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Review Article

Probiotics in dentistry: A boon or sham

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ABSTRACT

Probiotics are dietary supplements, which have been advocated for the prevention and the treatment of a wide range of diseases. These products consist of beneficial micro-organisms, which stimulate health promoting flora thus, suppressing the pathologic colonization and disease spread. Since, probiotics are now widely used in both medical (such as cancer risk reduction, gastrointestinal tract health, and urinary tract health) and dental specialties (reduction in caries development, in achieving periodontal health, reducing oral malodor, etc.), a thorough understanding of their risks and benefits are essential. This review focuses on the recent trends in use of probiotics in dentistry as well as the potential risks associated with them.

Key Words: Micro-flora, micro-organisms, probiotics

INTRODUCTION

"Probiotics" are with us since the time people have been eating fermented milk; however, its relation with health benefits drew attention only when Metchnikoff in 1907 observed that bacteria in the fermented milk competed with the micro-organisms that are injurious to health.[1] Lilley and Stillwell in 1965 described these beneficial micro-organisms in fermented milk using the term "probiotic." In 1989, Fuller defined them as a live microbial food supplement, which beneficially affects the host animal by improving its microbial balance.[2] The first probiotic species introduced into research were *Lactobacillus acidophilus* by Hull, *et al*. in 1984 and *Bifidobacterium bifidum* by Holcombh, *et al*. in 1991.[3]

The bacterial population of human gastrointestinal (GI) tract constitutes an enormously complex ecosystem. Most of these organisms are beneficial but some are harmful. Some dietary substances, so the term "prebiotics" and this term can favor the growth of these beneficial bacteria over that of harmful ones. Prebiotics are non-digestible food ingredients such as inulin, fructo-oligosachharides, and lactulose that cannot be digested by humans but support the growth of beneficial bacteria.[3] The term "synbiotic" is used when a product contains both probiotics and prebiotics. Because the word alludes to synergism, this term should be reserved for products in which the prebiotic compound selectively favors the probiotic compound.[4]

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COMPOSITION OF PROBIOTICS

Probiotics can be bacteria, molds or yeast. However, most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular. *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus lactis*, *Lactobacillus helviticus*, *Lactobacillus salivarius*, *Lactobacillus plantrum*, *Lactobacillus bulgaricus*, *Lactobacillus rhamnosus*, *Lactobacillus johnsonii*, *Lactobacillus reuteri*, *Lactobacillus fermentum*, *Lactobacillus del-brueckii*, *Streptococcus thermophilus*, *Enterococcus faecium*, *Enterococcus faecalis*, *B. bifidum*, *Bifidobacterium breve*, *B. longum*, and *Saccharomyces boulardii* are commonly used bacterial probiotics. A probiotic may be made out of a single bacterial strain or it may be a consortium

as well. Probiotics can be in powder form, liquid form, gel, paste, granules or available in the form of capsules, sachets, etc.[5]

Features of probiotics

A good probiotic agent needs to be non-pathogenic, nontoxic, resistant to gastric acid, adhere to gut epithelial tissue and produce antibacterial substances. It should persist, albeit for short periods in the GI tract influencing metabolic activities such as cholesterol assimilation, lactose activity, and vitamin production.

The survival of probiotic organisms in the gut depends on the colonization factors that they possess as well as on the organelles which enable them to resist the antibacterial mechanisms that operate in the gut. In addition to the antibacterial mechanisms, they need to avoid the effects of peristalsis, which tend to flush out bacteria with food. This can be achieved either by immobilizing themselves or by growing at a much faster rate than the rate of removal by peristalsis. The probiotic strain needs to be resistant to the bile acid, e.g., *Bifidobacteria* strains proved significantly less acid-resistant than the *Lactobacillus* strains, when exposed to human gastric juice.[5]

Mechanisms of action explaining beneficial probiotic effects include modulation of host immune response leading to strengthening of the resistance to pathogenic challenge and alteration of the composition and metabolic activity of host micro-flora at the specific location. Among paramount selection criteria for probiotics are:

1. Adhesion and colonization (at least transitory) in the human body. Adhesion may increase the retention time of a probiotic and place bacteria and host surfaces (body fluids and epithelial cells) in close contact, thus facilitating further probiotic activity.
2. Enhancement of the non-specific and specific immune response of the host.
3. Production of antimicrobial substances and competition with pathogens for binding sites.
4. Survival and resistance to human defense mechanisms during the oro-gastro-intestinal transit.
5. Safety to the macro-organism.[6]

Probiotics products

Probiotics are provided in products in one of the following basic ways:

1. A culture concentrate added to a beverage or food (such as a fruit juice).
2. Inoculated into prebiotic fibers.
3. Inoculants into a milk-based food (dairy products such as milk, milk drink, yogurt, yogurt drink, cheese, kefir, and bio-drink).
4. As concentrated and dried cells packaged as dietary supplements (non-dairy products) such as powder, capsule, gelatin tablets.[7]

Indications Sanders *et al*,[8] Saraf *et al*[9]

Proven indications

1. Rotavirus diarrhea
2. Reduction of antibiotic-associated side effects.

Possible indications

1. Food allergies and lactose intolerance
2. Actopic eczema
3. Prevention of vaginitis
4. Urogenital infections
5. Irritable bowel syndrome
6. Inflammatory bowel syndrome
7. Cystic fibrosis
8. Traveller's diarrhea
9. *H. pylori* infection
10. Various cancers.

Probiotics and oral cavity

Probiotics in controlling periodontal infection and halitosis

Periodontitis is a multifactorial disease that encompasses the hard- and soft-tissue, microbial colonization (with or without invasion), inflammatory responses and adaptive immune responses. The complexity of the local tissue components, including bacteria and/or their products and virtually all aspects of host response mechanisms, has complicated our ability to elucidate the critical protective functions in the tissues and has continually provided evidence for the potential of host destructive factors as the ultimate causative parameters in the disease. Treatment of periodontal diseases in recent years has moved towards an antibiotic/anti-microbial model of disease management. Probiotics might be a promising area of research in the treatment of periodontitis. Probiotics decrease the pH of the oral cavity so that plaque bacteria cannot form dental plaque and calculus that causes the periodontal disease.[10] They make excellent maintenance product because they produce antioxidants. Antioxidants prevent plaque formation by neutralizing the free electrons that are needed for the mineral formation. Probiotics are able to breakdown putrescence odors by fixating on the toxic gases (volatile sulfur compounds) and changing them to gases needed for metabolism. Teughels,

et al. reported that the subgingival application of a bacterial mixture including *Streptococcus sanguis*, *Streptococcus salivarius*, and *Streptococcus mitis* after scaling and root planning significantly suppressed the re-colonization of *Porphyromona gulae* (canine *P. gingivalis*) and *P. intermedia* in a beagle dog model.[11] This guided pocket re-colonization approach may provide a valuable addition or alternative to the armamentarium of treatment options for periodontitis.

Probiotics could also be used in the treatment of halitosis. Kang, *et al*. reported a significant reduction of volatile sulfur compounds after gargling twice daily with 15 ml *Weissella cibaria* CMU for 2 min.[12] Burton, *et al*. reported significant reductions in volatile sulfur compounds for the probiotic group compared to the placebo group when probiotic *Streptococcus* was used.[13]

Role of probiotics in dental caries

In caries, there is an increase in acidogenic and acid-tolerating species such as mutans streptococci and lactobacilli, although other bacteria with similar properties can also be found like *Bifidobacteria*, nonmutans streptococci, *Actinomyces* spp., *Propionibacterium* spp., *Veillonella* spp. and *Atopobium* spp. Use of probiotics and molecular genetics to replace and displace cariogenic bacteria with non-cariogenic bacteria has shown promising results. These studies have employed different approaches:[3]

1. Early studies concentrated on utilizing bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances that specifically prevented the growth of cariogenic bacteria.
2. One approach has been to identify food grade and probiotic bacteria which have ability to colonize teeth and influence the supra-gingival plaque.
3. Also, strains have been screened for suitable antagonistic activity against relevant oral bacteria.
4. Another approach utilized recombinant strain of *S. mutans* expressing urease, which was shown to reduce the cariogenicity of plaque in an animal model.
5. Similarly, genetically modified probiotics with enhanced properties can be developed ("designer probiotics"). For example, a recombinant strain of *Lactobacillus* that expressed antibodies targeting one of the major adhesions of *S. mutans* (antigen I/II) was able to reduce both the viable counts of *S. mutans* and the caries score in a rat model.

Probiotics and oral candidosis

Candida species constitute part of the commensal oral flora in about 50% of healthy subjects, but are able to cause a clinically apparent lesion if the immune defenses are breached either on the local or systemic level. One study has shown that the subjects who consumed cheese containing the probiotic *L. rhammnosus GG* exhibited reduction in the prevalence of oral *Candida* which subsequently may confer protective effect against oral candidosis. However, others investigated the effect of various lactobacilli and could not find an effect on oral *Candida*. This may be partly explained by the finding of the *ex vivo* experiment which demonstrated a profound but variable abilities of commercially available strain of lactobacilli probiotics to inhibit the growth of *C. albicans* possibly due to the low pH milieu produced by the lactobacilli. Relevant to this is the laboratory study which demonstrated that the *Candida*-infected mice which were fed with *L. acidophilus* exhibited accelerated clearance of *C. albicans* from the mouth.[14]

Probiotics and voice prosthesis

There is no research regarding relationship between dental restorative materials and probiotics. However, in larynx, the second barrier after oropharynx, probiotics strongly reduce the occurrence of pathogenic bacteria in voice prosthetic biofilms.[7] There is anecdotal evidence among patients in Netherlands that the consumption of buttermilk, which contains *Lactococcus cremoris*, *Lactococcus lactis* spp. that can produce antimycotics and other substances, prolongs the lifetime of indwelling voice prostheses.

Side effects and risks

Some live micro-organisms have a long history of use as probiotics without causing illness in people. Probiotics' safety has not been thoroughly studied scientifically. More information is especially needed on how safe they are for young children, elderly people, and people with compromised immune systems.

Side effects of probiotics, if they occur, tend to be mild and digestive (such as gas or bloating). More serious effects have been seen in some people. Probiotics might theoretically cause infections that need to be treated with antibiotics, especially in people with underlying health conditions. They could also cause unhealthy metabolic activities, too much stimulation of the immune system, or gene transfer (insertion of genetic material into a cell).[15]

Probiotic products taken by mouth as a dietary supplement are manufactured and regulated as foods, not drugs. Furthermore, uncertainty about specificity of probiotics effects and their mechanism of action is a cause of concern.

Precautions and contraindications

Since probiotics contain live micro-organisms, there is a slight chance that these preparations might cause pathological infection, particularly in critically ill or severely immunocompromised patients.[16] Probiotic strains of *Lactobacillus* have also been reported to cause bacteremia in patients with short-bowel syndrome, possibly due to altered gut integrity.[17-20] Caution is also warranted in patients with central venous catheters, since contamination leading to fungemia has been reported when *Saccharomyces* capsules were opened and administered at the bedside.[20,21] *Lactobacillus* preparations are contraindicated in persons with a hypersensitivity to lactose or milk.[22] *S. boulardii* is contraindicated in patients with a yeast allergy.[20,23] However, no contraindications are listed for *Bifidobacteria*, since most species are considered nonpathogenic and non-toxigenic.[16,17,19]

CONCLUSION

Probiotics are regulated as dietary supplements and are not subjected to the same rigorous standards as medications. A challenge with these products involves the complexity of quality control with live micro-organisms. As a result, individuals may obtain a product that is ineffective or that contains varying quantities of bacteria or yeast. Probiotic therapy uses bacterial interference and immunomodulation in the control of several infectious, inflammatory, and immunologic conditions. Similar to their better known actions in the GI tract, probiotics exert their effects in many ways also in the oral cavity. Based on the currently available clinical data, it seems that dietary probiotics do not confer a major risk for oral health. However, the risk of transferring antibiotic resistance from probiotics to virulent micro-organisms requires more evaluation. In conclusion, probiotics have made their way into oral healthcare and are more likely to be a boon rather than sham. Despite our rapidly increasing knowledge of pathogen–host interactions, the role of beneficial bacteria in preventing the emergence of pathogenic species and oral health remains obscure. There is a great need to elucidate the role of the oral beneficial microbiota, to identify beneficial bacteria and to conduct proper large-scale studies on the usefulness of probiotics to maintain or improve oral health.

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