

Review article**We can WAR against Tooth Decay, but are still “BREWING”**

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Abstract : Research is a part and parcel to reach to a correct regimen for any disease in existence and being a dental surgeon we too require to indulge in such experiments and come out with flashing new researches in our field of dentistry too which can make a drastic difference in approach of certain oral diseases and their regimen.

Keywords : Tooth Decay; Chewing Gums; Vitamin D; *S. Mutans*; Caries; Vaccine.

INTRODUCTION

Preventive part of Paediatric Dentistry has taken long strides in the direction of eliminating dental diseases, especially dental caries. It is like, imagine never having to face your dentist's drill again. No more needles, no more “floppy lips” or embarrassing drooling afterwards and no more pain.¹ In this venture a number of works have been brought up by dental surgeons and researchers. These upcoming experiments and researches have been worked upon since a long time, but they are still brewing and not yet reached to the Pedodontists worldwide, so as to help in irradiation of the most commonly occurring disease in young children and adolescents i.e. dental caries. Among the numerous studies going on regarding the above I would like to accustom the people reading my article with a few but important upcoming fighters that can war against dental caries but are still in the pipeline since a very long time. The warriors I will talk about comprise of carries vaccination, magic fluid, cousin mutant bacteria, cashew nuts, cheese, whole grape, pomace, apples & strawberries, Vitamin D and chewing gums, probiotics, licorice root, nutmeg, coconut tooth oil.

CARIES VACCINE: Amongst these the first and the most important warrior could be caries vaccine. A vaccine is a preparation of killed microorganisms, living attenuated organisms, or living fully virulent organisms that is administered to produce or artificially increase immunity to a particular disease. It is basically a Mutant bacteria used against an existing bacteria, to seize its existence. The various routes of administration for the above are via nasal route, oral route, active

gingivo-salivary route, systemic route and could be via active or passive immunization. The National Institute of Dental and Craniofacial Research (NIDCR) is the primary sponsor of research and research training in oral, dental and craniofacial diseases. The target for vaccine development in his research group has been the glucosyl transferases (GTF) and the glucan binding proteins (Gbp). The basic hypothesis is that mucosal induction of salivary IG antibody to GTF interferes with the accumulation of *S. mutans* in hard surfaces like glass and teeth. The enzyme is inhibited by this antibody both in vitro and in vivo. They have synthesized a variety of peptides from the catalytic domain and from the glucan-binding domain and prepared mono and diepitopic constructs. A peptide from GbpB has been shown to protect against caries.¹ The group has utilized several delivery methods, including subcutaneous injection, intra gastric intubation, oral capsules and topical application. More recently they have used intranasal administration in aluminum phosphate or PLGA micro particles.

At birth, there are no bacteria in the oral cavity, but there is subsequent colonization with certain “pioneer” oral bacteria that come essentially from the mother, including *S. midus* and *S. salivarius*. Teeth emerge at about 6 months and certain teeth-associated flora begins to be found, such as *S. sanguis*. *S. mutans* is not present (in a certain portion of individuals) until between 18 and 36 months of age. IG levels also rise and by 12 months children have adult levels of IG and of antibody to certain antigens. At 5 weeks of age one can find antibody salivary IgA to *S. midus* antigen in saliva. When infected, children can respond to a

variety of antigens associated with microorganisms. The group is convinced of the safety of the GTF, as exposure to multiple doses of orally and topically applied GTF did not cause any health problems. GTF is the only streptococcal component in vaccine materials. The plan is to use GTF as the antigen, administered with PLGA micro particles by the intranasal route, 2-3 doses between 12 and 24 months of age. This would be a phase I trial. The cost of the trial would be between 2 and 3 million dollars.¹

According to Katz in 1993, coupling of protective salivary immunoglobulin A with non toxic unit of the cholera toxin was effective in suppressing the colonization of streptococcus mutans. This approach was tried out as the cholera toxin effectively binds to the lymphoid cells and functions as an excellent adjuvant. It was tried via intra-oral route of administration.² According to Hamada in 1990, gave the novel concept of using hen egg-yolk antibodies against the cell associated glycosyl transferase of *S.mutans*. The vaccine used were formalin-killed whole cell in one and cell associated glucosyl transferase in the other. Caries reduction was found in both these cases.³

MAGIC FLUID: The fluid, devised by Amalia Aggeli and chemistry colleagues at the University of Leeds discovered how to “train” teeth to rebuild healthy enamel while cavities are still at the micro-pore stage. The secret is a tiny molecule called a peptide. Peptides are sort of like mini-proteins. Their structure is very similar to a protein, but usually much simpler. The doctors at Leeds discovered a special peptide called P11-4 can assemble itself into fibres. They’ve created a fluid that triggers this action and can be “painted” onto a tooth’s surface. When their “magic fluid” comes into contact with your saliva, it forms a gel. A gel loaded with these special peptide fibers that build a sort of scaffolding in the micro-pores. And here’s where it gets really interesting. Calcium the major building block of tooth enamel is attracted to P11-4. Calcium begins to build up on the scaffolding in the micro-pores and the tooth literally rebuilds itself. Now here’s the great part. This isn’t just a theory, but is still. The research team at

Leeds has already tested P11-4 on humans. When they painted it on teeth showing early signs of decay, the “scaffolding” formed inside micro-pores and the people’s teeth literally reversed the effects of decay.⁴

The corporation Planet Biotechnology has developed a synthetic antibody against *S. mutans*, branded CaroRx, which it produces using transgenic tobacco plants. This product may be considered a therapeutic vaccine, applied once every several months, and is in Phase II clinical trials as of October 2007. The International Association for Dental Research and American Association for Dental Research announced a study performed by the Chinese Academy of Sciences which looked at using an inhaled vaccine that uses a protein filament as a delivery vehicle.⁵

COUSIN MUTANT BACTERIA: Dr. Jeffrey D. Hillman of the University of Florida College of Dentistry in Gainesville has developed a genetically modified strain of the bug that doesn't make lactic acid, but is able to shoulder out competing bacteria. The new bacterium, dubbed BCS3-L1⁶, could theoretically prevent cavities by colonizing the mouth and getting rid of its cavity-causing cousin.

Hillman described his research on BCS3-L1 Saturday at the American Academy for the Advancement of Science's annual meeting in Boston. He has been working on developing bacterial replacement therapy for cavity prevention for 25 years. In the dentist's office, he said, the bacteria would probably be applied after tooth cleaning. "The dentist would simply squirt a suspension of our bacteria, our modified bacteria, onto your tooth surfaces for about 5 minutes, and then more than likely the dentist would pat you on the head and tell you to go home and eat sugar." Sugar, he explained, helps the genetically modified bug stick to tooth surfaces.⁷

CASHEW NUT OIL: Cashew oil may conquer cavities. Don't be surprised if nut-flavoured toothpaste makes its way to the drug store shelf sometime in the next decade. In their research, Masaki Himejima and Isao Kubo tested various tropical fruits

and vegetables for antimicrobial activity. The oil from the cashew nut shell, normally a waste product of the food industry, seemed to hold some potential, so the researchers extracted and tested 16 compounds from it. The oil and some of the extracts worked well against gram-positive bacteria, in particular *Propionibacterium acnes*, which causes acne, and *Streptococcus mutans*, which causes tooth decay.

When killing bacteria in the mouth, these compounds also appear to interfere with production of the microbes' enamel-eroding acids. "It has anti-plaque activity, too" says Kudo. The shell oil is not edible, but Kubo notes that its bacteria-fighting components also exist in the nut and in the juice of the surrounding fruit. This fruit, called cashew apple, is eaten in tropical countries with no ill effects. Kubo thinks the cashew compounds may prove safe when mixed into toothpaste or mouthwash. And he sees another benefit of their commercialization: The cashew represents a renewable resource and potentially important product from tropical forests.⁸

CHEESE: Four years ago, Mark Jensen, director of clinical studies at the University of Iowa, dental school in Iowa City, noticed that aged-cheddar, Swiss and Monterey Jack cheeses help fight tooth decay. Although the mechanism of action remains unknown, he and his co-workers have now confirmed that another nine cheeses--Edam, Gouda, Muenster, mozzarella, Port Salut, Roquefort, Romano, Stilton and Tilsit -- perform equally well in limiting tooth decay.

Ordinarily, when carbohydrates such as sugar become trapped in plaque, the film on tooth surfaces that incubates cavity-fostering bacteria and they are converted to tooth-destroying acids. But in a week-long study, electrodes implanted between the teeth in five volunteers recorded no significant increase in the acidity of plaque when a sucrose (table sugar) tooth rinse followed the subjects' consumption of any of the 12 cheeses. However, plaque acidity increased 1,000-fold--to a pH of 4--when the sugar rinses were not preceded by a cheese snack. In a related experiment involving only cheddar, Jensen found that consumption of this cheese four times daily for two weeks

caused a 20 percent remineralisation (tooth-surface rebuilding) in synthetic tooth-like materials temporarily attached to root areas and 5 to 10 percent remineralisation in materials similar to tooth-crown enamel.

These studies suggest that the 12 tested cheeses, when eaten as snacks or just chewed without swallowing--before a sweet meal, he adds, they might limit tooth decay by preventing the formation of tooth-demineralizing acids.⁹

WHOLE GRAPE: According to Dr. Dr. Koo's lab at the University of Rochester Medical Center, Rochester , (URMC) and the New York State Agricultural Experimental Station at Cornell University, examined the chemical composition of polyphenolic compounds obtained from whole grape and pomace, a slightly fermented grape mash consisting primarily of skins and seeds. The phenolic compounds from the different wine grape varieties were tested against *S. mutans* to determine the most effective disruptive agent.¹⁰

POMACE: The scientists determined that all wine grape varieties contained high levels of polyphenolic extracts. The extracts, however, did not kill *S. mutans*. Instead, the extracts were effective at disrupting the bacteria's ability to form the acidic biofilms that cause dental caries. The phenolic extracts obtained from the pomace were slightly more effective than the whole grape in inhibiting acidic bacterial biofilm production.¹⁰

APPLES AND STRAWBERRIS: Professor David James in 2000, a plant biotechnologist at the Horticulture Research International in Southern England, is trying to find ways to deliver the peptide into the mouth through apples and strawberries.¹¹

VITAMIN D: To reduce the risk and severity of dental caries, vitamin D produces cathelicidin and defensins. These proteins have antibacterial effects to fight bacteria that cause dental caries. They may also neutralize toxic byproducts. Having vitamin D blood levels above 30-40 ng/mL (75-100 nmol/L) may help reduce the risk of dental caries. To reach these levels one must take

1000-5000 IU/day of vitamin D3 (cholecalciferol).¹²

CHEWING GUMS: A chewing gum that can destroy the bacteria that cause tooth decay could be in the shops soon according to the Society of Chemical Industry. The gum is one of several products being developed by German chemical company BASF using the bacteria *Lactobacillus*, which is normally found in live yoghurt. BASF has discovered a new strain of *Lactobacillus* called *L. anti-caries*, which binds to *Streptococcus mutans*, the bacteria responsible for tooth decay. *S. mutans* sticks to the surface of teeth, where it produces an aggressive acid that breaks down the enamel. The friendly bugs in the gum will make the *S. mutans* clump together, preventing them from becoming attached to the tooth surface. The company's tests reveal that the chewing gum can reduce the amount of bacteria in the mouth by fifty times.

"With *Lactobacillus anti-caries* we have found an antagonist which effectively binds to the caries bacteria and prevents them adhering to the surface of the teeth", explains Dr Andreas Reindl, Project Leader at BASF Future Business. Although the company has said a *Lactobacillus* product is due to hit the supermarkets in 2007, it will not confirm whether it is the chewing gum and a new range of toothpastes and mouthwashes using *L. anti-caries* are also in the pipeline.¹³

PROBIOTICS: Probiotics (ProBiora3, G-U-M periobalance, GanEdenBC30, etc)^[14], is a 100% natural ingredient that helps to reestablish a healthy balance of oral micro flora and provides the additional benefits of whiter teeth, fresher breath and healthy gums and teeth. Certain common problems of the human oral cavity are dental caries, periodontal or gum disease and bad breath are known to result from an imbalance of the normal populations of certain bacteria. A small number of the more than 500 microbial species that inhabit the oral cavity can cause a negative shift from oral health when they are able to achieve sufficiently large numbers in localized areas of the teeth or gums. In contrast, it is known that a small number of bacterial species can help maintain a microflora population balanced in

favor of healthy gums and teeth. These beneficial strains are included in ProBiora3: *Streptococcus oralis* KJ3, *Streptococcus uberis* KJ2 and *Streptococcus rattus* JH145.

When the ProBiora³™ ingredient enters the mouth and contacts saliva, the freeze-dried probiotics activate and attach themselves to the teeth and gum tissue, establishing Colony Forming Units (CFU) of live, active bacteria both on the surface of the teeth and deep beneath the gum line. These colonies compete for both nutrients and space with the opportunistic bacteria known to be linked to pathogenic activity in the mouth. With daily replenishment, the ProBiora³ bacteria re-establish the natural microbial balance in the mouth and create whiter teeth, fresher breath and healthier teeth and gums. Without requiring lifestyle changes, the addition of the ProBiora3 probiotic ingredient can quickly, dramatically and painlessly affect the long term health and wellness of the mouth and the other health systems dependent on oral health. If oral health is managed with ProBiora3 supplementation daily, the majority of the population could greatly minimize the effects of this serious, costly and painful condition.¹⁵

Mr. Bonfiglio: Oragenics has been involved since its inception mostly in diseases of the mouth, and we are expanding now so that our primary focus at this point in time is on antibiotics, in fact a novel antibiotic that was actually discovered in the mouth from a group of antibiotics called lantibiotics. We are currently in the process of developing a lead compound to take forward into an IND and into human clinical trials by the middle of 2015.¹⁶

LICORICE ROOT: Stefen Gafner and his team of scientists behind the study conducted the American Chemical Society's Journal of Natural Products have recently revealed the use of licorice root as a means of impacting dental health. According to research, licorice root is capable of both preventing and fighting tooth decay and gum disease.¹⁷ The scientists found that two of the plant's main compounds, licoricidin and licoricoflavan A, are capable of inhibiting the growth of decay causing bacteria¹⁸,

particularly *S. mutans*, a bacteria which, as previously mentioned, releases enamel-decaying acid and provides a safe-haven for other bacteria to grow. By preventing the growth of this harmful bacteria, these two compounds largely reduce risk for the production of other potentially harmful substances that require the safety of a biofilm to grow, substantially reducing the possibility of decay.

The recent study also found that licoricidin and licoricoflavan A are capable of reducing the growth bacteria linked to periodontitis. Licorice candy is also flavored with anise oil rather than actual licorice root. Although research showed that the use of licorice root is capable of preventing tooth decay, it also showed that there are risks associated with consuming its supplements. In excess, the supplements may cause raised blood pressure, lower potassium levels, and cause water/salt retention.¹⁹

COCONUT TOOTH OIL: Researchers at the Athlone Institute of Technology, Ireland, reported at the Society for General Microbiology autumn conference at the University of Warwick, England that coconut oil has antibacterial qualities combating strains of *Streptococcus*, which commonly inhabit the human mouth.

Dr. Damien Brady, along with a team of researchers, found that digested coconut oil stopped most of the bacteria from multiplying. What the team found was that semi-digested coconut oil destroys *Candida albicans* yeast that causes thrush. They believe that coconut oil in a semi-digested state, may have commercially viable antimicrobial qualities for the oral health care industry.²⁰

NUTMEG: The specificity and fastness of an active principle present in the nutmeg against cariogenic oral bacteria, suggest that it could be used as an agent against tooth decay. A study was conducted by J.Y. Cheng and his collaborators from the Yonsei University, Seoul, Korea, to evaluate the anticariogenic properties of the extract of nutmeg (*Myristica fragrans*) and its compounds.

The occurrence of dental cavities is mainly related with cariogenic oral bacteria like

the *Streptococcus mutans*. Preliminary antibacterial studies showed that the extracts of nutmeg, vegetal specie widely used, have a strong inhibitory activity against the *S. mutans*. The anticariogenic compound was identified as "macelignan". The minimum concentrations that inhibit the growth of *S. mutans* were significantly low, even lower than other natural anticariogenic agents, such as sanguinarine, eucalyptol and menthol.

The tests showed that concentrations as low as 20 ug/ml of macelignan, completely inactivated *S. mutans* in less than one minute. The authors of the study concluded that the fastness and effectiveness of macelignan against cariogenic oral bacteria, strongly suggest that it could be used as a natural antibacterial agent when applied to foods and oral care products.²¹

Conclusion: All these above agents have their role in fighting against eradication or prevention of dental caries and other dental diseases. But as these researches are still undergoing and brewing, we can hope that these might come out soon with bright colours and bring a new boom in Pediatric Dentistry as well as Conservative Dentistry and Endodontics. Let us hope for the best and try ourselves to bring out such new researches to encourage better future of a pedodontist, endodontist and others too.

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