



REVIEW ARTICLE

THE POSSIBLE ROLE OF PROBIOTICS IN PERIODONTAL DISEASE: A SHORT REVIEW

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ABSTRACT

In recent times, probiotics have been brought to notice, by a lot of researchers. The paradigm has now been shifted from the elimination of specific bacteria's to altering the bacterial ecology of the oral cavity, all of which can be achieved by probiotics. Live micro-organisms which are resident flora of the oral cavity act as probiotics in the treatment of periodontal diseases and even beneficial for extra-oral/general health. Hence the incorporation of probiotics in the daily diet may significantly aid in reducing or delaying periodontal disease initiation/progression.

Key words:

Probiotics, Periodontal disease, Inflammation.

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INTRODUCTION

Inflammation is known as the human body's biological response to harmful pathogens and irritants and is the first line of the immune system's defence mechanism against the pathogens that have breached the continuity of the oral mucosal membrane (Serov, 1983). Chemicals released by the damaged tissue cells induce the swelling, while immune cells such as the dendritic cells, macrophages, histiocytes, Kupffer cells initiate inflammation (Serov, 1983). Just as rheumatoid arthritis, atherosclerosis, hay fever etc are inflammatory infections of the human body, similarly periodontitis is the inflammatory infection of the oral cavity (Mosteller, 1950). Our body is well equipped to combat the surplus existence of micro-organisms in our oral cavity (Mosteller, 1950). It is a fact that our oral cavity dwells within multifarious microbes some of which are beneficial to the host and the rest deleterious (Khavkin et al., 2015). Yet, even though our body has a layered defense system to protect the body from the minutest of the microbes, there are several possibilities for the microbes to breach the membranes, beginning from the physical barrier that prevents the entry of bacteria's and viruses, on failure of which body's innate immune system gets involved (Weir and Blackwell, 1983). However, unlike the adaptive immune system, the innate immunity does not offer long term immunity.

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Innate immunity performs fundamental functions such as recruiting immune cells to the site of infection through cytokines, identification of pathogens and foreign bodies, promotes clearance of dead cells and antibodies also helps in activating adaptive immunity (Hirsch, 1959). Adaptive immunity superintend actions of specific pathogens after which immunological memories are created to enhance the responses of subsequent responses of the same pathogen (Hirsch, 1959). Despite the multi-layered defence mechanism, microbes do enter the human body and cause inflammatory infections (Hirsch, 1959). Periodontitis has been a pressing dental issue for generations and it always boils down to the same old treatment modality of either treating it surgically or with antibiotics. However antibiotic resistance is threatening our ability to treat these bacterial infections. Instead, what if we could alter the bacterial ecology of the oral cavity all together to confer with the human health? This necessitates the development of novel and effective therapeutic strategies, adjunctive to clinical periodontal treatment. One of the greatest challenges encountered in the treatment of periodontitis, is the ability to suppress inflammation as well as regenerate lost bone

Mode of action of probiotics

Probiotics as we know are "live micro-organisms which when administered in adequate amounts confer a health benefit on the host" (Laleman and Teughels, 2015). Probiotics are useful in altering, halting or delaying diseases of the periodontium (Laleman and Teughels, 2015). They have recently only been

employed in the treatment of halitosis, since it assists with plaque modification as well as attachment loss and pocket depth that can be modified (Laleman and Teughels, 2015). Probiotics help in modulating the host immunity both systemically and locally (Laleman and Teughels, 2015). Studies have reported the presence of oral lymphoid foci in the interdental papillae that act as sites for immune modulation. Probiotics sensitize antigen presenting dendritic cells which results in expression of T-helper cells 1 and T-helper cells 2 (Dugas et al., 1999; West et al., 2009). These live microorganisms help to amplify the body's innate immunity. Th 1 response causes phagocytosis of intracellular pathogens whereas Th 2 response causes engulfment of extracellular pathogens (Dugas et al., 1999). A salient point to remember is that probiotics mimic pathogenic response except the deleterious effects on the periodontium. Certain other mechanisms such as the one with *Lactobacillus Casei* causes change in the composition of the salivary pellicle which prevents the bacteria within in the oral cavity from binding to it (Kobayashi et al., 2017). Another such principal mechanism is that of aggregation alteration where in several bacteria's co-aggregate to inhibit commensals. Hetrofermentative *Lactobacillus* acts as an inhibitor for *Aggregatibacter Actinomycetem Comitans*, *P. Gingivalis* and *Prevotella Intemedia*. *F. Nucleatum* aggregates with *Weissella Criberia* and *L. Rhamnosus* with *Fusobacterium Nucleatum*. Studies have shown that *Weissella Cibaria* produce an essential amount of hydrogen peroxide which help inhibit multiplication of *Fusobacterium Nucleatum* (Kang et al., 2005). These probiotic aggregations have reported to cause apoptosis of tumor cells and inhibit apoptosis of mucosal cells and mucous membrane. *Lactobacillus Reutri* secrete bacteriocins which aid in inhibition of proliferated pathogens and have anti-inflammatory effect by suppressing pro-inflammatory mediators. These are some of the applications presenting the use of probiotics for general health.

### The role of probiotics in periodontal disease

Shifting our focus onto the area of our concern, Probiotics have demonstrated an important role in treating periodontal diseases. The presence of *Streptococcus Oralis* and *Streptococcus Uberis* indicate healthy periodontium owing to contribution in inhibiting the growth of periopathogens such as *P. Gingivalis*, *T. Denticola*, *T. Forsythus* and *A. Actinomycetes* (Conrads et al., 2017). Probiotics can be administered via different modes. Various studies have been conducted where probiotics are administered either as mouth rinses that would help in considerably reducing plaque and adherent biofilms, incorporated in chewing gums which along with root planning help in reducing periodontitis as performed earlier and also as tablets (Allaker and Douglas, 2009; Laleman and Teughels, 2015). Various studies have been conducted on pigs and dogs where artificially created pockets, in which *S. Sanguis KTH-4*, *S. Salivarius TOVE* and *S. Mitis BMS* were locally applied only to see a considerable decrease of anaerobic bacteria and their reduced recolonization along with less bleeding on probing (Stamatova and Meurman, 2009; Yanine et al., 2013; Zambori et al., 2016). Krasse et al (Krasse et al., 2006) carried out a study to evaluate the effectiveness of *Lactobacillus Reutri* as a probiotic (incorporated in chewing gums). A randomized, double-blind, placebo controlled study was carried out comprising of 59 patients suffering from moderate to severe gingivitis. These patients were asked to chew this gum twice a day for 2 weeks at a concentration of  $1 \times 10^8$  CFU (colony

forming unit) accompanied by regular scaling and root planning. Clinical parameters were examined and reviewed after 2 weeks. Significant improvement was noticed in patients consuming probiotic incorporated chewing gum. An experimental placebo-controlled study was implemented on 72 subjects, where they were asked to rinse twice in the morning with 15 ml of rinse containing *Weissella Cibaria CMS-1* (Kang et al., 2006). Rinsing was then repeated in the afternoon and evening. Around 20% reduction in plaque score was noticed, implying that this probiotic possess the ability to inhibit production of biofilms. An in-vitro study carried out by Nara et al proposes the role of probiotics in promoting bone formation hence useful in repairing periodontal bone destruction. *Lactobacillus Helveticusdemon* strated the release of peptides which stimulate osteoblasts. Another study which was carried out, incorporated *Lactobacillus Salivaris T1 2711* into tablets (Matsuoka, 2006). Around 84 subjects were asked to consume this tablet 5 times a day for at least 8 weeks. These subjects showed a decrease in pigmented anerobic rods and *P. Gingivalis* count also decrease in bleeding on probing. Sunstar (Etoy, Switzerland) recently began marketing the first probiotic specifically formulated to fight periodontal disease. Gum Perio Balance contains a patented combination of 2 strains of *L. reuteri* specially selected for their synergetic properties in fighting cariogenic bacteria and periodontopathogens. Each dose of lozenge contains at least  $2 \times 10^8$  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. Additional studies are required to evaluate the long-term effects of using these products.

### Summary

Probiotics unlike antibiotics are free from the issue of developing resistance because they are the resident flora of body's own oral cavity. With advances in biotechnology, probiotics can be designed in a way it can treat diseases naturally. Periodontitis has been reported to cause many systemic diseases hence maintaining our periodontal health is of utmost importance. Probiotics can be labelled as a safe and natural solution to this dilemma. These micro-organisms used as probiotics sure help in combating periodontal problems however they have a limited effect and hence needs more randomized trials to be performed to increase the surety of these friendly bacteria's. Therefore, probiotics might not only suppress the emergence of endogenous pathogens or prevent the super infection with exogenous pathogens but also they might also protect us through the promotion of a beneficial host response as well as increase bone formation. However, despite the large number of clinical studies that demonstrate significantly positive effects on the diseased periodontium, there is a current need for in vitro studies in order to understand the underlying mechanism before the concept of probiotics, as an adjunct to periodontal care, can be widely adopted.

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