

# Concept of Probiotics in Dentistry

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## ABSTRACT

In recent years, probiotics have been used to promote oral health. The Time has come to shift the paradigm of treatment from elimination of specific bacteria to altering bacterial ecology by using probiotics. Probiotics are dietary supplements which contain potentially beneficial bacteria or yeasts. They help in stimulating health promoting flora and also suppressing pathogens which cause and spread diseases. The Probiotic approach has shown promising results in the oral health with respect to control of chronic disease such as dental caries, periodontitis, and recurring problems like candidal infections and halitosis. 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:** Oral diseases, Oral health, Probiotics.

## INTRODUCTION

The role of diet in well-being and overall health is universally acknowledged. With the evolution of the science of nutrition, research is now directed towards improving the understanding of specific physiologic effects of the diet beyond its nutritional effect.<sup>1</sup> In this aspect, probiotics are the subject of intense and widespread research in food and nutritional science. The term probiotic, is derived from the Greek language, meaning “for life”. It was first used by Lilly and Stillwell in 1965 and described probiotics as “substances secreted by one microorganism which stimulates the growth of another” and thus was contrasted with the term antibiotic.<sup>2</sup>

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.<sup>3</sup> 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.<sup>4</sup> An International Life Science Institute Europe consensus document, proposed a simple and widely accepted definition i.e. “Viable microbial food supplements which beneficially influence the health of human.” These bacteria must belong to the natural flora of body in order to resist gastric secretion and survive during intestinal transit. They must adhere to the intestinal mucosa and must have the ability to inhibit pathogens present in gut.<sup>5-7</sup>

## HISTORY

In the early 1900's, Dr. Metnikoff of Russia found that certain Bulgarians lived longer, disease-free, and pain-free lives. He attributed their diet for their healthy longevity. The diet consisted of yogurt, sour dough, bread, and buttermilk. Dr. Metnikoff discovered that these fermented foods contained beneficial bacteria that were able to take rotten putrescence food and digest them to release some by-products which are full of nutrients and which destroyed the foul odour. 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 lifespan of humans. The concept of probiotics was thus born which opened a new field of bacteriology.<sup>3</sup>

Lilley, and Stillwell introduced the term probiotics in 1965.

The term prebiotic was introduced by Gibson and Roberfroid who exchanged “pro” for “pre” which means “before” or “for”. Prebiotics is defined as a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.<sup>8</sup> More specifically, probiotics are short-length carbohydrates, such as fructooligosaccharides, that resist digestion or are fermented in the colon to produce short-chain fatty acids, such as acetate, butyrate, and propionate, which positively effects on colonic cell growth and stability, generate many of the same bacteria as provided in probiotics.<sup>1</sup>

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## PROBIOTIC BACTERIA FOR ORAL HEALTH

The most commonly used strains belong to the *Lactobacillus* and *Bifidobacterium* genera that are commonly found in the oral cavity, including caries lesions.<sup>9</sup> These were the first probiotic species to be introduced into research (*Lactobacillus acidophilus* by Hull et al. 1984 and *Bifidobacterium bifidum* by Holcomb et al., 1991).<sup>2</sup> *Lactobacillus rhamnosus* GG, ATCC 53103 has been proposed to reduce the risk for caries by producing a growth inhibitory substance against *Streptococcus sobrinus*.<sup>9</sup> It was originally isolated in 1985 from the human intestinal flora and named after the discoverers, Sherwood Gorbach and Barry Goldin.<sup>4</sup> *Streptococcus salivarius* strains appear to be excellent candidates for an oral probiotic, since they are amongst the most numerically predominant members of the tongue micro biota of healthy individuals and are early colonizers of oral surfaces.<sup>10</sup>

Other strains of probiotics in the oral cavity include: *L. acidophilus*, *L. casei* Shirota, *L. paracasei*, *L. casei*, *L. johnsonii*, *L. reuteri*, *propionibacterium*, *W. cibaria*.<sup>11</sup> A successful effector strain for replacement therapy of a bacterial disease must have some basic properties like it must not cause disease itself or otherwise predispose the host to other disease states by disrupting its residing ecosystem.<sup>12</sup> To be able to have probiotic effects in the mouth, a bacterium must adhere to oral surfaces and become part of the biofilm.<sup>13</sup> Finally, an effector strain should have a high degree of genetic stability.<sup>12</sup> Current evidence indicates that probiotic effects are strain-specific; so, a beneficial effect attributed to one strain cannot be provided by another strain, even if it belongs to the same species.<sup>14</sup>

## PROBIOTICS PRODUCTS

Probiotics are provided in products in four basic ways:

- As a culture concentrate added to a beverage or food (such as fruit juice).
- Inoculated into prebiotic fibers.
- Inoculants in a milk-based food (dairy products such as milk, milk drink, yogurt).
- As dietary supplements in concentrated and dried cells packaged (non-dairy products).

## PROPERTIES OF PROBIOTICS

- Should be non-toxic and non-pathogenic preparation
- Should produce beneficial effect
- Should withstand gastrointestinal juice
- Should have a good shelf life
- Should reinstate and replace the intestinal microflora

## MECHANISM OF PROBIOTIC ACTION ON ORAL HEALTH

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

- Modulation of immune response
- Normalization of intestinal microbiota
- Metabolic effects.<sup>15</sup>

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 IgA levels in saliva seem unaffected by probiotic use.<sup>16,17</sup> Normalization of intestinal/oral microbiota is supported by the ecological plaque hypothesis which suggests that the selective pressure present in environmental conditions can alter the balance between disease and oral health.<sup>18</sup> As bacteria can influence their environment, and both antagonistic and synergistic 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 some species that seem to be associated with oral health; however, it is still questionable that bacteria administered in food could be used as probiotics to normalize oral micro biota. There are many possible mechanisms for how pathogen exclusion may take place.

First, several probiotics 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 inhibit the expression of virulence functions by altering the gene expression program of pathogens.

Lastly, probiotics may create an unfavourable environment for pathogen colonization by altering the mucus layer, pH and other factors in the local surroundings.

## ROLE OF PROBIOTICS IN DENTAL CARIES

Dental caries is an infectious disease affecting most of the population. This multifactorial and complex disease process occurs along the interface between the enamel surface and dental biofilm. Several methods may be used to alter the cariogenicity of the biofilms responsible for dental caries. Researchers are developing “probiotic” methods to treat the caries causing infection. Probiotic, mechanisms are employed to selectively remove only the harmful pathogen while leaving the remainder of the oral ecosystem intact.<sup>19</sup> One of the replacement therapy options entails the application of a genetically engineered “effector strain” of *S. mutans* that will replace the cariogenic or “wild strain” to prevent or arrest caries and to promote optimal remineralization of tooth surfaces that have been demineralized but that have not become cavitated. *S. mutans* strain BCS3-L1 is a genetically

modified effector strain designed for use in replacement therapy to prevent dental caries. Recombinant DNA technology was used to delete the gene encoding lactate dehydrogenase in BCS3-L1 making it unable to produce lactic acid. This effector strain was also designed to produce elevated amounts of a novel peptide antibiotic called mutacin 1140 that gives it a strong selective advantage over most other strains of *S. mutans*.<sup>20</sup>

The pathogenicity of both *S. sorbinus* and *S. mutans* 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. These glucans are synthesized through glucosyltransferase B, glucosyltransferase C, and glycosyltransferase D genes. The introduction of mutated *gtfC* gene affects the ability of *S. mutans* to produce extracellular glucans resulting in a decrease in extracellular matrix component of mixed oral biofilms from 51 to 33% of the biofilm volume.<sup>21</sup> Several studies suggest that consumption of products containing probiotic lactobacilli or bifidobacteria could reduce the salivary concentration of mutans streptococci.<sup>22</sup>

A clinical trial began early in 2005 to test the effectiveness of replacement therapy. Thus, it is too early to determine the potential of this treatment method to prevent new caries lesions and to arrest existing lesions without any significant side effects. Another approach is based on a genetic modification of two plaque streptococci to create organisms that produce ammonia from urea and arginine. These organisms will reside in dental plaque, and the ammonia produced from salivary and dietary substrates will prevent the colonization of cariogenic bacteria and ensure internal pH homeostasis. If the effector strain is better adapted than the pathogen, colonization or outgrowth of the pathogen will be prevented by blocking the attachment sites, by competing for essential nutrients, or via other mechanisms. As long as the effector strain persists as a resident of the indigenous flora, the host is protected potentially for an unlimited period of time.<sup>20</sup>

## REVIEW OF THE STUDIES INVOLVING PROBIOTICS FOR DECREASING DENTAL CARIES

Comelli EM et al. (2002) studied 23 dairy bacterial strains for the prevention of dental caries and out of which, only two strains, namely *Streptococcus thermophilus* and *Lactococcus lactis*, were able to adhere to saliva-coated hydroxyapatite and were further successfully incorporated into a biofilm similar to the dental plaque. Furthermore, they can grow together with five strains of oral bacterial species commonly found in supragingival plaque. In this system, *Lactococcus lactis* was able to modulate the growth of the oral bacteria, and was particularly able to diminish the colonization of

*Streptococcus oralis*, *Veillonella dispar*, *Actinomyces naeslundii* and *Streptococcus sobrinus*.<sup>23</sup> *L. rhamnosus* is one of the most extensively studied probiotics in oral biology, since it does not readily ferment sucrose and is safer for teeth than lactic acid-producing bacteria. *L. Rhamnosus* was found to inhibit cariogenic *S. mutans*, but colonization of the oral cavity by *L. rhamnosus* seems improbable.

In a seven-month study on kindergarten by Nase et al. (2001), children received the probiotic *L. rhamnosus* and the caries risk was subsequently calculated according to clinical and microbiological data (*S. mutans* level in saliva and plaque). Results showed lower levels of *S. mutans* and less dental caries in the probiotic milk-consuming group.<sup>20</sup> A study aimed at showing the benefit of cheese containing *Lactobacillus rhamnosus* showed that probiotic intervention reduced the highest level of *Streptococcus mutans*.<sup>18</sup>

In order to assess whether naturally occurring oral lactobacilli have probiotic properties, lactobacilli were isolated from saliva and plaque in children and adolescents, with or without caries lesions. Twenty-three *Lactobacillus* sp. completely inhibited the growth of all mutans streptococci tested. The species with maximum interference capacity against mutans streptococci included *Lactobacillus paracasei*, *Lactobacillus plantarum*, and *Lactobacillus rhamnosus*.<sup>9</sup>

Few studies have reported that use of probiotic-containing yogurts causes a reduction in mutans streptococci levels in saliva, but it is not clear whether this decrease is due to the bactericidal activity of yogurt or other mechanisms. Petti S (2008) investigated the differences in susceptibility of strains of viridians streptococci. In vitro, yogurt with live bacteria showed selective anti-mutans activity, suggesting that the overall decrease in mutans streptococci in vivo could be due to a bactericidal effect on *S. mutans*.<sup>17</sup> Yogurt products containing *L. reuteri* showed a significant growth inhibitory effect against *S. mutans* while yogurts with lactobacilli other than *L. reuteri* did not show such inhibition. Moreover, a double-blind, placebo-controlled trial demonstrated that consuming yogurt with *L. reuteri* significantly reduced the oral carriage of mutans streptococci, compared to the placebo yogurt.<sup>16</sup> Knuutila YH et al. (2006) investigated the effect of the probiotic bacterium *Lactobacillus reuteri* on levels of mutans streptococci and lactobacilli, which was introduced by two different straws containing *L. reuteri* and lozenges containing *L. reuteri*; they concluded that short-term daily ingestion of lactobacilliderived probiotics delivered by prepared straws or lozenges reduced the levels of salivary mutans streptococci in young adults.<sup>13</sup> Calgar et al. evaluated the effect of xylitol and probiotic chewing gums on salivary mutans streptococci and lactobacilli and concluded that there is a reduction in the levels of salivary mutans streptococci on daily chewing of gums containing probiotic bacteria or xylitol in a significant way. However, a combination of xylitol gums and probiotic did not seem to enhance this effect.<sup>24</sup> In a

similar study, they noticed a reduction in the levels of salivary mutans on sucking a medical device containing the probiotic lozenge with *L. reuteri* once daily for 10 days.<sup>25</sup>

## CONCLUSION

The oral cavity with a well-maintained balance of species and species interactions may be a potential source for health-promoting probiotic bacteria. Probiotics play an important role in combating issues with overuse of antibiotics and antimicrobial resistance. It is right time to change the way bacteria are treated in today's new technological era. Further studies are required 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, randomized controlled trials and systematic studies are needed to find out the best probiotic strains and means of their administration in different oral health conditions and oral health promotion. With fast evolving technology and integration of biophysics with molecular biology, designer probiotics pose huge opportunity to treat diseases in a natural and non-invasive way.

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