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Is Sealing and Healing a Carious Lesion Possible? Recent Advances in Prevention of Dental Caries: A Review



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ABSTRACT

Dental caries is one of the most common infectious microbial diseases. It is said that prevention is better than cure. The philosophy of preventive dentistry gives meaning to the practice of dentistry. Dental caries is one of the most common infectious microbial diseases. It is rightly said that prevention is better than cure. Various steps in the prevention of dental caries have been taken, with which fluoride being the most common among them. Various non-fluoride agents are also present which helps in the prevention of dental caries. This paper reviews various recent advances in the prevention of dental caries.



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INTRODUCTION

Prevention of ill-health is not an altruist concept. ^[1] It is mankind's primary hope for upgrading health. Therefore, the tradition of emphasizing prevention through diet and modification of lifestyle encompasses a long record. Prevention is defined as an action taken before the emergence of a disease that eliminates the chance that the disease will ever occur. This review provides a perspective of the novel methods in the prevention of dental caries.

It can be classified as: -

- **Methods which modify the host: -**

- a) Remineralising agents-

1. Fluoride containing agents
2. Silver diamine fluoride
3. Fluoride containing dentifrices

- b) Non-fluoride containing agents

1. CPP-ACP
2. Bioactive glass



- **Methods that modify the microflora: -**

- a) Antimicrobial peptides

- b) Plant extracts

- c) Arginine

- d) Probiotics

- e) Prebiotics

- f) Replacement therapy

- g) Caries vaccine

- **Methods that modify the substrate:-**

a) Sugarpolyols

SILVER DIAMINE FLUORIDE (SDF)

38% SDF has been widely used, primarily for caries prevention and arrest in children. 38% SDF is an alkaline (pH 10) colourless solution, containing 24%-27% silver (Ag), 8.5%-10.5% ammonia (NH₃) and 5.0%-6.0% fluoride (F).² Excavation of caries is not required prior to application. Teeth are air-dried, and SDF is applied to the carious lesions using a micro brush for 1 minute and rinsed.³The effect of SDF diminishes over time, therefore follow-up applications are required as the lesion can revert to further carious demineralization in 24 months.⁴ The recommended safest maximum dose of SDF per visit is 1 drop/10 Kg.³ SDF affects the tooth structure and the caries process. The formation of silver phosphate turns SDF-treated carious lesions black.⁵Many studies have found that SDF is significantly effective in arresting the cavitated as well as incipient carious lesions.^{4,6,7}

CASEIN PHOSPHOPEPTIDE- AMORPHOUS CALCIUM PHOSPHATE

Amorphous calcium phosphate (ACP) was first described by Aaron S Posner in the mid-1960s. It has the ability to remineralize the early carious lesion, has a position over fluoride toothpaste when it comes to neutralizing acids in the oral cavity. CPP has the ability to stabilize calcium phosphate in solution as ACP nanocomplexes, thereby promoting the formation of small CPP-ACP clusters. CPP can stabilize the level of ACP in saliva as it acts as a reservoir of calcium and stabilizes the level of calcium. CPP-ACP clusters act as a pool of calcium and phosphate that binds to dental plaque and tooth surfaces. On acid challenge, the attached CPP-ACP liberates calcium and phosphate ions, thus a supersaturated mineral environment is maintained, thereby reducing demineralization and promoting remineralization.⁸Presence of agent CPP-ACP on dentine surfaces provoked lower demineralization and higher remineralization in comparison with the dentine surfaces without agent.⁹CPP-ACP may offer a safe and efficient alternative to fluorides with less mineral content loss and more remineralization of early caries lesion.¹⁰

BIOACTIVE GLASS

Bioactive glass (45S5) has been developed for dental application and applied in a number of studies to remineralize white-spot lesions. This has shown promising results in inducing

apatite formation when it contacts saliva or any physiological fluid. These apatites comprised of either hydroxyapatites or fluorapatite, if fluoride was incorporated into the chemical composition of the glass structure it has ‘smart’ properties, with increased remineralization activity in low pH environments.¹¹The bioactive glass-containing toothpaste was highly efficient in promoting enamel remineralization by the formation of deposits and a protective layer on the demineralized surface in comparison with other approaches.¹²

ANTIMICROBIAL PEPTIDE

Antimicrobial peptides (AMPs) are a heterogeneous group of molecules with similar antimicrobial properties that have a high potential for controlling bacterial infections and improving biofilms.

The specifically targeted antimicrobial peptide (STAMP) is a synthetic fusion peptide with 2 independent functional domains, comprising of a *Streptococcus mutans*-selective “targeting domain” designated as C16, and a “killing domain” designated as G2. C16 is derived from a fragment of the *S. Mutans* competence stimulating peptide (CSP), while G2 is derived from a broad-spectrum antimicrobial peptide. C16G2 had antimicrobial mechanisms similar to traditional amps, and critically, its membrane-disrupting activity specifically targets *S. Mutans* from multispecies biofilms without affecting closely related non-cariogenic oral streptococci.¹³

Their mechanism of action involves binding to the negatively charged moieties, e.g; Lipopolysaccharide (LPS), on the microbial membrane. The peptides lead to membrane disruption by insertion once they get bounded to the microbial surface, but may also translocate into the microbe and kill by intracellular mechanisms.

PLANT EXTRACTS

NEEM (*Azadirachta indica*)

The phytochemical components present in *neem* are nimbidin, Nimbin, nimbolide, Azadirachtin, gallic acid, epicatechin, catechin, and margolone. All these exhibit potent antibacterial activities. The chief active constituent of *neem* is azadirachtin, which is an effective antimicrobial agent.¹⁴

Neem exhibits antimicrobial effects against *S. Mutans* and *S. Faecalis*. Ethanolic extract of *Neem* leaves, sticks, and bark have shown remarkable antibacterial activity. Dried chewing

sticks of *Neem* exhibited significant antibacterial activity against *S. Mutans* when compared to other cariogenic organisms like *S. Salivarius*, *S. Mitis* and *S. Sanguis*.

TULSI (*Ocimum sanctum*)

Tulsi has been reported to exhibit antimicrobial properties against a variety of microorganisms like *Staphylococcus aureus*, *Klebsiella*, *Candida albicans*, *E. Coli*, and *proteus*. The antibacterial effect of Tulsi may be ascribed to the presence of methyl ester of salicylic acid which accentuates granulation and regeneration of tissues. Ursolic acid and carvacrol might also be responsible for their antimicrobial activity. **Agarwal et al.2010**; in their study demonstrated an antimicrobial potential of tulsi extract at various concentrations and achieved maximum antimicrobial potential at 4% concentration level.¹⁵

PRUNUS MUME

Prunus mume, known as Japanese apricot, is used as a traditional medicinal food in Korea, China, and Japan.¹⁶ It is considered to be the potential candidate for developing an oral antimicrobial agent to control or prevent dental diseases associated with oral pathogenic bacteria like *Streptococcus mutans*, *S. sobrinus*, *S. Mitis*, *S. Sanguinis*, *Lactobacillus acidophilus*, *P. gingivalis*, *Aggregatibacter actinomycetemcomitans*.¹⁷

GREEN AND BLACK TEA (*Camellia sinensis*)

Tea is an infusion of the leaves of the *Camellia sinensis* plant. **Smullen et al.2007**;¹⁸ have shown that extracts from unfermented green tea have a bacteriostatic effect on *Streptococcus mutans*. **Suyama et al. 2011**;¹⁹ evaluated enamel remineralization and the acquisition of acid resistance by using sugar-free chewing gum containing fluoride extracted from green tea and found that fluoride chewing gum (FCG) produced a superior level of remineralization and acid resistance, as compared to the placebo gum. The results suggest that regular use of FCG is useful for preventing dental caries.

HOP PLANT (*Humulus lupulus*): **Tagashira et al.**²⁰ reported the inhibition of *S. Mutans* and other oral streptococci, by the antimicrobial active ingredients of the hop plant. They found that all tested hop constituents inhibited the streptococci with minimum inhibitory concentration at pH7.5 ranging from 2 to 50 µg/ml.

MESWAK CHEWING STICKS (Twigs of *Salvadora persica*): Meswaksticks when embedded in agar or suspended above the agar plate had potential antibacterial effects against

all tested bacteria. This was suggested due to the presence of the volatile active antibacterial compound.

PROPOLIS: Propolis is a natural beehive product, has shown significant antibacterial activity against *S. Mutans* and/or *S. Sobrinus in vitro*^{21,22} Propolis extract when used as a mouthwash exhibits an *in vivo* antimicrobial activity against *S. Mutans* and might be used as an alternative measure to prevent dental caries.²³

ARGININE

Arginine, a common amino acid found in saliva is broken down by oral plaque bacteria to acid-neutralizing alkali. The production of acid by dental plaque is the direct cause of dental caries; it is noteworthy that increases in the proportions of aciduric organisms appear to occur at the expense of species that are less acidic and generally associated with dental health; including *Streptococcus sanguinis* and *Streptococcusgordonii*.^{24,25} Some of the less aciduric organisms associated with dental health derive protection from plaque acidification by hydrolyzing urea or arginine to ammonia, either by expressing a urease enzyme or by the **arginine deiminase system (ADS)**, respectively.

PROBIOTICS

The term probiotics were derived from the Greek words, meaning “for life”. In 1960, Lilly and Stillwell introduced the word probiotics as “Substances produced by microorganisms that stimulate the growth of another.” Caries is considered as an infectious disease, efforts were made to control the growth and spread of microorganism causing dental caries and probiotics had shown its significant effect in reducing the proliferation and adherence of cariogenic bacteria of which *Lactobacillus* and *Bifidobacterium* sp. were the most commonly used.²⁶ *Streptococcus mutans* is the main bacteria causing the initiation of tooth decay. *S. salivarius* BLIS M-18 was found to inhibit *Streptococcus mutans* which should help in preventing the development of dental caries.²⁷

PREBIOTICS

Prebiotics are "nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon."²⁸ They enhance the growth and activity of beneficial organisms and simultaneously suppress the growth and activity of potentially deleterious bacteria. Some commonly known prebiotics

are Lactose, Insulin, Galactooligosaccharides, Fructooligosaccharides, and Xylo oligosaccharides. Naturally, occurring prebiotics are in fruits like tomato, bananas, asparagus, garlic, onion, and wheat. The combination of prebiotics and probiotics may have additive and synergistic effects providing better oral health conditions.²⁹

REPLACEMENT THERAPY

Replacement therapy is a method that competitively reduces the pathogen composition in the oral microflora has emerged with the advances in gene engineering and DNA recombination technology. Replacement therapy necessitates the use of a harmless effector strain that is permanently colonized in the host's microflora. This effector strain is designed to prevent the colonization or outgrowth of a particular pathogen.³⁰

An effector strain for replacement therapy of dental caries is called BCS3-L1 has been constructed (Hillman & others, 2000) that took into account the following logical prerequisites: It must have a definitely reduced pathogenic potential, it must persistently and pre-emptively colonize the *S mutans* niche, thereby preventing colonization by wild-type strains whenever the host comes in contact with them, Ideally, it should combatively displace indigenous strains of *S mutans*, thereby allowing even previously infected subjects to be treated with replacement therapy and it must be generally safe and not predispose the host to other disease conditions.

CARIES VACCINE

It stimulates the production of a protective antibody and other immune mechanisms. Some of the possible ways antibodies might control bacterial growth are listed below:³¹

- i. The salivary immunoglobulin may act as a specific agglutinin interacting with the bacterial surface receptors and inhibiting colonization and subsequent caries formation. They might also inactivate surface glucosyltransferase, which will reduce the synthesis of extracellular glucans resulting in reduced plaque formation.
- ii. The salivary glands produce secretory IgA antibodies by direct immunization of the gut-associated lymphoid tissue (GALT), from where sensitized B-cells may be home to the salivary glands. The salivary IgA antibodies have, of course, direct access to the tooth surface. They may prevent *S. mutans* from adhering to the enamel surface or they may prevent the formation of dextran by inhibiting the activity of glucosyltransferase (GTF).

SUGAR POLYOLS

Xylitol is a five-carbon sugar alcohol (Polyol) that appears and tastes similar to sucrose. Xylitol cannot be utilized and fermented by MS or other microorganisms in the oral cavity, however, it may be directly absorbed by the human small intestine and eventually metabolized. Both *in vitro* and *in vivo* studies^{32,33} showed that the plaque pH is not affected by the intake of xylitol, and it was found that xylitol has a bacteriostatic effect on *S. mutans* by forming a futile cycle that utilizes cellular ATP. In a futile cycle, Xylitol is transported across the bacteria cell membrane by a phospho-transferase system, producing xylitol-5-phosphate which cannot be metabolized and may eventually be dephosphorylated and exported at the cost of ribitol-5-phosphate. Xylitol declines the degree of Mutans streptococci (MS) in plaque and saliva by disrupting their energy generation processes, leading to a futile energy cycle and cell death.

CONCLUSION

For caries prevention, oral hygiene measures, fluoride application, pit-and-fissure sealants, the utilization of xylitol, the development of a dental caries vaccine, and the role of the primary caregiver for infants have been established. For both demineralization prevention and remineralization stimulation, one vital concept that may anticipate the benefit of the therapy is effective drug retention on the surface of the tooth. Even with recent dental caries research, restorative treatment is the method that is followed by most clinical practitioners once decay has been detected. Further education and clinical research efforts should be continued to accentuate early detection and caries prevention.

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