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Research Paper

Recent Advances in Remineralization Therapies For Caries: A Review Article

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ABSRACT: *Dental caries is a common and complex oral disease, posing significant health care for communities has become challenges for centuries. Various remineralizing agents support the remineralization process to halt disease advancement and enhance the teeth's form and functionality. Remineralization is the process in which essential minerals, mainly phosphate and calcium, are added and integrated into areas of dental decay that have lost these minerals due to the demineralization of tooth structure. The current article explains about various materials that facilitate and encourage the remineralization of dental structure along with their implementation in clinical practice.*

KEYWORDS*: Dental caries,Nanoparticles, Polydopamine, Recent advances, Remineralizaion.*

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I. INTRODUCTION:

Dental caries is a condition that is prevalent and affects teeth, characterized by demineralization and cavitation. It ultimately results in discomfort and pain, which restricts function and diminishes face attractiveness [1,2]. Caries should not be viewed simply as a constant and one-way process of mineral loss instead; it is a cyclical occurrence marked by phases of demineralization followed by remineralization [3]. When the demineralization process predominates, it leads to cavitation. Mineral loss occurs at the leading edge of the lesion, beneath the enamel surface, triggering the demineralization process. This includes the transfer of acid ions from the plaque to the advancing forward, as well as the transfer of mineral ions from the advancing forward and then to the plaque [4]. Remineralization is the process in which essential minerals, mainly phosphate and calcium, are added and integrated into areas of dental decay that have lost these minerals due to the demineralization of tooth structure.This process promotes growth through the addition of hydroxyapatite crystals, and when fluoride is present, it results in the formation of fluorapatite. [5]. Remineralization can occur naturally or through therapeutic interventions, with fluoride (F)-based treatments receiving the most support from evidence. Fluoride use is the main factor in reducing dental caries globally. However, its effectiveness has limitations in some individuals, and its impact on caries reduction is reaching a plateau. Consequently, researchers are developing new therapies primarily to improve fluoride treatments, while patients who prefer non-fluoride alternatives may also consider them. This article summarizes recent advancements in remineralization therapies [6].

II. FLUROIDES:

All remineralization systems, whether used independently or in conjunction with one another, must evaluate the remineralization efficacy of fluoride in addressing caries against this benchmark [7]. Fluoride is well-established for its anti-caries properties, primarily by facilitating the formation of fluorapatite, which is more acid-resistant than hydroxyapatite. It promotes remineralization, disrupts ionic interactions during pellicle and plaque formation, and inhibits microbial growth and metabolism [8]. Soi et al. identified four methods by which fluoride exerts its effects. Fluoride stops demineralization because the crystals that are made when enamel apatite crystals interact with fluorapatite crystals are stronger against acid erosion than hydroxyapatite crystals. Then, fluoride helps remineralization by speeding up the formation of new fluorapatite crystals are formed by combining

phosphate and calcium ions together. Later, it makes acidogenic cariogenic bacteria less effective by stopping the production of phosphoenolpyruvate (PEP), which is an important step in the glycolytic cycle of bacteria. F− ions attach strongly to tooth enamel, oral mucosal tissue, and dental plaque, helping to minimize demineralization and encourage remineralization [9]. The dentistry market is experiencing an increasing prevalence of acidulated fluoridated products. Products of this nature typically include sodium fluoride mouthrinse with phosphoric acid at a pH of 3.0–4.0, as well as gels and foams [10]. Walsh et al., 2010 has proved various fluoride therapies have been effective in arresting caries lesions, with a dose-response relationship observed in fluoride toothpastes. Toothpastes containing 5000 ppm fluoride have been shown to be more effective in remineralizing root caries lesions compared to those containing 1000–1500 ppm fluoride [6]. Overexposure to fluoride may result in fluorosis. These constraints have compelled researchers to seek non-fluoridated alternatives for remineralization [11].

III. CPP-ACP:

Eric Reynolds with his team team produced a protein nanotechnology by employing CPP, a protein which is produced from milk, to stabilize aggregates of ACP into CPP–ACP complexes. At a neutral pH, the "acidic motif" within CPP acts as a highly charged area that can effectively bind to minerals, including Mn2+, Fe2+, Se2+, Zn2+, and Ca2+ [12]. This protein nanotechnology integrates a specific ratio of 96 phosphate ions, 6 peptides of CPP, 144 calcium ions. The dimensions and electroneutrality of the CPP nanocomplexes facilitate their diffusion along the concentration gradient into the sub-surface lesion [13,14]. Researchers also believe that CPP has antibacterial and buffering properties against plaque, as well as the ability to inhibit the growth and adhesion of Streptococcus mutans and Streptococcus sorbinus are examined [15]. When applied intraorally, these nanocomplexes adhere to tooth surfaces and dental tissues. Plaque, inducing a state of supersaturation of calcium and phosphate ions in the oral biofilm. This process enhances the availability of bioavailable calcium and phosphate ions, facilitating remineralization and altering the dynamics of demineralization-remineralization events during cariogenic challenges, thereby preventing caries development [16].In 2008, Morgan et al. conducted a two-year in vivo investigation, which demonstrated that CPP-ACP It effectively inhibited the progression of enamel caries on proximal surfaces. In a similar vein, Shadman et al. in 2015, Zalizniak et al. in 2013, Rao et al. in 2009, Wong RH et al. in 2010 conducted both in vitro and in vivo research on CPP-ACP, consistently yielding positive results [17].

IV. SELF-ASSEMBLING PEPTIDE:

Recent progress in research has brought attention to the importance of peptide-based treatments in dentistry. These treatments have two effects: they increase mineral gain and stop mineral loss from teeth at the same time [18,19]. The β-sheet-forming peptide P114 self-assembles into 3D scaffolds under specific conditions, enabling hydroxyapatite (HAP) nucleation by attracting Ca2+ ions through its anionic side chains and thereby inducing in situ HAP precipitation [19]. P114 is a safe, non-invasive, and patient-friendly treatment that stands apart from other "filling without drilling" approaches. Its use of a biomimetic peptide gives it the unique benefit of helping with "natural" repair by making it easier for the mineral to grow back [20]. When P114 is applied to the tooth, the peptide diffuses into the subsurface micropores and constructs a three-dimensional scaffold composed of fine Fibers was demonstrated by Schlee et al. These scaffold mimetic proteins are implicated in tooth growth and facilitate the crystallization of hydroxyapatite surrounding them, promoting the regeneration of tooth enamel over a span of three months [12].

V. BIOACTIVE GLASS:

Dr.Larry hench established bioactive glass in the year 1960s. It serves as a biomimetic mineralizer, aligning the body's fundamental mineral composition characteristics and influencing cellular signalling, thus enhancing the repair of tissue structure and function [21]. Fluoride-containing bioactive glass (f-BG) releases fluoride over 12 hours in the oral environment. Unlike conventional bioactive glasses that form hydroxycarbonate apatite, aiding remineralization, f-BG produces fluorapatite, which is more resistant to acid degradation [22]. Wefel (2009) and Burwell et al. (2009) evaluated the potential of this bioactive glass material for remineralization and concluded that, although the technology appeared promising, further research was necessary [6]. Novamin Technologies Inc. (Alachua, FL, USA) produced a bioactive glass named Novamin which has been clinically shown to reduce tooth hypersensitivity. This is achieved by incorporating fine particulate bioactive glass (<90 μm) into water-based toothpastes, which promotes the occlusion of dentinal tubules through the formation of a hydroxycarbonate apatite (CAP) layer [23].

VI. NANOMATERIALS:

Nanohydroxyapatite, a biocompatible and bioactive substance, operates by directly occluding the micropores in initial carious lesions ,acting as a model in the remineralization process by consistently drawing in significant amounts of phosphate and calcium ions from oral fluids into the area of decay, which in turn promotes the growth of crystals [24].Nanoparticles are commonly incorporated as inorganic fillers in restorative materials such as resin composites because of their improved ability to release ions. They help in releasing fluoride, phosphate and calcium ions, which support the remineralization of dental hard tissues [25]. Xu HHK et al. demonstrated that incorporating nanoCaF□ enhances cumulative fluoride release compared to traditional glass ionomer cements [17].

VII. THEOBROIME:

Theobromine is a white crystalline powder that belongs to the methylxanthine family. It is found in cocoa at a concentration of 240 mg per cup, while chocolate contains approximately 1.89% theobromine. The primary distinction between caffeine and theobromine is the presence of one methyl group, specifically in the structure of 1,3,7-trimethylxanthine [26]. In a 1993 animal study conducted by Falster et al., it was demonstrated that pure cocoa powder effectively prevents dental caries [27]. Amaechi et al. observed that toothpaste containing theobromine and fluoride resulted in significantly greater mineral gain compared to artificial saliva [28]. An enhancement in enamel microhardness application of theobromine on the enamel surface was demonstrated by Grace Syafira et al. [29].

VIII. CONCLUSION:

There is considerable evidence indicating that the application of ion-releasing restorative materials in dentistry can reduce the likelihood of biological failure, especially by aiding in the prevention of secondary caries. Calcium fluoride (CaF□), Nano-sized amorphous calcium phosphate (NACP), and bioactive glass (BAG) are frequently utilized remineralizing agents in resin-based materials.

Research has primarily concentrated on creating resin-based composite formulations, with less attention paid to the development of dental adhesives, crown cements and resin-based sealants. The bioactive materials releases ions which is crucial to this process. The ability to neutralize acidic environment surrounding the restorative materials, promote remineralization of the tooth structure, and indirectly influence the modulation of oral biofilms. Additionally, the combination of remineralizing agents with other bioactive compounds, such as quaternary ammonium, has shown synergistic antibiofilm effects, offering dual-action protection against secondary caries. Future research should prioritize the comprehensive evaluation and characterization of these materials to better understand their mechanical and antibacterial properties. Moreover, clinical translational studies are essential for assessing the performance of these bioactive formulations under in vivo conditions.

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