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Probiotics and Prebiotics: A Review

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Abstract

Probiotics are live microbes that can be formulated into many different types of products, including foods, drugs, and dietary supplements. Traditionally, probiotics have been associated with gut health, and most clinical interest has been focused on their use for the prevention or treatment of gastrointestinal infections and diseases; however, during the past few years, several investigators have also suggested the use of probiotics for oral health purposes. Additionally, Prebiotics are nondigestible food ingredients that help in increasing populations of probiotic bacteria. Hence, promote the growth of beneficial micro-organisms that comprise part of the resident microbiota. This article presents a clear picture and evidence for the use of pro or prebiotics for the prevention of caries, periodontal diseases and their role in overall oral health.

Keywords*: probiotics, prebiotics, caries, periodontal disease, oral health.*

Introduction

Probiotics can be defined as living microbes, or as food ingredients containing living microbes, that beneficially influence the health of the host when used in adequate numbers. 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[1]. These bacterial genera are regarded as a part of the normal human microbiota. In the oral cavity, lactobacilli usually comprise fewer than 1% of the total cultivable microbiota, but no species specific to the oral cavity has been found[2,3]. Species commonly isolated from saliva samples include *L. paracasei, L. plantarum, L. rhamnosus,* and *L. salivarius.* Culture-based studies suggest that bifidobacteria are among the first anaerobes in the oral cavity[4,5]. During the last few years, several authors have suggested that probiotic bacteria originally planned for gut health could also be beneficial to oral health[4,5,6,7,8]. Additionally, prebiotics are the compounds in food that add to the growth and/or increase the activity of the probiotic organisms in the host. These prebiotics are basically fibrous compounds that are nondigestible. Thus, they pass through upper gastrointestinal (GI) tract undigested, acting as the substrate for the advantageous microorganisms, helping in their growth and enhanced biological activity. One need not take prebiotic for probiotic organisms to act, but together prebiotics make probiotic organisms more effective. Studies of prebiotics have mainly been focused on gastrointestinal microbiota and health benefits; there has been little work in the oral cavity[7]. A complete understanding of the broad ecological changes induced in the mouth by probiotics or prebiotics will be essential to assess their long-term consequences for oral health and disease[8].

Probiotics

Probiotics is a term derived from Greek language, which means “for life.” They include many microbial species and strains.

Desirable Probiotic Properties

In order for a potential probiotic strain to be able to exert its benefcial effects, it is expected to exhibit certain desirable properties[9]. The ones currently determined by in vitro tests are:

- Should be non-toxic and non-pathogenic preparation.
- Produce beneficial effect.
- Should withstand gastrointestinal juice.
- Should have good shelf life.
- Should replace and reinstate the intestinal microflora

Guidelines for Use of Probiotics

FAO/WHO in 2002 issued guidelines for the evaluation of probiotics for use in food products.

1. Probiotic organisms must be a live organism.
2. The organism must be identified up to species level.
3. It should have a proven safety data.
4. When used in a defined value and delivery system, must have a physiological effect on the host.
5. When used as food additive, must be biologically and genetically stable.
6. It should be economical.
7. It should maintain long-term stability on storage (adequate shelf life).
8. It should be nonpathogenic and nonhazardous.
9. It should be able to influence local metabolic activity

Mechanism of action of Probiotics

The general mechanisms of probiotics can be divided into three main categories: normalization of the intestinal microbiota, modulation of the immune response, and metabolic effects[10]. They have an antimicrobial effect through modifying the microflora, secreting antibacterial substances, competing with pathogens to prevent their adhesion to the intestinal epithelium, competing for nutrients necessary for pathogen survival, producing an antitoxin effect and reversing some of the consequences of infection on the intestinal epithelium, such as secretory changes and neutrophil migration[10]. Probiotics are also capable of modulating the immune system, regulating the allergic immune cell response of the body and reducing cell proliferation in cancer. The effects of these agents may go beyond the gastrointestinal tract to distant areas, such as the urogenital and respiratory mucosa, oral cavity and it may not be necessary to administer the intact probiotic organism to achieve benefits.

Mechanism effects in oral cavity

The ecological plaque hypothesis suggests that selective pressure in environmental conditions can change the balance between oral health and disease[10]. As bacteria can also influence their environment, and both synergistic and antagonistic interactions are suggested for bacteria in dental plaque, the environmental pressure described in the ecological plaque hypothesis could be introduced partly by bacteria. Second, it is well recognized that the normal microbiota protect the oral cavity from infections.

Finally, just as there are bacterial species associated with oral diseases, there are also species that seem to be associated with oral health[11,12].

Probiotic products and clinical applications in dentistry

The literature on the health benefits of probiotics has often focused on disease states using either animal models of such diseases or studies in human populations. More recently, investigators have been asking how to measure the impact of probiotics on healthy individuals, such as reducing the risk of developing disease or optimizing physiological function within normal ranges. The distinction between research aimed at maintaining general and oral health and that aimed at treating a disease has important regulatory implications; the former can be applied to foods and supplements, whereas the latter is confined to drugs.

Probiotics and caries-associated microbes.

Several studies suggest that consumption of products containing probiotic lactobacilli or bifidobacteria could reduce the number of *mutans streptococci* in saliva[13-17]. In most of these studies, the levels of salivary lactobacilli have also been measured, which resulted in increase in the number of salivary *Lactobacillus*[12,16]. It is important to realize that the salivary level of caries-associated microbes does not equate to dental caries. In fact, the microbiota of unstimulated whole saliva resembles that of the tongue more than of dental plaque. Thus, no conclusive statement about the effects of probiotic bacteria on dental caries can be made.

Probiotics and periodontal disease

Riccia and colleagues in 2007 studied the anti-inflammatory effects of *Lactobaillus brevis* in a group of patients with chronic periodontitis[18]. Anti-inflammmatory effects of *L.brevis* could be attributed to its capacity to prevent the production of nitric oxide and consequently the release of PGE2 and activation of MMPs induced by nitric oxide. Patients with various periodontal diseases, gingivitis, periodontitis, and pregnancy gingivitis, were locally treated with a culture supernatant of a *L. acidophilus* strain. Significant recovery was reported for almost every patient. There has been significant interest in using probiotics in treatment of periodontal disease recently, too. The probiotic strains used in these studies include *L. reuteri* strains, *L. brevis* (CD2), *L. casei Shirota, L. salivarius* WB21, and *Bacillus subtilis. L. reuteri* and *L. brevis* have improved gingival health, as measured by decreased bleeding on probing. The use of probiotic chewing gum containing *L. reuteri* ATCC 55730 and ATCC PTA 5289 also decreased levels of pro-inflammatory cytokines in GCF, and the use of *L. brevis* decreased MMP (collagenase) activity and other inflammatory markers in saliva[19,20]. Use of tablets containing *L. salivarius* WB21 has

been shown to decrease gingival pocket depth, particularly in high-risk groups such as smokers, and also affect the number of periodontopathogens in plaque.

Probiotics role in halitosis

Halitosis is not a disease but a discomfort, although some oral diseases including periodontitis may be the underlying cause; however, in approximately 90% of cases, the origin can be found in the oral cavity, and probiotics are marketed for the treatment of both mouth- and gut-associated halitosis[21,22]. Despite that, only a few clinical studies have found different probiotic strains or products to be efficacious. The studied strains include *E. coli* , *S. salivarius* K12, three *Weissella confusa* isolates, and a lactic acid–forming bacterial mixture, not specified by the authors of that work.[22]

Probiotics role in orthodontic therapy

Fixed orthodontic appliances are considered to jeopardize dental health due to accumulation of microorganisms that may cause enamel demineralization, clinically visible as white spot lesions[23].Furthermore, the complex design of orthodontic bands and brackets may create an ecological environment that facilitates the establishment and growth of cariogenic *mutans streptococci* strains[24]. Cildir et al. (2009) conducted a clinical study with probiotics and found out that daily consumption of fruit yogurt with *Bifidobacterium* could reduce the salivary levels of *streptococci mutans* in orthodontic patients with fixed appliances[25]. Further studies are needed to clarify if this approach is an alternative strategy for prevention of demineralization and white spot formation during orthodontic treatment[25,26].

Probiotics and the immune system

There is growing evidence that probiotics help maintain a strong immune system. The most powerful and important aspect of the immune system involves the body's probiotic bacteria. The human body houses more than 32 billion beneficial and harmful bacteria and fungi at any particular time. When beneficial bacteria are in the majority, they constitute 70-80% of the body's immune response. They stimulate the body's immune cells, activating the cell-mediated response, the humoral response, and indirectly, the body's exterior barrier mechanisms through immunoglobulin stimulation[27]. Three decades of medical research has indicated that probiotics stimulate T-cells, B-cells, macrophages and NK-cells with smart messages that promote specific immune responses. They also activate cytokines and phagocytic cells directly to coordinate their intelligent immune response[27].

Role of probiotics in oral cancer

The anticancer effects of probiotics were long recognized but evidence in literature is minimal. Evidence is cropping up that probiotics can interfere at various stages of cancer process, more so by interference with chromosomal and DNA damage. However, more research is required to develop specific regulations on their consumption[28,29]

Prebiotics

The term prebiotics was coined in 1995 by Gibson and Roberfroid as a "non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria already resident in the colon"[1].

Mechanism of action

The ability of certain oligosaccharides to enhance the growth of resident commensal gut bacteria, particularly Bifidobacteria and Lactobacilli, is well documented[30,31] Thus, the major mechanism of action of prebiotics is assumed to be indirect, i.e. facilitating the proliferation of beneficial components of the resident microflora, with probiotic effects resulting from the actions of these bacteria as described above.

Types of Prebiotics

There are many types of prebiotics. Majority of them are a subset of carbohydrate groups and are mostly oligosaccharide carbohydrates (OSCs). The relevant are mainly on OSCs, but there are also some pieces of evidence proving that prebiotics are not only carbohydrates[8,32].

Fructans

This category consists of inulin and fructo-oligosaccharide or oligofructose. Previously, some studies implicated that fructans can stimulate lactic acid bacteria selectively. However, over recent years, there are some investigations showing that the chain length of fructans is an important criterion to determine which bacteria can ferment them. Therefore, other bacterial species can also be promoted directly or indirectly by fructans.

Galacto-Oligosaccharides

Galacto-oligosaccharides (GOS), the product of lactose extension, are classified into two subgroups: (i) the GOS with excess galactose at C3, C4 or C6 and (ii) the GOS manufactured from lactose through enzymatic trans-glycosylation. GOSs can greatly stimulate *Bifidobacteria* and *Lactobacilli*. Bifidobacteria in infants have shown high incorporation with GOS. Enterobacteria, Bacteroidetes, and Firmicutes are also stimulated by GOS, but to a lesser extent than Bifidobacteria[33]. There are some GOSs derived from lactulose, the isomer of lactose. This lactulose-derived GOSs are also considered as prebiotics[34].

Starch and Glucose-Derived Oligosaccharides

There is a kind of starch that is resistant to the upper gut digestion known as resistant starch (RS). RS can promote health by producing a high level of butyrate; so it has been suggested to be classified as a prebiotic[35]. Polydextrose is a glucose-derived oligosaccharide. It consists of glucan with a lot of branches and glycosidic linkages. There is some evidence that it can stimulate Bifidobacteria, but it has not been confirmed yet[36].

Other Oligosaccharides

Some oligosaccharides are originated from a polysaccharide known as pectin. This type of oligosaccharide is called pectic oligosaccharide (POS). They are based on the extension of galacturonic acid (homogalacturonan) or rhamnose (rhamnogalacturonan I). Various types of sugars (e.g., arabinose, galactose, and xylose) or ferulic acid are linked to the side chains[37]. Their structures vary significantly depending on the sources of pectic oligosaccharides.

Non-Carbohydrate Oligosaccharides

Although carbohydrates are more likely to meet the criteria of prebiotics definition, there are some compounds that are not classified as carbohydrates but are recommended to be classified as prebiotics, such as cocoa-derived flavanols. In vivo and in vitro experiments demonstrate that flavanols can stimulate lactic acid bacteria.

Conclusion

Maybe because long-term colonization by probiotic bacteria is unlikely, potential adverse effects of probiotic bacteria in the oral cavity have not been a subject of much intensive research; however, probiotic products are used widely; therefore, when dental health is considered, the acidogenicity of lactobacilli and bifidobacteria cannot be overlooked. The effect of widespread use of safe and effective

probiotic products on society-wide economic and quality-of-life indicators should be assessed with end points such as reduction of common infectious diseases in developing and developed nations. Such information could provide support for sustained research in this field. 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.

There is evidence from multiple studies that prebiotic arginine can inhibit caries development and probiotic supplements seem to reduce caries incidence in preschool children and schoolchildren with a high caries risk. Due to ethical research issues for arginine and the risk of bias for both the pre- and probiotic studies, the confidence in effect estimate is limited. More trials are needed to gain better knowledge of pre- and probiotic supplements and to confirm that their use is beneficial and cost-effective in caries care.

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