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Review Article

PROBIOTICS IN ORAL HEALTH PROMOTION: The New Approach

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ABSTRACT
Probiotics have been extensively studied for in the gastrointestinal tract. They are dietary supplements containing potentially beneficial bacteria or yeasts. Since few years, probiotics are looked upon in the oral health perspective. It is attempted to discuss the mechanisms of bacterial adhesion, potential of probiotics in oral cavity colonization, interspecies interactions, and possible effects on immunomodulation, and also the means of administration. There are claims that probiotics strengthen the immune system. Recent randomized controlled trials have shown that certain gut bacteria, in particular species of *Lactobacillus* and *Bifidobacterium,* may exert beneficial effects in the oral cavity by inhibiting cariogenic streptococci and *Candida* sp. and thus aid in the treatment of dental ailments as a whole.

Keywords: *Probiotics, Lactobacillus, Bifidobacterium, Candida, Oral Health*

INTRODUCTION
Research in microbiology and immunology marks a resurgence in the concept of oral foci of infection. In 1900, William Hunter a British physician, first developed the idea that oral microorganisms were responsible for a wide range of systemic conditions that were not easily recognized as being infectious in nature (Dussault and Schiehem, 1982; Newman, 1996). He believed that the degree of systemic effect produced by oral sepsis depended on the virulence of the infection and the individual's degree of resistance. The human gut contains 10 times more bacteria than cells elsewhere (Moore and Holderman, 1974). More than 400 different types of bacteria characterize oral human flora just few days after birth. Following tooth eruption, a more complex colonization with even more than 500 different species is reported (Socransky and Haffajee, 1997), although, most are commensal and beneficial. The eco-system gets disrupted when exposed to toxics in the form of polluted water and food, as well as injudicious use of antibiotics (Minna *et al.,* 2002). This causes destruction of beneficial bacteria leaving the resistant ones, pathogenic.

Of late, the failure of conventional therapy in prevention and treatment of diseases and antibiotic resistance, has prompted the health care professionals to seek alternative therapeutic options. There are claims that probiotics strengthen the immune system to combat allergies, stress, HIV infection and cancers, mostly, the colo-rectal carcinomas. Strains of genera lactobacillus and bifidobacterium are the most widely used probiotic bacteria (Izumita, 2001; Meurman, 2005).

Definition
Probiotics are bacterial cultures or living microorganisms upon ingestion in certain quantity promote and enhance health benefits (Minna *et al.,* 2002). World Health Organization defines Probiotics as Live microorganisms which when administered in adequate amounts confer a health benefit on the host. These bacteria should belong to the natural flora in order to resist gastric secretion and survive during intestinal transit. They should also adhere to the intestinal mucosa and finally should have the ability to inhibit gut pathogens. Prebiotics are non digestible food ingredients such as fructooligosaccharides (FOS), lactulose and inulin that beneficially affect the host by selectively stimulating growth and/or increase activity of a limited number of probiotic like bacteria in a colon (Suvarna and Bobby, 2005). The use of probiotics in cases of antibiotic resistance is termed microbial interference therapy. This concept in oral health prevention is an important one since oral infections constitute the most common forms of infections in humans.

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History

Drugs were first used to treat infectious disease when Paul Ehrlich treated syphilis with salvarsan. Later sulfonamides were introduced and antibiotics became clinically available. In 1907, the Ukrainian born biologist and Nobel laurete Elie Metchnikoff realized that consumption of Bulgarian yogurt was good for health. Over the last century, different microorganisms have been used for their ability to prevent and cure diseases, leading to the coining of the term probiotics, although the term was first proposed by Lilley and Stillwell in 1965, as an autonym for the term antibiotic (Patil and Reddy, 2006). Mann and spoering in 1974 discovered that the fermented yogurt reduced blood serum cholesterol (Patil and Reddy, 2006). In 1984 Hull identified the first probiotic species, the *lactobacillus acidophilus*. Later in 1991, Holcombh identified *bifidobacterium bifidum* and WHO in 1994 described the probiotics as next most important in immune defense system following antibiotic resistance. These incidences paved way for a new concept of probiotics in medicine and dentistry (Manisha *et al.*, 2001). Recently there are reports of usage of lactic acid bacteria in microbial infections and cancer due to their immunostimulatory properties (Meurman, 2005). These microorganisms can inhabit the plaque bio-film and actually protect oral tissue from disease. They also have cariostatic activity; help in preventing candidal colonization and act as antioxidants(Patil and Reddy, 2006).

Species in Health Promotion

Probiotics can be varied; they can be yeast, bacteria or moulds. But most commonly, bacterial species are predominant. Some of the species are: (Suvarna and Bobby, 2005)

1. Lactic acid producing bacteria (LAB): Lactobacillus, bifidobacterium, streptococcus.
2. Non lactic acid producing bacterial species: Bacillus, propionibacterium
3. Non pathogenic yeasts: saccharomyces
4. Non spore forming and non flagellated rod or coccobacilli

The lactobacillus species help in production of enzymes to digest and metabolize proteins and carbohydrates. They aid in synthesis of Vit. B and Vit.K and facilitates breakdown of bile salts. More than 100 species of L. acidophilus, L. brevis, L. casei, L. rhamnous, L. salivarius has been identified. They are usually dispensed in gel, paste, power and liquid forms. Not only do they enhance innate and acquired immunity, but also help inhibit pro-inflammatory mediators as well. More recently, a study demonstrated that long term consumption of milk caused a significant reduction in caries risk (Meurman, 2005). *Bifidobacterium species* are strictly anaerobic and predominate the large intestines. Over 30 species had been identified. The benefits from these include metabolization of lactose, generatelactic ions from lactic acid and synthesize vitamins. They also ferment indigestible carbohydrates and produce beneficial short chain fatty acids. They are believed to be beneficial in reducing antibiotic associated diarrhea and traveller's diarrhea. They relieve constipation, alleviate inflammatory bowel disease and prevent DNA damage. Finally they may prevent or delay the onset of cancers (Dominique *et al.*, 2007; Nicole and Martjjn, 2000). *Streptococcus thermophillus and Lactobacillus bulgaricus* are primary cultures used in yogurt production. Most noted benefits are to metabolize lactose, improve lactose intolerance and antimicrobial activity (Nicole and Martjjn, 2000). *Saccharomyces boulardii* is a non colonizing lactic acid producing yeast. It prevents or treats antibiotic- associated diarrhea, C. difficle associated disorders, acute diarrhea, traveller's diarrhea in tube fed patients. They are also useful in AIDS related diarrhea and to prevent relapse of Crohn's disease. Most noted feature is that they secrete proteases and other substances that breakdown bacterial enterotoxins and inhibits their binding to intestinal receptors. They also help in immune function enhancement. Most of the beneficial species enhance vitamin production and reduce serum-cholesterol level and in anticarcinogenic activity (Meurman and Stamatova, 2007).

Selection of Probiotics (Patil and Reddy, 2006)

The criteria for considering certain product should be:

1. They should be non toxic and non pathogenic preparation.
2. Produce beneficial effect
3. Should withstand gastrointestinal juice

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4. Should have good shelf life
5. Should replace and reinstate the intestinal microflora

Probiotics and Prebiotics could affect the host in combination by synergistic action. In India, sporolac, saccharomyces boulardii and yogurt (L. bulgaricus + L. thermophillus) are the most common ones used. Sporolac is manufactured using sporolactobacilli. Lactobacilli solution is an example of a probiotic, usually given to pediatric patients. The latest and recent addition to the list of probiotics in India is made up of genetically modified Bacillus mesentricus which act as an alternate to B-complex capsules. Only sporulating lactobacilli are used with some of the antibiotic preparations (Suvarna and Bobby, 2005).

Mechanism of Action on Immunity (Elisa and Scott, 2008)

Regulatory t lymphocytes (tregs) are thought to play a critical role in limiting inflammation in response to the nonpathogenic antigens, and defects in the t-cell subset have been implicated in the pathogenesis of few gastro-intestinal disorders. Toll-like receptor signaling triggers dendritic cell maturation, which primes naive T lymphocytes towards specific T helper cell types 1 and 2 immune responses. Although a t helper cell type balance may be important in modulating allergic responses, t regulatory cells that suppress certain immune responses maybe critical in immune regulation. The effect is produced either by absorption of a soluble antigen or by translocation of 'lactobacilli' through the gut wall into the blood stream. Lactobacilli which adhere to human intestinal epithelial cells are capable of activating macrophages. Another class of pharmacologic agents, the histone/protein deacetylase inhibitors (HDACs), has recently been shown to improve treg function and increase treg numbers in mice. HDACs regulate chromatin remodeling and affect gene expression by modifying histones via acetylation. Murine models demonstrate an important role for IL-10 in Treg-mediated control of intestinal inflammation; however, the source of IL-10 may not be entirely treg derived.

Probiotics and HIV

Recently it has been postulated that the probiotic bacteria may slow down AIDS progression. Lin Tao and his colleagues screened hundreds of bacteria taken from the saliva of volunteers. The results showed that some *Lactobacillus* strains had produced proteins capable of binding a particular type of sugar found on HIV envelope, called mannose (Lin, 2008). The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract, forming colonization. One strain secreted abundant mannose-binding protein particles into its surroundings, neutralizing HIV by binding to its sugar coating. They also observed that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harboring HIV and prevent them from infecting other cells.

Probiotics and Cancer

The anticancer effects of probiotics were long recognized, but evidence in literature is minimal. Recently, there has been growing interest in proving their interrelationship. Individuals who consume high amount of animal protein and fats apparently showed increased risk of colon cancer. The refined diet has also been implicated in causation of breast and prostate carcinoma. It has been postulated that microflora of GI tract are involved in inducing colorectal carcinoma (Min, 2008). Present studies have suggested that prebiotics also possess protective effect against colon carcinogenesis, mainly attributed to the production of short chain fatty acids upon its fermentation by gut microflora, and alteration of gene-expressions in tumor cells (Minna *et al.,* 1999). Notably, some of the newer studies showed that short-lived metabolite mixtures isolated from milk that was fermented with strains of Lactobacillus bulgaricus and streptococcus thermophilus are more effective in deactivating etiologic risk factors of colon carcinogenesis than are cellular components of microorganisms (Min, 2008). In humans, the ingestion of probiotics leads to the excretion of urine with low concentrations of components that are genotoxic in human colon cells and high concentrations of components that induce oxidized DNA bases.

Probiotics and Calcium Absorption

Milk is considered to be abundant with calcium apart from other dietary sources. Individuals with lactose intolerance may probably develop osteoporosis due to decreased consumption of milk containing diet. Calcium absorption is favored in acidic pH. So if probiotics are fed to lactose intolerance patients, then milk lactose is hydrolyzed by probiotic strains and favors calcium absorption (Minna *et al.,* 1999).

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Probiotics Usage in Gastrointestinal Disorders

Chronic constipation is one of the most frequent complaints in childhood. Although there is evidence that gastrointestinal flora is important in gut motility, there is little evidence that gut flora is abnormal in constipation. Lactobacilli and bifidobacteria increase stool frequency and decrease consistency in normal individuals. But, according to several reviews, the evidence of probiotics for efficacy in constipation is limited. Fiber supplements, lactose-free diets, and lactobacillus supplementation are effective in the management of children with recurrent abdominal pain and irritable bowel syndrome (IBS) (Vandenplas and Benniga, 2009). IBS is a common disorder and available therapies have limited efficacy. Mucosal inflammation and alterations in gut microflora may contribute to the development of IBS symptoms, and researchers have hypothesized that probiotics might improve these symptoms (Brenner *et al.,* 2009). *Bifidobacterium infantis* 35624 showed significant improvement in the composite score for abdominal pain/discomfort, bloating/distention, and/or bowel movement difficulty compared with placebo ($P<0.05$) in the recent study (Brenner *et al.,* 2009). No other probiotic showed significant improvement in IBS symptoms in the randomized controlled trial. Because some probiotics react with antigens in the intestine, these products might be useful in the treatment of food allergies and that probiotic use might reduce cases of colic ulceration and malabsorption.

Probiotics and Oral Health

Mouth represents the first part of the gastrointestinal tract. Probiotics have been successful for treating digestive related diseases. These can be introduced into the oral cavity at much higher concentration with minimal loss in number. Many of the beneficial bacteria are destroyed by the hydrochloric acid in the stomach. The way to avoid this pitfall is to freeze the bacteria and put them in a pill (Meurman, 2005). In the oral cavity, Probiotics should adhere to dental tissues to establish a cariostatic effect and thus should be a part of the bio-film to fight the cariogenic bacteria. The duration of their stay locally also is important for beneficial effect. Ideal vehicles of probiotics installation are yogurt, milk and cheese. Some of the hypothetical mechanism of probiotics action in the oral cavity is by: (Izumita, 2001; Suvarna and Bobby, 2005; Huovinene, 2001)

1. Direct interaction in dental plaque
2. Involvement in binding of oral micro-organisms to proteins
3. Action on plaque formation and on its complex ecosystem by competing and intervening with bacterial attachments.
4. Involvement in metabolism of substrate and production of chemicals that inhibit oral bacteria

Indirect probiotic actions are also featured such as:

1. Modulating systemic immune function.
2. Effect on local immunity.
3. Effect on non-immunologic defense mechanisms.
4. Regulation of mucosal permeability.
5. Probiotics as an antioxidants and produce antioxidants.
6. Prevent plaque formation by neutralizing the free electrons.

The literature review showed only few studies available on the prevalence, role and effects of probiotic bacteria in the mouth. Lactic acid bacteria are considered detrimental to dental health because they ferment sugars and lower pH of these bacteria. When lactic acid bacteria are consumed in milk products, the buffering capacity of milk influences the acidity. The presence of calcium and other constituents may also protect tooth surfaces and inhibit the adherence of dental pathogens. Russian scientists have reported that probiotic bifidobacteriuim sp. reduce gingival and periodontal inflammation (Grudianov *et al.,* 2002). One study showed inhibitory effect on salivary counts of Strepto. Mutans and yeast by using a combination of LGG and Bifidobacteria. A Specially manufactured cheese was used as the vehicle of administration for 3 weeks. Eating cheese also enhanced remineralization and prevents demineralization of hard tissues in saliva (Montalto *et al.,* 2004).

The prevalence of oral candidiasis is often seen by prosthodontists in geriatric population. A 16-week, randomized, double-blind, placebo-controlled trial on 276 elderly people was done in order to assess the

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effectiveness of probiotic cheese in controlling candidial infection (Hatakka *et al.,* 2007). It was found that the probiotic intervention reduced the risk of high yeast and fungal counts by 75% and the risk of hyposalivation by 56%. Thus, probiotic bacteria can be effective in controlling oral *Candida* and hyposalivation in the elderly.

Halitosis, or bad breath is an embarrassing social problem more than being a dental health problem. Dental clinicians have the responsibility to diagnose, treat and prevent oral malodor for at least 85% of these have an oral source. The gram- negative anaerobic bacteria associated with gingivitis and periodontitis cause halitosis by their proteolysis, which produces volatile sulfide compounds (Kang *et al.,* 2006). It was inferred in recent studies that by administering probiotic bacteria, it was possible to suppress the odour- producing bacteria, thus resulting in the decrease in foul smelling gase in mouth (Kang *et al.,* 2006; Burton *et al.,* 2006). Even though there is good number of studies indicating the reduction of severity and occurrence of mucosal lesions, specifically aphthous ulcers and anticarcinogenic effect in intestines, there are no long term studies done over the effect of probiotics on premalignent and malignant conditions of oral cavity (Wegener *et al.,* 1997). Further research needs to be directed towards the action of probiotics on oral cavity and also on its pathological conditions.

Conclusion

The mechanisms of probiotic action appear to link with colonization resistance and immune modulation. This concept prompts a new horizon on the relationship between diet and periodontal health. However, data is still sparse on the probiotic action in the oral cavity. There is every reason to believe that the putative probiotic mechanisms of action are the same in the mouth as they are in other parts of the gastrointestinal tract. Because of the increasing global problem with antimicrobial drug resistance, this concept merits further research in the fields of oral medicine and dentistry. Furthermore, it can be used as passive local immunization against dental caries. Clinical trials should be directed to assess the method of probiotic administration in oral cavity and dosages for different therapeutic uses.

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