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OUR TRILLION FRIENDS: PROBIOTICS IN DENTISTRY

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ABSTRACT

Probiotics are microorganisms that play a beneficial role in maintaining health, including the health of the oral cavity. This article reviews the potential of probiotics in dentistry and the future perspective in developing probiotics that can serve as highly efficacious adjuvants to- , or, even as alternatives to conventional treatment.

KEYWORDS: Probiotics, prebiotics, dental caries, Lactobacillus

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INTRODUCTION

The human gut comprises of over 400 known bacterial species which contribute to human health. This eco-system gets disrupted when exposed to toxins and injudicious use of antibiotics, causing destruction of beneficial bacteria leaving the resistant pathogenic flora behind.[1] This has led to the search of alternative therapeutic options like “Probiotics”, which are defined as live microbial food ingredients that have a beneficial effect on human health.[2] Prebiotics are dietary substances (mostly consisting of non starch polysaccharides and oligosaccharides poorly digested by human enzymes) that nurture a selected group of microorganisms living in the gut.[2] The dual combination of live microbial ingredients and dietary additives that promote selective microbial growth are known as Synbiotics.[2] Oral infections constitute some of the most common forms of infections in humans. The concept of microbial ecological change as a mechanism for preventing dental diseases is an important one.[3] This paper aims at viewing the benefits of probiotics in the treatment of oral health conditions.

HISTORY OF PROBIOTICS

The concept of probiotics evolved around 1900 when Henry Tissier, a French Paediatrician, observed that children with diarrhoea had a low number of Bifidobacterium compared to healthy children.[4] The original observation of beneficial bacteria was by Russian scientist and Nobel laureate Eli Metchnikoff, who introduced in his diet sour milk fermented with the bacteria he called "Bulgarian Bacillus" and found that his health benefitted.[4] The term “probiotics” was first introduced in 1965 by Lilly and Stillwell. In 1984 Hull identified the first probiotic species, the Lactobacillus *acidophilus*. In 1991 Holcombh identified Bifidobacterium *bifidum*.[1]

CHARACTERISTICS OF PROBIOTIC STRAINS[4,5,6,7]

- Non-toxic, non-pathogenic and resistant to bile & acid.
- Genetically stable, capable of survival, proliferation and metabolic activity at target site.
- Produces antimicrobial substances – including bacteriocins, hydrogen peroxide and organic acids.
- Able to compete with the normal microflora and antagonistic toward pathogenic/cariogenic bacteria.
- Immunostimulatory
- Amenable to production processing: adequate growth, recovery, concentration, freezing, dehydration, storage, and distribution.
- Free of plasmid-encoded antibiotic resistance genes.

Table 1
Mechanisms of Action of Probiotics[8]

Antimicrobial Activity • Decrease luminal pH • Secrete antimicrobial peptides • Inhibit bacterial invasion • Block bacterial adhesion to epithelial cells	**Immunomodulation** • Effects on epithelial cells • Effects on dendritic cells • Effects on monocytes/macrophage • Effects on lymphocytes (B lymphocytes, NK cells and T cells)
Enhancement of Barrier Function • Increase mucus production • Enhance barrier integrity	

PROBIOTICS IN ORAL HEALTH

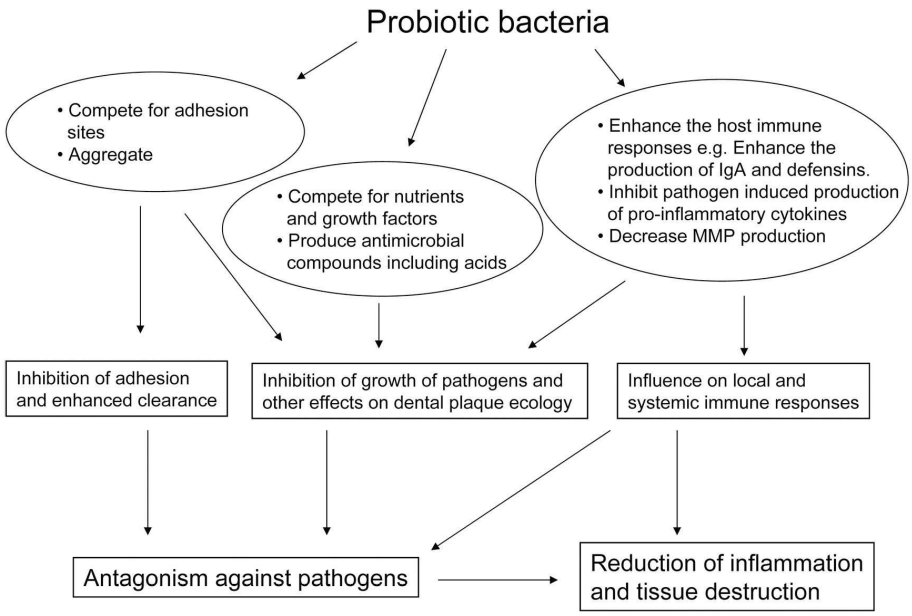

Figure 1
Mechanism of probiotic actions in the oral cavity[9]

PROBIOTICS IN DENTAL CARIES

Lactobacilli plays a role in the eco physiology of oral microbiota.[10-13] Lactobacillus *paracasei*[14,15], Lactobacillus *plantarum*[14,15], and Lactobacillus *rhamnosus*[3,16] have maximum interference capacity against mutans Streptococci. A study in Finland[17] concluded that a regular intake of probiotic bacteria could prevent dental caries in young children and the efficiency may vary by age. In a Swiss study[18] it was seen that Lactococcus *lactis* was able to diminish the colonisation of Streptococcus *oralis*, Veillonella *dispar*, Actinomyces *naeslundii* and carcinogenic Strepticocus *sobrinus.* L.*acidophilus* strains may inhibit the in-*vitro* growth of other bacteria by producing low molecular weight bacteriocins. In another study, [19] L. *rhamnosus* strains, L. *paracasei* and L. *reuteri* were unable to ferment sucrose, thus revealing information about the relative safety of probiotic strains in caries-prophylactic perspective. However, since Lactobacilli are also known to play a role in the pathogenesis of dental caries, it is advised not to advocate regular consumption of lactobacilli-derived probiotics to children with open, untreated dental cavities.[17] The oral administration of probiotics, both in capsules and in liquid form, significantly increases salivary counts of Lactobacilli, whereas S.*mutans* populations are not significantly modified.[20] Therefore the dental health of patients undergoing long-term probiotics treatment requires closely monitoring.

PROBIOTICS IN GINGIVITIS

In a study by Harini PM[21], probiotics containing L.*reuteri* were found to be effective in reducing plaque accumulation and gingival inflammation compared with chlorhexidine. Kang MS *et al*[22] did a study in which they found that subjects who rinsed with a solution containing W.*cibaria* exhibited plaque-index reduction.

PROBIOTICS IN PERIODONTITIS

L.*reuteri* plays a key role in the prevention of periodontal disease by inhibiting the colonisation of pathogenic bacteria in plaque biofilm and supporting immune function.[23] Lactobacilli has the capacity to inhibit the growth of periodontopathogens including P.*gingivalis*, Prevotella *intermedia* and A.*actinomycetemcomitans*.[24] Subgingival application of a mixture including S.*sanguis*, S.*salivarius* and S.*mitis* after scaling and root-planing significantly suppressed the re-colonization of P.*gingivalis* and P. *intermedia* in a beagle dog model.[25]

L.*helveticus* produces short peptides that act on osteoblasts and increases their activity in bone formation. These bioactive peptides contribute to reducing the bone resorption associated with periodontitis.[24]

PROBIOTICS AND ORAL CANDIDIASIS

In testing the pattern of colonization of L.*acidophilus* and L.*fermentum*, Ehali *et al*[26] showed a rapid decline in C.*albicans* in mice after the intake of probiotic strains by inducing the production of IL-4 and IFN-γ in lymph nodes and nitric oxide (NO) in the saliva. Santos AL[27] showed that after the use of probiotics there was significant reduction of 65% Candida of which 98% were C.*albicans* and 2% C.*tropicalis* by inhibiting its adhesion to epithelial cells.

PROBIOTICS AND HALITOSIS

Successful reduction in the concentration of volatile sulphur compounds (VSC) in the exhaled breath has been observed with S.*salivarius* K12.[28] In children, a marked reduction in the level of H_2S and CH_3SH was registered after gargling with W.*cibaria* containing rinse.[22] Burton *et al* further reported that the S.*salivarius* strain K12 produced two antibiotic bacteriocin compounds that were inhibitory to strains of several species of Gram-positive bacteria implicated in halitosis.[29]

Table 2
Summary of controlled clinical intervention studies in the oral cavity with Lactobacilli- and Bifidobacteria-derived probiotics.[17]

Reference	No of samples / average age	Vehicle, time	Species	Outcome in oral cavity
Näse *et al*	594/1–6 years RCT, DB	Milk, 7 months, placebo	L. *rhamnosus*	Decrease counts of MS in saliva, reduced caries
Ahola *et al*	74/18–35 years RCT, DB	Cheese, 3 weeks, placebo	L. *rhamnosus*	Decreased counts of yeast and MS in saliva
Nikawa *et al*	40/20 years, RCT, cross-over	Yoghurt, 2 weeks, placebo	L. *reuteri*	Decrease counts of MS in saliva
Montalto *et al*	35, 24–33 years RCT, DB	Liquid, 45 days	Lactobacillus spp.	Increased salivary counts of LB, MS unchanged
		Capsules, 45 days placebo	Lactobacillus spp.	Increased salivary counts of LB, MS unchanged
Caglar *et al*	26/21–24 years, RCT, cross-over	Yoghurt, placebo	Bifidobacteria	Decreased counts of MS in saliva
Caglar *et al*	120/21–24 years, RCT, DB	Water/straw, 3 weeks	L. *reuteri*	Decreased counts of MS in saliva
		Lozenges, 3 weeks		
		Placebo	L. *reuteri*	Decreased counts of MS in saliva
Krasse *et al*	58/adults, RCT, DB	Gums, 2 weeks, placebo	L. *reuteri*	Decreased gingivitis
Hatakka *et al*	294/70–100 years	RCT, DB Cheese16 weeks, placebo	L. *rhamnosus*	Decreased prevalence of oral candida

(DB, double blind; LB, lactobacilli; MS, mutans streptococci; RCT, randomized controlled trial)

SAFETY ASPECTS

Probiotics are generally considered safe but each probiotic strain has specific properties that should be considered before its use in any patient. Furthermore, all patients should be screened for certain medical conditions which may predispose them to sepsis. Table 3 lists proposed risk factors for Probiotic sepsis.[31]

Table 3
Major and Minor factors for risk of sepsis

Major risk factors	Minor risk factors
• Immune compromise, including a debilitated state or malignancy • Premature infants	• Central venous catheter • Impaired intestinal epithelial barrier, e.g., diarrheal illness, intestinal inflammation • Concomitant administration of broad spectrum antibiotics to which probiotic is resistant • Probiotics with properties of high mucosal adhesion or known pathogenicity • Cardiac valvular disease (Lactobacillus probiotics only)

FUTURE PERSPECTIVES

The following future applications of probiotics may be identified:

1. Genetic engineering of already identified probiotics.[4]
2. Biotherapy using antibiotic-sensitive bacteria to displace resistant strains.[32]
3. Microbiota removal: Reducing the adherence of S.*mutans* to the tooth's surface to create a microbial community with less S.*mutans*[32]
4. Passive immunization[32]
5. Interference with signalling mechanisms involving Competence Stimulating Peptide (CSP) as the signalling molecule. The addition of a high concentration of CSP can interfere with signalling events of S. mutans and induce the death of the bacterium, thus exhibiting a potential beneficial effect against dental caries.[32]
6. Targeted antimicrobial therapy via a novel STAMP technology[33]

CONCLUSION

The emerging science behind Probiotics promises several novel applications in Oral Sciences and Dentistry. The fundamental advantage that Probiotic species offer is that they permit clinicians to disrupt or alter biofilms in a highly effective manner, utilizing the biologic species-specific traits of various organisms. Additional bioengineering and genetic manipulation of these organisms will permit future clinicians to create new methods to control and stabilize microbial populations responsible for various disease states.

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