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CASEIN PHOSPHOPEPTIDE-AMORPHOUS CALCIUM PHOSPHATE (CPP-ACP) MODIFIED GLASS IONOMER CEMENT- A REVIEW ARTICLE

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ABSTRACT Glass ionomer cements (GIC) have been extensively used for over forty years in dentistry because of their unique biological properties. This is credited to their ability to release long-term antimicrobial agents. However, they do suffer as restorative materials because of their poor mechanical property and development of secondary caries. Therefore, many efforts have been made to improve the anticariogenic potential of the cement. Particularly, for achieving this goal various bioactive agents possessing antibacterial property have been incorporated into GIC and tested. One such agent is Casein Phosphopeptide-Amorphous Calcium Phosphate (CPP-ACP), a milk protein derivative that helps in remineralising subsurface enamel lesions and slows progression of caries by replenishing the lost minerals like calcium and phosphate. This review article gives an understanding into the CPP-ACP modified GIC.

KEYWORDS : CPP-ACP, GIC, remineralization, demineralization

INTRODUCTION

Dental caries is one of the most prevalent chronic diseases of microbial origin that affects people worldwide. The disease process is initiated by acidic by-products from bacterial fermentation of dietary sugars that cause localized destruction of susceptible hard tissues. It is a multifactorial disease that is affected by several factors- salivary flow and its composition, fluoride exposure, consumption of dietary sugars and preventive behaviors. It is often not a self-limiting process but can be arrested and potentially reversed in its early stages. Thus, this highlights the significance of anti-cariogenic agents involving calcium and phosphate that supplement the effect of fluoride in an approach to prevent and manage caries experience.[1]

The glass ionomer family of materials is a set of clinically established acid-base cements that have been widely used since their introduction in 1972. They were developed by Wilson and Kent primarily as a result of the search for a replacement for the silicate cements. They are water-based, tooth-colored restorative materials that are based on a setting reaction between ion-leachable glass powder and polyalkenoic acid. GICs have shown to be capable of remineralising carious enamel and dentin, preventing demineralization and ceasing bacterial growth. These excellent biological properties make it a popular dental material which is best attributed to its ability of sustained fluoride release.[2]

Dairy products (milk, milk concentrates and cheese) have shown to possess anti-cariogenic potential which is attributed to direct chemical effect by milk components such as casein, calcium and phosphate.[3] Casein is a principal phosphoprotein found in bovine milk. Casein phosphopeptide, derived from casein by tryptic digestion, possess marked ability to stabilize calcium and phosphate ions in solution thus inhibiting tooth demineralization and promoting remineralization.[4]

These actions make CPP-ACP a promising addition to the restorative materials. This article gives an overview of CPP-ACP modified GIC in comparison with conventional GIC.

Composition:

The glass-ionomers are more precisely known as glass-polyalkenoate cements. They are prepared from an aqueous solution of either a 47.5% solution of homo-polymer or a copolymer of 2:1 polyacrylic acid with maleic acid, itaconic acid and other monomers. The powder is usually a calcium aluminosilicate glass with high fluoride content but it is a complex structure based on three important constituents- silica (SiO_2), alumina (Al_2O_3) and lime (CaO) which is often substituted by strontium or zinc oxide. In addition they also contain Fluorite (CaF_2) as a source of fluoride release, and some phosphate and soda (Na_2O). The additives differ according to the manufacture and no two products are identical.[5]

Powder content:

Silica	SiO_2	29%
Alumina	$Al2O_3$	16.6%
Aluminium fluoride	AlF_3	5.3%
Calcium fluoride	CaF_2	34.3%
Cryolite	$Na3AlF_6$	5%
Aluminium phosphate	$AlPO_4$	9.8%
Lanthanum, strontium, barium		In traces

Setting reaction:

The setting reaction is typically a conventional acid-base reaction. Following the mixing of the powder with the liquid, the surface of the glass is attacked by the polyacrylic acid causing dissolution at the surface and release of ions (Ca^2+ and Al^3+) and fluoride. The cations then migrate to interact with the polyacid anions to form the metallic salt bridges. The set cement is composed of glass particles in a matrix of polycarboxylate salts sheathed by silica hydrogel.[6] Fluoride does not take part in the reaction and lies free within the matrix. Thus, it is able to leach out and return without affecting the physical properties of the set cement. Thus, glass ionomers can be regarded as a fluoride reservoir.[7]

Classification:

Based on clinical applications they have been classified as follows: (Wilson and McLean 1988)

Type 1: Luting and bonding materials

- For cementation of crown, bridges, inlays and orthodontic appliances
- Powder: liquid ratio is 5:1 or 3.8:1

Type 2: Restorative

II.I Restorative (aesthetic) auto cure and resin modified

- For any aesthetic restorations with minimal load
- Powder: liquid ratio is 3:1

II.2 Restorative materials

- For rapid set and high physical properties
- Powder: liquid ratio is 3:1 to 4:1

Type 3: Lining or base cements

- Can be used as a lining or a base under restoration
- Powder: liquid ratio for lining is 1.5:1
- Powder: liquid ratio for base is 3:1

In the recent years, several modifications of glass ionomer cement have come into the market.

Properties:

GICs possess certain inherent unique properties that make them advantageous as restorative and adhesive dental material. These include adhesion to all teeth tissues, anticariogenic property attributed to fluoride release, thermal compatibility due to low coefficient of thermal expansion, favorable biocompatibility and low cytotoxicity. However, poor mechanical properties such as low fracture toughness and wear offer limited application in stress bearing (posterior) areas.[7] In addition, micro leakage around restorations may occur that may lead to formation of secondary caries.[9] They are also regarded as technique sensitive due to its sensitivity to moisture contamination.

Physical and mechanical property:

The 24 hour compressive strength of glass ionomer cements ranges from 90 to 230 MPa and the tensile strength is seen to be from 4 to 6 Mpa.

Fluoride release and Anti-cariogenicity:

A sustained, long-term fluoride release is considered to be one of the biggest assets of the glass-ionomer cements. Fluoride is added as a flux during the manufacturing process of the glass powder and is not an integral part of the matrix. At the time of mixing, there is considerable release of free fluoride which shows a pattern of initial rapid release followed by a decline over the next month to largely stabilize at a lower level.[10] Fluoride release increases in acidic conditions or at high temperatures.[11] As the inherent fluoride levels deplete, the cement has the ability to be recharged from fluoride exposure in the ambient environment. Hence, it acts as a fluoride reservoir. The amount of released fluoride depends on content in both the storage media and the restorative material. It is also referred to as "smart material" since it allows incorporation of bioactive molecules including calcium, phosphate and strontium in a controlled fashion in response to the environment.[10] The fluoride ion enhances remineralization, prevents demineralization by inhibiting the metabolism of acid-producing bacteria and renders the surrounding tooth structure resistant to acid attack.

In an approach to further reinforce the biological properties of a novel dental material like glass ionomer; investigators have explored new modifying agents that can reconstruct the depleted tissues with hydroxyapatite, which has the same inorganic content as enamel. One such remineralising agent is a calcium phosphate based system, casein phosphopeptide-amorphous calcium phosphate.

CPP-ACP

ACP

Aaron S Posner first described amorphous calcium phosphate in mid-1960s. It precipitates from a supersaturated calcium phosphate solution and can convert into stable crystalline phases, for instance octacalcium phosphate and apatitic products. It has good bioactivity and osteoconductivity. The unstable ACP combines with fluoride to form flouroapatite.[12]

Development of CPP

Casein phosphopeptide- amorphous calcium phosphate is a bioactive agent which is derived by the process of tryptic digestion of the milk protein, casein. It contains cluster sequence of Ser(P)-Ser(P)- Glu- Glu. These multiple phosphoseryl residues significantly accelerate the solubility of calcium phosphate thus stabilizing the ions as amorphous nanocomplexes under normal and alkaline conditions.[13] The presence of CPP prevents rapid growth of calcium phosphate to the critical size required for phase transformation by binding to the nanoclusters of amorphous calcium phosphate. This maintains the ions in a bioavailable form for remineralization of subsurface lesions in tooth enamel.[14]

Actions of CPP-ACP

CPP-ACP functions in a dose dependent mechanism.

Calcium phosphate reservoir: remineralization

CPP- ACP has the ability to localize ACP at the tooth structure and can be regarded as a calcium phosphate reservoir. It maintains a state of super saturation thereby promoting remineralization and reducing demineralization. It makes the tooth surface more resistant to subsequent acid attack.

Antibacterial property

It inhibits the adherence of cariogenic flora inducing the formation of non- cariogenic plaque. With the presence of extracellular free calcium ion concentration; it has a bactericidal or bacteriostatic effect thereby possibly affecting biofilm formation. It also has an anti-calculus action. The CPP-ACP formation responds to pH; binding reduces as the pH falls and vice-versa.

Flouroapatite formation

It is seen that CPP-ACP interacts with fluoride synergistically to form amorphous calcium fluoride phosphate (ACFP). It promotes remineralization by formation of flouroapatite. CPP-ACP can be added to GIC and studies have demonstrated the enhanced resistance to acid challenge[15].

CPP-ACP modified GIC

The goal of addition of CPP-ACP into GIC is to produce a material with improved biological properties while retaining acceptable physical and working properties.

Mazzaoui et al incorporated 1.56% w/w CPP-ACP into GIC and investigated cements physical and chemical properties. It displayed escalated release of calcium, phosphate and fluoride ions at neutral and alkaline ph. and amplified protection of adjacent dental tissues to acid challenge. The micro tensile bond strength was 33% higher and was believed to be due to the fusion of CPP-ACP nanoparticles into the cross-linked matrix. The compressive strength was 23% higher than control.[16]

The Addition of 3% CPP-ACP also enhanced ion release with no significant adverse effects on the surface hardness or change in mass.[17] Similar finding were noted by several researchers.[9] The colonization and establishment of streptococcus mutans biofilm was evaluated and it was concluded that 3% CPP-ACP inhibited the biofilm development.[19]

In another study conducted by Al Zraikat et al, physical and mechanical properties were evaluated. The addition of 3 or 5 % CPP-ACP substantially reduced the demineralized enamel area adjacent to GIC with heightened calcium and inorganic phosphate release, which was in agreement with the previous studies. But, it lessened the cements strength and prolonged the setting time. However, the values were within the ISO limits. The probable rationale was the alteration in the powder: liquid ratio. It also demonstrated a significant reduced fluoride release which may be attributed to the precipitation of calcium fluoride following release of ions.[20]

Applications

It helps in remineralization of white spot lesions which is a common finding in orthodontic patients and children. It has shown less micro leakage in cementation of orthodontic bands. Additionally, it can be used in early childhood caries. It has been seen to be helpful in treating dentinal hypersensitivity. It has an anti-erosive property. CPP-ACP probably interacts with the hydrogen ions, forming calcium hydrogen phosphate and restores the center areas of the enamel prisms which are dissolved in enamel erosion and also it maintains the orientation of crystal fibrils which were confirmed by enamel surface roughness measurements. It can also be used in restoring root dental caries due to its buffering action.[12]

CONCLUSION

CPP-ACP has provided a new level to the preventive dentistry. It is a promising additive to the restorative material and can be used as a useful adjunct in the non-invasive management of early carious lesions. Incorporation of 3% CPP-ACP into the conventional GIC increases the anticariogenic potential by substantial release of calcium, phosphate and fluoride ions without significantly affecting the materials mechanical and physical properties.

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