

Oral Probiotic: A Role in Oral Cavity

Dolyawee Chaowadee

Singapore Intercultural School, South Jakarta, Indonesia, 12440

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***Corresponding author:**

Dolyawee Chaowadee, Singapore
Intercultural School, South Jakarta,
Indonesia, 12440

E-mail:
dolyawee.ch@gmail.com

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ABSTRACT

Probiotics are live microorganisms promoted with claims that they provide health benefits when consumed. It has attracted the attention of both professionals and patients in recent decades. The purpose of this paper is to describe the role and beneficial effects of probiotics in the prevention and treatment of oral diseases. Probiotics can produce antimicrobials, compete for cell adhesion sites, modulate the immune system, and perform other mechanisms that aid in the prevention and treatment of dental caries, periodontitis, and many other oral health diseases, according to the findings. Probiotics may be a valuable adjunct to the conventional treatment that causes problems. However, there are still questions about the best bacterial strain combination for each disease, appropriate dosage, and potential side effects. Therefore, further studies are required.

Keywords: Bacterial strain, Microorganisms, Oral diseases, Probiotics

Introduction

For centuries, dentists have struggled with oral problems. It is widely recognized that an individual's age, physical well-being, nutritional condition, lifestyle, and—most importantly—the variety of resident bacteria all have a significant impact on oral health. The oral cavity is a dynamic ecosystem with constant environmental change and commensal bacterial interaction, which helps to prevent the colonization of pathogenic microorganisms. In addition, the oral microbiota is heterogeneous and diverse. Its imbalance may result in the development of a number of significant diseases, including dental caries, periodontitis, halitosis, candidiasis, and gingivitis. Adopting mechanical techniques to remove bacterial plaque and administering antimicrobial medication therapy are two common conventional treatments for these oral diseases [1]. However, recently there is a development of resistance regarding the use of these antibiotics [1]. Therefore, it's time to shift the paradigm of treatment from eliminating the pathogenic bacteria to altering the bacterial ecology by using probiotics to avoid the possibility of returning back to pre-antibiotic dark ages [2]. Probiotics are beneficial bacteria that naturally live in the human body, especially in the oral cavity. It helps to maintain the oral health through interaction with the oral microbiome, contributing to healthy microbial equilibrium and antagonistic to the harmful bacteria [3, 4].

The introduction of probiotics is interesting to global professionals because it provides an effective alternative to the conventional therapeutic way and also free from concerns of developing resistance because probiotics are counterparts of antibiotics. Furthermore, they are the body's own residential flora hence are most easily adapted to host [5].

This review is written with the purpose to update and summarize the currently available data regarding the characteristics, types, mechanisms of probiotics which aid in the treatment of several diseases, along with their offered applications.

Characteristics of probiotics

'Probiotics' is a Greek term which translates as 'for life.' They are hence microorganisms that have been established to exert beneficial impacts on both human and animal health. In addition, probiotics are referred to as 'live microorganisms that, when administered in adequate amounts, confer a health benefit to the host' by The Food and Agricultural Organization of the United Nations (FAO) and The World Health Organization (WHO). This affirmed with the prior interpretation of the Greek's probiotics term. Even though probiotics have just gained a massive amount of interest recently, some professionals have seen the prospects since 1994 as WHO stated that they are the next most important

immune defense system when commonly prescribed antibiotics are rendered useless by antibiotic resistance. Therefore, it can be simply summarized that probiotics are non-pathogenic living microorganisms, principally bacteria, that are safe for consumption, which are used to prevent various medical conditions. However, to be called a probiotic, a bacterial strain must be fully characterized. According to the recommendation from the FAO and the WHO, probiotics bacterial strains are characterized by their spectrum of resistance to antibiotics and hemolytic activities, their capacity to produce toxins, their infectious power in immunocompromised animal models and their side effects in humans. Most commonly they are bacteria. Some of their species are (1) Lactic acid producing bacteria (LAB), including *Lactobacillus*, *Bifidobacterium*, and *Streptococcus*; (2) Non-LAB species, including *Bacillus* and *Propionibacterium*; (3) Non-pathogenic yeasts, including *Saccharomyces*; and (4) Non spore forming and non-flagellated rod or *Coccobacilli*. [6]

Types of probiotics

The genera *Lactobacillus* and *Bifidobacterium* contain the majority of the probiotic strains. In oral biofilm, *lactobacillus* is regarded as a typical component. It accounts for approximately 1%. The *Lactobacillus* species from which probiotic strains have been isolated include *L. acidophilus acidophilus*, *Lactobacillus johnsonii*, *Lactobacillus casei*, *Lactobacillus rhamnosus*, *Lactobacillus gasseri*, and *Lactobacillus reuteri*. For *Bifidobacterium*, they are only marginally generated in oral biofilm. The strains include *B. bifidum*, *B. longum*, and *B. infantis* [7, 8] At the present, although there is scarce amount of information regarding the indigenous probiotics to evidence their benefits, these strains are rarely involved in human infections and form the majority of probiotics in general. In fact, some studies also show that these bacteria have a symbiotic relationship with human beings. For instance, Koll-Klais et al. reported that healthy oral cavity was populated with *Lactobacillus gasseri* and *Lactobacillus fermentum*, whereas periodontitis patients were free of these two species but populated with *Lactobacillus plantarum* [9].

Mechanism of action of probiotics

Several mechanisms have been proposed regarding the action of probiotics which help in competing with the oral pathogens and providing health benefits to the host. Firstly, the probiotics compete with the pathogens for the adhesion sites on mucosa. This prevents the pathogen from adhering to the host tissues. In fact, the adhering ability is one of the characteristics that probiotic candidates should have as it should be able to successfully establish itself in the oral biofilm to exert health benefits. Some examples of bacterial strains that are reported to possess strong binding activity (more

than 20%) are *L. rhamnosus* and *L. paracasei*. After the probiotics have adhered and colonized on the oral surface, they compete with oral pathogens for nutrients and growth factors, and also produce antimicrobial compounds, including organic acids, hydrogen peroxide, carbon peroxide, diacetyl, and low molecular weight antimicrobial substances, bacteriocins, and adhesion inhibitors [3]. These substances inhibit the growth of pathogens, which further help in decreasing the possibility of disease initiation. Furthermore, other health-beneficial mechanisms of probiotics are enhancement of the non-specific and specific immune response of the host, degradation of toxins, and modification of the surrounding environment such as pH and/or oxidation and reduction potential which may compromise the establishing ability of pathogens [6].

Probiotics and oral health diseases

The advancement in dentistry and scientific fields has led to a paradigm shift away from treating dental diseases by targeting specific oral pathogens towards an ecological and microbial community-based approach [10]. Studies have shown that the oral cavity is a habitat for a large diversity of microorganisms, dominantly bacteria, which are all associated with oral infections. The balance between microflora and the host is significant in order to maintain an appropriate oral health. A shift in the balance between them can result in several diseases of the oral structures such as dental caries and periodontitis [11]. Therefore, probiotics, which contribute to an appropriate balance in microflora, can play a vital role in the prevention and treatment of oral diseases when consumed regularly.

Probiotics and dental caries

Dental caries is commonly known as cavities or tooth decay. It can be generally defined as a localized chemical dissolution of the tooth surface resulting from metabolic events in a biofilm (dental plaque) covering the affected area. It leads to many painful symptoms such as toothache, tooth sensitivity, staining on the tooth, etc [12]. Elements that must be present for disease initiation and progression are host, bacteria, and nutrients as they are required to foment the production of organic acids and the subsequent demineralization activity. The removal of any element leads to the interception of the disease process [5]. However, all the elements are present in the oral cavity most of the time, therefore there is a high possibility of dental caries formation. In case of dental caries, there is an increase in acidogenic and acid tolerating species such as *lactobacilli*, and especially, *streptococcus mutans* [2]. Studies have shown that elevated levels of *S.mutans* are strongly associated with increased risk of dental caries [13]. Hence, many recent prevention strategies are focusing on inhibiting the proliferation of *S.mutans* and its adherence to the oral surfaces as it is capable of producing acids from carbohydrates fermentation.

These acids can demineralize and destroy the dental tissues. According to an established global dental practice, the treatment and control of dental caries can be done by mechanically removing the carious lesion along with using antimicrobial. However, according to the stated issue of increasing resistance strains and the arise of positive probiotic studies, probiotics have been proposed as an adjunct method to dental caries management strategies as they adhere to oral tissues, and prevent the colonization of caries pathogens and formation of pathogenic biofilm. In addition, some of them are also capable of producing inhibitors of cell adhesion and antibacterial agents, and consuming nutrients before caries pathogens can further use them [1] (Figure1).

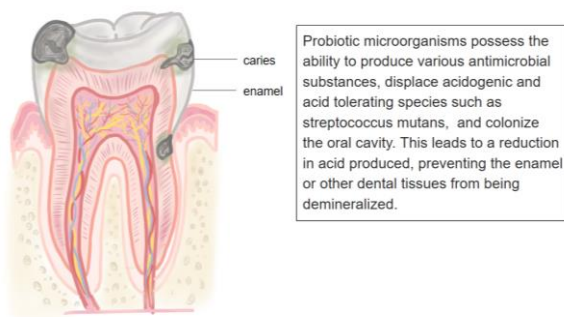


Figure 1 Carious lesions resulting from the dissolution of minerals in enamel and dentin by acids produced during the metabolism of food residues by microorganisms colonizing tooth surfaces

Probiotics and periodontitis

Periodontal diseases, including periodontitis, are a group of inflammatory pathologies of the periodontium that lead to teeth loss principally due to dysregulated, immune-mediated destruction of the periodontal ligaments and tooth-supporting structures [16]. They are the most common inflammatory destructive conditions that negatively affect many people. According to WHO, 15-20% of middle-aged adults encounter tooth loss due to severe periodontal diseases. The disease is initiated by components of the plaque which develops on the hard surface adjoining the soft tissues that support periodontium. Treatment is needed as soon as possible because the disease can further extend to the gingiva or to deeper supporting structures leading to the destruction of the periodontal ligament and the alveolar bone in the worst case [12]. In the disease development, there is an increase in obligate anaerobic and proteolytic bacteria which might be reduced by the administration of probiotics. In fact, three factors that determine whether disease will develop in a subject are a susceptible host, the reduction or absence of beneficial bacteria, and the presence of pathogenic species such as *Porphyromonas gingivalis*, *Treponema denticola*, *Tannerella forsythia*, *A. actinomycetemcomitans*, *Bacteroides* sp., *Actinomyces* sp.,

Staphylococcus intermedius, and *Candida albicans* [5, 17]. According to studies, the disease could be inhibited via probiotics by lowering the salivary pH and producing antioxidants that utilize the free electrons required to mineralize plaque [3]. To be simple, the probiotics will alter the oral microbial ecology.

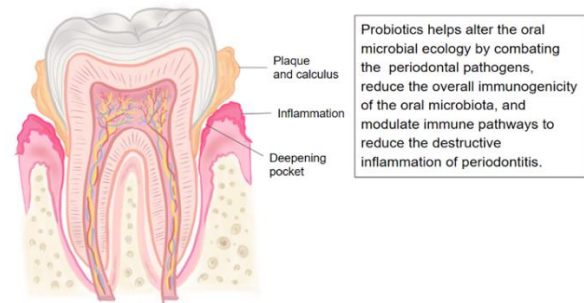


Figure 2 Bacterial plaque formation around the tooth and inflammation of bacterially-infected tissue leads to periodontitis.

They will firstly combat dysbiosis by competitive inhibition of periodontal pathogens and reduce the overall immunogenicity of the oral microbiota, and secondly modulate active disease-associated immune pathways to reduce the destructive inflammation of periodontitis, leading to immune homeostasis that could be maintained by the host in the long term.[17] Even though the conventional treatment of periodontitis, which involves the mechanical removal of the subgingival plaque, is more popular among professionals, removing the bacterial plaque in low-access sites can be difficult. This could lead to the relapse of periodontitis due to the huge amount of remaining bacteria left in the plaque [18]. As a result, probiotics are required to aid in this process (Figure 2).

Table 1. List of probiotics studied for limiting the progress of oral diseases and their causative pathogens

Disease	Causative agent	Therapeutic probiotics	Results	References
Dental caries	<i>Streptococci mutans</i> , <i>Streptococcus sobrinus</i> <i>Bifidobacteria nonmutans</i> <i>Streptococci</i> , <i>Actinomyces</i> <i>spp.</i> , <i>Propionibacterium</i> <i>spp.</i> , <i>Veillonella spp.</i> , and <i>Atopobium spp.</i> , <i>Fusobacterium nucleatum</i> , and <i>Prevotella intermedia</i>	<i>L. reuteri</i> ,	Administration of <i>L. reuteri</i> , in lozenge, straw, and tablet forms, <i>L. rhamnosus</i> in milk, Bifidobacterium in yogurt have shown a reduction in salivary <i>S. mutans</i> levels	Parihar, Anuj Singh, and Vartika Katoch (2015) ⁵
		<i>L. rhamnosus</i> , and <i>Bifidobacterium</i>		
		<i>L. rhamnosus GG</i>	<i>L. rhamnosus</i> GG has the highest adhesion value and inhibits Streptococcus by producing antimicrobial components such as organic acid, hydrogen peroxide, carbon peroxide, and diacetyl bacteriocins.	Piqué, Berlanga, and Miñana-Galbis (2019) ¹⁴
		<i>Streptococcus dentisani</i>	Probiotic <i>Streptococcal species</i> , <i>Streptococcus dentisani</i> , isolated from dental plaque of caries-free individuals. The strain was shown to inhibit the growth of major oral pathogens like <i>S. mutans</i> , <i>Fusobacterium nucleatum</i> , and <i>Prevotella intermedia</i> through the production of bacteriocins, and also buffers acidic pH of the oral cavity.	López-López et al. (2017) ¹⁵

Disease	Causative agent	Therapeutic probiotics	Results	References
Periodontitis	<i>Porphyromonasgingivalis</i> , <i>Treponema denticola</i> , <i>Tannerella forsythia</i> , <i>Aggregatibacter actinomycetemcomitans</i> , <i>Bacteroides sp.</i> , <i>Actinomyces sp.</i> , <i>Staphylococcus intermedius</i> and <i>C. albicans</i>	<i>Lactobacillus rhamnosus</i> GG (LGG), <i>Bifidobacterium animalis subspecies lactis Bb-12</i> (BB-12)	The short-term consumption of <i>Lactobacillus rhamnosus</i> GG (LGG) and <i>Bifidobacterium animalis subspecies lactis Bb-12</i> (BB-12) reduces the amount of plaque and it is clinically relevant for the reduction of gingival inflammation.	Toiviainen et al. (2015) ²⁰
		<i>L. salivarius</i> <i>L. reuteri</i>	Administration of mouthwash using selected strains of <i>L. reuteri</i> or tablets containing 6.7×10^8 colony forming units of <i>L. salivarius</i> and Xylitol (280 mg/tablet) reduced the accumulation of gingivitis and plaque. ⁽⁷⁾	Reddy, Swapna, and others (2011) ⁷
		<i>L. casei</i> 37 <i>L. salivarius</i> TI 2711	When compared to a placebo, an <i>L. salivarius</i> WB21-containing tablet demonstrated insignificant differences in pocket probing depth and bleeding on probing indices. <i>L. casei</i> 37 can reduce the number of most common periodontal pathogens, and <i>L. salivarius</i> TI 2711 inhibits <i>P. gingivalis</i> when given for 4 or 8 weeks.	Grajek, Olejnik, and others (2005) ¹⁹

Applications of probiotics

Probiotics could be provided in products in different ways, such as inoculants in dairy products and prebiotic fibers, concentrated culture in food and beverages, and dietary supplements [21]. The supplement is an easy and popular way. However, for the best results in the prevention or treatment of dental diseases, specifically targeted applications with slow release of probiotics may be required. Some carriers available currently are capsule and liquid form, chewing gum, and tablet [5]. According to the studies that are currently available, chewing gum and tablets have more support than capsules and liquids. A tablet containing a probiotic mix of Acilact and Bifidumbacterin was developed by Grudianov et al. in 2002. The product helps to normalize the micro flora and prevent gingivitis and periodontitis. In addition, *L. reuteri* Prodentis chewing gum has recently been invented for twice-daily consumption. This gum can regulate *S. mutans* levels and aid in caries prophylaxis.[5] However, despite these inventions, there are still no studies that define the most suitable means of delivery and dosages of probiotics for various oral health purposes. Furthermore, the fact that a probiotic can be made from a single or multiple combination strains makes determining the best treatment strains even more difficult. Nevertheless, there are some ideal requirements of probiotic products that the researcher can rely on in order to identify the suitable strains. These criteria stated that the product should show the beneficial effect in host animals, should be non-pathogenic and nontoxic, should be capable of surviving and metabolizing in the oral environment, and finally, should remain viable under storage for duration [6].

Conclusion

Probiotics are living microorganisms that are made out of single or multiple strains. They are used to treat various oral health problems through their direct and indirect mechanisms. They offer an advantage to the human oral ecosystem without any other systemic harmful effects or drug resistance. Probiotics bring the advancement toward the research area of oral medicine, the examination of the close relationships between food and oral health. In order to administer the probiotics, health professionals are in an ideal position to help and guide their patients toward appropriate therapeutic uses of probiotics that deliver the desired beneficial health effects [5]. However, probiotics are still unaccepted by some professionals nowadays due to insufficient amount of supporting substantial evidence. Therefore, further clinical studies are required to prove their role in oral health, and to select the best-suited probiotic for each issue. Future research should focus on obtaining substantial data from blind, large-scale, long-term, randomized, placebo-controlled clinical trials studies with the emphasis on strain efficacy, dose effects, and delivery vehicles to determine the most effective

probiotic strain combination that are accepted by different age groups and conditions.

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