Mehmet Sarikaya, et al.
Tooth Remineralization

http://www.sci-news.com/medicine/biogenic-dental-product-05912.html

New Biogenic Dental Product Rebuilds Tooth Enamel, Treats Cavities

A team of scientists at the University of Washington has developed a new dental product that uses protein amelogenin-derived peptides to remineralize tooth enamel and treat cavities...
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The study authors accomplished this by capturing the essence of amelogenin — a protein crucial to forming the hard crown enamel — to design amelogenin-derived peptides that biomineralize and are the key active ingredient in the new technology....

“These peptides are proven to bind onto tooth surfaces and recruit calcium and phosphate ions,” said study co-author Deniz Yucesoy, a doctoral student at the University of Washington.

The peptide-enabled technology allows the deposition of 10 to 50 micrometers of new enamel on the teeth after each use...

“Remineralization guided by peptides is a healthy alternative to current dental health care,” said study’s lead author Professor Mehmet Sarikaya, from the Department of Chemical Engineering and the Department of Oral Health Sciences at the University of Washington...

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Biomimetic Tooth Repair: Amelogenin-Derived Peptide Enables In Vitro Remineralization of Human Enamel.
Sami Dogan et al.

White spot lesions (WSL) and incipient caries on enamel surfaces are the earliest clinical outcomes for demineralization and caries. If left untreated, the caries can progress and may cause complex restorative procedures or even tooth extraction which destroys soft and hard tissue architecture as a consequence of connective tissue and bone loss. Current clinical practices are insufficient in treating dental caries. A long-standing practical challenge associated with demineralization related to dental diseases is incorporating a functional mineral microlayer which is fully integrated into the molecular structure of the tooth in repairing damaged enamel. This study demonstrates that small peptide domains derived from native protein amelogenin can be utilized to construct a mineral layer on damaged human enamel in vitro. Six groups were prepared to carry out remineralization on artificially created lesions on enamel: (1) no treatment, (2) Ca2+ and PO43– only, (3) 1100 ppm fluoride (F), (4) 20?000 ppm F, (5) 1100 ppm F and peptide, and (6) peptide alone. While the 1100 ppm F sample (indicative of common F content of toothpaste for homecare) did not deliver F to the thinly deposited mineral layer, high F test sample (indicative of clinical varnish treatment) formed mainly CaF2 nanoparticles on the surface. Fluoride, however, was deposited in the presence of the peptide, which also formed a thin mineral layer which was partially crystallized as fluorapatite. Among the test groups, only the peptide-alone sample resulted in remineralization of fairly thick (10 μm) dense mineralized layer containing HAp mineral, resembling the structure of the healthy

enamel. The newly formed mineralized layer exhibited integration with the underlying enamel as evident by cross-sectional imaging. The peptide-guided remineralization approach sets the foundation for future development of biomimetic products and treatments for dental health care.

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REAGENTS AND METHODS FOR MINERALIZATION OF TOOTH ENAMEL

Inventor(s): SARIKAYA et al.

Reagents and methods for whitening and remineralizing teeth using biomineralizing peptides are described.

BACKGROUND

Accumulation of various chromogcns/discolorants, for example, food and tobacco that come into contact daily onto tooth surfaces and their subsequent penetration into deeper regions (dentin), cause tooth discoloration. Furthermore, the process of aging, disease, trauma, certain medications, certain congenital conditions, and environmental effects can also cause teeth to become discolored. Although discolored teeth do not cause health problems, since bright white teem arc usually considered to be cosmetically desirable, there is a great deal of interest in developing compositions and methods for whitening teeth.

There arc several techniques for whitening or bleaching of teeth. Professional whitening methods, also known as "in-clinic" whitening strategics, arc considered presently as the most effective methods. These in-clinic whitening strategies typically involve the application of high-concentration peroxide products (up to 35%) and other abrasive chemicals to the discolored area. These peroxide species penetrate the stained area (up to underlying dentin layer) and dissolve the accumulated discoloring agents through an oxidation process. To achieve desired effects more quickly, such oxidation reactions on teeth arc often assisted with external laser light application, which heats up the reaction site and thereby increases the rate oxidation reaction. Furthermore, utilization of titanium dioxide up to 10% is often preferred to facilitate these photo- catalytic reactions. Other in-clinic whitening techniques involve superficially removing the enamel layer with abrasive instruments or pumice followed by treatment with additional caustic agents.

There arc several drawbacks of these in-clinic techniques. First of all, the abrasive chemicals and peroxide agents causes enamel demoralization and results with teeth sensitivity. In most cases sorc/injurcd gums as well as bad taste of the product itself cause much discomfort to the patients. Further, patients arc required to make a clinic appointment to get this medical service.

Other existing products for at-home use contain considerably lower concentrations of active oxidizing agents and, thus, arc generally less effective than in- clinic whitening strategics and products. Therefore, dramatic whitening effect can only be achieved by the repeated applications of these reagents for several weeks. These treatments often assisted with bleaching trays (night-guard) in order to better localize bleaching products and, thereby, maximize the whitening effect However, even though these at home products contain active whitening agents in lower concentrations, similar side effects as those associated with professional treatments arc very common. In addition, there arc paint-on, at-home whitening products, also known as "tooth varnishes", as well as whitening strips intended to eliminate the need for dental trays. However, these products require more frequent applications, usually 3-timcs in a day, to complete whitening procedure. Finally, among the variety of at-home use products, whitening toothpastes and gels are the least effective form of whitening products due to their short contact time with the tooth surfaces. Although bleaching agent additives augment the effectiveness, the whitening effect is primarily as a result of removal of surface stains via mechanical action of brushing and other polishing ingredients (for example, silica particles).

Dental caries is one of the major public health problems and it is a highly prevalent disease among the global population. Incipient caries and white spot lesions (WSL) as well as hypersensitivity, arc the earliest clinical evidence of enamel dcmincralization and dental caries. Dental caries occurs when tooth enamel is exposed to acid produced by cariogenic bacteria. As a result, acid diffuses into surface enamel and dissolves hydroxyapatite (HAp) mineral. Due to its non-rcgenerative nature, enamel is unable to heal and repair itself post-dcmincralization. Traditionally, fluoride (F) has been used as the key agent in prevention of caries. Fluoride functions primarily via topical mechanisms. It is believed that fluoride forms a thin layer of new but harder mineral, namely fluorapatitc (FAp) which is incorporated into the existing HAp mineral on the tooth surface. There is a trend of enhancing the rcmincralization effect of fluoride with calcium and phosphate supplementation in high risk individuals. Although controversial, the use of fluoride products remains the primary treatment modality for caries prevention and rcmincralization, with major limitations regarding the efficacy of these products for the reversal or prevention of dental caries. Fluoride delivery systems, therefore, arc not sufficient to overcome the high caries risk especially in younger and elderly population.

There is presently an unmet need for tooth whitening and mineralization methods and products that reduce or eliminate the need for concentrated, abrasive oxidizing agents and attendant side effects such as dcmincralization-associatcd tooth sensitivity and gum line injuries.

SUMMARY OF THE INVENTION

Herein we provide methods and compositions for whitening teeth where the natural color of teeth is restored and improved upon by generating newly formed thin mineral layer on discolored tooth surface using one or more biomineralizing polypeptides. Herein we also provide methods and compositions for mineralizing teeth.

In a first aspect, the present application provides a method for whitening teeth, comprising administering to a subject in need thereof an amount effective to whiten the teeth of a biomineralizing polypeptide. In some embodiments, the method for whitening teeth comprises administering to a subject in need thereof an effective amount of a composition comprising a biomineralizing polypeptide. In some embodiments, the biomineralizing polypeptide comprises an amino acid sequence selected from the group consisting of:

(PGYIN(L/F)SYE(K/N) SHSQAIN(T/V)DRTA)|.,0(ADP5; SEQ ID NO: 13), or a functional equivalent thereof. In some embodiments, the biomineralizing polypeptide comprises the amino acid sequence (PGYINFSYENSHSQAINVDRTA)i-io (ADP5H; SEQ ID NO: 15), or a functional equivalent thereof. In some embodiments, the biomincralizing polypeptide comprises the amino acid sequence...
