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PROBIOTICS AND PERIODONTAL HEALTH

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ABSTRACT

The interest in probiotics and the modulation of the microbiota for restoring and maintaining health have gained a lot of attention over the past decade. Researchers have been keenly investigating the beneficial effects of probiotics on human health and focusing upon the different mechanisms, such as their ability to compete with pathogenic micro organism for adhesion, to antagonize the pathogens, or to modulate the host's immune response. This has led to a widespread use of probiotics in the management of systemic infections and disease. In the field of periodontics, probiotics have come up as an attractive alternative to antibiotics. They target particular periodontal pathogens, thus increasing the long-term success of periodontal therapy. This review evidence the use of various probiotic strains in periodontal diseases.

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INTRODUCTION

The TERM PROBIOTICS derived from the Greek word, meaning "for life." Endorsed by the Food and Agriculture Organization and the World Health Organization, the definition of probiotics, in 2001, describes them as live micro-organisms, which when administered in adequate amounts confer health benefits on the host (Nympha Pandit, Inder kumar Pandit, Deepika Bali 2013). According to the currently adopted definition by FAO/WHO (The Food Agricultural Organization/World Health Organization), "probiotics are living organisms, principally bacteria that are safe for human consumption and when ingested in sufficient quantities, have beneficial effects on human health, beyond the basic nutrition". (Deepa Shetty, Shreya Hegde 2016) Such non-pathogenic organisms (yeasts or bacteria, particularly lactic acid bacteria) are present in food, and can have a favourable impact on host health. Probiotics have been used for decades in fermented products, but potential use of probiotics as a nutritional medical therapy has not been formally acknowledged.

Micro organisms (pathogens) are capable of causing disease, but there are some that actually are beneficial to human. The first probiotic species to be introduced was 'lactobacillus acidophilus' by Hull et al in 1984, followed by 'bifidobacterium bifidium' by Holcomb et al in 1991.

Given the widespread emergence of bacterial resistance to antibiotics, the concept of probiotic therapy has been considered for application in oral health. The interest in probiotics and the modulation of microbiota for restoring and maintaining health have gained a lot of attention in past decade, and since then probiotics are been deliberately added to the commercially available products owing to their beneficial effects on human health.

The presence of periodontal pathogens could be regulated by means of antagonistic interactions. A decrease in gum bleeding and reduced gingivitis has been observed by Krasse et al with the application of L. reuteri. Koll-Klais et al reported that resident lactobacilli flora inhibits the growth of *Porphyromonas gingivalis* and *Prevotella intermedia* in 82% and 65%, respectively. (Dr. Sumit Narang, Dr. Ruby Gupta, Dr. Anu Narang 2011)

Probiotics can improve patient condition in medical disorders such as diarrhea, gastroenteritis, short-bowel syndrome, and inflammatory intestinal diseases (Crohn's disease and ulcerative colitis), cancer, immunodepressive states, inadequate lactase digestion, pediatric allergies, growth retardation, hyperlipidemia, liver diseases, infections with *Helicobacter pylori*, genitourinary tract infections, and others. (Nympha Pandit, Deepika Bali 2013)

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Probiotics Guidelines

To be considered for use as probiotic following criteria needs to be fulfilled.

1. It should capable of exerting a beneficial effect on the host animal, e.g. increased growth or resistance to disease.
2. It should be of human origin.
3. It should have high cell viability.
4. It should be non-pathogenic and non-toxic.
5. It should be able to interact or to send signals to immune cells.
6. It should have capacity to influence local metabolic activity
7. It should be capable of surviving and metabolising in the gut environment e.g. resistance to low pH and organic acids.
8. It should be stable and capable of being viable for longer duration under storage and field conditions.

Safety of Probiotics

Properly prepared and tested probiotic strains are, for the most part, extremely safe for human oral and extra oral use. New strains and products wishing to be designated as probiotics should be proven in human studies to be safe. Clear labelling is recommended when a strain has some limitations in its use, such as for patients with a leaky gut or at risk of blood borne infection. Eg. *S.bouraldii* (*S. cerevisiae*)

Probiotics in Systemic Health

Probiotics have proven to be effective in the treatment of several systemic and infectious diseases, such as Crohn’s disease, cancer, hyperlipidemia, immunodepressive states, acute diarrhea, inadequate lactase dilation, liver diseases, infection with *Helicobacter pylori* and genitourinary tract infections. (Deepa Shetty, Shreya Hegde 2016)

Probiotics in Oral Health

Periodontal diseases, dental caries and halitosis are major areas of concern in dentistry. An essential requirement for a microorganism to be an oral probiotic’ is its ability to adhere to and colonize surfaces in the oral cavity. Microorganisms generally considered as probiotics may not have oral cavity as their inherent habitat and, subsequently, their possibility to confer benefit on oral

health is then questionable. Studies suggest that lactobacilli as members of resident oral microflora could play an important role in the micro-ecological balance in the oral cavity. The studies further demonstrated that lactobacilli strains with probiotic properties may indeed be found. Yet there is no evidence whether these lactobacilli strains were detected due to the frequent consumption of dairy products leading to temporary colonization only, or if the oral environment is their permanent habitat.

Probiotics in Dental Caries

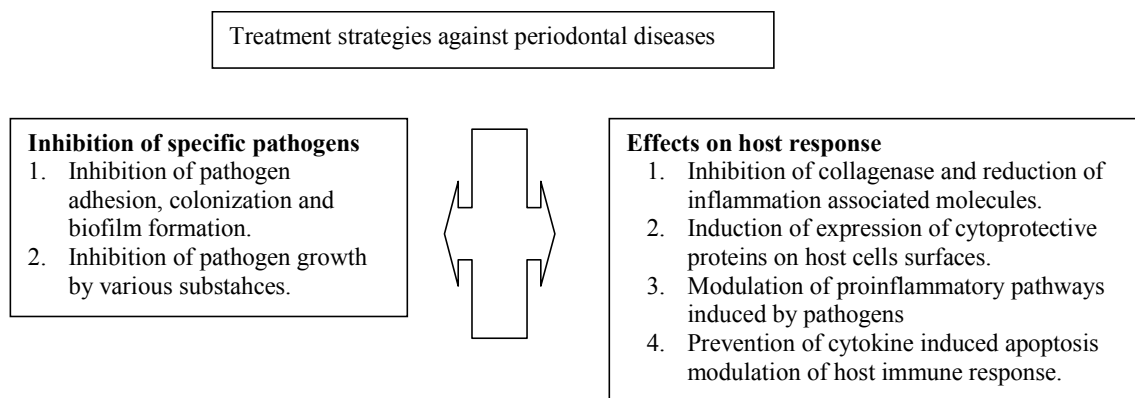
Dental caries is a disease where bacterial process effect damage hard tissue structure of the tooth, characterized by demineralization of the tooth enamel. This leads to the formation of cavities on the surface of the tooth. It is well recognised that *Streptococcus mutans* is the most destructive bacterial strain in the mouth as it attaches easily to teeth and produces acid. A statistically significant reduction of *S. mutans* was recorded in individuals that consumed probiotic yogurt.

Probiotics and Periodontal Disease

Periodontal diseases are classified into two major types- gingivitis and periodontitis. Gingivitis is characterized by inflammation of gingiva, whereas periodontitis is a progressive, destructive disease that affects all supporting tissues of teeth, including the alveolar bone. The main pathogenic agents associated with periodontitis are *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter* (formerly *Actinomyces*) *actinomycetemcomitans*. These bacteria have a variety of virulent characteristics allowing them to colonize the subgingival sites, escape the host defense system and cause tissue damage. (Sandeep Lawande 2012)

Mechanisms of action of Probiotics

Probiotics can help prevent and treat disease through several mechanisms including direct interaction, competitive exclusion and modulation of host immune response. The treatment strategies conferred by probiotics against periodontal diseases are mainly anticipated to be either by inhibition of specific pathogens or by altering the host immune response through the following multiple factors:



Flow chart 1 Theoretical possibilities for probiotics to affect periodontal health

Inhibition of specific organisms

Inhibition of pathogen adhesion, colonization and biofilm formation Inhibition of pathogen growth by various substances such as organic acids, hydrogen peroxide and bacteriocins against oral pathogens.

Effects on host response

Inhibition of collagenases and reduction of inflammation associated molecules Induction of expression of cytoprotective proteins on host cell surfaces Modulation of pro-inflammatory pathways induced by pathogens Prevention of cytokine-induced apoptosis Modulation of host immune response

For micro organisms to exert their probiotic action in the oral cavity, they have to:

- Resist oral environment conditions and defence mechanism.
- Adhere to saliva coating surfaces.
- Colonize and grow in mouth.
- Inhibit oral pathogens.
- Be safe for host.

The primary etiological factor for the development of periodontal diseases are bacteria in supra and sub gingival biofilm, probiotics lower the pH so that plaque bacteria cannot form plaque and calculus that forms the periodontal diseases. They make an excellent maintenance product because they produce antioxidants. Anti oxidants prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation.

Shimauchi et al reported significant decrease in plaque index and pocket depth in smokers after the oral administration of a tablet containing *Lactobacillus Salivarius* and also observed marked reduction in salivary lactoferin at the end of an 8 week trial. *Grudianav et al* also carried out a clinical study using a probiotic mix of *Acilact* and *Bifidumbacterin* in tablet forms and found that there was normalization of micro flora and reduction in signs of gingivitis and periodontitis.

Krasse et al assess the effect of probiotic *L. Reuteri* against gingivitis, which was incorporated into chewing gum, and it was noticed after 14 days of ingestion that moderate to severe forms of gingivitis had been colonized by *L. Reuteri*, and the plaque index had reduced. Shimazaki and colleagues, in an epidemiological study found that individuals, particularly nonsmokers, who regularly consumed *yoghurt* or beverages containing *lactic acid* exhibited lower probing depths and less loss of clinical attachment than individuals who consumed few of these dairy products. A similar effect was however not observed with milk or cheese.

Twetman et al used *L. reuteri* containing chewing gum in 42 healthy patients and assessed its effects on crevicular fluid volume, cytokine (interleukin-1 β , interleukin-6, interleukin-10, and TNF- α) levels, and bleeding on probing. Crevicular fluid volume, as well as TNF- α and interleukin-8 levels, and bleeding were significantly reduced.

Effects of Probiotics in Halitosis

Halitosis or oral malodour is the unpleasant odour volatile sulphur compounds (VSC) emanating from the oral cavity. The bacteria responsible for oral malodour are *Fusobacterium*

nucleatum, *Porphyromonas gingivali*, *Prevotella intermedia* and *Treponema denticola*.

Kang et al reported that a probiotic strain *Weissella cibaria* inhibited VSC production in both invitro and invivo conditions most probably due to its ability to co-aggregate with VSC producing species like *F. nucleatum*, thus reducing the source of malodorous compounds in the oral cavity and also by producing hydrogen peroxide which inhibits *F. nucleatum*. *Burton et al* showed that lozenges and gum containing *S. salivarius* decrease VSC by producing bacteriocins, which inhibit bacteria producing VSC.

Kazor et al reported that *L.salivarius* was the most predominant species detected in healthy subjects, whereas it was detected in only one of the subjects with halitosis at very low levels.

Probiotic Products

Probiotics in the form of chewing gums, lozenges, tablets or tooth pastes are available.

Gum PerioBalance (marketed by Sunstar, Etoy, Switzerland)

This is probably the first probiotic specifically formulated to fight periodontal disease. It contains a patented combination of two strains of *L.reuteri* specially selected for their synergistic properties in fighting cariogenic bacteria and periodontopathogens. Each dose of lozenge contains at least 2×10^8 living cells of *L. reuteri* Prodentis. Users are advised to use a lozenge every day, either after a meal or in the evening after brushing their teeth, to allow the probiotics to spread throughout the oral cavity and attach to the various dental surfaces.

PeriBiotic

This toothpaste is an all-natural, fluoride-free oral hygiene supplement containing Dental-Lac, a functional *Lactobacillus paracasei* probiotics not found in any other toothpaste.

Bifidumbacterin, Acilact, Vitanar (marketed by Alfarm Ltd., Moscow, Russia)

This probiotics preparation of a complex of five live LYOPHILIZED LACTIC ACID bacteria, is claimed to improve both clinical and microbiologic parameters in gingivitis and mild periodontitis patients. After routine mechanical debridement, 2 tablets to be dissolved in the mouth, three times a day for 20-30 days for improved outcome.

Wakamate D (Wakamoto Pharmaceutical Co., Tokyo, Japan)

This probiotic tablet contains 6.5×10^8 colony forming units (CFU) per tablet of *Lactobacillus salivarius* WB21 and xylitol (280 mg/ tablet) was originally prepared to contribute for the intestinal microbial balance by providing acid tolerant *L. salivarius* WB21.

Prodentis (BioGaia, Stockholm, Sweden)

This probiotic lozenge is a blend of two *Lactobacillus reuteri* strains containing a minimum of 1×10^8 colony forming units (CFU) for each of the strains DSM 17938 and ATCC PTA 5289

Yakult

Staab *et al* showed that the probiotic L.casei strain Shirota was associated with reduction in elastase activity and matrix metalloproteinases-3 (MMP3)

CONCLUSION

Recent advances in technology have led to a constant drive to develop novel strategies for the treatment of periodontal diseases. The probiotics concept essentially entails the introduction of specific viable microbial species in order to confer health benefits upon a host by functioning via different mechanisms. The literature review shows that use of oral probiotics is associated with improvement in periodontal health. However, the effects of probiotics on periodontal health and its maintenance including means of administration, dosage and safety aspects are not clear. Numerous randomized clinical studies will be required to clearly establish the potential of probiotics in the prevention and treatment of periodontal diseases. There is no doubt that with further significant progress, probiotics may have an important role to play in the near future within the periodontal arena.

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