



DENTISTRY WITH PROBIOTICS: A REVIEW

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ABSTRACT

Probiotics are dietary supplements, that have been advocated for the prevention and the treatment of various diseases. These products consist of essential micro-organisms, which stimulate health promoting flora thus, suppressing the pathologic colonization. Now time has arrived so that paradigm of treatment is shifted from elimination of specific bacteria to altering bacterial ecology by using probiotics. They have shown promising effects in the oral health with respect to control of chronic disease like periodontitis, dental caries and recurring problems like candidal infections, halitosis, aphthous ulcers etc. Probiotics form a biofilm in oral cavity that is protective against oral diseases. Since, probiotics are now widely used in both medical and dental specialties, a thorough understanding of their risks and benefits are essential. This review focuses on the recent trends in use of probiotics in dentistry, to understand the mechanism of action of probiotic bacteria in the oral cavity as well as the potential risks associated with it.

Key Words: Dentistry, Probiotics, Oral diseases, Oral Flora, Oral Health

INTRODUCTION:

The World Health Organization has defined probiotics as “Live microorganisms which, when administered in adequate amounts, confer a health benefit to the host¹.” It was used first by Lilly and Stillwell in 1965 to describe “substances secreted by one microorganism which stimulates the growth of another” and it contrasted with the term antibiotic². In the initial years 1900 Ukrainian bacteriologist Metchnikoff regarded as the originator of concept of probiotics claimed that longevity of some populations in Bulgaria, Turkey and Armenia was due to regular consumption of fermented milk products rich in live lactic acid bacteria which may neutralize deleterious effects of gut pathogens, thus extending life span³. In 1989, Fuller defined them as a live microbial food supplement, which beneficially affects the host animal by improving its microbial balance⁴. The first and foremost probiotic species

introduced into research were *Bifidobacterium bifidum* by Holcomb, *et al.* in 1991 and *Lactobacillus acidophilus* by Hull, *et al.* in 1984⁵. Gibson and Roberfroid defined prebiotics as a “non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth⁶. Traditionally, probiotic microorganisms have been used to prevent or treat diseases in the gastrointestinal tract. In the past few decades, there has been an increased interest in possible oral health effects of probiotics. An International Life Science Institute Europe consensus document, proposed a widely accepted definition i.e. “The Viable microbial supplements which beneficially influence the health of human beings.” And these bacteria must belong to the natural flora of body in order to resist gastric secretion and survive during intestinal transit. They must adhere to the intestinal mucosa and must have the ability to inhibit pathogens present in gut^{7,8}. Various in vitro studies have shown promising results with growth inhibition of mutans streptococci and *Candida albicans*. There are only a few clinical studies with caries development as the primary outcome while more studies have been focusing on control of caries risk factors or so-called surrogate outcomes. Several studies have evaluated the effects of probiotic bacteria on MS in saliva and/or plaque, and a number of probiotic strains show ability to reduce the number of MS. Probiotic bacteria have not been shown to permanently colonize the oral cavity; in early-in-life interventions or in subjects with a mature microbiota¹. This the aim of this review is to focus on the recent trends in use of probiotics in dentistry, to understand its mechanism of action in the oral cavity and the potential risks associated with it.

PREBIOTIC AND SYNBIOTIC

Probiotics should not be confused with prebiotic. The term prebiotic was introduced by Gibson and Roberfroid¹⁹ who exchanged “pro” for “pre” which means “before” or “for”. Prebiotics are the food segments that are inedible but advantageously influences the host by specifically stimulating the growth or activity limited number of beneficial microscopic organisms in the colon. These are short-length carbohydrates, such as gluco-oligosaccharides, fructooligosaccharides, galctosaccharides and inulin which resists digestion. They are fermented in the colon to produce short-chain fatty acids, such as acetate, butyrate, and propionate and also have positive effects on colonic cell growth and stability. Synbiotic term is used when a product contains both probiotics and prebiotics and includes both the live cells of the beneficial bacteria and the selective substrate⁹.

COMPOSITION OF PROBIOTICS

Probiotics can be bacteria, molds or yeast. However, most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular. *Lactobacillus acidophilus*, *Lactobacillus lactis*, *Lactobacillus helveticus*, *Lactobacillus casei*, *Lactobacillus salivarius*, *Lactobacillus plantrum*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus*, *Lactobacillus johnsonii*, *Lactobacillus fermentum*, *Streptococcus thermophilus*, *Enterococcus faecium*, *Enterococcus faecalis*, *B. bifidum*, *Saccharomyces boulardii*, *Bifidobacterium breve*, *B. longum*, are commonly used bacterial probiotics. A probiotic can be made of a single bacterial strain or it may be a consortium as well. Probiotics can be in liquid form, powder form, gel form, granules and is also available in the form of capsules, sachets, etc¹⁰

FEATURES OF PROBIOTICS

A good probiotic agent needs to be non-pathogenic, nontoxic, resistant to gastric acid, adhere to gut epithelial tissue and produce antibacterial substances. It should persist, albeit for short periods in the GI tract influencing metabolic activities such as cholesterol assimilation, lactose activity, and vitamin production. The survival of probiotic organisms in the gut depends on the colonization factors that they possess as well as on the organelles which enable them to resist the antibacterial mechanisms that operate in the gut. They also need to avoid the effects of peristalsis, which tend to flush out bacteria with food. This can be achieved either by immobilizing themselves or by growing at a much faster rate than the rate of removal by peristalsis. The probiotic strain needs to be resistant to the bile acid, i.e. Bifidobacteria strains have significantly shown less acid-resistant than the strains of Lactobacillus, when exposed to human gastric juice¹⁰.

MECHANISM OF ACTION¹¹⁻¹³

In oral health, possible mechanisms is

1. Production of antimicrobial substances such as Organic acids, Hydrogen peroxide and Bacteriocins. Some produce lactase.
2. Binding in Oral Cavity (Compete with pathogens for adhesion sites and Involvement in metabolism of substrates (competing with oral micro-organisms for substrates available) as well as for available nutrients and growth factors).
3. Immuno modulatory (Stimulate non specific immunity and Modulate humoral and cellular immune response Effect on local immunity)
4. Modify oral conditions (Modulating pH, Modification of oxidation reduction potential, Regulation of mucosal permeability, Selection pressure on developing oral microflora towards colonization by less pathogenic species.
5. Probiotics act on dental plaque formation, its complex ecosystem and are involved in binding of oral microorganisms to proteins. They stimulate macrophages, produce cytokines, escalate natural killer cell and raise the levels of immunoglobulins. The increase in the number of Immunoglobulin A producing cells is the most remarkable property induced by probiotic organisms and also by fermented milk yogurt. Other mechanism of action includes the down regulation of inflammatory responses, mucin production, defensin production, inhibiting collagenases, inhibit pathogen induced production of pro-inflammatory cytokines, decreasing Matrix Metalloproteinase (MMP) production, induction of expression of cytoprotective proteins on host cell surfaces, etc. Since mouth represents the first part of the gastrointestinal tract, some probiotic mechanisms may also play a vital role in this part of the system and can also be introduced here at much higher concentration with minimal loss in their number. Probiotics inhibit pathogens but do not inhibit

friendly bacteria. Studies have shown that once the pathogenic organisms are replaced the reintroduction of the pathogen does not occur easily.

PROBIOTIC SOURCES¹⁴⁻¹⁶

Probiotics are mainly available in the form of food and dietary supplements. Yogurt and other fermented foods, soybeans, asparagus are the main sources of naturally occurring probiotic bacteria in the diet and are considered as ideal vehicles. The dairy sources of probiotics are rich in calcium and thus may prevent demineralization of teeth. Other carriers for probiotics may include kombucha, miso, kefir, biodrink etc. Probiotics are provided in products in one of the five basic ways.

- Available in the form of Culture concentrate which is added to a beverage or food (such as a fruit juice).
- Inoculated into prebiotic fibers.
- Inoculants into a milk-based food (dairy products such as milk, milk drink, yoghurt, cheese).
- Available in concentrated forms and also dried cells packaged as dietary supplements (non-dairy products) such as powder, capsule, gelatin tablets
- They can also be supplied as mouth washes, lozenges, chewing gums, tooth pastes and straws.

In India, Sporlac, *Saccharomyces boulardii* and yoghurt are commonly used. Lactobacilli solution is an example of probiotic given to pediatric patients. *Bacillus mesentericus* acts as an alternative to B-Complex capsules. A combination of pro- and pre-biotic e.g. BION is prescribed as single dose before meals in the morning on daily basis. Swallowing a single tablet cannot do as much for the oral ecology as letting it dissolve in the mouth. Probiotics are administered in different quantities that allow for colonization. Daily consumption of probiotics has been recommended for optimal results. The probable benefits increase with an early childhood use. Maternal use of some probiotic strains have shown to influence the composition of breast milk. However, administration of probiotics in children should be given with proper protocols because their oral microflora is not been established yet. Recent evidence indicates that effects of probiotic are strain-specific; thus, a beneficial effect attributed to one strain cannot be assumed to be provided by another strain, even when it belongs to the same species. A combination of strains can enhance effects in a synergistic manner.

CRITERIA FOR SELECTION OF PROBIOTICS¹⁷⁻¹⁹

Fuller in 1989 listed the features of good probiotic. An ideal probiotic must have following properties:

- Nontoxic and non pathogenic preparation.
- Produce beneficial effects to host.
- Should withstand gastrointestinal juices and be capable of surviving and metabolizing in gut environment.
- Should have good shelf life.
- Should replace and reinstate the intestinal microflora.
- Should be present as viable cells, preferably in large numbers.
- There should be a high degree of genetic stability in Effector strain
- They should be of human origin.

PROBIOTIC PRODUCTS²⁰

Probiotics are provided in products in four basic ways: As a culture concentrate added to a beverage or food (such as fruit juice), Inoculated into prebiotic fibers, Inoculants in a milk-based food (dairy products such as milk, milk drink, yogurt) and as dietary supplements in concentrated and dried cells packaged (non-dairy products).

ROLE OF PROBIOTICS IN DENTISTRY:

- **Dental caries:** It is an infectious multifactorial disease affecting most of the population and occurs along the interface between the enamel surface and dental biofilm. Various methods have been used to alter the cariogenicity of the biofilms responsible for the same. Researchers are developing “probiotic” strategies to treat the caries causing infection, the mechanism of which are employed to selectively remove only the harmful pathogen but leaving the remainder of the oral ecosystem intact. One of the replacement therapy options require the application of a genetically engineered “effector strain” of *S. mutans* which will replace the cariogenic or “wild strain” to arrest caries and to promote the remineralization of tooth surfaces that have been demineralized but that have not become cavitated and its strain BCS3-L1 is modified genetically and is used in replacement therapy to prevent dental caries. Recombinant DNA technology was used to delete the gene encoding lactate dehydrogenase in BCS3-L1 making it unable to produce lactic acid and was also designed to produce increased amounts of a novel peptide antibiotic called mutacin 1140 which gave it a strong selective advantage over other strains of *S. mutans*. In a randomized double-blind study, it was demonstrated that the administration of the probiotic *Lactobacillus paracasei* SD1 in milk increased the levels of the peptide HNP1-3, which seems to be interested in the reduction of the presence of caries in children.

These human neutrophils peptides as HNP1-3 are antimicrobial peptides cationic that provide the first line of host defense against a broad spectrum of microorganisms. These are released by the submandibular salivary glands and secreted into the saliva. They are also present and release in the gingival crevicular fluid. The preventive role of HNP1-3 against dental caries was suggested by the finding of a significant increase in levels of HNP1-3 salivary in children with the absence of caries. Since one of the mechanisms of probiotics has been involved in the regulation of the immune system of the host, it was therefore assumed that the administration of probiotics may help to prevent dental caries through their ability to increase and modulate the production of salivary HNP1-3²¹⁻²³

- Probiotics in periodontal-health** *P. gingivalis*, *A. actinomycetemcomitans*, *T. forsythia*, *T. denticola* are the main periopathogens. Probiotics reduces the pH of the oral cavity as due to which plaque bacteria do not form dental plaque and calculus causing the periodontal disease. Probiotic mouth wash has shown to reduce the incidence of plaque formation and gingivitis in 6-8 year old children. In vitro study of *L. salivarius* TI 2711 behaviour isolated from a healthy human volunteer showed inhibitory action on *Prevotellaintermedia*, *P. gingivalis*, and *Prevotellanigrescens* after 6-12 hrs co-culturing. Some of the studies showed that prevalence of lactobacilli, particularly *Lactobacillus fermentum*, and *L. gasseri*, in the oral cavity was greater among healthy participants than among patients with chronic periodontitis. some studies concluded that inhibition of the growth of periodontopathogens can be done by lactobacilli, including *Prevotellaintermedia*, *P. gingivalis*, and *A. actinomycetemcomitans*. All these observations suggest that lactobacilli residing in the oral cavity could play a role in the oral ecological balance^{24,25}.
- Probiotics and Halitosis** Halitosis has many causes such as consumption of particular foods, respiratory tract infections, metabolic disorders, however in most cases it is associated with an imbalance of the commensal microflora of the oral cavity i.e. results from the action of anaerobic bacteria which degrade the salivary and food proteins to generate amino acids, that are in turn transformed into volatile sulphur compounds, including hydrogen sulphide and methanethiol. Previous studies have reported that various strains of *W. cibaria* have the capacity to inhibit the formation of volatile sulphur compounds by *F. nucleatum* and concluded that this fruitful effect was due to the production of hydrogen peroxide which in turn reduced the proliferation of *F. nucleatum*. These authors also found that gargling with a solution containing *W. cibaria* was associated with the reduction in the formation of methanethiol and hydrogen sulphide and finally helped in reduction in bad breath^{26,27}.
- Candidiasis** A reduction in the prevalence of *Candida Albicans* in elderly after consumption of probiotic cheese which contained *Propionibacterium freudenreichii* ssp. *shermanii* JS and *L. rhamnosus* strains (GG and LC705) has been demonstrated. Lactobacilli probiotics inhibits the growth of *C. albicans* possibly due to the low pH milieu produced by the lactobacilli. *Candida*-infected mice fed with *L. acidophilus* exhibited accelerated clearance of *C. albicans* from the mouth. Also *Lactobacillus fermentum* appears to be promising. Hasslof P et al (2010) found that two *L. plantarum* strains and *L. reuteri* ATCC 55730 displayed the strongest inhibition on *Candida albicans*. *B. animalis* reduces the incidence and severity of mucosal candidiasis^{28,29}.
- Orthodontics** The presence of fixed orthodontic appliances in the mouth can allow microorganisms to accumulate, causing enamel demineralization that produces white spot lesions. Various Studies resulted that

short-term consumption of fruit yogurt containing bifidobacteria alters the levels of salivary mutans streptococci and lactobacilli in patients with fixed appliances. In one study 200 g once daily fruit yogurt containing *Bifidobacterium animalis* subsp. *lactis* N 173010 significantly reduced salivary mutans streptococci counts in two weeks. No effect was produced on lactobacilli counts. A study showed that the consumption of probiotic curd (Active plus) and the topical application of probiotic toothpaste (GD) caused significant decreases in the S mutans levels in the plaque around the brackets of orthodontic patients^{30,31}

- **Voice Prosthesis** Turkish yogurt containing *Streptococcus thermophilus* and *Lactobacillus bulgaricus* effectively abolished the biofilm formation on indwelling voice prostheses. Patients in Netherlands consuming buttermilk containing *Lactococcus cremoris*, *Lactococcus lactis* spp. which produces antimycotics and other substances prolonged the lifetime of indwelling voice prostheses. Lactobacilli species have capacity to interfere with the adhesion of uropathogens to epithelial cells and catheter materials, while *S. thermophilus* can effectively compete with yeasts in their adhesion to substratum surfaces, like silicone rubber^{14,32}.
- **Xerostomia** Evidence suggests that probiotics can also efficiently lessen the risk xerostomia²⁹.
- **Probiotics and aphthous ulcer** A study conducted by Nalini et al showed that by the use of synbiotic there is reduction in the recurrence of aphthous ulcers. Even though there are many other treatment modalities for aphthous ulcers study done on synbiotic bifilac lozenges showed better results. There are no significant side effects for synbiotic instead it is more beneficial for the host³³.
- **Probiotics and oral cancer** There is minimal evidence about the anticancer effects of probiotics. Few evidences cropping up that probiotics can interfere the DNA and chromosomal damage. More researches needs to be done about regulation on their consumption³⁴.

FUTURE TRENDS³⁵

Through probiotics passive neighbourhood immunization can be completed towards dental caries. Early mucosal colonization with Ecolab bacteria in new child stimulates mucosal immune gadget to supply unique antibodies as properly nonspecific secretory immunoglobulins. Studies are directed at the reduction of severity and prevalence of mucosal lesions, particularly aphthous ulcers however Efficient methods of probiotic administration in oral cavity, their dosages for different optimum therapeutic uses, their actions on various pathogens in the oral cavity and also on the safety of use of these in various pathological conditions should be determined.

PRECAUTIONS AND CONTRAINDICATIONS^{36,37}

Side effects of probiotics tend to be mild and digestive (such as gas or bloating). They possibly can cause unhealthy metabolic activities, too much stimulation of the immune system, or gene transfer. Uncertainty about specificity of probiotics effects is a cause of concern. There always remains the possibility that probiotic consumption can cause infection and that individuals will respond in different ways to a specific strain. Probiotics might cause infections in critically ill or severely immunocompromised patients. *Lactobacillus* strains have been reported to cause bacteremia in patients with short-bowel syndrome. Fungemia has been reported when *Saccharomyces* capsules were opened

and administered in patients with central venous catheters. Lactobacillus preparations are contraindicated in persons with a hypersensitivity to lactose or milk. *S. boulardii* is contraindicated in patients with a yeast allergy. Liver abscess was reported in an individual on *L. rhamnosus* GG. Stimulation of immune system by probiotics showed degradation in autoimmune diseases, and transferred antibiotic resistance to pathogens. The mode and time of the administration as well as the age of the subject taking probiotics is crucial.

CONCLUSION

The probiotic application in near future may provide an end to many infections occurring in oral cavity. The selection of the best probiotic for oral health is an issue that calls for further study. Probiotics provide an effective, non invasive and economic means to overcome oral diseases. Thus, a slight change in diet by including probiotic foods may stop, retard, or even significantly delay the pathogenesis of oral diseases, promoting a healthy lifestyle to fight oral infections. A complete understanding of the broad ecologic changes they induce in the mouth is essential to assess their long term consequences for oral health and disease and there is a great need to explain the role of the oral beneficial microbiota, to identify beneficial bacteria and to conduct proper large-scale studies on the usefulness of probiotics to maintain or improve oral health.

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