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# Oral Probiotics on the Horizon: A Review

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For the past few decades, bacteria known as probiotics have been added to food because of their beneficial effects on human health. Probiotics are a part of our daily food consumed as fermented foods with specially added active live cultures; such as in yogurt or as dietary supplements. Probiotics act by competing with pathogenic microorganisms for adhesion sites, antagonising these pathogens or by modulating the host's immune response. The potential application of probiotics for oral health has gradually garnered the attention of several teams of researchers. Although only a few clinical studies have been conducted so far, the results to date suggest that probiotics could be useful in the prevention and treatment of oral infections, including dental caries, periodontal disease and halitosis. This article briefly summarises the currently available data on the potential benefits of probiotics for oral health.

**KEYWORDS:** Dental Caries, Halitosis, Oral Health, Periodontal Disease, Probiotics

## INTRODUCTION

The term Probiotics was derived from the Greek word which means 'for life'. The concept of probiotics dates back to 1908, when the Nobel Prize winner, Ukrainian bacteriologist Ilya Metchnikoff suggested that the long life of Bulgarian peasants resulted from their consumption of fermented milk products. The term "probiotic" was first used in 1965, by Lilly and Stillwell for describing substances secreted by one organism which stimulates the growth of another. The knowledge that the intestinal flora can protect humans against infection and that their disturbance can increase susceptibility to infection forms the crude basis for the belief in the beneficial effects of probiotics. The bacteria present in yogurt and fermented milk products comprise the most important source of probiotics for humans. The vast majority of probiotic bacteria belong to the genera *Lactobacillus*, *Bifidobacterium*, *Propionibacterium* and *Streptococcus*.<sup>1</sup>

Prebiotics are non-digestible oligosaccharides that tend to alter the proliferation of bacteria considered as residents of the gastrointestinal tract. Prebiotics and probiotics can work simultaneously and when they are used in the same product, they are termed synbiotics. Synbiotics have the ability to increase the survival rate of microorganisms, which results in the

increase in growth of the bacteria in the intestinal tract.<sup>2</sup>

## MECHANISM OF PROBIOTICS

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

1. Immune Modulation
2. Normalization of the intestinal microbiota
3. Metabolic effects<sup>3</sup>

## Microorganisms used as Probiotics

1. ***Lactic acid producing bacteria***
  - *Lactobacillus* species
    1. *L. acidophilus*
    2. *L. bulgaricus*
    3. *L. casei*
    4. *L. crispatus*
    5. *L. fermentum*
    6. *L. gasseri*
    7. *L. johnsonii*
    8. *L. lactis*
    9. *L. plantarum*
    10. *L. reuteri*
    11. *L. rhamnosus* GG
  - *Bifidobacterium* species
    1. *B. adolescentis*
    2. *B. animalis*
    3. *B. bifidum*
    4. *B. breve*
    5. *B. infantis*

6. *B. lactis*
7. *B. longum*

## 2. *Non-lactic acid producing bacteria*

- *Bacillus cereus*
- *Propionibacterium*
- *Enterococcus faecalis*
- *Enterococcus faecium*
- *Escherichia coli* Nissle
- *Streptococcus thermophilus*

## 3. *Non-pathogenic Yeast*

- *Saccharomyces boulardii*

## 4. *Non-spore forming and non-flagellated rods or coccobacillus*

Probiotics act by creating a biofilm in the oral cavity, which acts as a protective lining for oral tissues against oral diseases. Such a biofilm keeps the bacterial pathogens off oral tissues, by filling the space which could have served as a niche for pathogens in future and by competing with the growth of cariogenic bacteria and periodontal pathogens.<sup>4</sup> The possible mechanism of Probiotic Action in the Oral Cavity can be depicted (Figure 1).<sup>5</sup>

## PROBIOTICS AND ORAL HEALTH

The increasing incidence of antibiotics that are bacterial resistant is the main reason behind the use of probiotics in oral diseases. Dental caries, periodontal disease and halitosis are a few among the oral disorders that have been targeted.

### Properties of Probiotics:

1. Dental surface binding
2. Antimicrobial substances production
3. Alteration of environmental conditions of mouth
4. Reduction of inflammatory response

In humans, 1% of the cultivable oral microflora comprises of *Lactobacilli*. Their potential to remain aciduric aids them to withstand a pH as low as 3.5, which is an ultimatum for the survival of the low-pH transition into the intestines. *Bifidobacteria* play a crucial role in maintaining the equilibrium among normal flora, as they are the predominant anaerobic bacteria seen to naturally occur within the small intestinal lumen.<sup>6</sup>

Haukioja et al (2006)<sup>7</sup> assessed the survival in the saliva of various probiotics in the dairy industry in saliva and their adherence to oral surfaces and found that all the tested strains survived well in saliva, having a varied capacity to adhere to oral surfaces. A substantial finding was that the species in the genus *Lactobacillus* had an adherence capacity superior to that of the *Bifidobacterium* species. Studies with regard to *L.rhamnosus* GG, *L. reuteri* have well-grounded their potential in interacting with *S. mutans* and reducing its number, thus suggesting a role of probiotics in Caries prophylaxis. Furthermore, researchers have observed the reduction of oral *Candida* counts in elderly who were administered with probiotics, which is a new strategic finding in the control of oral yeast infections.<sup>8-10</sup>

## PROBIOTICS AND DENTAL CARIES

Dental caries manifests with an increase in cariogenic pathogens which can be of both acidogenic and non-acidogenic species like *Streptococcus mutans*, *Lactobacilli* and various other species like *Propionibacterium* spp., *Bifidobacteria*, non-mutans streptococci, *Actinomyces* spp., *Veillonella* spp., and *Atopobium* spp.

A probiotic must have the potential of adherence to dental surfaces and integration into the bacterial colonies which constitute the dental biofilm, the ability to compete and antagonize with the cariogenic bacteria, thus interfering with their proliferation, to have a profitable outcome in preventing or limiting dental caries.<sup>1</sup> Probiotics can result in the reduction of the risk for a high *S. mutans* level occurrence.<sup>11</sup> In a comparative study of the *S. mutans* reduction effects by various probiotic administration forms by Caglar et al. (2006)<sup>12</sup>, a reduced *S. mutans* level was seen in patients receiving fluid or tablet probiotic forms. Caglar et al (2007)<sup>13</sup> also evaluated the effect of xylitol and probiotic chewing gums on salivary *S.mutans* and *Lactobacilli* in a study which showed a reduced *S. mutans* level in subjects using probiotics or xylitol-enriched chewing gum, with no synergic effect seen when combining both agents.

Nikawa H et al (2004)<sup>14</sup> reported that consuming yoghurt containing *L. reuteri* over a period of 2

weeks resulted in a significant reduction in the concentration of *S. mutans* in the saliva by up to 80%. Children consuming milk containing probiotic, those 3–4 years of age, in particular, had fewer dental caries and lowered salivary counts of *S. mutans* than the controls in a study by Nase L et al (2001).<sup>15</sup>

## PROBIOTICS AND PERIODONTAL DISEASE

Treatment strategies against periodontal disease using probiotics can be summed up (Figure 2).<sup>16</sup> Grudianov et al (2002)<sup>17</sup> studied the effect of probiotics tablets on gingivitis and different grades of periodontitis. Twetman et al (2009)<sup>18</sup> assessed the effects of *L. reuteri* on crevicular fluid volume, cytokine (interleukin- $\beta$ , interleukin-6, interleukin-10, and TNF- $\alpha$ ) levels, and bleeding on probing in 42 healthy patients who were provided with *L. reuteri* containing chewing gums which showed a significant reduction. Patients with moderate to severe gingivitis were given either one of two *L. reuteri* formulations subsequently presented with reduction in plaque and gingivitis scores compared to a placebo group in a similar study conducted by Krasse P et al (2006).<sup>19</sup>

The regular (three times daily for eight weeks) consumption of tablets containing *Lactobacillus salivarius* (*L.salivarius*) WB21 showed a beneficial effect in terms of plaque index and pocket probing depth in individuals who were at a high risk of periodontal disease (smokers) compared to a placebo control group.<sup>20</sup> Riccia et al (2007)<sup>21</sup> reported the anti-inflammatory effects of *L.Brevis*, with significant improvements in the plaque index, gingival index, bleeding on probing for patients with Chronic Periodontitis who were treated with lozenges containing *L. Brevis* over a period of 4 days.

Although promising results have been observed stating that *Lactobacilli* residing in the oral cavity could play a vital role in the oral ecological balance, the studies have been fairly brief and the difference produced quite small, though statistically significant.

## PROBIOTICS AND HALITOSIS

Oral halitosis refers to bad breath originating from the oral cavity. It is a common finding seen to affect about one in four adults and is caused by

bacteria infecting the dorsal surface of the tongue, producing volatile sulphur compounds (VSCs).<sup>22</sup>

Increased VSC levels might play a role in linking oral infection with systemic diseases like heart disease and preterm low birth weight. Certain gram-negative anaerobic bacteria residing in periodontal pockets and on the dorsal surface of tongue tend to degrade food and salivary proteins, producing amino acids, which are further converted into volatile sulphur compounds (VSC) like hydrogen sulphide and methanethiol.<sup>23,24</sup>

Probiotics aid in treating Halitosis is by fixating on the VSC's and result in their conversion into gases required for metabolism, thus breaking their unpleasant odour. *S. salivarius* are known to produce bacteriocins which result in the reduction of the quantity of VSC-producing species.<sup>25</sup>

## SAFETY OF PROBIOTICS

Although certain probiotic strains have been established as a safe natural alternative to medication, most probiotic bacteria are weakly proteolytic like *Lactobacillus bulgaricus*, which was shown to lack the ability to degrade some host tissue components. Few cases of bacteraemia and fungaemia associated with probiotic use have been reported in immune-compromised subjects or those suffering from chronic disease.<sup>26</sup>

A report of a subject developing *Lactobacillus* endocarditis following dental treatment in Finland was suggested to be due to prior consumption of *L. rhamnosus* in a probiotic preparation.<sup>27</sup> In animal models, a strain of *L. salivarius* has the potential to induce caries, whereas another tends to make a biofilm model more cariogenic, suggesting that different strains of the same species possess differing traits, thus demanding scrupulous strain selection before being labelled as a probiotic.<sup>28</sup>

## FUTURE OF PROBIOTIC THERAPY

Advances in biomedical engineering is necessary to develop systems that deliver bacteria to the host, which may include encapsulation of probiotics to rehydrate at specific sites, and encasing prebiotics in nano-aggregates thus providing protection in the gastric acidic environment ensuring delivery at a pH of 7.4.<sup>29</sup> Capsules coated with biosensors that can ascertain

the favourable conditions for release of probiotic contents are on the horizon in macromolecular research. Probiotics are already administered as passive local immunization vehicles against dental caries in oral immunology.<sup>30</sup>

## CONCLUSION

Probiotics is a natural means of maintaining health and protecting oral tissues from disease, at an early start of childhood. Yet it remains to be seen that there is a greater extent to which probiotics are applicable to promoting oral health. Although the results of existing studies are promising, still more research is required for the identification of probiotics that are best suited to enhance oral health, as well as the most appropriate vehicles for its delivery. With rapidly evolving technology and an alliance of biophysics with molecular biology, oral probiotics pose a huge opportunity to treat oral health conditions in a natural and non-invasive way.

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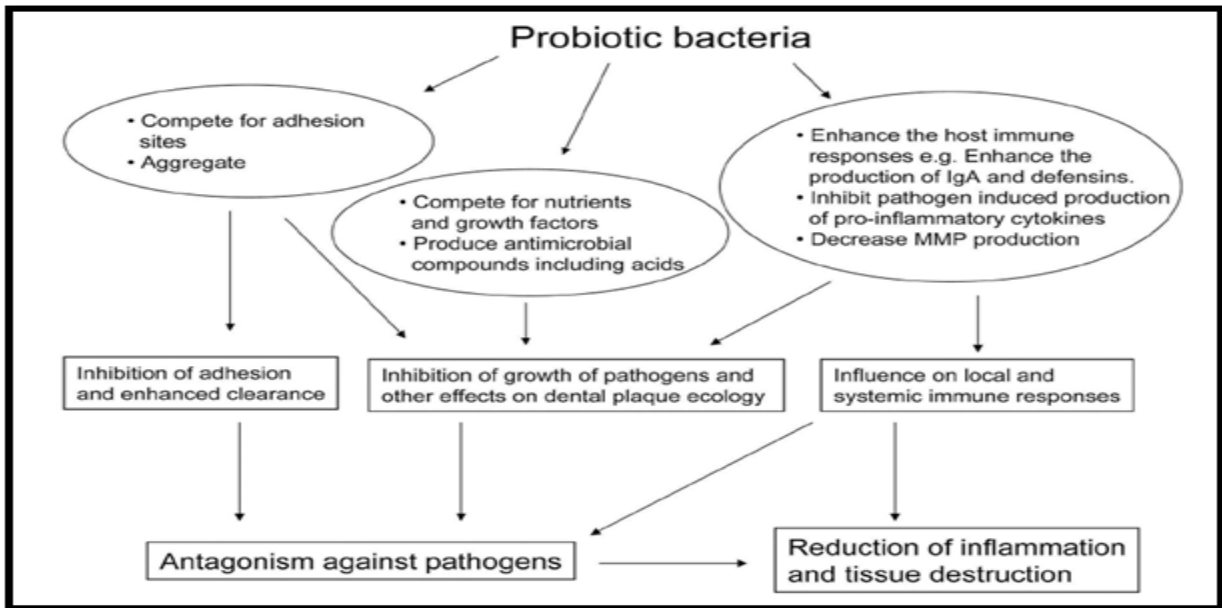


Figure 1. Mechanisms of Probiotic Action in the Oral Cavity<sup>5</sup>

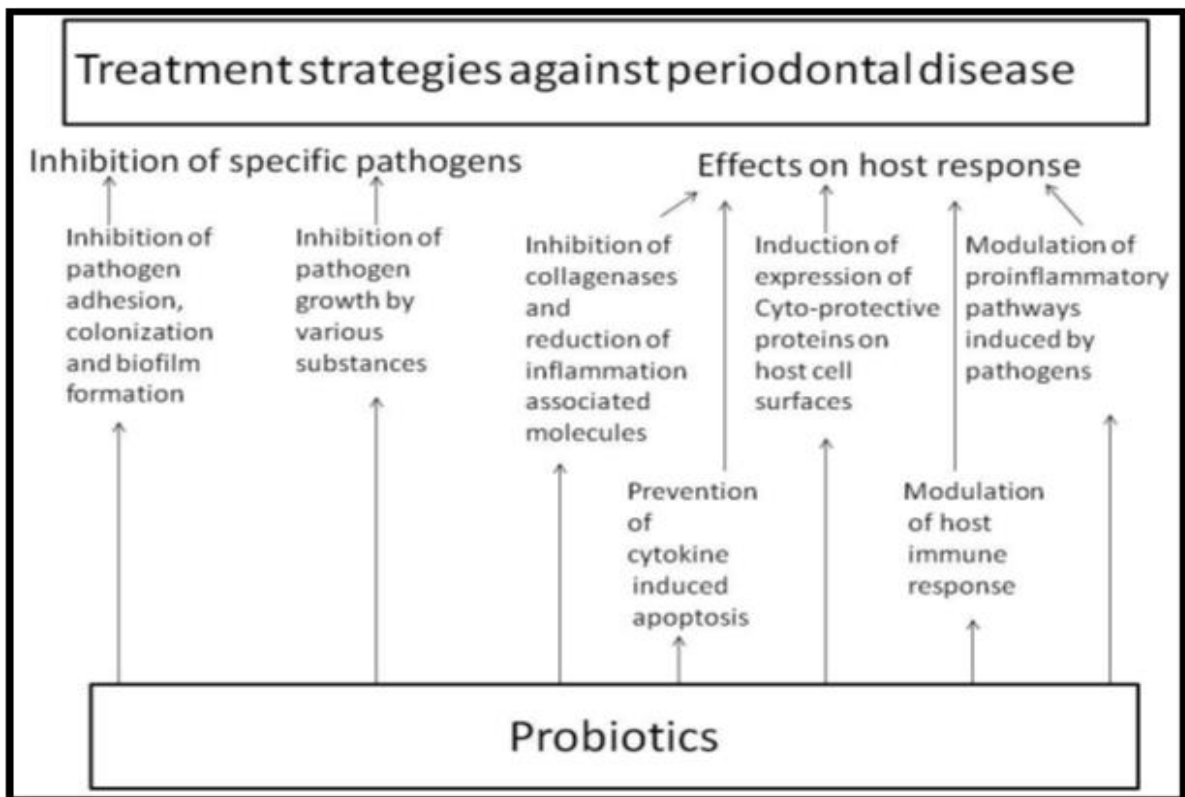


Figure 2. Treatment Strategies against Periodontal Disease<sup>16</sup>