

Review Article

Probiotics in Human Health

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INTRODUCTION

Human beings live in close association with vast numbers of microorganisms present on the skin, in the mouth/oral cavity, and gastrointestinal tract (GI tract). The greatest concentration of commensal organisms is found in the GI tract, which comprises more than 400 m² of surface area, and contains a rich microflora of over 500 bacterial species, some of which have important functions in maintaining human health. The gut flora is acquired rapidly after birth, remains relatively stable throughout the life and is essential for human homeostasis.^[1]

The golden era of antibiotics began in 1928 when Alexander Fleming found that a mold on a discarded culture plate had an antibacterial action, and called this mold “penicillin.”^[2] Introduction of antibiotics revolutionized the field of medicine- life expectancy increased, with improvement in the quality of human life due to a decrease in the mortality rate. However, the major drawback with antibiotics is that besides killing harmful bacteria they also kill good bacteria, thus disturbing the ecosystem of the body, and can, in turn, result in superinfection and drug resistance.

HISTORY

The dietary use of living microorganisms has a long history. Mention of cultured dairy products is found in the Bible and the sacred books of Hinduism. It is

ABSTRACT

Probiotics are bacterial cultures or living microorganisms, which on ingestion in a certain quantity, promote, and enhance health benefits. A few conventional foods containing probiotics include yogurt, fermented and unfermented milk, cheese, etc. Strains of genera *Lactobacillus* and *Bifidobacterium* are the most widely used probiotic bacteria. Conventionally, probiotics have been associated with the gastrointestinal tract; however, recently several investigators have suggested the use of probiotics for oral health. This article describes the mechanism of action and role of probiotics in general and oral health and discusses the potential benefits of probiotics in oral health.

KEYWORDS: *Bifidobacterium*, *Lactobacillus*, *Probiotics*

thought that sacred milk and cultured dairy products such as *kefir*, *koumiss*, *liben*, and *dahi*, have been used therapeutically before the existence of microorganisms was recognized.^[3]

Élie Metchnikoff (1907) hypothesized that the apparent longevity of Bulgarian peasants was due to their consumption of large quantities of fermented milk products such as curd and buttermilk. He believed that the lactic acid bacteria in these products replaced the harmful organisms found in the intestines, thus reducing the production of toxins which lead to disease and infection.^[2]

The term “probiotic” was first used by Lilly and Stillwell (1965) for describing substances secreted by one organism which stimulate the growth of another.^[4] Hull (1984) identified the first probiotic species, the *Lactobacillus acidophilus*, while, Holcomb (1991) identified *Bifidobacterium bifidum*.^[3]

PROBIOTICS

The word probiotic is derived from the Latin word “pro” meaning “for” and the Greek word “biotic” meaning “life.”^[5] It means that mechanisms are employed to selectively remove only the pathogen.

The Food and Agriculture Organization and World Health Organization (2001) have defined probiotics

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as “live microorganisms which when administered in adequate amounts confer a health benefit on the host.”^[4-6]

The most commonly used strains belong to the genera *Lactobacillus* and *Bifidobacterium*.^[2,4,7]

MICRO-ORGANISMS USED AS PROBIOTICS IN HUMANS

Lactic-acid producing bacilli

- i. *Lactobacillus* acidophilus, sporogenes, rhamnosus, reuteri, fermentum, lactus, brevis, paracasei, gasseri, salivarius, and casei
- ii. *Bifidobacterium*: Bifidum, Lactis
- iii. *Streptococcus*: Lactis, salivarius, thermophiles.^[5]

Nonlactic acid producing bacterial species

- i. *Bacillus propionibacterium*
- ii. Nonpathogenic yeasts: *Saccharomyces*.^[2]

PREBIOTICS

A prebiotic is defined as “a selectively fermented ingredient that allows specific changes, both in composition and/or activity in gastrointestinal microflora that confers benefits upon host well-being and health.” (Gibson and Roberfroid - 1995)^[8]

They include nondigestible food ingredients such as fructooligosaccharides, lactulose, and inulin which beneficially affect the host by selectively stimulating growth and/or increase in the activity of probiotic-like bacteria in the colon. Unlike probiotic bacteria, prebiotic carbohydrates do not undergo any changes during cooking – this property makes them interesting in the food industry. Synergistic combinations of probiotics and prebiotics are called synbiotic.^[8]

CHARACTERISTICS OF IDEAL PROBIOTICS

Fuller (1989) stated that the features of a good probiotic were as follows:^[2]

- It should be capable of exerting a beneficial effect on the host, for example, increased growth or resistance to disease
- It should be nonpathogenic and nontoxic
- It should be present as viable cells, preferably in large numbers
- It should be able to survive and metabolize in the gut environment, for example, resistance to low pH, organic acids acid, and bile.

MECHANISM OF ACTION

Several mechanisms have been proposed to explain the action of probiotics:^[1,7,9]

- Normalization of the intestinal microflora of the host

- Capacity to stimulate the nonspecific immunity and modulate the humoral and cellular immune response
- Alteration of the composition and metabolic activity of host microbiota at the specific location
- Secretion of various antimicrobial substances such as organic acids, hydrogen peroxide, and bacteriocins
- Competition with pathogenic agents for adhesion sites on the mucosa
- Modifying the surrounding environment by modulating the pH and/or oxidation-reduction potential, which may compromise the ability of pathogens to become established.

VEHICLES

Probiotics can be provided in products in any of the following ways:^[6]

- Culture concentrate added to a beverage or food (such as fruit juice)
- Inoculated into prebiotic fibers
- Inoculated into a milk-based food or dairy products (milk, milk drinks, yogurt, cheese, kefir, biodrink) asparagus, and soybeans
- Concentrated and dried cells packaged as dietary supplements (nondairy products such as powder, capsule, and gelatin tablets).

PROBIOTICS IN GENERAL HEALTH

Conventionally, probiotics have been associated with gut health, and mainly used in the prevention or treatment of gastrointestinal infections and diseases; however, during the past decade, clinical interest has focuses on an increasing number of established and proposed health effects of probiotic bacteria.^[10]

Prevention and/or reduction of diarrhea

Probiotic bacteria such as *Lactobacillus*, *Lactobacillus casei*, *B. Bifidum*, and *Streptococcus thermophilus* have been shown to preserve the intestinal integrity and mediate the effects of inflammatory bowel diseases, irritable bowel syndrome, colitis, and alcoholic liver disease.^[11] The intestinal effects of probiotics are to promote recovery from diarrhea (rotavirus, travelers’ and antibiotic-induced), produce lactase, alleviate symptoms of lactose intolerance and malabsorption, relieve constipation, treat colitis, and stimulate gastrointestinal immunity.^[2]

Diarrhea is a major cause of infant death worldwide and can be incapacitating in adults; hence, the use of probiotics could be an important, noninvasive means in its prevention and treatment, particularly in developing countries.

Lactose intolerance

S. thermophilus, *Lactobacillus delbrueckii* subsp. *bulgaricus* and other lactobacilli in fermented milk

products provide bacterial lactase to the intestine and stomach and can alleviate lactose intolerance symptoms.^[2]

Calcium absorption

Milk is considered to be abundant with calcium apart from other dietary sources. Calcium absorption is favored in acidic pH. The use of probiotics in lactose intolerant patients, results in hydrolysis of milk lactose by the probiotic strains, thus favoring calcium absorption.^[2]

Reduction of concentration of cancer-promoting enzymes in the gut

It has been suggested that probiotics also possess a protective effect against colon carcinogenesis.^[3] This is attributed to the production of short-chain fatty acids on its fermentation by gut microflora, and alteration of gene-expressions in tumor cells. Gut flora, especially after the ingestion of resistant starch, induces the chemopreventive enzyme glutathione transferase in the colon. Together, these factors lead to a reduced load of genotoxic agents in the gut and to increased production of agents such as butyrate, which deactivate toxic components.^[3]

Immune response

Probiotics can enhance specific and non-specific immune responses, by activating macrophages, increasing levels of cytokines, increasing natural killer cell activity, and/or increasing levels of immunoglobulins. This can inhibit pathogen growth and translocation, and reduce the chance of infection from common pathogens such as salmonella, *Shigella*.^[2]

Prevention or alleviation of allergies and atopic diseases in infants

Probiotics may exert a beneficial effect on the allergic reaction by improving mucosal barrier function. In addition, probiotic consumption by young children may beneficially affect the development of the immune system.^[2]

Anti-hypertensive

Two tripeptides, valine-proline-proline and isoleucine-proline-proline, isolated from fermentation of a milk-based medium by *Saccharomyces cerevisiae* and *Lactobacillus helveticus* are thought to function as angiotensin-I-converting enzyme inhibitors and reduce blood pressure.

Other health effects of probiotics

Probiotics can also be used to reduce the risk of certain cancers (colon, bladder), detoxify carcinogens, suppress tumors, and lower serum cholesterol. They are also used in the prevention of allergies and respiratory tract

infections (common cold, influenza), as well as treatment of urogenital infections and to optimize effects of vaccines (e.g., rotavirus vaccine, typhoid fever vaccine).

Miscellaneous

Probiotics have been used in agriculture to restore soil fertility, to eliminate odor in waste-water systems, and as supplements in animal and poultry foods.

PROBIOTICS AND ORAL HEALTH

The oral cavity provides an intricate habitat to a great diversity of microbial species. The environment within the mouth supports distinct yet overlapping communities of hundreds of species. It is estimated that there are over 1000 bacterial species present in the oral cavity. The tongue dorsum also possesses a unique microbiota: one-third of oral species is exclusively harbored on the tongue and cannot be isolated from any other oral niche.^[7]

Bacteria reside in the mouth either in planktonic state or are finely integrated in oral biofilm on various oral surfaces. Saliva plays an integral role in propagating oral biofilms. Salivary flow can easily lead to detachment of some microbes from biofilm surfaces and thus modulate microbial colonization. Saliva also contains different proteins with a bactericidal, bacteriostatic, or inhibitory activity that can collectively damage a variety of species in the planktonic state.^[6]

Some of the proposed hypothetical mechanisms of probiotic action in the oral cavity include direct interaction in dental plaque; involvement in the binding of oral microorganisms to proteins; action on plaque formation by competing and intervening with bacterial attachments; and involvement in the metabolism of substrate and production of chemicals that inhibit oral bacteria.^[3,12]

Indirect actions of probiotics are modulation of systemic immune function, the effect on local immunity and non-immunologic defense mechanisms, mucosal permeability regulation, antioxidant action, and prevention of plaque formation.

Candida infection

Probiotics such as *Lactococcus lactis*, *L. helveticus*, *Lactobacillus rhamnosus* is used to control *Candida* infection in elderly patients, who are more prone to this infection provoked by chronic diseases, medication, poor oral hygiene, reduced salivary flow, and impaired immune response. A study by Hatakka *et al.*^[13] found that probiotic intervention resulted in an increase in unstimulated salivary flow and reduced the risk of high yeast counts by 75%. It is suggested that probiotics can also reduce hypo-salivation and dryness of mouth.^[2]

Dental caries

Streptococcus mutans is the main causative micro-organism in development of caries due to its ability to produce highly branched, water-insoluble glucan, mutan, which facilitate its establishment in the oral biofilm. Studies have found that probiotic administration reduces *S. mutans* bacteria in the oral cavity. This is thought to be due to the competition for binding sites in oral biofilms^[7] Caglar *et al.* (2005)^[14] recorded a reduction in salivary mutans streptococci after consumption of a probiotic yogurt containing *Bifidobacterium* and stated that probiotic bifidobacteria in yogurt might reduce the levels of selected caries-associated microorganisms in saliva. Since most probiotics are in dairy forms containing high calcium, they can possibly reduce demineralization of teeth.^[2]

Periodontal disease

The use of probiotics for enhancing oral health was first studied in the treatment of periodontal inflammation. Patients with various periodontal diseases, gingivitis, periodontitis, and pregnancy gingivitis, were locally treated with a culture supernatant of a *Lactobacillus acidophilus* strain.^[15] Probiotic strains that have been used in recent studies include *Lactobacillus reuteri*, *Lactobacillus brevis*, *L. casei*, *Lactobacillus salivarius*, and *Bacillus subtilis*. Studies by Riccia *et al.*^[16] and Deepa and Mehta^[17] have found that administration of *Lactobacillus* in the form of tablets/lozenges reduces gingival inflammation and decreases the probing pocket depth.

Halitosis

Halitosis results from the action of anaerobic bacteria that degrade salivary and food proteins to generate amino acids, which are in turn transformed into volatile sulfur compounds.^[18] *Streptococcus salivarius* strains appear to be excellent candidates for an oral probiotic since they are colonizers of oral surfaces and also happen to be among the numerically predominant members of the microbiota of healthy individuals. They have great potential for the control of halitosis and prevention of a variety of oral bacterial infections.^[1,15]

REPLACEMENT THERAPY

The term replacement therapy (bacteriotherapy or bacterial interference) is occasionally used interchangeably with probiotics. Replacement therapy, however, involves direct application of the effector strain on the site of infection to displace or prevent colonization of a pathogen. Unlike probiotics, it causes dramatic and long-term changes in the indigenous microbiota and has a minimal immunological impact.^[4]

SAFETY EFFECTS

The increase in probiotic consumption inevitably leads to increased concentrations of these species in the host organism. *Lactobacillus* bacteremia is a rare entity, and in the past 30 years around 180 cases have been reported.^[6] Any viable microorganism is capable of causing bacteremia; however, especially in patients with severe underlying diseases or in immune-compromised states and hence like any other medication, probiotics should also be used judiciously.

ADMINISTERING PROBIOTICS

Probiotics can currently be administered in the form of sachets or capsules or can be added to the food supply. Dairy products supplemented with probiotics are a natural means of oral administration and can be easily adopted in a dietary regimen.^[4]

COMMONLY AVAILABLE FORMULATIONS

Cap Vibact (USV)

Streptococcus faecalis 30 million, *Clostridium butyricum* 2 million, *Bacillus mesentericus* 1 million, *Lactobacillus sporogenes* 50 million.

Cap Vitagut (Medley-Suprakare)

L. acidophilus 662.5 million, *Lactobacillus rhamnosus* 362.5 million, *Bifidobacterium longum* 67.5 million, Fructooligosaccharides 100 mg, *Saccharomyces boulardii* 137.5 million, *Streptococcus thermophilus* 50 million.

Cap Sporocek (Indoco Remedies)

S. faecalis 30 million, *C. butyricum* 2 million, *Bacillus mesentericus* 1 million, *Lactobacillus sporogenes* 50 million.

Cap Becelac-PB (Dr. Reddy's)

S. faecalis 30 million, *C. butyricum* 2 million, *Bacillus mesentericus* 1 million, *Lactobacillus sporogenes* 50 million.

Cap Nutrolin-B Plus (Cipla)

Lactobacillus 40 million, Thiamine mononitrate 3 mg, Riboflavin 3 mg, Pyridoxine hydrochloride 1 mg, Nicotinamide 25mg, Cyanocobalamin 7.5 mcg, Folic acid 750 mcg.

Cap Vizylac (Unichem)

Lactobacillus sporogenes 40 million, Thiamine HCl 2.5mg, Riboflavin 2.5mg, Pyridoxine HCl 0.75mg, Nicotinamide 22.5mg, D-panthenol 2.5mg, Folic acid 0.5mg.

CONCLUSION

Probiotics are an emerging field in oral medicine. This concept casts new light on the connections between

diet and health, including oral health. Probiotics have a wide-range of beneficial effects which could justify the addition of not one but potentially several probiotics to commonly consumed foods, which in turn could achieve population-wide health benefits. The existence of probiotics in the indigenous oral microflora of humans requires further exploration because these bacteria offer the advantage of being perfectly adapted to the human oral ecosystem.

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Conflicts of interest

There are no conflicts of interest.

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