

Probiotics in Dentistry – A Review

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Abstract

The development of resistance to a range of antibiotics by some important pathogens has raised the possibility of a return of humans to the pre-antibiotic dark ages. Time has come to shift the paradigm of treatment from specific bacteria elimination to altering bacterial ecology by probiotics. Probiotics are dietary supplements containing potentially beneficial bacteria or yeasts. They help in stimulating health promoting flora and also suppressing pathogens which cause and spread diseases. The aim of this review is to understand the mechanism of action of probiotic bacteria in the oral cavity and summarize observed effects of probiotics as well as their varied applications in the field of dentistry.

Keywords: Probiotics; Lactobacillus; Bifidobacterium

Introduction

The human gut contains 10 times more bacteria than cells elsewhere in human body. The enormous biomass consists of over 400 known bacterial species that generate intense metabolic activity and are of key importance for human health. This ecosystem gets disrupted when exposed to toxics in the form of polluted water and food as well as injudicious use of antibiotics [1-3]. Antibiotic resistance, with the emergence of multiple resistant strains, is an increasingly important global problem [4]. This causes destruction of beneficial bacteria leaving resistant ones, pathogenic. Of late it has been realized by health care professionals and prompted them to seek alternative therapeutic options. One such alternative is the use of beneficial bacteria, the probiotics, which stimulate health – promoting indigenous flora and reverting back the change [1,2,5].

Definition

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 [6]. 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.” Guarner et al. [4] 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 [2,3,5].

Prebiotics are non digestible food ingredients such as fructo-oligosaccharides (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 [1].

History

The idea of probiotics dates back to the first decade of 1900s when the Ukrainian bacteriologist and Nobel Laureate Metchnikof (1908) studying the flora of the human intestine developed a theory that senility in humans is caused by poisoning of body by the products of some of these 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 [6]. Lilley and Stillwell (1965) introduced the term probiotics. Mann and Spooring 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, Holcomb 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 [5,7,8].

Potential Mechanisms of Probiotic Effects in Oral Cavity

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 [9]. 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 [10,11].

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 [12] 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

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oral microbiota, in particular in adults [13]. 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. There are many possible mechanisms for how pathogen exclusion may take place. 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 [14].

Several pharmacologic/metabolic effects have been attributed to probiotics (Figure 1). 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 [15].

Species of Probiotics

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

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, powder and liquid forms. They enhance innate and acquired immunity as well as help in inhibition of pro-inflammatory mediators [4,5].

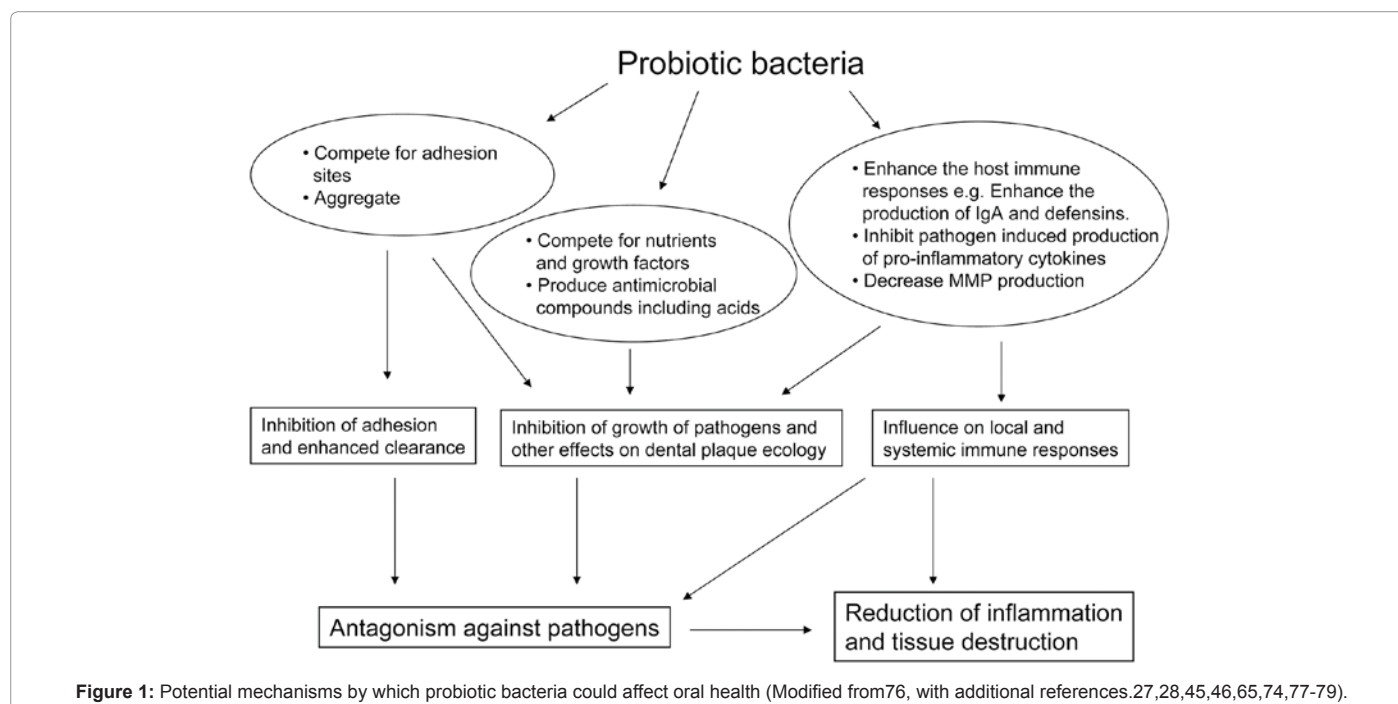
Bifidobacterium species are strictly anaerobic and predominate the large intestines. Over 30 species had been identified. The benefits from these include metabolization of lactose, generate lactic acid and synthesize vitamins. They also ferment indigestible carbohydrates and produce beneficial short chain fatty acids [16].

Streptococcus thermophilus and *lactobacillus bulgaricus* are primary cultures used in yogurt production. Most noted benefits are to metabolize lactose, improve lactose intolerance and antimicrobial activity [16].

Saccharomyces boulardii: It is a non colonizing lactic acid producing yeast. It prevents or treats antibiotic associated diarrhoea. It secretes proteases and other substances that breakdown bacterial enterotoxins and inhibits their binding to intestinal receptors. It also helps in immune function enhancement. It also enhances vitamin production and reduces serum-cholesterol level and in anticarcinogenic activity [16].

Properties of Probiotics

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

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 [17]. Several mutated strains of *S. mutans* that lack the machinery to efficiently metabolize 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 glucosyltransferase 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 [18].

Several studies suggest that consumption of products containing probiotic lactobacilli or bifidobacteria could reduce the number of mutans streptococci in saliva [19,20]. Using randomized controlled trials, Meurman and colleagues demonstrated that long term consumption of milk containing the probiotic *Lactobacillus rhamnosus* GG strain reduced initial caries in kindergarten children. Nase et al. [17], Caglar et al. [21] 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. [21].

In addition to the classical probiotic strains, other oral residents or genetically modified strains have also been tested for their ability to inhibit cariogenic microbes. Hillman and his colleagues introduced a non acid producing *S. mutans* strain that produces a bacteriocin active against other *S. mutans* strains into the oral cavity to replace the naturally occurring cariogenic strains [22].

Role of probiotics in periodontitis

Riccia and colleagues in 2007 studied the anti inflammatory effects of *Lactobacillus brevis* in a group of patients with chronic periodontitis. Anti-inflammatory effects of *L. brevis* could be attributed to its capacity to prevent the production of nitric oxide and consequently the release of PGE2 and activation of MMPs induced by nitric oxide [23].

The use of probiotic chewing gum containing *L. reuteri* ATCC55730 and ATCCPTA5289 also decreased levels of pro-inflammatory cytokines in GCF [24] and the use of *L. brevis* decreased MMP (collagenase) activity and other inflammatory markers in saliva [23].

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* [25] and thus can prevent halitosis.

Another species, *Streptococcus salivarius* is detected most frequently among people without halitosis and is therefore considered a commensal bacterium of the oral cavity. *S. salivarius* is known to produce bacteriocins, which contribute in reducing the number of bacteria that produce Volatile sulphur compounds (VSC). The use of gum or lozenges containing *S. salivarius* K12 reduce levels of VSC among diagnosed with halitosis [26].

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 [27] 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 [28]. White spot lesion formation can be seen as an imbalance as an imbalance between mineral loss and mineral gain and recent systematic reviews have examined methods to prevent this side effect of orthodontic treatment [29]. Cildir et al. [30] 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 [30].

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 [3,16].

Role of probiotics in infections and oral diseases

Only two studies have investigated the effects of probiotic bacteria on oral candida infection in humans [19,31]. 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 [19].

In a shorter study with younger subjects, no significant difference was observed between effects of probiotic and those of control cheese on salivary candida counts [20].

Recently it has been postulated that the probiotic bacteria may slow down AIDS progression. Lin Tay and his colleagues screened hundreds of bacteria taken from 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 [32].

Delivery mechanisms of probiotics

Advances in biomedical engineering will prove to be equally important to molecular biology in terms of the developing systems that deliver bacteria and / or nutritional factors to the host. These will include encapsulating probiotics, such that they rehydrate at specific sites, and encasing prebiotics in nano-aggregates that protect against stomach acid and deliver their payload when the pH reaches 7.4. Potentially, such nano encapsulation will also allow delivery in foods such as biscuits, whereas targeted, water protected macrocapsules containing probiotic organisms may prove useful in animal food pellets and perhaps in liquids, which currently cannot be used because of problems with shelf stability. At the macromolecular level, it will soon be possible to coat capsules with biosensors that detect the optimal conditions for the release of probiotic contents [33].

In summary, molecular, nano, biochemical, microbiological and engineering sciences hold the key to future advances in the clinical applications of probiotic and prebiotic products.

Conclusion

Probiotics play an important role in combating issues with overuse of antibiotics and antimicrobial resistance. Today's new technological era would be the right time to change the way bacteria are treated. Further studies to understand the ability of probiotic bacteria to survive, grow, and have a therapeutic effect when used for treatment or when added to foods, to fix the doses and schedules of administration of probiotics. Hence, systematic studies and randomized controlled trials are needed to find out the best probiotic strains and means of their administration in different oral health conditions. With fast evolving technology and integration of biophysics with molecular biology, designer probiotics poses huge opportunity to treat diseases in a natural and non invasive way.

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