures can increase the occurrence of abnormal cells, among them chemical exposures. Cancer-causing chemicals (carcinogens) can be ingested in a normal diet or generated by metabolic activity of microbes that live in the gastrointestinal system. It has been hypothesized that probiotic cultures might decrease the exposure to chemical carcinogens by

- Detoxifying ingested carcinogens;
- Altering the environment of the intestine and thereby decreasing populations or metabolic activities of bacteria that may generate carcinogenic compounds;
- Producing metabolic products (e.g., butyrate) which improve a cell's ability to die when it should die (a process known as apoptosis or programmed cell death);
- Producing compounds that inhibit the growth of tumor cells; or
- Stimulating the immune system to better defend against cancer cell proliferation **(**Sanders, 2007**).**

Urogenital Tract Disorders and infections

Excluding sexually transmitted diseases, almost all infections of the vagina and bladder are caused by microorganisms that originate in the bowel. There is a strong correlation between presence of commensals, particularly lactobacilli in the vagina with health, and an absence of these microorganisms in patients with urogenital infections. There is some evidence that probiotic microorganisms delivered as foods and topical preparations have a role in preventing urogenital tract disorders and infection. The criteria for selection of effective probiotic strains have been proposed and should include verification of safety, colonization ability in the vagina and ability to reduce the pathogen count through competitive exclusion of adherence and inhibition of pathogen growth (Reid and Bruce, 2001). Several hundred million women are affected by urinary tract infection (UTI) annually. Uropathogenic *Escherichia coli* originating in the bowel is the responsible agent in up to 85% of cases. There is evidence, including randomized controlled data to suggest that once weekly

vaginal capsules of freeze dried *Lactobacillus* strains GR-1 and B-54 (Reid *et al*., 1995) prepared with addition of skim milk, and once daily oral capsule use of *Lactobacillus* strains GR-1 and RC-14 (Reid *et al*., 2001b), can result in the restoration of a lactobacilli dominated vaginal flora and lower risk of UTI recurrences. By creating a lactobacilli barrier in the vagina, it is believed that fewer pathogens can ascend into the bladder, thereby blocking the infectious process. Bacterial vaginosis (BV) is a disease of unknown etiology resulting from the overgrowth of various anaerobic bacterial species and associated with the disappearance of lactobacilli, which dominate the normal vagina. There is some clinical evidence to suggest that oral and vaginal administration of lactobacilli can eradicate asymptomatic (Reid *et al.*, 2001a; 2001b) and symptomatic BV (Hilton *et al.*, 1995; Sieber and Dietz, 1998). Oral administration of *Lactobacillus acidophilus* and yogurt has been used in the prevention and therapy of candidal vaginitis (Hilton *et al*., 1992).

Lactose Intolerance

The inability of adults to digest lactose, or milk sugar, is prevalent worldwide. Consumption of lactose by those lacking adequate levels of lactase produced in the small intestine can result in diarrhea, bloating, abdominal pain and flatulence (http://www.foodreactions.org/intolerance/index.html).

These symptoms are due to the undigested lactose reaching the large intestine and being fermented by the colonic microbes, which can produce gases and products that lead to watery stool**.** The consumption of dairy products – important for supplying calcium and preventing osteoporosis – by people with lactose intolerance can be facilitated by probiotic bacteria**.** It has been documented scientifically that many lactose intolerant individuals are better able to consume fermented dairy products, such as yogurt, with fewer symptoms than the same amount of unfermented milk, even though yogurt contains about the same amount of lactose as milk. Yogurt was found to aid digestion of lactose because the lactic acid bacteria used to make yogurt produce lactase and digest the lactose before it reaches the colon. In addition to yogurt starter bacteria, *L. acidophilus* and bifidobacteria have been shown by several studies to improve digestion of lactose, although generally to a lesser extent than the yogurt starter cultures, *Lactobacillus bulgaricus* and *Streptococcus thermophilus* **(**Sanders, 2007**).**

Pancreatitis

Pancreatic necrosis and associated pancreatic infection are determinants of poor outcome in patients with severe acute pancreatitis. Colonization of the lower gastrointestinal tract and oropharynx with gram-negative organisms often precedes contamination of the inflamed pancreas. Human studies in which patients with acute pancreatitis received *L. plantarum* 299v showed a decrease in occurrence of pancreatic infection/abscess and a shorter hospital stay (Olah *et al*., 2002; Pezzilli and Fantini, 2006).These human findings were supported by trials of probiotics (L. plantarum 299v and S. boulardii) in animal models of acute pancreatitis in which intestinal microbial translocation was reduced (Akyol *et al*., 2003).

HIV and Immune System Stimulation

The immune system provides the primary defense against microbial pathogens that have entered our bodies. The immune system is extremely complex, involving both cell-based and antibody-based responses to potential infectious agents. Immunodeficiency can result from certain diseases (e.g., cancer, AIDS, leukemia) or, to a lesser extent, from more normal conditions such as old age, pregnancy, or stress.

Autoimmune diseases (e.g., allergies, rheumatoid arthritis, inflammatory bowel diseases) also can occur due to misdirected immune system activity **(**Sanders, 2007**)**. Probiotic cultures have been shown in a variety of test systems to stimulate certain cellular and antibody functions of the immune system. Animal and some human studies have shown an effect of yogurt or lactic acid bacteria on enhancing levels of certain immunoreactive cells (e.g. macrophages, lymphocytes) or factors (cytokines, immunoglobulins, interferon)].

In addition, some studies have shown improved survival of pathogen-infected laboratory animals consuming probiotic cultures as compared to animals consuming a control diet. Results accumulated so far suggest that probiotics may provide an additional tool to help your body protect itself **(**Sanders, 2007**)**. Animal models and human studies provide a baseline understanding of the degree and type of probiotic-induce immune response. From these studies, it appears that probiotic bacteria are able to enhance both non-specific and specific immune responses by activating macrophages (Sanders, 1999**).**

Kidney Stones

A high oxalate level in the urine is a risk factor for the development of kidney stones. Use of oxalate by intestinal microbes limits its absorption. A probiotic preparation that contained bacteria able to degrade oxalate in vitro was shown to reduce oxalate fecal excretion in six patients. This study suggests that manipulation of the gut flora with the right probiotic bacteria may improve gastrointestinal tract oxalate levels and may decrease oxalate absorption **(**Sanders, 2007**).**

Antibiotic Therapy Disease

The purpose of antibiotics is to kill harmful bacteria. Unfortunately, they frequently kill normal bacteria as well, often resulting in disruption of the bacterial flora, leading to diarrhea and other intestinal disturbances.

Replenishing the flora with normal bacteria during and after antibiotic therapy seems to minimize disruptive effects of antibiotic use. Studies show that probiotics can prevent antibiotic associated diarrhea, but that no strong effect on the ability of probiotics to treat diarrhea exists. Not all studies have shown positive results in the prevention of antibiotic associated diarrhea or other symptoms associated with antibiotic therapy **(**Sanders, 2007**).**

CONCLUSIONS

Probiotics are becoming an important part of the complex world of foods that are good for health. They are foods that contain live bacteria. It is the bacteria and metabolites which they produce that give these probiotics their health-promoting properties. These can boost the immune system, prevent allergies and stop eczema and heal the intestine. A good diet, supplemented with a high quality probiotic will improve the balance between good and bad bacteria and have nutritional and therapeutic properties. In spite of the problems with dosage and viability of probiotic strains, lack of industry standardization and potential safety issues, there is obvious considerable potential for the benefits of probiotics over a wide range of clinical conditions. Ongoing basic research will continue to identify and characterize existing strains of probiotics, identify strain-specific outcomes, determine optimal doses needed for certain results and assess their stability through processing and digestion. Available data from traditional medicine and clinical use clearly state that probiotics have great health potential, particularly today with the increasing threat of antibiotic over-usage and prevalence of antibiotic resistant microorganisms.

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