

## Probiotics and periodontal health

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**Abstract:** In recent years there is an increase in the studies related to the use of probiotics for oral diseases. It has been effectively used for the control of dental caries but its use in the treatment of periodontal disease is still under study. This article aims at understanding how probiotics work and its application in the field of periodontology.

**Key Words:** probiotics, periodontitis, gingivitis,

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### I. Introduction

Periodontitis is one of the most common diseases seen among the population today. The etiology of this disease is a well established fact. A number of pathogenic bacteria have been associated with this disease. The treatment modality for periodontitis is aimed mainly at eliminating the entire microflora irrespective of their pathogenicity. But there is now an emergence of researches and studies to prove the effectiveness of probiotics in restoring periodontal health.

Probiotics are defined by the World Health Organization<sup>1</sup> as living microorganisms which, when administered in adequate amounts, confer a health benefit on the host. The use of probiotics is rapidly gaining momentum and there is now increasing evidence that the usage of probiotics may have oral health benefits. The concept of beneficial-for-health microorganisms dates back to the ideas of Nobel Prize laureate Ilya Metchnikov in the early years of the 20<sup>th</sup> century.<sup>2</sup> He laid down the scientific foundations of probiotics.<sup>2</sup>

### II. Periodontitis

The current view on plaque related periodontitis is<sup>3</sup>

- a susceptible host
- the presence of pathogenic species
- the reduction or absence of the so called beneficial bacteria.

Mechanical subgingival debridement in combination with improved oral hygiene, shifts the subgingival flora to a less pathogenic composition which is only temporary as re-colonization occurs within 1-2 weeks.<sup>3</sup> Therefore the focus is now being aimed at the third etiological factor, the reduction or absence of beneficial bacteria. This can be brought about with the help of probiotics. Probiotics not only suppress the emergence of endogenous pathogens or prevent the super infection with exogenous pathogens, they might also protect us through the promotion of a beneficial host response.<sup>3</sup>

### III. Mechanism of action of probiotics

Probiotics used in the oral cavity must be able to adhere to oral surfaces to produce a prolonged effect of the probiotics.<sup>5</sup> They must colonize periodontal tissue and be a part of the biofilm.<sup>7</sup> The effect of probiotics come mainly from three modes of action.<sup>6</sup>

1. Modulation of host immune response- they interact and strengthen the immune system to combat periodontal disease.
2. Direct interaction- probiotics interact directly with the disease causing microbes and produce antimicrobials<sup>7</sup> against periodontal pathogens
3. Competitive exclusion- beneficial microbes directly compete with the pathogenic microbes for nutrition or adhesion sites.

#### Immune modulation

Probiotics are known to modulate the host immune response.<sup>5</sup> They can act on a wide variety of cells and produce anti inflammatory action.<sup>7</sup> Increased phagocytic capacity of macrophages when challenged with probiotics has been reported ( Perdigon et al.2002) the expression of phagocytic receptors in the neutrophils in healthy individuals are seen( Pelto et al 1998) it also enhances natural killer cell activity ( Takeda et al 2006). Dendritic cells scattered in the mucosal surfaces of lymphatic tissues in the oral cavity are pivotal in the front line bacterial recognition and in activating T-cell responses.<sup>5</sup> Probiotics enhances innate immunity and modulate pathogen induced inflammation through “toll-like receptors” on the dendritic cells.<sup>4</sup> Intracellular pathogens are phagocytosed by T-helper 1 response and the extracellular pathogens are taken care by T-helper 2 response.<sup>4</sup>

Della Riccia et al (2007) tested in vivo the immunomodulatory effects of *Lactobacillus brevis* on periodontal disease which resulted in a significant decrease in the inflammatory markers in the saliva like metalloproteinase and nitric oxide synthase activity, prostaglandin E2 and interferon gamma levels.<sup>7</sup>

#### Direct interaction

Probiotics can produce a wide range of compounds with antimicrobial activity<sup>7</sup> such as lactic acid, hydrogen peroxide, bacteriocins and bacteriocin like inhibitory substances (Gillor et al 2008, Gordon 2009, Oelschlaeger 2010).

#### Competitive exclusion

Gause's law<sup>7</sup> states that two species that compete for the same resources cannot stably co-exist. One of the two will always have an advantage over the other eventually leading to the extinction of the second competitor or a shift of this species to another niche. It either blocks the adhesion of pathogenic bacteria or they compete for the same nutrition.

It has been shown that streptococci strains can hinder colonization of periodontopathogens to hard and soft tissues in vitro (Teughels et al 2007, Sliepen et al 2008, Van Hoogmoed et al 2008, Sliepen et al 2009). Probiotics may also produce biosurfactants that prevent adhesion (Van Hoogmoed et al 2000). Haukioja et al 2008 showed that certain strains modify the salivary pellicle composition by removing an adhesion protein (agglutinin gp340) to decrease colonization.

Elli et al 2000 has shown that bacteria can compete for essential nutrients or chemicals required for growth thus inhibiting pathogen growth.

Certain *Lactobacillus* species like *L. casei*, *L. rhamnosus*, *L. bulgaricus* and *L. acidophilus* co-aggregate with *Fusobacterium nucleatum* and prevent its binding with other bacteria. It might thus affect the formation of oral biofilms and modify resident microflora.<sup>5</sup>

They are also known to stimulate apoptosis<sup>4</sup> of tumour cells through end product formation. It also inhibits apoptosis of mucosal cells. Probiotic mixture has been reported to protect epithelium barrier by maintaining tight junction protein expression and preventing apoptosis of mucous membrane.<sup>4</sup> Probiotics also decrease the pro inflammatory cytokines.<sup>4</sup>

Probiotics lower the pH so that plaque bacteria cannot form dental plaque and calculus that cause periodontal disease.<sup>6</sup> They produce antioxidants which prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation.<sup>6</sup>

### **IV. Probiotics for periodontal health**

Probiotics are mainly categorised into two genus *Lactobacillus* and *Bifidobacterium*. Various studies were done to prove the effectiveness of probiotics in the maintenance of periodontal health.

#### Gingivitis

Grudianov et al<sup>8</sup> studied the effects of probiotics tablets on gingivitis and different grades of periodontitis and has concluded that probiotics treatment resulted in better microbiota normalization than the control group. A study by Krasse et al<sup>10</sup> showed that patients with moderate and severe gingivitis when given *L.reuteri* formulations had reduced plaque and gingivitis scores than the placebo group.

#### Periodontitis

Koll-Klaise et al<sup>9</sup> reported the ability of lactobacilli to inhibit the growth of *P.gingivalis*, *P. intermedia* and *A. actinomycetemcomitans*.

Vivekanda et al<sup>11</sup> also confirmed the plaque inhibitory, anti inflammatory and anti microbial effects of *L.reuteri*. Riccia<sup>12</sup> and colleagues studied the anti inflammatory effects of *L.brevis* and observed a reduction in salivary levels of prostaglandin E2 and matrix metalloproteinases. Probiotic strains included in periodontal dressings at optimal concentration were shown to reduce the number of most commonly isolated periodontal pathogens: *Bacteroides* sp., *Actinomyces* sp. and *S. intermedius* and also *C. albicans*.<sup>13</sup>

The oral administration of a tablet containing *L. salivarius* WB21 was able to decrease the plaque index and the pocket probing depth significantly, in subjects who were smokers.<sup>14</sup> Another finding in this clinical trial was the ability of *L. salivarius* WB21 to successfully bring down the prevalence of periodontal pathogens.

*L. acidophilus* contained in a tablet named Acilact was first clinically tested by Pozharitskaia et al in 1994<sup>15</sup> and they found improved clinical parameters in periodontitis patients and shifts in local microflora towards gram positive cocci and lactobacilli.

### V. Administration of probiotics

The different vehicles used to administer probiotics are<sup>16</sup>

1. Lozenge
2. Straw, tablet
3. Cheese
4. Rinse solution
5. Capsule, liquid
6. Yogurt drink

### VI. Commercially available Probiotics for periodontal disease management

Few products containing probiotics (such as tablets, lozenges, chewing gums or tooth pastes) are currently 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  $2 \times 10^8$  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.<sup>17</sup>

PeriBiotic (Designs for Health, Inc.)

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.<sup>17</sup>  
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.<sup>8</sup>

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

This probiotic tablet contains  $6.5 \times 10^8$  colony forming units (CFU) per tablet of *Lactobacillus salivarius* WB21 and xylitol (280 mg/ tablet). It was originally prepared to contribute for the intestinal microbial balance by providing acid tolerant *L. salivarius* WB21.<sup>14</sup>

Prodentis(BioGaia, Stockholm, Sweden)

This probiotic lozenge is a blend of two *Lactobacillus reuteri* strains containing a minimum of  $1 \times 10^8$  colony forming units (CFU)<sup>11</sup>

The following table shows us the effect of different probiotics purely against periodontal disease<sup>1</sup>

Probiotics	Means of administration	Effect	Reference
<i>L. casei</i> 37	Periodontal dressing	Reduction of periopathogens and extension of remission period	Volozhin et al. 2004 <sup>13</sup>
Probiotic mix	Tablets Acilact and Bifidumbacterin	Normalization of microflora and reduction of signs of gingivitis and periodontitis	Grudianov et al. 2002 <sup>8</sup>
<i>L. acidophilus</i>	Tablet Acilact	Improved clinical parameters in periodontitis patients and shift in local microflora towards gram-positive cocci and lactobacilli	Pozharitskaia et al. 1994 <sup>15</sup>
<i>L. reuteri</i>	Study-tailored formula	Reduction of gingivitis and plaque in patients with gingivitis	Krasse et al. 2006 <sup>10</sup>
<i>S. sanguinis</i> , <i>S. salivarius</i> , <i>S. mitis</i>	Application of streptococci after root planing	Delay in subgingival recolonization by periopathogens, Inhibitory effect on <i>A. actinomycetemcomitans</i> recovery and colonization	Teughels et al. 2007 <sup>18</sup>
<i>L. brevis</i>	<i>L. brevis</i> -containing lozenge	Amelioration of periodontitis associated symptoms and signs	Riccia et al. 2007 <sup>12</sup>
<i>L. salivarius</i> WB21	Tablet taken three times daily	Improvement of clinical signs of periodontal disease in smoker and non-smoker patients	Shimauchi et al. <sup>14</sup>

### Safety concerns

The issue of safety is of special concern during the past few years due to the increased probiotics supplementation of different food products. Criteria of an ideal microorganism used as a probiotic<sup>4</sup>

- High cell viability, resistant to low pH and acids
- Ability to persist
- Adhesion to cancel the flushing effect

- Able to interact or to send signals to immune cells
- Should be of human origin
- Should not be pathogenic
- Resistance to processing
- Must have capacity to influence local metabolic activity

### Designer Probiotics

Designer probiotics are a part of Patho-Biotechnology. It involves assigning genetic elements to probiotics bacteria, which are necessary to overcome stress outside and inside the host and antagonise invading pathogens. This approach employs probiotics to be engineered to express receptor mimic structures on their surface. The stress tolerance of the probiotics cultures are increased which causes improved tolerance to processing stress and prolongs survival during subsequent storage.<sup>4</sup> Thus a larger proportion of administered probiotics would reach the desired location in a bioactive form.<sup>4</sup>

### Uses of probiotics

- As dietary supplements and are able to exert a beneficial effect without permanently colonizing the site.<sup>4</sup>
- Rarely dramatic and long term microbiological change.<sup>4</sup>
- Exerts beneficial effects by influencing the immune system.<sup>4</sup>

## VII. Conclusion

Probiotic use refers to the basic idea of replacing pathogenic bacteria by supplementing commensalisms, which have the same affinity for tooth surface adherence. They are the body's own resident microflora and hence are more easily adapted to the host.<sup>4</sup> With technology developing quickly, designer probiotics poses a huge opportunity to treat diseases. Probiotics are a promising, safe and natural option<sup>4</sup> and there is a need for further exploration in depth for periodontal application.

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