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Fluoride Alternatives in the Prevention of Dental Caries: A Review

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There is no doubt that fluoride has been playing an important role in the prevention of dental caries and has been incorporated in various products (in both topical and systemic forms). However, few researchers consider fluoride to be a double edged sword as its use as an anticaries agent has been marked by various controversies because of the health concerns associated with the excessive use of the fluorides with its chronic use has been found to be associated with dental fluorosis, skeletal fluorosis, osteoporosis of long bones, carcinomas, renal and gall bladder calcification etc. The efficacy of fluorides to pit and fissured of the tooth surface is also questioned as its effect only seems to be limited to the smooth surface to the tooth. Hence, this review provides the readers with alternative fluoride free delivery mechanisms for caries prevention which can be used as an effective public health measure.

KEYWORDS: Fluoride, Pit and Fissure Sealants, Probiotics, Remineralization Therapy

INTRODUCTION

Many researchers agree that dental caries is a major public health problem and one of many diseases of modern civilization affecting approximately 90% of the children and 60% adults across the globe.¹

Preventing dental caries is based on the concept of breaking the chain of events that promotes its formation. In earlier times, the only available treatment was extraction, and debridement and restoration was introduced only during 1800s. While preventive dentistry has taken giant leaps of modernization since then and according to the principle of lege artis, all our efforts should concentrate on preventing, controlling and arresting dental caries therefore, modern philosophy in caries management highlights the concept of active prevention and early detection.²

The major breakthrough in caries reduction was achieved by the early findings of Trendley H. Dean in 1934 who for the first time demonstrated that fluoride in the concentration of 1 ppm caused significant reduction in dental caries. Since then, fluoride occupies an important position in preventive dentistry and has been used across the world as the major instrument for caries reduction in topical and systemic forms with its contribution leading to significant reduction in dental caries

experienced by most industrialized countries in the latter part of the 20th century.³

The journey of fluoride since its discovery as an anticaries agent has been marked by various controversies because of the health concerns associated with the excessive use of the fluorides with its chronic use has been found to be associated with dental fluorosis, skeletal fluorosis, osteoporosis of long bones, carcinomas, renal and gall bladder calcification etc. Further the effectiveness of fluoride is also being questioned on the basis that the protective effect of the fluoride is restricted to the smooth surfaces only whereas 80% of the caries occurs in the occlusal pits and fissures where the fluoride is least effective.³

This presented the need to explore the use of alternative fluoride free delivery mechanisms for the caries prevention which can be used effectively as an effective public health measure and hence, this review describes various alternatives to fluoride used in the prevention of dental caries which include:

1. Pit and fissure Sealants
2. Specific Fluoride alternatives
3. Remineralization Therapy

4. Caries Vaccine
5. Probiotic Approaches
6. Others

1 Pit and fissure sealants

For the past few decades, a significant reduction in the prevalence of dental caries in children of United States of America (USA) has been well documented. It was also reported that fluoride has played a large role in decreasing the amount of smooth surface decay, but had the least preventive effect on pit and fissure caries with the National Dental Caries Prevalence Survey highlighting that a whopping 84 percent of caries in 5- to 17-year old children involved surfaces with pits and fissures.

In this context, the use of dental sealants are one of the most effective ways of preventing dental caries in pits and fissures. Fissure sealants are materials which are designed to prevent pit and fissure caries when they are applied to the occlusal surface of the teeth in order to obturate occlusal fissures and to remove the sheltered environment in which dental caries may thrive. Currently there are two types of pit and fissure sealants available: resin based and glass ionomer cements. The resin based sealants are further divided into generations according to their mechanism for polymerisation or content.⁴

Safety and Efficacy Data of Sealants⁵

ADA Specification No. 39 established the following requirements:

1. Working time for type I sealants is not less than 45 seconds.
2. Setting time is within 30 seconds of the manufacturer's instructions and does not exceed three minutes.
3. Curing time for type II sealants is not more than 60 seconds,
4. Depth of cure for type II sealants is not less than 0.75 millimeters,
5. The uncured film thickness is not more than 0.1 mm.
6. Sealants meet the biocompatibility requirements of American National Standard/American Dental Association Document No. 41 for Recommended Standard Practices for Biological Evaluation of Dental Materials.⁶

Efficacy of the Pits and Fissure Sealants: Dental pit and fissure sealants have been scientifically

proven to be highly effective and beneficial in the prevention of pit and fissure caries. Data from a Cochrane meta-analysis (2004) on the effectiveness of sealants analyzed data from eight clinical trials, of which seven were split-mouth studies and one a parallel-group study with the results implicating that the overall effectiveness of resin-based sealants in preventing dental decay on first permanent molars was very high. A reduction in caries from 86% at 12 months to 57% at 48-54 months was also observed in the meta-analysis.⁶

The Glass Ionomer based sealants have been documented to be equally effective in caries reduction as compared to their resin counterparts because of their fluoride releasing properties. Even after the partial loss of the sealant material the GIC based sealants are effective in caries prevention. However the main disadvantage with the use of Glass ionomer based sealants is inadequate retention and loss over period of time.⁷

2. Specific Fluoride Alternatives

G.C. Forward in the year 1994 classified specific fluoride alternatives as:⁸

- **Phosphorus-containing agents:** These agents represent the greatest number of potential non-fluoride anticaries agents and include simple inorganic salts ranging from sodium and potassium to the more complex polyphosphates, such as trimetaphosphate and pyrophosphate. They also include, but are not limited to organic phosphates such as glycerophosphate and phytate whose data on animal studies show cariostatic activity.
- **Calcium-containing agents:** Calcium lactate has been documented to be a potential anticaries agent in at least two animal caries studies (1.2% and 2.15% levels were used in the diet of animals). Another potential method to raise calcium and phosphorus levels in plaque by physically entrapping particles, e.g., calcium salts and support for this possibility was first observed by Duke (1986), who investigated calcium-carbonate-based toothpastes, which were compared with alumina-based toothpastes by a modification of the Frostell (1970) technique.⁸ Another fact to note is that while calcium carbonate is a well-known antacid, alumina-based toothpastes have a limited plaque acid buffering potential.

• **Antimicrobials:** To decrease the incidence of human dental caries, the use of antimicrobial control to control the flora of the dental plaque may be beneficial as an alternate to fluoride and sugar restriction. Early studies have sufficiently demonstrated that antibiotics could reduce levels of mutans streptococci in the oral mucosa thus reducing the dental caries activity.⁹ In contrast, there is general agreement that antibiotics are inappropriate for routine use as anti-plaque agents and should be only be restricted for use in medicine. Antibiotics range from penicillin to the well-known anti-plaque agents, Chlorhexidine and Alexidine. In human studies, both Chlorhexidine and Triclosan have been shown to reduce plaque acid production.³ Human trials across the globe support the view that antimicrobials have anti-carries potential and it has been proven that penicillin employed systemically, Vancomycin and Kanamycin applied in trays have all resulted in a decrease in dental caries in humans.

• **Anti-plaque agents:** These include the bis-biguanides such as chlorhexidine and phenolic compounds such as Triclosan, metal ions (for example, copper, zinc, or stannous). Topical chlorhexidine probably has the most human clinical trial support data among all non-fluoride anticaries agents and has proved to be one of the most effective antiplaque agents to date. Apart from major disadvantages like altered taste sensation, Superficial desquamation of tissue and Hypersensitivity, is inactivated by most dentifrice surfactants and, therefore it is not included in dentifrices. Also, because of this inactivation, it is critical for dental professionals to alert patients not to use chlorhexidine mouthrinses within 30 minutes before or after regular tooth brushing.

Triclosan (a phenolic compound) is a broad spectrum antimicrobial agent which has been incorporated successfully into dentifrice formulations. Through combination with a polyvinyl methyl ether maleic anhydride copolymer and in combination with zinc, another antimicrobial agent Triclosan shows a markedly increased anti-plaque effect.¹⁰

• **Essential oils:** Listerine antiseptic was the first OTC antiplaque mouth rinse to be approved by the ADA. Patients are advised to rinse twice daily

with 20 ml of Listerine for 30 seconds, in addition to their usual oral-hygiene regimen. Listerine has been used as a mouthrinse for more than 110 years. The active ingredients are thymol, menthol, eucalyptol and methyl salicylate, termed as essential oils. The original formula contains 26.9% alcohol and microorganisms are unable to develop any resistance to the antibacterial effects of essential oils, which include clove oil (eugenol) and thyme oil (thymol).⁵

• **Metals:** A whole range of metals has been investigated in many different types of animal studies and insitu experiments. Although many metals have shown the anticaries potential but aluminium, copper, and iron have the most positive information. However the probable toxicity of many of these metals (e.g., aluminium, molybdenum, barium, and copper) and organoleptic problems associated with their use in the oral products restrict the concentration at which they could be safely used.⁸

• **Miscellaneous Agents:** The agents like Glycerol Monolaurate, Monolaurin, Nonanoic Acid, Lysine Phosphate, Propolis, Bacteriocins, Urea Peroxide and Sodium Lauryl Sulphate shown to have anti-carries activity in animal caries studies. Citrate has also shown anticariogenic activity in most of the plaque acid clinical trials and it might be expected that it interfere with parts of the enzyme systems which produce acids in plaque, e.g., phosphofructokinase

3. Remineralization Therapy

In various in vitro studies, Schemehorn et al., Munoz et al., and Kardos et al. found that a dual-phase toothpaste increased fluoride uptake, reduced enamel solubility, re-strengthened weakened enamel and prevented demineralization more effectively than a conventional fluoride toothpaste.²

• **TMP:** Since a long time, trimetaphosphate ion (TMP) has been proposed to have anti-carries activity and while the potential mode of action of TMP is not fully understood, it is likely to involve adsorption of the agent to the enamel surface, thereby slowing the exchange of ions with the oral environment, and hence reducing demineralization during acid challenge.¹¹

- **Hydroxyapatite:** Hydroxyapatite has many excellent properties, such as being able to bound to a wide variety of molecules and most of the therapeutic agents for bone diseases under physiological conditions. It is an excellent biomaterial widely considered to be the main bone filler and bone substitute in surgery.¹²
- **Ozone Therapy:** Ozone is a powerful agent that disinfects by destroying, neutralizing, or inhibiting the growth of pathogenic microorganisms. It has been found to be an effective alternative biocide to chlorine and possesses the added advantages of acting rapidly in lower concentrations and of having no side effects such as taste and odour, which are characteristic of other disinfecting agents. Ozone also decomposes to a harmless, non-toxic, environmentally safe material (oxygen)

4. Caries Vaccine

Current Approaches and Findings in Active Immunization:¹³ Over a period of a few years, numerous surface or secreted products of mutans streptococci have been proposed as vaccine antigen candidates, and currently, researchers' attention has become focused on three protein antigens: the surface fibrillar adhesions known as AgI/II (synonyms: antigen B, Pi, SpaP, PAc, SpaA, PAg), the glucosyltransferases (GTF) and the glucan-binding proteins, all of which have demonstrable associations with virulence and the process of tooth surface colonization.

Passive Immunization – An Alternative Approach:¹³ An alternative approach lies in the development of antibodies suitable for passive oral application against dental caries. This has considerable potential advantage in that it completely avoids any risks that might arise from active immunization. Conversely, in the absence of any active response on the part of the recipient, there is no induction of immunological memory, and the administered antibodies can persist in the mouth for only a few hours at most or up to 3 days in plaque.

Subunit Vaccines:¹⁴ Subunit vaccines, which contain structural elements of the Ag I/II adhesin family, GTFs or GbpB, have been designed for a variety of reasons. It had been observed that immune responses in animals protected by

immunization with intact proteins were associated, at least in part, with in vitro measures of functional inhibition. subunit vaccines can be designed to include the salivary-binding domain(s), but exclude sequence bearing the potential for induction of unwanted antibody responses. Subunit vaccines with inherent adjuvant potential could also be constructed by including some or all of the sequence of effective immune adjuvants.

Conjugate Vaccines:¹³ Another vaccine approach which may intercept more than one aspect of mutans streptococcal molecular pathogenesis is the chemical conjugation of functionally associated protein/peptide components with bacterial polysaccharides. Added to the value of including multiple targets within the vaccine is that the conjugation of protein with polysaccharide enhances the immunogenicity of the T-cell-independent polysaccharide entity. This principle was first demonstrated by Landsteiner (1936) and Avery and Goebel (1929) and has been applied with great success in the Hemophilus influenzae type B (Hib) conjugate vaccines to induce protective immunity to the capsular polysaccharide of H. influenzae in infants and young children.

5. Probiotic Approaches

The term probiotics refers to —live microorganisms, which, when administered in adequate amounts, confer a health benefit on the host. The concept of probiotics evolved from Elie Metchnikoff's ideas that the bacteria in fermented products could compete with microbes that are injurious to the host and thus are beneficial for health. Classic probiotic strains, such as those that belong to the genera Lactobacillus and Bifidobacterium, have been tested for their ability to confer probiotic effect in the oral cavity. This also includes the application of S. mutans types that cannot produce acids or other bacteria that interfere with the pathogenic effects of S. mutans. While these approaches show therapeutic effects against S. mutans experimentally, the conversion into commercial products remains a challenge, due to safety and shelf life issues. New high-tech approaches, such as quorum sensing interference of pathogenic bacteria or targeted antimicrobial therapies, offer novel ways to achieve probiotic

effects against dental caries.³

6. Other Fluoride Alternatives

- The Anticaries Effect of a Food Extract (Shiitake) Anti-cariogenic properties of tea (*Camellia Sinesis*)
- Inhibition Of Salivary And Bacterial Amylases
- **Chinese Medicinal Herbs:**¹⁶ He et al. conducted a systematic screening of the group of herbs and found that *Glycyrrhiza uralensis* (Chinese name “Gancao” or Chinese licorice) exhibited a strong antimicrobial activity against *S. mutans*. This extract has been formulated into a lollipop and has been clinically tested in a limited human study with promising results.
- **Tribulus Terrestris:**¹⁷ *T. terrestris* has a hard texture and bitter taste and it is odorless and pungent. In traditional Chinese medicine, *T. terrestris* is used for treating toothache, dental caries, periodontal disease, eye diseases, cutaneous pruritus, edema, inflammation and tracheitis.
- **Magnolol:** It inhibit secretion of acidity, Anti-dental caries and anti-periodontal disease. It is an Anti-tumor and cancer, Inhibits or prevents the growth or development of malignant cells.

Reasons to continue to seek alternatives to fluorides:

1. A high-fluoride strategy cannot be followed, since, to avoid the potential for adverse effects (e.g., fluorosis) due to overexposure to fluoride, legislation limits the amount of fluoride that may be used.
2. Fluoride is highly effective on smooth-surface caries, its effect would seem to be more limited on pit and fissure caries.
3. Although fluoride presents no problems when used properly, among certain groups of the world there has been the suggestion that fluoride exposure should be limited. Indeed, in some countries, non-fluoride dentifrices exist to serve the needs of these individuals.

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