Scholastic Dental Sciences (ISSN: 3107-1657) Review Article

Volume 2 Issue 3 March 2026

A Comprehensive Review and Application of Probiotics in Dentistry

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Received: March 23, 2026; **Published:** March 26, 2026

Abstract

Knowledge is providing us the tool to detect and take care of the disease earlier than it causes harm. Designed for some decades currently,bacteria identified as probiotics have been supplementary to a mixture of foods for the reason that of their helpful special effects for human being physical condition. The make use of antibiotics, immunosuppressive therapy and irradiation amongst other means of treatment may cause alterations in the composition and have an effect on the Gastro-intestinal (GI) Tract flora. Probiotics are dietary supplements containing potentially valuable bacteria or a few yeasts. They help in motivating health promoting flora and also suppressing pathogens which cause and spread diseases. A balanced oral microbial environment is essential for the promotion of health & prevention of diseases. Probiotic technology represents a break through approach to maintain oral health by using natural beneficial bacteria, commonly found in oral cavity of healthy individuals, to provide a natural defense against those bacteria which are thought to be harmful to structures of oral cavity. These products usually contain streptococci, lactobacilli, or bifidobacteria. The application of probiotic strategies may in near future provide an end to many infections occurring in oral cavity. This article describes on action, reimbursement, wellbeing issues and potential aspects of probiotics for oral health.

Key words: Bacteria,Probiotics, disease, action, oral health.

Introduction

The role of diet in health and well-being across the world accredited. With the advancement of the knowledge of nutrition, research is now being directed towards improving the tolerant of specific physiologic effects of the diet further than its nutritional effect.More specifically, prebiotics are short-length carbohydrates, such as fructooligosaccharides, that resist digestion or are fermented in the colon to produce short-chain fatty acids, such as acetate, butyrate, and propionate, which have positive effects on colonic cell growth and stability, generate many of the same bacteria as provided in probiotics. [1]

The term synbiotic is used when a product contains both probiotics and prebiotics.[2] According to this approach, a food or food supplement will include both the live cells of the benefi cial bacteria and the selective substrate. The idea being that the beneficial bacterial cells can grow quickly and competitively because of the presence of selective substrate and establish their predominance. [3]

Probiotics reminds of the very old and forgotten concept of 'Bacteriotherapy' which stated that beneficial bacteria occurring naturally in the human body can be administered in the patient's body to restore patient's health and wellbeing (Meurman, 2005).Bacteriotherapy gave rise to the concept of modern day probiotics. Probiotics have been

extensively studied for their intestinal benefits.The human intestine has a reservoir of microorganisms naturally inhabiting the intestine as symbiont. They are referred to as 'gut or the intestinal flora'.

In lieu of the shelter that the human body provides, the intestinal flora performs several important functions in the human body such as fermenting undigested energy substrate, strengthening the immune system, protection against the growth of the pathogenic bacteria, promoting gut development, production of vitamins (Vitamin K and Biotin) and production of hormones for fat storage.

The process whereby probiotics are used to restore the normal intestinal microflora to provide resistance against antibiotics is termed 'Microbial interference therapy'**.** Probiotics being safe for human consumption and resistant to bile and acidic environment survives in the intestine, colonize the human gut and show bacteriocin production to block the invasion of intestine cells by enteroinvasive bacteria. On the other hand, Broad spectrum antibiotics, being unable to distinguish between beneficial and harmful bacteria, kill both and alter the number of natural microbiota. This results in a downfall in host's health. Earlier, Probiotics were associated with only gut health but recently several investigators have suggested their potential applicability in the improvement of oral health. [4]

Defination:

Probiotics can be defined as living microbes, or as food ingredients containing living microbes, that beneficially influence the health of the host when used in adequate numbers. [5] As adopted by the International Scientific Association for probiotics and prebiotics, "Live microorganisms, which when administered in adequate amounts, confer beneficial effect on the health of the host." [6]

An International Life Science Institute Europe consensus document proposed a simple and widely accepted definition of probiotics as"Viable microbial food supplements which beneficially influence the health of human." 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 [7,8,9]. Prebiotics are non digestible food ingredients such as fructooligosaccharides(FOS), Lactulose and inulin that beneficially affect the host by selectively stimulating growth activity of a limited number of probiotic like bacteria in a colon [10].

History

In 20th century, Russian scientist and noble laureate Elie Metchnikoff was the first one to suggest the possibility to modify the gut microflora by replacing the harmful microbes with the useful microbes. Metchnikoff observed that certain rural populations in Europe, for example, in Bulgaria and the Russian steppes who mainly depended on milk fermented by lactic acid bacteria for their sustenance had comparatively longer lives. By that time, it was known that milk fermented with lactic acid bacteria inhibits the growth of proteolytic bacteria because of its low pH which is caused by the fermentation of lactose. Based on these facts, Metchnikoff proposed that consumption of fermented milk would 'seed' the intestine with harmless lactic acid bacteria,decreases the intestinal pH thereby suppressing the growth of proteolytic bacteria. *Bifidobacteria* was the first isolated probiotic bacteria. Henry Tissier (1905) isolated it from a breast-fed infant.

Tissier (1906), a french pediatrician, observed a low number *Bifidobacteria* in the stool of the infants with diarrhea as compared to the healthy infants. Metchnikoff introduced into himself the sour milk fermented with the bacteria he called "Bulgarian bacillus"and found his health benefitted. (Metchnikoff, 1907)(4)

The Ukranian bacteriologist and Nobel Laureate Metchnikof (1908) studying the flora of the human intestine developed a theory that senility in humans is caused by poisioning of body by the products of some of thses bacteria. To prevent the multiplication of these organisms he proposed a diet containing milk fermented by lactobacilli, which produce large amounts of lactic acid that could increase the life span of humans. The concept of probiotics was thus born and a new field of bacteriology was opened [11].

The *Escherichia coli* strains isolated from the faeces of an unaffected soldier was used for the treatment of acute gastrointestinal infections by German professor Alfred Nissle (1917) when the antibiotics were not yet available.1930s witnessed the first clinical trials on probiotics for their effect on constipation [4].

Lilley and Stillwell (1965) introduced the term probiotics. Mann and Spooering in 1974 discovered that the fermented yogurt reduced blood serum cholesterol. In 1984 Hull identified the first probiotic species, the lactobacillus acidophilus. Later in 1991, Holcombh identified *bifidobacterium bifidum*. 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 [11].

Mechanism of Action :

The general mechanisms of probiotics can be divided into three main categories:

(a) normalization of intestinal microbiota,

(b) modulation of immune response, and

(c) metabolic effects [12].

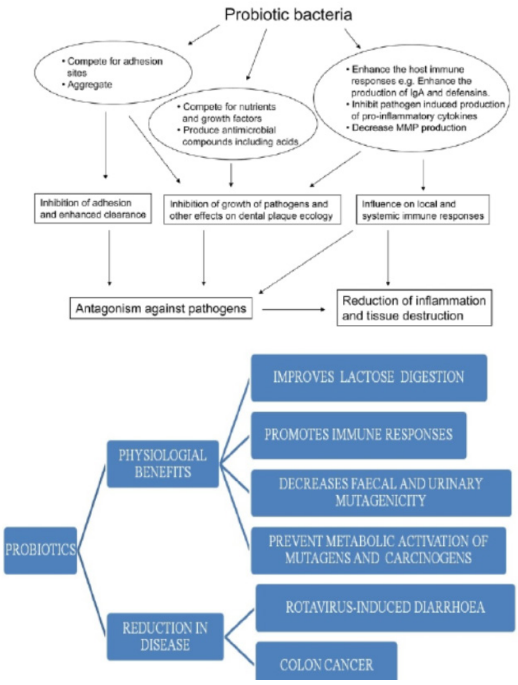
The mechanisms of probiotic action in the oral cavity could be analogous to those described for the intestine. Thus far oral colonization by probiotic bacteria has often been considered essential for them to exert oral effects; however, the possibility of systemic effects cannot be excluded, although the total sIgA levels in saliva seem unaffected by probiotic use [13,14].

Normalization of intestinal/oral microbiota is supported by the ecological plaque hypothesis which suggests that selective pressure in environmental conditions can change the balance between oral health and disease [15] As bacteria can influence their environment, and both synergistic and antagonistic interactions are suggested for bacteria in dental plaque, the environmental pressure described in the ecological plaque hypothesis could be introduced partly by bacteria. As there are bacterial species associated with oral diseases, there are also species that seem to be associated with oral health; however, it is questionable whether bacteria administered in food could influence relatively stable oral microbiota, in particular in adults [16]. Such friendly bacteria can be used as probiotics to normalize oral microbiota. Immunomodulation Rather than directly inhibiting the growth or viability of the pathogen, probiotics may compete for an ecological niche or, otherwise, create conditions that are unfavorable for the pathogen to take hold in the intestinal tract. First, several probiotics have been demonstrated to alter the ability of pathogens to adhere to or invade colonic epithelial cells in vitro. Second, probiotics could sequester essential nutrients from invading pathogens and impair their colonization ability.

Third, probiotics may alter the gene expression program of pathogens in such a way as to inhibit the expression of virulence functions. Lastly, probiotics may create an unfavorable environment for pathogen colonization by altering pH, the mucus layer, and other factors in the local surroundings. It is important to note that although many of these

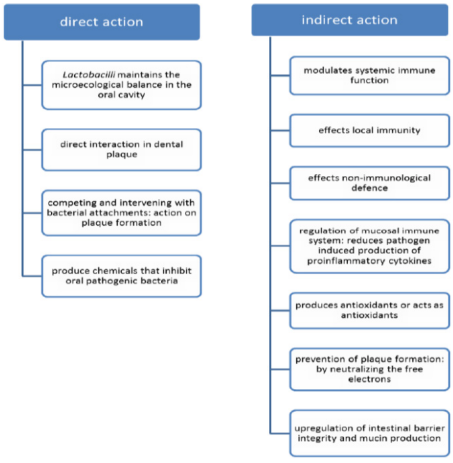
possible effects have been demonstrated in vitro, the ability of probiotics to exclude pathogens in vivo remains to be proven [17].

These include increased disaccharide activity,the production of antibacterial substances, competition for bacterial adhesion, stimulation of various immune defense mechanisms and in case of saccharomyces, antisecretory/protease effects against toxins as well trophic effects on the mucosa [18].



The methods by which probiotics can be administered [4].

1. Icecreams
2. Capsules
3. Liquid
4. Mouth Rinse
5. Yoghurt
6. Cheese
7. Lozenges
8. Tablets



Species of Probiotics Includes:

Probiotics can be varied. They can be yeast, bacteria or moulds. But most commonly, bacterial species are predominant. Some of these species are

a) Lactic acid producing bacteria (LAB) : Lactobacillus,bifidobacterium, streptococcus

b) Non lactic acid producing bacterial species: Bacillus, propionibacterium.

c) Non pathogenic yeasts: Saccharomyces

d) Non spore forming and non flagellated rod or coccobacilli [11]

Properties of Probiotics[11]

1. Should be non toxic and non pathogenic preparation
2. Produce beneficial effect
3. Should withstand gastrointestinal juice
4. Should have good shelf life
5. Should replace and reinstate the intestinal microflora
6. Binding to dental surfaces8
7. Produce antimicrobial substances against pathogens9
8. Alteration of ecological conditions of the mouth
9. Reduction of the inflammatory response.

Probiotics in General Health

1. Reduction of the concentration of cancer-promoting enzymes and/or putrefactive (bacterial) metabolites in the gut.
2. Prevention and alleviation of unspecific and irregular complaints of the gastrointestinal tracts in healthy people.
3. Prevention of respiratory tract infections (common cold, influenza) and other infectious diseases as well as treatment of urogenital infections.
4. Prevention and/or reduction of duration and complaints of rotavirus-induced or antibiotic-associated diarrhoea as well as alleviation of complaints due to lactose intolerance.
5. Prevention or alleviation of allergies and atopic diseases in infants.
6. Normalization of passing stool and stool consistency in subjects suffering from constipation or an irritable colon.
7. Beneficial effects on microbial aberrancies, inflammation and other complaints in connection with: inflammatory diseases of the gastrointestinal tract, helicobacter pylori-infection or bacterial overgrowth. [19]

Probiotics in Oral Health

As the bacterial resistance to antibiotics is emerging wide spreadly, the concept of probiotic therapy has been considered for application in oral health. Dental caries, periodontal disease, halitosis, and oral candidosis are among the oral disorders that have been targeted. An essential condition for a microorganism to represent a probiotic of interest for oral health is its capacity to adhere to and colonize various surfaces of the oral cavity[20] Lactobacilli constitutes about 1% of the cultivable oral microflora in humans. Lactobacilli are extremely aciduric and can withstand a pH as low as 3.5, which is a prerequisite to survive the

low-pH transition into the intestines. Bifidobacteria are the predominant anaerobic bacteria naturally occurring within the small intestinal lumen and play a critical role in maintaining the equilibrium among normal. [21]

The survival of various probiotics used by the dairy industry (specifically, species of both Lactobacillus and Bifidobacterium) in saliva and their adherence to oral surfaces was assessed by Haukioja et al.They found that all of the tested strains survived well in saliva, but they varied widely in their capacity to adhere to the surface of teeth and oral mucosa. More specifically, species in the genus Lactobacillus had an adherence capacity superior to that of the Bifidobacteriumn species. [22]

Role of probiotics in dental caries

Dental caries is an infectious disease that affects most of the population. This multifactorial and complex disease process occurs along the interface between the dental biofilm and enamel surface. Several methods may be used to alter the cariogenicity of the biofilm which is responsible for dental caries. Probiotic and molecular genetic techniques have been used to replace cariogenic organisms such as mutans streptococci and Lactobacillus species with strains of bacteria that are not cariogenic [23]. Several mutated strains of *S. mutans* that lack the machinery to efficiently meatbolize fermentable carbohydrates to organic acids have been developed. One example is *S. mutans* with a glucosyltransferase C (gtfC) gene mutation.

The pathogenicity of both *S. mutans* and *S. sorbinus* is related to their acidogenic potential and ability to form water insoluble extracellular and enzymatically undegradable polysaccharides from sucrose. These extracellular polysaccharides (glucans) promote adhesion and colonization of cariogenic organisms and mediate protection against antimicrobial agents and resistance to toxic compounds. Synthesis of these glucans is via glucosyltransferase B, glucosyltransferase C and glycosyltransferase D genes. The introduction of mutated gtfC gene that affects the ability of *S. mutans* to produce extracellular glucans has resulted in a decrease in extracellular matrix component of mixed oral biofilms from 51 to 33% of the biofilm volume [24].Using randomized controlled trials, Meurman and colleagues demonstrated that long term consumption of milk containing the probiotic *Lactobacillus rhamuosus* GG strain reduced initial caries in kindergarten children. Nase et al.[23], Caglar et al. It also showed that administration of probiotic bacterium *Lactobacillus reuteri* ATCC 55739 or *Bifidobacterium* DN-173 010 induced significant reduction of cariogenic *S. mutans* in saliva Caglar, et al. [25]

Role of probiotics in periodontitis

The use of probiotic chewing gum containing *L. reuteri* ATCC55730 and ATCCPTA5289 also decreased levels of pro-inflammatory cytokines in GCF and the use of *L.brevis* decreased MMP (collagenase) activity and other inflammatory markers in saliva .The common organisms involved in halitosis are *Fusobacterium nucleatum*, *P. gingivalis*, *P.intermedia* and *Treponema denticola*. These organisms degrade aminoacids, which are in turn transformed into volatile sulphur compounds which cause halitosis. Kang and colleagues reported that various strains of *Weissella cibaria* have the capacity to coaggregate with *fusobacterium nucleatum* and to adhere to epithelial cells and these bacteria produce hydrogen peroxide as well as a bacteriocin which inhibited the proliferation of *F. nucleatum*. These properties could enable *W. cibaria* to effectively colonize the oral cavity and limit the proliferation of *F. Nucleatum* and thus can prevent halitosis.[26,27,28].

Probiotics and halitosis (Oral malador)

Oral halitosis (malador) refers to bad breath originating from the oral cavity. It regularly affects about one in four adults and frequently is caused by anaerobic bacteria that degrade salivary and food proteins to generate amino acids, producing volatile sulfur compounds (VSCs). [29] Halitosis is considered to be an aesthetic problem, with multiple local and systemic etiological factors. The main local etiologies include periodontitis, poor oral hygiene, deep dental caries, tongue coating, and faulty restorations.

"Physiologic" is a term used to describe halitosis as the result of imbalance of the microbiota in the oral cavity without any organic lesion, in contrary to "pathologic" halitosis where patients usually presented with organic lesion most commonly periodontitis.A recent study has shown that patients with genuine physiologic or pathologic halitosis benefited significantly from two-week therapy with tablets containing L. salivariusWB21 in addition to a significant reduction in the level of the volatile compounds and gingival bleeding on probing from periodontal pockets. [30]

Probiotics and Oral Candidosis

Candida species constitute part of the commensal oral flora in about 50% of healthy subjects, but able to cause a clinically apparent lesion if the immune defenses were breached either on the local or systemic level.[31] One study has shown that the subjects who consumed cheese containing the probiotic L. rhammnosus GG and Propionibacterium freudenreichiisp exhibited reduction in the prevalence of oral Candid which subsequently may confer protective effect against oral candidosis. A concomitant feature of the probiotic activity observed in this study was the diminished risk of hypo salivation and the feeling of dry mouth of the subjects.[32]

Role of probiotics in orthodontic treatment

Fixed orthodontic appliances are considered to jeopardize dental health due to accumulation of microorganisms that may cause enamel demineralization, clinically visible as white spot lesions [33] Furthermore, the complex design of orthodontic bands and brackets may create an ecological environment that facilitates the establishment and growth of cariogenic mutans streptococci strains [34]. Cildir et al in 2009 conducted a clinical study with probiotics and found out that daily consumption of fruit yogurt with *Bifidobacterium animalis* subsp. Lactis DN -173010 could reduce the salivary levels of mutans streptococci in orthodontic patients with fixed appliances. Further studies are needed to clarify if this approach is an alternative strategy for prevention of demineralization and white spot formation during orthodontic treatment [35].

Role of probiotics in oral cancer

The anticancer effects of probiotics were long recognized but evidence in literature is minimal. Evidence is cropping up that probiotics can interfere at various stages of cancer process, more so by interference with chromosomal and DNA damage. However, more research is required to develop specific regulations on their consumption [8,36].

Role of probiotics in infections and oral diseases

Only two studies have investigated the effects of probiotic bacteria on oral candida infection in humans . When a test group of elderly people consumed cheese containing *L. rhamnosus* strains GG and LC705 and *Propionibacterium freudenreichii* ssp. Shermanii JS for 16 weeks, the number of high oral yeast counts decreased but no changes were observed in mucosal lesions [37].

Recently it has been postulated that the probiotic bacteria may slow down AIDS progression. Lin Tay and his colleagues screened hundreds of bacteria taken form 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. 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 described that immune cells trapped by lactobacilli formed a clump. This configuration would immobilize any immune cells harbouring HIV and prevent them from infecting other cells.[38,39].

Voice prostheses and probiotic therapy:

A voice prosthesis is an artificial device, usually made up of silicone that is used to help the laryngectomized patients to speak. This device has a very short life time because of the excessive growth of the microorganisms, especially *Candida* species on its surface. As a result, there is improper closure of the valve of prostheses leading to leakage of food into the wind pipe,

causing breathing troubles. Since yeast and bacterial colonization of esophageal side of prosthesis impedes fluent speech, respiration and swallowing because of either leakage or increased airflow resistance.

Therefore, it is needed to replace the voice prostheses regularly, every 1-2 weeks to 3-4 months.

In a study, the buttermilk containing *Lactobacillus lactis* and *Lactococcus lactis ssp. cremoris* and a fermented milk drink containing *L. casei* Shirota were examined for their ability to decrease the amount of bacteria and yeast on voice prostheses in both in vitro and in vivo studies. The results showed that the consumption of fermented milk containing *L. casei* Shirota increased the lifetime of voice prostheses by four times [4].

Probiotics and HIV :

Recently the role of probiotics to slow down the progression of AIDS (Acquired immunodeficiency syndrome) has been postulated by Lin Tao and colleagues (2008). A screening of saliva taken from hundreds of volunteers showed that some *Lactobacillus* strains produced proteins capable of binding a particular type of sugar, called mannose, found on HIV envelope. The binding of the sugar enables the bacteria to stick to the mucosal lining of the mouth and digestive tract and colonize them. One of the strain showed abundant mannose-binding protein particles into its surroundings which binded to the sugar coating and hence neutralized HIV. 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.[38]

Probiotic Dosage :

Probiotics are supplied next to with prebiotic in type of powder sachet, gelatin capsules or suspension. Permutation of pre and probiotic has 0.48 billion spores of Lactobacillus bifidum, Streptococcus thermophilus. 0.10 billion spores of Saccharomyces boulardi along with 300 mg of fructo-oligosaccharides, is given once in a day before meals in the morning. No consensus exists regarding the minimum number of microorganisms that must be ingested to obtain a beneficial effect. Typically, a probiotic should contain several billion microorganisms to increase the likelihood of adequate gut colonization . A variety of studies have reported diverse values, $1\times10^{8-10}$, $1\times10^{9-10}$, $1\times10^{10-11}$. [40,41]

Future Strategies :

Genetically modified microbes bring a new dimension to the concept of probiotics. Their main thrush is on reducing the harmful properties of pathogenic strains naturally colonizing the oral cavity. The modified strain could then be used to replace the original pathogen. One ambitious and promising example is the generation of an S. mutans strain with a complete deletion of the open reading frame of lactate hydrogenase and thus significantly reduced cariogenicity.[42] Another option could be to enhance the properties of a potentially beneficial strain.

Therefore; the new probiotic products targeted for oral health purposes do not necessarily comprise the same species as products now in market. Potential future uses of probiotics include inflammatory disease control, the treatment, and prevention of allergies, cancer prevention, immune stimulation, and a reduction in respiratory disease. Such effects could justify the addition of not one but potentially several probiotics to commonly consumed foods, which could achieve population-wide health benefits. In field of oral immunology, probiotics are being used as passive local immunization vehicles against dental caries (C3). Bacteriophages, viruses that kill bacteria, have been detected in oral pathogens, such as Actinobacillus actinomycetemcomitans, and they may play a role in the pathogenicity. Subsequently, future studies should be conducted to investigate if phage therapy might be applied for oral and dental diseases in the same way as has been attempted for systemic infections. The selection of the best probiotic for oral health is also an issue that calls for further study [43].

Conclusion

The attention in oral probiotics has been increasing since the preceding decades. Probiotics on the other hand is an innovative and attention-grabbing field of research in medical and dental faculty. The bulk of studies have been conducted with probiotic strains initially suggested for gut health. A journalism reviews shows that probiotics use in associated to an improvement in oral health, which is mainly due to significantly reduced levels of cariogenic as well as periodontal pathogens. The perception casts innovative glow on the associations between diet and oral health.

They are almost certainly going to play an significant role in skirmishing troubles arising from do to excess of antibiotics and antimicrobial resistance. Milk, milk drinks, or yoghurt containing one or more probiotic strains could be a management option in the long-standing hindrance of infancy caries. Some of these technologies may be parenterally administered to treat critical infections and rising drug-resistant organisms.The invasion of studies expected in the upcoming years, will most likely make clear some of these issues.

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