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Remineralizing Agents a Boon to Dentistry: A Review

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Abstract

Oral diseases are the most prevalent chronic diseases worldwide, and is burden to health care services. Among oral diseases dental caries is a highly prevalent multifactorial disease and has been a major public health problem for many centuries. It is not simply endless and unidirectional process of the demineralization of the mineral phase, but a cyclic event with periods of demineralization and remineralisation. Various sorts of remineralizing agents are explored and many of them are getting utilized clinically, with positive outcomes. This article reviews about the various agents that enhance and promote remineralization of tooth structure and thus are discussed in detail.

Keywords: Demineralization, Remineralisation, Remineralizing agents, non invasive treatment

Introduction

The mouth may be a battlefield of activities of demineralization and remineralization. The proportion among demineralization and remineralization is critical, deciding the hardness and quality of tooth structure. Demineralization results from a complex chemistry between bacteria, diet, and salivary components[1]. It involves loss of minerals at the advancing front of the lesion, at a depth below the enamel surface, with the transport of acid ions from the plaque to the advancing front and mineral ions from the advancing front toward the plaque[2].A drop in the pH in the oral cavity results in demineralization i.e. the oral environment becomes undersaturated with mineral ions, relative to a tooth's mineral content[1] finally resulting in dental caries. Remineralization happens under close unbiased physiological pH conditions whereby calcium and phosphate mineral particles are re-deposited inside the caries injury area thereby prompting the arrangement of fresher HAP gems, which are bigger and progressively invulnerable to corrosive dissolution[3]. Minimum intervention as the term refers to the principle of treatment in dentistry in which early intervention minimizes tooth destruction because the disease is diagnosed prior to the destruction of the tooth. Hence it is possible to remineralize the carious lesions[4]. The chemical basis of the demineralization–remineralization process is analogous for enamel, dentin, and root cementum. However, the different structures and relative quantity of mineral and organic tissue content of each of these materials cause significant differences in the nature and progress of the carious lesion.[5]

The early enamel lesions have a potential for remineralization with an increased resistance to further acid challenge, particularly with the use of enhanced remineralization treatments[6]. Thus invasive treatments of precavitated lesions are not required. Various in-vitro and in-vivo studies have been done regarding remineralizing agents and many of them are discussed in detail.

Requirements of An Ideal Remineralizing Material[7]

- It should diffuses into the subsurface or deliver calcium and phosphate into the subsurface
- It should not deliver an excess of calcium
- Should not favor calculus formation
- Should Work at an acidic pH
- Should be able to Work in xerostomic patients
- Should boost the remineralizing properties of saliva
- For novel materials which should shows more benefits over fluoride.

Fluorides

Fluorides are a significant subordinate in the avoidance of dental caries. Fluoride levels of around 3 sections for every million (ppm) in the lacquer are required to move the parity from net demineralization to net remineralization[8]. Fluoride is known for its anti-caries effect as it promote the development of fluorapatite, which is more corrosive safe than hydroxyapatite; HELPS IN remineralization; obstruct THE ionic holding during pellicle and plaque arrangement; and restraint THE microbial development and metabolism[9]. Fluoride can be utilized in blend with sodium, tin, or titanium. Titanium fluoride (TiF) displays improved uptake of calcium, and TiF-pretreated finish shows less loss of calcium during demineralization[10]. Nordstrom and Birkhed, 2010 showed a superior preventive effect of a 5,000-ppm dentifrice compared with a 1,450-ppm-F dentifrice in a two-year clinical trial in adolescents. Numerous clinical trials have demonstrated the efficacy of a high-concentration fluoride varnish in high-caries-risk individuals (Autio-Gold and Courts, 2001; Bader et al., 2001; Ferreira et al., 2009; Du et al., 2011)[11-14]. However high amounts of fluoride in dentifrices and systemic fluorides have shown signs of toxicity which later led to the development of NON FLUORIDATED AGENTS as effective remineralizing agents[15]. Thus there are various reasons to seek alternatives to fluorides like: Fluoride is highly effective on smooth-surface caries; but limited on pit and fissure caries, development of fluorosis due to overexposure to fluoride. Although fluoride presents no problems when used properly, among certain parts of the world, there has been the suggestion that fluoride exposure should be limited[16]

Calcium Phosphate Compounds

Calcium phosphate is found to be main form of calcium found in bovine milk and blood. As the major components of hydroxyapatite (HA) crystals, concentrations of calcium and phosphate in saliva and plaque play a key role in influencing the tooth demineralization and remineralization processes. At equal degrees of supersaturation, an optimal rate of enamel remineralization can be obtained with a calcium/phosphate ratio of 1.6. In the plaque fluid, the

Ca/P ratio is approximately 0.3. So additional calcium supply may augment enamel remineralization[24].β-TCP Studies have shown that the combination of TCP with fluoride can provide greater enamel remineralization and build more acid-resistant mineral relative to fluoride alone. When used in toothpaste formulations, it forms a protective barrier created around the calcium and allowing it to coexist with the fluoride ions. During toothbrushing, TCP comes into contact with saliva, causing the barrier to dissolve and releasing calcium, phosphate, and fluoride[17,18].

Amorphous Calcium Phosphate

It was first described by Aaron S Posner in the mid-1960s. It energizes from a significantly supersaturated calcium phosphate course of action and can be changed over speedily to stable crystalline stages, for instance, apatitic items or octacalciumphosphate. ACP has been exhibited to have favored in vivo osteoconductivity over HYDROXYAPETITE, best biodegradability over tricalcium phosphate, and incredible bioactivity yet no cytotoxity. ACP has been widely applied in the biomedical field because of magnificent bioactivity, high cell grip, flexible biodegradationrate, and great osteoconduction. However, unstabilized ACP quickly changes to crystalline stages in the mouth and in doing so may act to promote dental calculus. Within the sight of fluoride ions, the unstabilized ACP may deliver fluorapatite. The development of fluorapatite intraorally would sequester accessible fluoride particles along these lines decrease the capacity to remineralize subsurface lacquer during corrosive test. Thus, the dependability of ACP is an issue[19].

Casein Phosphor Peptide - Amorphous Calcioum Phosphate (CPP-ACP) It is used as CPP-ACP (casein phophopeptides with amorphous calcium phosphate) or CPP-ACFP (casein phophopeptides with amorphous calcium fluoride phosphate)[1]. CPP-ACP can restrict ACP at the tooth structure , expanding the degree of calcium phosphate in plaque and henceforth may go about as a calcium phosphate reservoir, buffering the free calcium and phosphate particle exercises, there-by serving to maintain condition of supersaturation, decline the demineralization and improve remineralization[20].Morgan et al in 2008 conducted 2 year in vivo study and resulted that CPP-ACP significantly slowed progression of enamel caries on proximal surfaces[21]. Similarly Rao et al in 2009,Wong RH et al in 2010, Zalizniak et al in 2013, Shadman et al in 2015 etc did both in vivo and in vitro studies from time to time regarding CPP-ACP and ended the study with positive results[22-25]. CPP also is believed to have an antibacterial and buffering effect on plaque and interfere in the growth and adherence of Streptococcus mutans and Streptococcus sorbinus. CPP-ACP fundamentally diminished caries action in a subordinate way, as 1% CPP-ACP delivered about a 55% decrease in smooth surface caries and a 46% decrease in gap caries movement, which is comparative essentially to that created by 500 ppm of fluoride. Combined with fluoride, CPP-ACP has an additive effect on caries activity[26]. Use of CPP-ACP along with fluoride-containing dentifrice has proved to be beneficial in reducing the demineralization around orthodontic brackets and remineralizing white spots caused by demineralization[27]. Ramalingam et al found that adding CPP-ACP to soft drinks can reduce their erosion capacity[28]. CPP-ACP has additionally been added to dentifrices, mouthrinses, biting gums, capsules, and cow-like milk. An investigation by Walker et al found that in spite of the fact that milk contains casein phosphate, expansion of CPP-ACP brings about upgraded remineralization[29]. A portion of

5 gm of CPP-ACP delivered 148% more remineralization contrasted with 2 gm of CPP-ACP per liter of milk. CPP-ACP has proved a new arena to preventive dentistry .It has shown anticariogenic, anti – erosive efficiency and reduces dentine hypersensitivity. It is delivered in the form of chewing gum, mouthwashes, dentifrices, and also added in various restorative materials. Hence it is proven as adjunctive treatment to fluorides in the non- invasive management of early lesion, root caries lesions, root dentinal caries, dental erosion and dentine hypersensitivity[30]

Sodium Calcium Phosphosilicate (Bio Active Glass)

Bioactive glass (Bioglass) was invented by Dr. Larry Hench in1960s. It acts as a biomimetic mineralizer matching the body's own mineralizing traits while also affecting cell signals in a way that benefits the restoration of tissue structure and function[31]. Bioactive glass interacts with salivation, quickly discharges sodium, calcium, and phosphorous particles into the spit that are accessible for remineralization of the tooth surface. The particles discharged structure hydroxycarbonate apatite (HCA) legitimately. They additionally adjoin to the tooth surface and keep on discharging particles and remineralize the tooth surface after the underlying application. These particles have been appeared to discharge particles and change into HCA for as long as about fourteen days. At last, these particles will totally change into HCA[32].Bioactive glass Nanoparticles (Novamin) holds fast to uncovered dentin surface and structures a mineralized layer that is precisely solid and impervious to corrosive. There is consistent arrival of calcium after some time, which keeps up the defensive impacts on dentin[49]. The NovaMin Technology was created by Dr. Len Litkowski and Dr. Gary Hack. Recently available things in the market are DenShield Conditioner with NovaMin, NuCare-Prophylaxis Paste with NovaMin, and Oravive,NuCare-Root NovaMin: SootheRx, [33,34.]

Sugar Substitutes

Xylitol is a tooth friendly nonfermantable sugar alcohol which has shown noncariogenic as well as cariostatic results. Its anticariogenic effects is done by the inactivation of S. mutans and inhibition of plaque's ability to produce polysaccharides and acids. When consumed as mints or gum, it will stimulate an increased flow of alkaline and mineral-rich saliva from small salivary glands in the palate. Increased salivary flow results in increased buffering capacity against acids and high mineral content will provide the minerals to remineralize the damaged areas of enamel[35]. Sorbitol is another sugar substitute that is utilized as a counterfeit sugar. The capacities of xylitol and sorbitol to remineralize early veneer caries appear to be nearly similar[36]. Isomalt is a noncariogenic sugar that is generally utilized as a sugar substitute. Adding isomalt to a demineralizing arrangement has appeared to fundamentally decrease tooth mineral loss[37]

DICALCIUM PHOSPHATE DIHYDRATE (DCPD)

DCPD is a precursor for apatite that readily turns into fluorapatite in the presence of fluoride[38]. Researches have shown that inclusion of DCPD in a dentifrice increases the levels of free calcium ions in the plaque fluid, and these remain elevated for up to 12 hours after brushing, when compared to conventional silica dentifrices[39].

Nanomaterials

Nanoparticles have better ion release profiles than microparticles. Since it is difficult to directly use nanomaterials to remineralize teeth in the oral environment, these materials are often added to restorative materials as inorganic fillers, such as resin composites to release calcium, phosphate, and fluoride ions for remineralization of dental hard tissues[40]. Various nano particles used are Calcium Fluoride Nanoparticles (Xu HHK et al. have shown that the addition of nanoCaF2 increases the cumulative fluoride release compared to the fluoride release in traditional glass ionomer cements), Calcium Phosphate-based Nanomaterials (includes nanoparticles of HAP, TCP, and ACP as sources to release calcium/phosphate ions and increase the supersaturation of HAP in carious lesions), NanoHAP Particles Nano-sized HAP (n-HAP) is similar to the apatite crystal of tooth enamel in morphology and crystal structure. So it can be substituted for the natural mineral constituent of enamel for repair biomimetically[40].

Phenolic Acid (PA)

Is a bioflavonoid, containing benzene–pyran–phenolic acid molecular nucleus. Grape seed separate (GSE) contains PA[41], which can shape outwardly insoluble HA buildings when blended in with a remineralizing arrangement at pH 7.4. Cheng-tooth Tan et al. seen a fixation subordinate increment in the microhardness when caries-like corrosive scratched demineralized dentine was treated with proanthocyanidins-rich GSE. Additionally, Epasinghe et al. have demonstrated in vitro the synergistic impact of PA when joined with CPP indistinct calcium fluoride phosphate (CPP-ACFP) on remineralization of fake root caries in which they saw an improved mineral addition and expanded the hardness of fake root caries[42].

Polydopamine

The oxidative polymerization of dopamine in fluid arrangements immediately frames polydopamine, imitating DOPA, which displays a solid cement property to different substrates under wet conditions. In demineralized dentin, the collagen fibers when coated with polydopamine, remineralization was promoted, which shows that polydopamine binding to collagen fiber act as a new nucleation site that will be favorable for HA crystal growth[43].

Theobromine

Theobromine is a member of the xanthine family, seen in cocoa (240 mg/cup) and chocolate (1.89%), and has shown to enhance crystalline growth of the enamel[44]. Amaechi et al., observed a significantly higher mineral gain with theobromine and fluoride toothpaste relative to artificial saliva. Grace Syafira et al. have shown an increased enamel micro-hardness after treatment with theobromine on the enamel surface[45]. Meanwhile, Abdillah Imron Nasution has noticed that the increase in hardness of the enamel surface by fluoride application is higher than the theobromine.

Arginine Bicarbonate

Arginine bicarbonate is an amino acid with particles of calcium carbonate, which is capable of adhering to the mineral surface. When the calcium carbonate dissolves, the released calcium is available to remineralize the mineral while the release of carbonate may give a slight local pH rise[46]. The studies on the demineralized bovine enamel blocks by Yamashita et al. with arginine and fluoride formulations have shown that when used in combination with fluoride, arginine significantly increased fluoride uptake compared with fluoride alone, and lesions treated with arginine containing toothpaste also showed superior fluoride uptake compared with those treated with conventional fluoride toothpaste[47].

Self-Assembling Peptide

Recent developments in research have revealed the role of treatment with peptide where it proved a combined effect of increased mineral gain and inhibition of mineral loss from the tooth. The β-sheet-forming peptides, P_{11-4}, that self-assemble themselves to form three-dimensional scaffolds under defined environmental conditions have been shown to nucleate hydroxyapetite. The anionic groups of the P_{11-4} side chains attract Ca++ ions, inducing the precipitation of hydroxyapetite in situ[48].

Conclusion

In current year, the motive of restorative dentistry has been adminstered towards conservative approach, out of which remineralization procedures are the mostly preferred. In this review, an attempt has been made to review the various remineralization materials and technologies currently being employed to remineralize enamel and dentin. Initially, fluoride formulations were only the material relied on, which responded by rebuilding the hydroxyapatite crystals, supplying the necessary ions, which were partially lost from the lattice network. Later the researches could successfully introduce newer biomimetic remineralization products having the capability to create apatite crystals within completely demineralized collagen fibers. It is expected that further experiments in this field would definitely bring out better products and technologies for clinical application with optimal responses and results.

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