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RESEARCH ARTICLE

A REVIEW OF PROBIOTICS IN TREATING ORAL MICROBIAL INFECTIONS

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ABSTRACT

Probiotics are live microorganisms thought to be beneficial to the host organism with proven health benefits. Traditionally, probiotics have been associated with gut health, and most clinical interest has been focused on their use for prevention or treatment of gastrointestinal infections and diseases. However during the last decade several investigators have also suggested the use of probiotics for oral health purposes. This article discusses about the significance of probiotic therapy as a means to fight common dental conditions.

Keywords:

Probiotics, Oral health,
Lactobacillus,
Bifidobacterium.

INTRODUCTION

In recent years, with the threat of widespread antibiotic resistance rendering many antibiotics useless against important diseases, there is an increased necessity not only to minimise antibiotic use and develop novel non-antibiotic-based treatments, but also to raise the profile of disease prevention. There is a public appetite for new therapies that are perceived to be natural through, for example, manipulation of the resident microbiota by the ingestion of probiotic bacteria or prebiotics. There has been a shift away from treating dental diseases by targeting specific oral pathogens towards an ecological and microbial community-based approach to understand conditions, such as caries and periodontal diseases^(4,5). These approaches recognise the importance of maintaining the natural balance of the resident oral microbiota and the need to carefully modulate host immune responses to the microflora at a site.

Probiotics

Etymologically, the term appears to be a composite of the Latin preposition pro ("for") and the Greek adjective (bios, "life") (Hamilton-Miller et al., 2003). Probiotics are defined as viable micro-organisms that confer health benefit when administered in sufficient doses. According to the currently adopted definition by FAO/WHO, probiotics are: "Live microorganisms which when administered in adequate amounts confer a health benefit on the host". (Report of a Joint FAO/WHO, 2001) Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics; but certain yeasts and bacilli may also be helpful.

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The organisms that have been used as probiotics are primarily certain species of lactobacilli and bifidobacteria, and *Saccharomyces* spp., but some streptococci, enterococci and commensal *Escherichia coli* have also been claimed to have beneficial effects in certain situations. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures; such as in yogurt, soy yogurt, or as dietary supplements.

Oral microbiota

Given the complexity of the oral microbiota; more than 700 species have been detected in the human mouth and the resident microbiota of one individual may comprise 30 to >100 species. A wide variety of sites in the mouth are heavily colonised. Supragingival and subgingival plaque form through sequential and specific adhesive interactions that result in a complex climax community. The tongue is heavily colonised and micro-organisms on the dorsum of the tongue are reservoirs for supragingival and subgingival plaque and salivary microbial populations. Many oral bacteria, especially streptococci, also survive within buccal epithelial cells. The following species are listed as 'true' oral commensal micro-organisms: *Streptococcus mitis*, *Streptococcus oralis*, *Actinomyces naeslundii*, *Fusobacterium nucleatum*, *Haemophilus parainfluenzae*, *Eikenella corrodens* and some species of *Prevotella*. Other studies have generated an increasingly long list of culturable and unculturable bacteria with a significant association with healthy sites.

Origin and vehicles for probiotic delivery

Probiotic bacteria are natural inhabitants of the intestinal flora and the vast majority of the strains and species that are

examined in research for their probiotic properties are isolated from healthy humans although there are some that originate from fermented food. The increasing interest for replacement therapy has, however, opened a market for other consumer products such as lozenges, sucking tablets and chewing gums.

Probiotics are provided into the food items in one of four basic ways:

- As a culture concentrate added to beverages (e.g. fruit juice);
- Inoculated into prebiotic fibres which promote the growth of probiotic bacteria?
- Inoculated into milk and milk based foods (e.g. milk drinks, yoghurt, cheese, bio drinks)
- As lyophilized, dried cells packaged as dietary supplements (tablets, chewing gums, straws).

The archetypical probiotic food is yoghurt and daily consumption of dairy products seems to be the most natural way to ingest probiotic bacteria. Another advantage is that milk products contain basic nutrients for the growing child; they are also considered safe for the teeth with possible beneficial effects on the salivary microbial composition and inhibition of caries development, due to their natural content of casein, calcium, and phosphorous. A formulation of approximately 10⁸ probiotic bacteria per gram or millilitre with an intake of 1.5–2 dL per day is recommended and the dairy products should preferably be non-sweetened and contain only natural sugar.

Dental caries (Meruman and Stamatova, 2007; Gibson et al., 1995; Burton et al., 2005; Corcoran et al., 2004; El-Nezami et al., 2006)

The advantage of incorporating probiotics into dairy products lies in their capacity to neutralize acidic conditions. For example, it has already been reported that cheese prevents demineralization of the enamel and promotes its remineralization. Comelli and colleagues reported that of 23 bacterial strains used in the dairy industry, *Streptococcus thermophilus* and *Lactobacillus lactis* spp. *Lactis* were the only ones with the capacity to integrate into a biofilm present on a hydroxyapatite surface and to interfere with development of the cariogenic species *Streptococcus sobrinus*. More recently, it was demonstrated that isolates of *W. cibaria* had the capacity to inhibit, both in vitro and in vivo, biofilm formation by *S. mutans* and to prevent proliferation of this bacterial strain. In other studies, one strain of *L. rhamnosus* and the species *L. casei* inhibited in vitro growth of 2 important cariogenic streptococci, *S. mutans* and *S. sobrinus*.

Containing *S. thermophilus* and *L. bulgaricus* had selective bactericidal effects on streptococci of the *mutans* group. Several clinical studies have demonstrated that regular consumption of yoghurt, milk or cheese containing probiotics led to a decrease in the number of cariogenic streptococci in the saliva and a reduction in dental plaque. More specifically, Nikawa and colleagues reported that consumption of yoghurt containing *Lactobacillus reuteri* over a period of 2 weeks reduced the concentration of *S. mutans* in the saliva by up to 80%.

Comparable results were obtained by incorporating probiotics into chewing gum or lozenges.

Probiotics and Periodontal Disease (Meruman and Stamatova, 2007; Burton et al., 2005; El-Nezami et al., 2006)

Periodontal disease is classified into 2 types: gingivitis and periodontitis. Gingivitis is characterized by inflammation limited to the unattached gingiva, whereas periodontitis is a progressive, destructive disease that affects all supporting tissues of the teeth, including the alveolar bone. The main pathogenic agents associated with periodontitis are *P. gingivalis*, *Treponema denticola*, *Tannerella forsythia* and *Aggregatibacter actinomycetemcomitans*. These bacteria have a variety of virulent characteristics allowing them to colonize the subgingival sites, escape the host's defence system and cause tissue damage.

The persistence of the host's immune response also constitutes a determining factor in progression of the disease. In one recent study, the prevalence of lactobacilli, particularly *Lactobacillus gasseri* and *L. fermentum*, in the oral cavity was greater among healthy participants than among patients with chronic periodontitis. Various studies have reported the capacity of lactobacilli to inhibit the growth of periodontopathogens, including *P. gingivalis*, *Prevotella intermedia* and *A. actinomycetemcomitans*. Together, these observations suggest that lactobacilli residing in the oral cavity could play a role in the oral ecological balance.

Oral candida (Hatakka et al., 2007)

It has been suggested that oral *Candida* incidence increases with age (Lockhart et al., 1999), possibly because of impaired immunity. Several elements in the immune system, such as T-lymphocytes, granulocytes, NK-cells, mast cells, and macrophages, account for the protection against *Candida* infections (Peterson, 1992). *Lactobacillus GG* and *Propionibacterium JS* cause enhanced T-cell and B-cell proliferation in mice (Kirjavainen et al., 1999). Probiotics have also stimulated the production of IFN enhanced phagocytic capacity (Arunachalam et al., 2000), and increased the proportions of helper T-lymphocytes and the activity of natural killer cells in elderly patients (Gill et al., 2001). Probiotics may also inhibit the *Candida* growth by producing antimicrobial compounds (Ström et al., 2002; Strus et al., 2005), and may inhibit its adhesion to epithelial cells (Reid et al., 1995).

In an in vitro model mimicking gastrointestinal conditions, *Lactobacillus* suppressed the growth of *Candida* after antibiotic treatment (Payne et al., 2003) possibly by competing for the same receptor sites. They tested 4 denture cleaners - Dentural, Medical Interporous, Steradent Active Plus, and Boots Smile. They found that all of the denture cleansers were effective at both removing the yeast (*Candida albicans*) biofilm and disinfecting the denture but some biofilm still remained that led to regrowth. They noted that despite the soaking the dentures were recolonizing with the yeast biofilm. Therefore, as they put it, "alternative mechanical disruptive methods are required to enhance biofilm removal." So that means you need to brush the dentures as well as soak them to get the best result.

Probiotics and Halitosis (Kang et al., 2006; Yli-Knuutila et al., 2006; Corcoran et al., 2004)

Halitosis (bad breath) is a discomfort rather a disease. Strains used as probiotic for mouth and gut associated halitosis include *E.coli* Nisle1917, *S.salivarius* K12, three *Weisellaconfusa* isolates and a lactic acid forming bacterial mixture. The administration of bacteriocin producing *S.salivarius* after an oral antimicrobial mouthwash reduces oral volatile sulphur compound levels. The outcome of this preliminary study indicates that the replacement of bacteria implicated in halitosis by colonization with competitive bacteria such as *S.salivarius* K12 may provide an effective strategy to reduce the severity of halitosis²⁷. Reduced levels of volatile sulfur compounds produced by *Fusobacterium nucleatum* after taking *Weisella* have been observed by Kang et al²⁸. The effect could be due to hydrogen peroxide production by *W.cibaria*, causing *Fusobacterium nucleatum* inhibition.

Prebiotics and probiotics

Prebiotics when combined with probiotics have many advantages. Basically, prebiotics selectively stimulate the growth of probiotics, which is dose and strain dependent. Prebiotics serve as a selective growth substrate for the probiotics strain during fermentation, during the period of storage, or during its passage through the gut. These two combinations implant live microbial dietary supplements and create a congenial environment for their survival in gut flora. Thereby, this environment in gut flora improves healthy microbial balance. So, the combination of prebiotics and probiotics may have additive and synergistic effect in providing better oral health conditions. Paster et al in an attempt to determine bacterial diversity in the human subgingival plaque by using culture-independent molecular methods have estimated that the total species diversity in the oral cavity ranges between 500 and 600 species. This number was further extended by Kazor et al, who detected 200 additional unknown species on the dorsum of the tongue, making the number of species in the mouth to reach 700.

Lactobacilli make approximately 1% of the cultivable oral microflora [38,43]. The most common lactobacilli species recovered from saliva in a study by Teanpaisan and Dahlen were *L. fermentum*, *L. rhamnosus*, *L.salivarius*, *L. casei*, *L. acidophilus* and *L. plantarum*. Three of them are probiotic strains used in dairy products. These findings indicate that lactobacilli as members of resident oral microflora could play an important role in the microecological balance in the oral cavity [57]. These studies further demonstrated that lactobacilli strains with probiotic properties may indeed be found in the oral cavity.

Contraindications

Because probiotics are live bacteria, immunocompromised patients will not be a candidate for any probiotics. People who are undergoing chemotherapy are not candidates, as well as those who present with HIV/AIDS. Other conditions also drive down the immune system, and those patients are not good candidates either. Often, these patients need oral biofilm management, and xylitol products are a better option.

As medicine alters the human physiology with medications, environmental and dietary stresses contribute to oral changes; the time is right for oral probiotics to support oral health.

Summary and Conclusion

The interest in oral probiotics has been growing during the last decades. At least some of the probiotic bacteria used in various probiotic products may colonize the oral cavity during the time they are in use; thus, the effects of probiotic bacteria in the oral cavity are important to understand. Probiotic bacteria seem to affect both oral microbiota and immune responses. On the other hand, the extent to which bacteria in food or in food ingredients can influence relatively stable oral microbiota is difficult to predict. Thus, both research to unravel the mechanisms of possible probiotic action and long-term clinical trials are needed if probiotics are to provide a new scientifically proven means of preventing or treating oral diseases.

Several health-promoting effects of probiotic bacteria are well documented and there is no reason to restrict the use of probiotic products because their effects on oral health are not yet well understood; however, their recommendation for dental health purposes is not yet justified. Genetic modification of probiotic strains to suit the oral conditions is thus needed. Systematic studies and randomized control trials are therefore needed to find out the best probiotic strains and means of administration in different oral health conditions.

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