

## Current Evaluation At Trend Remineralization Agents

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**ABSTRACT :** Changing trend approaches with developing technology have also changed with certain prognoses and the contents of treatments. The use of lower doses with highly effective materials has become more effective in remineralization treatments. The use of drugs and herbal materials in nanoparticle form with low chemical content has become widespread over the world. Nanocomposites, nanoglass ionomers, nanoceramics, ceramic nano cells, nanotechnological restorative materials, nanotechnological prosthetic materials, dental implants, nanotechnological orthodontic devices, nanotechnological endodontic devices, nanotechnological materials used in nano bone tissue engineering are the current materials produced with the same idea. The increase in human population and the need for oral and dental health treatment bring that the preventive dentistry practices should be also more developed rapidly. Demineralization and remineralization in healthy tissues make their progress in a certain balance in the oral system. The disruptions of this balance in the direction of demineralization initiate the formation of caries. The demineralization and remineralization cycle is the most important factor determining the prognosis of caries. While demineralization always causes dissolution on the crystalline network surface of the enamel tissue, the remineralization mechanism can be defined as the natural repair of lesions in which cavitation is not observed. Remineralization agents have a very important place in preventive dentistry in terms of preventing tooth decay. Within the aim of this review, remineralization agents that are frequently mentioned in the literature and have become routinely used in the clinics are explained. This review has been prepared to shed light on pharmacists, dentists and all researchers interested in the department of biochemistry.

**KEY WORDS:** Nanotechnology; preventive dentistry; remineralizing agents

### I. INTRODUCTION

Developing a new drug patent is complex and difficult. Optimizing the bioavailability of existing patented drugs may be a more effective way to use these drugs in the clinics. The high doses of drugs used in the preparation of known traditional and conventional drug carrier systems such as solution, emulsion, suspension, powder, tablet, capsule, and the resulting features such as high side effects, low therapeutic/pharmacological effect, first pass effect are the disadvantages of traditional drug carrier systems and also limit their use.<sup>1</sup> Different and new drug carrier systems should be also developed because the plasma level of the absorbed active substance fluctuated in these traditional drug carrier systems and the constant changes in the drug concentration in the plasma can not be observed and fixed.<sup>3</sup> These systems have also become a trend in the development of remineralization agents.<sup>4-5</sup> Preventive dental care is essential to maintain good oral health and keep the patients healthy during their life. Preventive dentistry is a combination of routine oral examinations, hygiene habits, dental treatments, preventive procedures such as fluoride applications and sealants, education, and proactive guidance and diagnostic procedures.<sup>6-7-8</sup> The aim of preventive dentistry is the early prevention of tooth decay rather than invasive restorative treatments.<sup>9</sup> However, efforts to promote oral hygiene and fluoride use, dental caries are the most common oral disease and also a major public health problem.<sup>10</sup>

### II. REMINERALIZATION AGENTS

In this section, some remineralization agents that have an important place in clinic and practice are explained.

**Bioactive Glass :** Bioactive glass is an inorganic component consisting of silica, sodium, phosphate and calcium and is actively found in the human body. Bioactive glass material is biocompatible and has the ability to form chemical bonds with tissues. Bioactive glass in contact with saliva rapidly releases calcium, phosphorus and sodium ions into the environment, and as a result of this release, hydroxycarbonate apatite is formed and remineralization begins.<sup>11</sup> Bioactive glass is an important material used in many areas of dentistry, such as remineralization of dental hard tissues, vital pulp treatments, antibacterial treatments, dentin sensitivity removal and bone regeneration.<sup>12</sup>

**Fluoride** : One of the most preferred alternative for prophylaxis is fluoride. The fluoride mechanism focuses on the principles of preventing demineralization and promoting remineralization. Prevention pellicle formation and dental plaque formation, at the same time reducing the acid production of the microorganisms contained in the plaque to an optimum level, converting the hydroxyapatite structure in the enamel structure into fluorohydroxyapatite, a form more resistant to demineralization, making the layer formed predominantly by calcium phosphate ions precipitated on the tooth surface more dense. The antibacterial effect of fluoride was supported by studies and these studies explain that this material has demineralization inhibition mechanism and remineralization-promotion properties.<sup>13</sup> When fluoride ions interact with the outer surface layer of the enamel, fluorapatite and calcium fluoride are formed in the environment and the fluoride mechanism is based on this step.<sup>13-14</sup>

**Hydroxyapatite** : The first artificially produced hydroxyapatites are microstructured particles and these particles differ from the hydroxyapatite in enamel tissue. Since these microstructured particles have a higher surface/volume ratio, the solubility of nano hydroxyapatite particles is higher than hydroxyapatite particles. The researchers showed that the glass ionomer restorative materials containing micro and nano hydroxyapatite in the experimental groups are effective on remineralization and compared the effects of these materials.<sup>15</sup> As a result of that, both of these materials provide remineralization activity; however, they reported that glass ionomers containing micro hydroxyapatite had less remineralization capacity than glass ionomers containing nano hydroxyapatite. In their in vitro studies, they compared the remineralization effect of nano hydroxyapatites with aminfluoride-containing pastes and concluded that nano hydroxyapatites provided higher remineralization.

**Casein Phosphopeptide Amorphous Calcium Phosphate** : CPP-ACP complex; casein, which is found in almost all products obtained from animal food, consists of the phosphoseryl structures contained in the phosphopeptide and amorphous calcium phosphates. Precipitation of casein in solutions should not be used. Therefore, the casein complex is filtered before it reaches its actual size. CPP-ACP maintains its demineralization inhibitory effect by preventing the increase of the bacterial population, increasing the Ca and P ion level and transport in the plaque, and preventing the release of free Ca and P ions.<sup>16</sup> In recent years, studies using CPP-ACP; corresponding with the current data, the positive effect of this material on remineralization has been clearly demonstrated.<sup>17</sup> For this reason, this material was introduced by adding it to the structure of prophylactic materials such as toothpaste, mouthwash and sugar-free gum.

**Casein Phosphopeptide Amorphous Calcium Fluoride Phosphate** : There is a significant number of studies showing an increase in remineralization potential when CPP-ACP is combined with fluoride. In a study comparing the remineralization effects of CPP-ACP and solutions containing CPP-amorphous calcium fluoride phosphate (ACFP) on incipient caries, it shows that CPP-ACFP is more effective than CPP-ACP and also it has been stated that solutions containing CPP-ACFP have more remineralization potential than solutions containing CPP-ACP.<sup>18</sup>

**Chitosan** : Chitosan is a hydrophilic polysaccharide and it can be used by multifactorial areas, the main ingredient of which is chitin. The second most common aminopolysaccharide in nature is chitin. Chitin is found in plankton, in the cell walls of fungi, in the skeletal structure of insects, and in shellfish. It is a substance that shows a wide antibacterial spectrum against fungi, gram-positive and gram-negative bacteria. In dentistry, chitosan is mainly used as an antibacterial agent. Chitosan provides its remineralization activity by increasing the pH value by affecting the acidity of the environment.<sup>19</sup>

**Isomalt** : One of the bestknown sugar alcohols is isomalt. Isomalt cannot reduce extracellular polysaccharides such as xylitol and cannot be degraded by pathogenic bacteria. For this reason, isomalt has no antibacterial properties and is nonacidogenic. Isomalt derives its remineralizing effect from increasing the buffering capacity of saliva. It binds calcium phosphate structures with the same mechanism as xylitol. In their study, they concluded that the use of xylitol together with fluoride significantly increased the remineralization capacity.<sup>21</sup>

**Hesperidin** : Hesperidin is a citrus extract with antimicrobial and remineralizing properties. Also, it is a flavonoid glycoside. In a study investigating the effect of hesperidin on bovine dentin, it was stated that it reduces the proteolytic activity in dentin and the sensitivity of dentin to demineralization, protects the collagen structure of dentin and contributes positively to the remineralization process.<sup>24</sup>

**Sorbitol** : Sorbitol, which is fermented by pathogenic microorganisms more slowly than glucose and sucrose, lowers the pH level less than other sugar alcohols. For this reason, sorbitol is classified as a noncariogenic

substance. In studies comparing sorbitol and xylitol, it was concluded that the noncariogenic effect of sorbitol was less than xylitol.<sup>22</sup>

**Xylitol :** Xylitol is a five-carbon sugar alcohol. Xylitol, obtained from cellulose, can be found in toothpastes, mouthwashes, chewing gums, some medicines and gels. Xylitol has antibacterial properties. Its degradation by pathogenic bacteria explains this feature. Another feature of xylitol is that this substance reduces the amount of extracellular polysaccharides. When the amount of extracellular polysaccharide is reduced, acidogenic bacteria stop to adhere to the tooth surface, thus preventing a demineralization attack. Xylitol simultaneously increases the salivary flow rate.<sup>22-23-25</sup>

**Tricalcium Phosphate :** The biomaterial found in hard tissues such as teeth and bones, as well as alpha and beta formulas, is tricalcium phosphate. The alpha form of tricalcium phosphate increases the level of free calcium and phosphate. For this reason, it is thought to contribute positively to the progress of remineralization. The alpha form of tricalcium phosphate is generally used in prophylactic products. CPP-ACPF and TCP are very successful agents to promote remineralization of early-stage caries lesions. In a study, the remineralization activities of nano-hydroxyapatite were compared with the use of agents containing fluoride and tricalcium phosphate and the product containing tricalcium phosphate performed the highest remineralization potential than other products.<sup>20-23-25</sup>

**Perspective, Conclusions and Future Trends :** According to the findings, all supplements in this article explained are effective to promote remineralization mechanism. In order to reduce the occurrence of mineral loss, innovative techniques and more high-quality researches should be highlighted. Most of the studies show an in vitro accomplishment in the biomimetic remineralization of dentine using various approaches, which includes the use of remineralization agents as well as biomaterials derived from natural sources have great performance. The first stage of biomimetic dentine remineralization is the creation of crystallized nanoprecursors. A variety of remineralization agents containing bioactive glass are successful in interfibrillar and intrafibrillar remineralization of the demineralized dentine matrix. Conclusively, it is pertinent to develop a universal method to assess biomimetic remineralization with these remineralization agents.

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