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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
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. 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. 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. The dual combination of live microbial ingredients and dietary additives that promote selective microbial growth are known as Synbiotics. 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. 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. 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. 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.

CHARACTERISTICS OF PROBIOTIC STRAINS

- 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

<table>
<thead>
<tr>
<th>Antimicrobial Activity</th>
<th>Immunomodulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Decrease luminal pH</td>
<td>• Effects on epithelial cells</td>
</tr>
<tr>
<td>• Secrete antimicrobial peptides</td>
<td>• Effects on dendritic cells</td>
</tr>
<tr>
<td>• Inhibit bacterial invasion</td>
<td>• Effects on monocytes/macrophage</td>
</tr>
<tr>
<td>• Block bacterial adhesion to epithelial cells</td>
<td>• Effects on lymphocytes (B lymphocytes, NK cells and T cells)</td>
</tr>
</tbody>
</table>

Enhancement of Barrier Function

| • Increase mucus production |
| • Enhance barrier integrity |
**PROBIOTICS IN ORAL HEALTH**

**PROBIOTICS IN DENTAL CARIES**
Lactobacilli plays a role in the eco physiology of oral microbiota. L. paracasei, L. plantarum, and Lactobacillus rhamnosus have maximum interference capacity against mutans Streptococci. A study in Finland 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 it was seen that Lactococcus lactis was able to diminish the colonisation of Streptococcus oralis, Veillonella dispar, Actinomyces naeslundii and carcinogenic Streptococcus sobrinus. L. acidophilus strains may inhibit the in-vitro growth of other bacteria by producing low molecular weight bacteriocins. In another study, 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. 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. Therefore the dental health of patients undergoing long-term probiotics treatment requires closely monitoring.

**PROBIOTICS IN GINGIVITIS**
In a study by Harini PM, probiotics containing L. reuteri were found to be effective in reducing plaque accumulation and gingival inflammation compared with chlorhexidine. Kang MS et al 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. Lactobacilli has the capacity to inhibit the growth of periodontopathogens including P. gingivalis, Prevotella intermedia and A. actinomycetemcomitans. 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.
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 AL27 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 H₂S and CH₃SH 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 |

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

(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 |

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

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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. mutans32
4. Passive immunization32
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 technology33

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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