Review Article

Role of Probiotics in Prevention of Dental Caries: A Review

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Abstract:
Despite the use of age old conventional physical and chemotherapeutic methods for caries management, dental caries still continues to be the most prevalent form of oral infectious disease. Thus, there is a need for additional approaches to deal with dental caries. The aim of this comprehensive review is to present an update about the recent advances in probiotic use for the prevention of dental caries. Authors concluded that studies conducted recently in this discipline show that probiotics have got immense potential in dental caries prevention. **'**An apple a day keeps doctor away' the famous quote now in recent years will definitely modify into 'Probiotics per day keeps doctor away'.

Key words: Dental caries, Probiotics, streptococcus mutans,

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Introduction

The term probiotic, meaning "for life," is derived from the Greek language. It was first used by Lilly and Stillwell in 1965 to describe "substances secreted by one microorganism which stimulates the growth of another" and thus was contrasted with the term antibiotic.[1] It can be defined as "Live microorganisms that when administered in adequate amounts confer a health benefit on the host" (FAO/WHO 2001). There has been a paradigm shift towards an ecological and microbial community-based approach to understanding oral diseases. This has significant implications for approaches to therapy and has raised the possibility of developing novel strategies through manipulation of the resident oral microbiota and modulation of host immune responses. The increased popularity of using probiotic bacteria supplements to improve gastrointestinal health has prompted interest in the utility of this approach for oral applications.[2]

Dental caries is one of the most common preventable childhood diseases; people are

susceptible to this ailment throughout their lifetime. Various approaches including Chemoprophylactic agents, Antibiotics, Caries Vaccines, Sugar Substitutes, Fluorides, Restorative materials have been in use, however the anti-caries effects of these approaches are still limited. Hence the main aim of this review is to discuss the role of probiotics in dental caries prevention.

Micro-organisms commonly used as Probiotics[3]

Lactobacillus:	acidophilus casei plantarum delbreukii sp., bulgaricus reuteri gasseri fermentum salivarius
Pediococcus:	pentosaceus
Saccharomyces:	cerevisiae boulardii

Bifidobacterium:	bifidum lactis
Enterococcus:	faecium
Bacillus:	subtilis cereus coagulans licheniformis
Aspergillus:	oryzae

Mechanism of action in oral cavity[1, 2]

1. Prevention of adhesion of pathogens to host tissues.
2. Stimulation and modulation of the mucosal immune system, e.g. by reducing production of pro-inflammatory cytokines through actions on NFkB pathways, increasing production of anti-inflammatory cytokines such as IL-10 and host defence peptides such as b-defensin 2, enhancing IgA defences and influencing dendritic cell maturation.
3. Modulation of cell proliferation and apoptosis through cell responses to, for example, microbially produced short chain fatty acids.
4. Improvement of intestinal barrier integrity and upregulation of mucin production.
5. Killing or inhibition of growth of pathogens through production of bacteriocins or other products, such as acid or peroxide, which are antagonistic towards pathogenic bacteria.
6. Involvement in binding of oral micro-organisms to proteins (biofilm formation).
7. Action on plaque formation and on its complex ecosystem by competing and intervening with bacteria-to-bacteria attachments.
8. Involvement in metabolism of substrates (competing with oral micro-organisms of substrates available).

Ideal properties of Probiotics[4]

An effective probiotic should:

1. Exert a beneficial effect on the host
2. Be non-pathogenic and non-toxic
3. Contain a large number of viable cells
4. Be capable of surviving and metabolizing in the gut
5. Remain viable during storage and use
6. Have good sensory properties
7. Be isolated from the same species as its intended host.

Role of Probiotics in Prevention of Dental Caries

In caries, there is an increase in acidogenic and acid-tolerating species, such as mutans streptococci and lactobacilli, although other bacteria, like *Bifidobacteria, nonmutans streptococci, Actinomyces spp., Propionibacterium spp., Veillonella spp. and Atopobium spp.,* with similar properties can also be found. The use of probiotics and molecular genetics to replace and displace cariogenic bacteria with noncariogenic bacteria has shown promising results.[5] Here we are going to discuss about the various studies conducted in this regard.

Anti-caries effect of various Probiotics as per their mechanism of action

1. **Improvement of intestinal barrier integrity and upregulation of mucin production:** Long-term consumption of milk containing *Lactobacillus rhamnosus* GG strain can reduce initial caries in kindergarten children. Ingestion of *Lactobacillus reuteri* ATCC 55739 or *Bifidobacterium* DN-173 010 can induce significant reduction of cariogenic *S. mutans* in saliva.[6] Mollstam, et al. disclosed several new strains of *Lactobacillus*, including *L. reuteri* CF2-7F (ATCC PTA-4965), *L. reuteri* MF2-3 (ATCC PTA-4964) and especially *L. reuteri* FJ1 "Prodentis" (ATCC PTA-5289) and *L. reuteri* FJ3 (ATCC PTA-5290), that have good antimicrobial activity against *S. mutans* and good binding characteristics to oral mucin and thereby prevent, reduce or treat dental caries.[7]

2. **Involvement in binding of oral micro-organisms to proteins (biofilm formation), action on plaque formation and on its complex ecosystem by competing and intervening with bacteria-to-bacteria attachments:** Several mutated strains of *S. mutans* that lack the machinery to efficiently metabolize fermentable carbohydrates to organic acids have been developed. In one case, a non-acid-producing *S. mutans* strain BCS3-L1 that produces an antibiotic called mutacin 1140 active against other *S. mutans* strains to replace the naturally occurring cariogenic strains in oral cavity has been developed. This strain was significantly less cariogenic than the parent strain JH1140 due to the delete of lactic acid dehydrogenase open reading frame.[6] In another study, the ability of *S. mutans* to produce extracellular glucans is blocked in a mutation by deleting the GTF-C gene. Introducing this new strain into an *in vitro* mixed biofilm model resulted in a decrease in extracellular matrix component from 51 to 33 percent of the biofilm volume.[8]

3. **Killing or inhibition of growth of pathogens through production of bacteriocins or other products, such as acid or peroxide, which are antagonistic towards pathogenic bacteria. Involvement in binding of oral micro-organisms to proteins (biofilm formation):** Calgar et al (2007) evaluated the effect of xylitol and probiotic chewing gums on salivary *mutans streptococci* and *lactobacilli* and concluded that daily chewing on gums containing probiotic bacteria or xylitol reduced the levels of salivary *mutans streptococci* in a significant way.[9] Hasslof et al reported that at concentrations ranging from 10^9 to 10^5 CFU/ml, all lactobacilli strains inhibited the growth of the MS strains completely with the exception of *L. acidophilus* La5 that executed only a slight inhibition of some strains at concentrations corresponding to 10^7 and 10^5 CFU/ml. *L. acidophilus* La5 had a statistically significant weaker inhibition capacity in comparison with the other probiotic strains. At the lowest cell concentration (10^3 CFU/ml), only *L. plantarum* 299v and *L. plantarum* 931 displayed a total growth inhibition while a slight

inhibition was seen for all five MS strains by *L. rhamnosus* LB21, *L. paracasei* F19, *L. reuteri* PTA 5289 and *L. reuteri* ATCC 55730. *L. rhamnosus* GG ATCC 53103 diluted to 10^3 CFU/ml inhibited the growth slightly for three of the five MS strains (*S. mutans* NCTC 10449, *S. sobrinus* OMZ176 and *S. mutans* P1:27) while low concentrations of *L. acidophilus* La5 did not affect MS growth.[10] Cildir et al demonstrated that daily consumption of fruit yogurt with *Bifidobacterium animalis* subsp. *Lactis* DN-173010 could reduce the salivary levels of mutans streptococci in orthodontic patients with fixed appliances.[11] Suzuki N et al evaluated the capacity of *E. faecium* WB2000 to inhibit biofilm formation by oral viridans group and mutans group streptococci. *E. faecium* WB2000 inhibited biofilm formation by the clinical mutans group streptococci, except for *S. mutans* SMW09, which was an exception to the probiotic effect of *E. faecium* WB2000.[12] Heng et al reported that *S. salivarius* M18 (formerly strain Mia) exhibited broad-spectrum inhibitory activity against several streptococcal pathogens, notably the caries-causing *Streptococcus mutans.*[13] Twetman et al carried out a study to assess the effectivity of probiotics in caries reduction in children and reported a significant caries reduction in 3 to 4 year-old children after 7 months of daily consumption of probiotic milk.[14] Singh et al reported that probiotic ice-cream containing Bifidobacterium lactis Bb-12 ATCC27536 and Lactobacillus acidophilus La-5 can reduce the levels of certain caries-associated micro-organisms in saliva.[15] Keller et al concluded that selected lactobacilli displayed co-aggregation activity and inhibited growth of clinical mutans streptococci. The growth inhibition was strain-specific and dependent on pH and cell concentration.[16] B. adolescentis SPM1005 cells decreased the growth of S. mutans, which is a risk factor for dental caries. Therefore, authors suggested that this Bifidobacterium strain may be a useful probiotic microorganism for prevention of dental caries that does not have adverse effects.[17] Glavina et al reported significant reduction in S. mutans and Lactobacillus spp. salivary counts in children after 14 days consumption of commercially available yoghurt containing Lactobacillus rhamnosus ATCC53103 - LGG (Bioaktiv LGG, Dukat, Croatia).[18] Bosch et al also concluded that lactic acid bacteria show promising properties to be used as potential probiotics for improving oral health.[19] In several other reviews and studies it was found that probiotics showed significant reduction in the count of cariogenic bacteria.[20, 21, 22, 23, 24]

New Approaches to achieve Probiotic Effects

Interference with signaling mechanisms: Several pathogenic properties of *S. mutans* are regulated by quorum sensing mechanism involving Competence Stimulating Peptide (CSP) as the signaling molecule. Addition of a high concentration of CSP can interfere with signaling events of *S. mutans* and induce the death of the bacterium, thus exhibiting a potential beneficial effect against dental caries.[25]

Targeted antimicrobial therapy via a novel STAMP technology: Eckert *et al.* reasoned that, with the exception of a limited number of pathogens, the majority of indigenous oral microorganisms are benign or beneficial. Currently available antimicrobials exhibit broad spectrum killing properties Indiscriminate killing of all microbes by these conventional antimicrobials disrupts the ecological balance of the indigenous microbiota with unknown clinical consequences. These investigators formulated a new class of antimicrobials called Specifically Targeted Anti-Microbial Peptides (STAMPs). A

"STAMP" is a fusion peptide with two moieties: a killing moiety made of a nonspecific antimicrobial peptide and a targeting moiety containing a species-specific binding peptide. The targeting moiety provides
specific binding to a selected pathogen and facilitates the targeted delivery of an attached antimicrobial peptide.[25]

Safety concerns

Probiotics like Lactobacilli, bifidobacteria, and lactococci have generally been regarded as safe. There are other probiotic organisms, such as *Enterococcus, Bacillus*, and other spore-forming bacteria, as well as streptococci, that are not generally regarded as safe but have been
used as probiotics, their use is associated with increased risk of Bacteremia and endocarditis development.[26] Till date only few studies were reported in relation to safety of probiotics in the field of dentistry. Mackay et al [27] reported the development of L. rhamnosus endocarditis (strain not specified) after a dental extraction in a 67 year old man with mitral regurgitation who was taking probiotic capsules daily.

Future Aspects:

In the present day, technology has improved drastically. Very soon, people will be able to go into space to live on the planets like the moon. NASA of USA is carrying out research to develop probiotic products which enable humans live in space.[28]

Importance to paediatric dentists

In this review, we discussed the recent developments in the use of probiotics for dental caries prevention. It is essential for the paediatric dentists to know about all the preventive measures against dental caries as they are the one who deal with the children and encounters dental caries very frequently. 'An apple a day keeps doctor away' the famous quote now in recent years will definitely modify into 'Probiotics per day keeps doctor away'.

Conclusion

Probiotics have got immense potential in dealing with dental caries as revealed by the studies conducted recently in this discipline. More studies are needed to explore the use of probiotics appropriately in the field of dentistry.

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