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Review

Novel Remineralizing Agents In Tooth Repair: *A Review*

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Abstract

A new area of dentistry is represented by remineralizing agents. The aim of modern dentistry is to manage non-cavitated caries lesions non-invasively through remineralization in an attempt to prevent disease progression and improve aesthetics, strength, and functionThey can be categorised as fluoride agents, agents made of calcium and phosphate, agents made of herbs, or agents in mixtures. Remineralizing agents can be administered orally by dentifrices, mouthwashes, lozenges, or chewing gum. Fluoride use has been effective in preventing dental caries, but more innovative strategies and exciting new caries prevention products need to be developed and tested. This article provides an overview of various newer reminerlizing agents their role and mechanism of action on tooth.

Key Words: caries, dentistry, fluoride, remineralizing agents

Introduction

Dental caries is an infectious microbiologic disease that causes damage to calcifies tissues. Caries is a dynamic process which occurs when demineralization exceeds remineralisation. Remineralization is a new procedure in preventative dentistry as a result of early detection of developing carious lesions. Use of remineralizing agents is the final mode of treatment for caries management. Currently fluoride, calcium phosphate-based systems, calcium sodium phosphosilicate etc that help in remineralization are available commercially. [1]

Modern day dentistry has shifted the focus from Black's extension for prevention to prevention of extension. Nowadays, non-invasive management of non-cavitated carious lesions through remineralization is being emphasized in order to prevent disease progression, and to enhance aesthetics, improve strength and function of teeth.[2]

The balance between pathogenic elements that support demineralization (cariogenic bacteria, fermentable carbohydrates, salivary dysfunction) and those that are protective (antibacterial agents, enough saliva, remineralizing ions) determines whether a lesion advances or reverses.[3]

reverses.[3]

Remineralization of white-spot lesions and carious lesions may be possible with a variety of currently available agents containing fluoride, bioavailable calcium and phosphate, and casein phosphopeptide in amorphous calcium phosphate, self-assembling peptide. The current concept further bridges the traditional gap between prevention, non-invasive and surgical procedures which is just what dentistry needs for the current age.[4]

Present article highlights the uses of fluoridated, non- fluoridated agents, nanomaterials, self-assembling peptide and herbal remineralizing agents in repair and prevention of dental caries.

Classification

On the basis of composition, various remineralising agents are classified as follows: (Fig-1)

1. *Fluorides*

The most popular remineralizing agent is fluoride. Fluoride present in the microenvironment stops enamel disintegration as soon as the acid attacks the enamel surface, causing the pH to rise. Fluoride crystals containing fluorhydroxyapatite grow larger and newer as

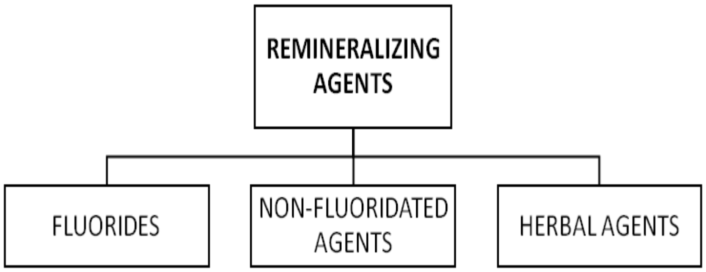

Figure –1

the pH rises, limiting enamel demineralization and promoting remineralization. Dental caries can be prevented by fluoride in a variety of ways. It accelerates post-eruptive maturation, increases resistance to acid demineralization, encourages remineralization of developing lesions, interferes with the development and operation of dental plaque microorganisms, and modifies tooth shape. [5]

Fluoride accelerates the formation of the new fluorapatite crystals by bringing calcium and phosphate ions together, which improves remineralization. Also, the F^- is retained on dental hard tissue, on the oral mucosa, and in the dental plaque to decrease demineralization and enhance remineralization. [3]

Dentrifices containing fluoride are thought to be the most efficient way to stop enamel demineralization. Numerous studies have demonstrated the effectiveness of conventional toothpastes with 1,000 ppm fluoride, but there is evidence that toothpaste with 5,000 ppm fluoride can further reduce demineralization and improve remineralization. [5]

2. Non fluoridated agents

2.1 Calcium phosphate compounds

The main calcium type present in milk and blood from cows is calcium phosphate. Concentrations of calcium and phosphate in saliva and plaque, which are the main constituents of HAP crystals, have a significant impact on the processes of dental demineralization and remineralization. [3]

2.1.a Casein Phosphopeptide- Amorphous Calcium Phosphate-(CPP-ACP)

Calcium and phosphate interact with the phosphor-protein found in milk called casein. The amount of amorphous calcium phosphate that is bound to the substance rises as the material's pH rises, stabilising free calcium and phosphate in the process.[6] In the year 1998, the remineralizing agent casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), (Tooth Mousse, GC India), was introduced. Alpha 1 and 2, as well as β-caseins, predominate among the diverse family of proteins known as caseins. Casein phosphopeptides (CPPs) are phosphorylated casein-derived peptides that are created when casein is triedptically digested. The ability to bind and stabilize calcium and phosphate in solution is possessed by the CPP component, which comprises the amino acid cluster sequence -Ser(P)-Ser(P)-Ser(P)-Glu-Glu.[5]

Additionally, it has been demonstrated that the CPPs maintain fluoride ions in solution, enhancing the efficacy of fluoride as a remineralizing agent. CPP-ACP has been trademarked as Recaldent, and is available in chewing gums, mouthrinse and confectionary. Moreover, a sugar-free, water-based cream containing RECALDENT TM (CPP-ACP) is also available in market. (Prospec MI Paste/ GC Tooth Mousse). [2]

2.1.b Amorphous calcium phosphate

In order to prevent the calcium and phosphorous components from interacting with one another prior to usage, the ACP technique requires a two-phase delivery method. Calcium sulphate and dipotassium phosphate are the two salts that are now used as sources of calcium and phosphorous. The two salts quickly combine to create ACP, which has the potential to precipitate onto the tooth surface. Dr. Ming S. Tung created the ACP technique. ACP was first added to toothpaste in 1999 under the brand name Enamelon. Church & Dwight then reintroduced it in Enamel Care toothpaste in 2004. [1]

2.1.c Sodium calciumphosphosilicate (bioactive glass)

Bioactive glass materials have been introduced in many fields of dentistry and are considered as a breakthrough in remineralizing technology.[5] When bioactive glass comes in contact with saliva, it rapidly releases sodium, calcium, and phosphorous ions into the saliva that are available for remineralization of the tooth surface.[1] They also bind to the suface of tooth and continue to release ions and aid in remineralization after the initial application. It has been observed that these particles release ions and convert into HCA for upto 2 weeks.[2] The bioactive glass is traded as Novamin, which was formulated by Dr. Len Litkowski and Dr. Gary Hack. [2]

2.1.d. Tri-calcium Phosphate

Tricalcium phosphate, a newer remineralizing agent, comes into contact with the tooth surface and is moistened by saliva, the protective barrier breaches, allowing calcium to be absorbed.[6] It also possesses structural resemblance with the hydroxyapatite of tooth enamel. The calcium environments of TCP are well protected in order to prevent premature interaction between calcium and fluoride.[2]Inclusion of the functionalized TCP ingredient in NaF formulations has been shown to produce stronger, more acid-resistant mineral relative to fluoride alone in laboratory and clinical evaluations.[5]

2.1.e. Dicalcium Phosphate Dihydrate (DCPD)

Dicalcium Phosphate Dihydrate is a precursor for apatite, which in the presence of fluoride readily converts into fluorapatite.[5] Inclusion of dicalcium phosphate dehydrate (DCPD) in a dentifrice increases the levels of free calcium ions in plaque fluid, and these remain elevated for up to 12 hours after brushing, when compared to conventional silica dentifrices.[1]

2.1.f. Trimetaphosphate ion

Trimetaphosphate ion (TMP) works by adhering to the enamel surface to provide a barrier coating that prevents or delays interactions between the crystal surface and its fluid environment, hence lowering demineralization during acid challenge.[1]

3. Nanomaterials

3.1.a. Calcium fluoride nanoparticles

Inorganic fillers like resin composites that release calcium, phosphate, and fluoride ions are frequently supplemented with nanoparticles in restorative materials to remineralize tooth hard tissues.[3]

3.1.b Calcium phosphate-based nanomaterials

It contains HAP, TCP, and ACP nanoparticles as sources to release calcium/phosphate ions and boost HAP supersaturation in carious lesions.[3]

3.1.c.Nanohydroxy Apatite

One of the most biocompatible and bioactive mate-rilas is nano-hydroxyapatite (n-HAP), which has shown remarkable growth in popularity in dentistry in recent years. That is resemblance between apatite and nano-HAP (n-HAP) tooth enamel crystal in terms of shape and crystal structure. Hence, it can be substituted for the natural mineral component of enamel for physiological enamel repair.[2] A concentration of 10% nanohydroxy apatite may be optimal for the remineralization of early enamel caries.[1]

3.1.d. ACP Nanoparticles

They are tiny, spheroidal particles of nanoscale dimensions (40–100nm). Composite resins, ionomer cements, and adhesives have all incorporated ACP nanoparticles as a source of calcium and phosphate ions.[3]

3.1.e. Nanobioactive glass materials

NanoBG particles have been shown by Sheng et al. to increase dentin's resistance to acid and to encourage mineral formation on dentin surfaces.[3]

4. Self Assembling Peptide

Dental therapies have a great deal of potential as a result of recent advances in tissue engineering, material sciences, and stem cell research. Research in this area is focused on peptide therapy for early caries lesions. Because increased mineral gain and prevention of mineral loss work together to increase net mineral gain, peptide therapy has a major impact on this. An intelligently created self-assembling peptide is called anionic P114. In response to particular environmental triggers, self-assembling peptides form well-defined hierarchical three-dimensional fibrillar scaffolds, providing a new generation of well-defined biopolymers with a variety of possible applications.[4] The extra benefit of using a bimimetic peptide like P114 by replenishing the mineral itself, of achieving "natural" repair.[2]

4.1.Electric field-induced remineralization

By using electrophoresis in the absence of calcium phosphates and their analogues, this technology was able to remineralize the fully demineralized dentin collagen matrix and reduce the mineralization time.[3]

4.2. Arginine bicarbonate

The amino acid arginine bicarbonate contains calcium carbonate granules and can adhere to the surface of minls.

Minerals.While the release of carbonate may cause a modest local pH rise, when calcium carbonate dissolves, the calcium that is released is available to remineralize the mineral.[3]

5. Herbal remineralizing agents

5.1. Xylitol

A non-fermentable sugar alcohol, xylitol is made from hardwoods high in xylan, such as birch and beech wood. It has anti-cariogenic actions by inactivating S. mutans and inhibiting the production of acids and polysaccharides in plaque. Additionally, it promotes greater saliva production when chewed as gum, increasing the body's ability to buffer acids, and its high mineral content supplies the minerals needed to remineralize teeth. Because cariogenic bacteria cannot ferment xylitol, it does not lower the pH of plaque, limiting demineralization of the enamel and bacterial growth.[2]

5.2. Grape seed extract

Proanthocyanidin (PA), a type of polyphenol, is present in grapeseed extract. Plant-derived compounds known as polyphenols have antioxidant and anti-inflammatory effects. Proanthocyanidin works by hastening the transformation of soluble into insoluble collagen. Proanthocyanidin-treated collagen matrices are biocompatible and stop the action of enzymes like F-ATPase, glucosyl transferase, and amylase. Streptococcus mutans-produced glucosyl-transferases are inhibited by PA, which prevents dental caries. [2]

5.3. Hesperidine

Lebreton was the first to isolate hesperidine, a flavanoneglucoside, from the white interior orange peels. It causes remineralization by interacting with the collagen matrix. Collagen matrix becomes more stable as a result, and remineralization is promoted since it serves as a scaffold for mineral deposition.[2]

5.4. Yogurt Extract

By adhering to the enamel surface, milk proteins prevent demineralization of the enamel. Additionally, milk enzymes contribute to the reduction of cariogenic bacterial development.Yogurt releases calcium ions at an acidic pH, aiding in the remineralization of enamel. Yogurt extract was shown to be useful in preventing enamel demineralization in a study by Varghese et al.[2]

5.5. Psidium Cattleianum Leaf Extract

Another name for Psidium cattleianum is strawberry guava. Flavonoids are the primary active substances found in P. cattleianum. These tannins (ellagic acid) and flavanoids (primarily kaempferol, quercetin, and cyanidin) have antibacterial properties. The action of P. cattleianum leaf extract involves suppressing the expression of proteins involved in general metabolism, particularly the metabolism of carbohydrates in S. mutans biofilms. Glycosyl transferases and other membrane-associated proteins are thus blocked. Psidium cattleianum aqueous extracts boost enamel remineralization by increasing microhardness, according to Crivelaro de Menezes TE et al.[2]

Challenges for future

Despite the fact that the science of cariology in regards to microbiome dysbiosis, caries lesion remineralization, and caries risk assessment is highly developed, one of the biggest challenges is turning all of this knowledge into useful, evidence-based treatment recommendations for practise and at-home care.[7]

Remineralization is more likely to occur in active white spot lesions than in dormant lesions. This is due to the fact that their surface is more porous, which allows ions to penetrate it more effectively. The suggested methods include acid etching, microabrasion, bleaching/deproteination or their combination. Another issue is that these new remineralizing agents still need direct clinical validation to ensure efficacy because the clinical performance of these non-fluoridated remineralizing agents may not always be predicted by pre-clinical models.[4]

Engagement of the patient is essential for success and requires careful consideration of literacy-related concerns and an understanding that dental caries is a treatable condition that may require various interventions over the course of the patient's lifetime. To shift the dental profession toward preventive and low intervention dentistry, financial incentives must be put in place. To meet these objectives, electronic record-keeping systems need to be updated.[7]

Conclusion

An effort has been made in the current review to examine the various remineralization approaches and technologies currently used to remineralize enamel and dentin.

A number of factors, including changes in lifestyle, food, and longer life expectancy, have had an impact on the health and aesthetics of dental enamel and dentin during the past few decades. A more favourable relationship where remineralization happens more frequently than demineralization can be established with a better understanding of the application of these remineralizing agents and new technology that are available to dentists.

The process of tooth structure demineralizing and remineralizing is ongoing. Incipient carious lesions exhibit the remineralization process. Many people stand to gain from non-fluoride remineralization technology. We can restore the health of oral tissues using contemporary non-fluoride procedures without worrying about the negative effects of fluorides.

It is anticipated that additional research in this area will result in better clinically applicable goods and technology with optimal responses and outcomes.

Conflict of Interest

None Declared

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