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Novel rechargeable calcium phosphate dental nanocomposite

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ABSTRACT

Objectives. Calcium phosphate (CaP) composites with Ca and P ion release can remineralize tooth lesions and inhibit caries. But the ion release lasts only a few months. The objectives of this study were to develop rechargeable CaP dental composite for the first time, and investigate the Ca and P recharge and re-release of composites with nanoparticles of amorphous calcium phosphate (NACP) to achieve long-term inhibition of caries.

Methods. Three NACP nanocomposites were fabricated with resin matrix of: (1) bisphenol A glycidyl dimethacrylate (BisGMA) and triethylene glycol dimethacrylate (TEGDMA) at 1:1 mass ratio (referred to as BT group); (2) pyromellitic glycerol dimethacrylate (PMGDM) and ethoxylated bisphenol A dimethacrylate (EBPADMA) at 1:1 ratio (PE group); (3) BisGMA, TEGDMA, and Bis[2-(methacryloyloxy)ethyl] phosphate (BisMEP) at 2:1:1 ratio (BTM group). Each resin was filled with 20% NACP and 50% glass particles, and the composite was photo-cured. Specimens were tested for flexural strength and elastic modulus, Ca and P ion release, and Ca and P ion recharge and re-release.

Results. NACP nanocomposites had strengths 3-fold of, and elastic moduli similar to, commercial resin-modified glass ionomer controls. CaP ion recharge capability was the greatest for PE group, followed by BTM group, with BT group being the lowest ($p < 0.05$). For each recharge cycle, CaP re-release reached similarly high levels, showing that CaP re-release did not decrease with more recharge cycles. After six recharge/re-release cycles, NACP nanocomposites without further recharge had continuous CaP ion release for 42 d.

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Significance. Novel rechargeable CaP composites achieved long-term and sustained Ca and P ion release. Rechargeable NACP nanocomposite is promising for caries-inhibiting restorations, and the Ca and P ion recharge and re-release method has wide applicability to dental composites, adhesives, cements and sealants to achieve long-term caries-inhibition.

1. Introduction

Resin composites and adhesives are increasingly used in dental restorations [1–6]. Tooth cavity restorations cost the United States approximately $46 billion annually [7]. Secondary (recurrent) caries is a frequent reason for the failure of dental restorations [8–10], and replacing the failed restorations accounts for 50–70% of all restorations performed [11,12]. According to the minimally-invasive treatment concept, more dentin tissues are recommended to be preserved, which are accompanied by a certain amount of caries-infected and caries-affected dentin with residual bacteria in the prepared cavity [13–16]. In addition, microleakage along the restoration margins can provide pathways for new invading bacteria from the oral environment [17–20]. The bacteria growth and biofilm formation can produce acids to demineralize the tooth structure and cause caries.

A promising approach to combat caries is the development of calcium phosphate (CaP) composites that can release calcium (Ca) and phosphate (P) ions [21–27]. Traditional CaP composites contained CaP particles with sizes of 1–55 μm and achieved successful remineralization of tooth lesions [21–24]. Re-incorporation of minerals into the demineralized dentin matrix is important since the precipitated mineral may serve as sites for further nucleation, and the remineralized tissues may be more resistant to degradation [28]. Recently, nanocomposites containing nanoparticles of amorphous calcium phosphate (NACP) with a mean particle size of 116 nm were developed [27,29–31]. The nanocomposites released high levels of Ca and P ions while having mechanical properties 2-fold those of traditional CaP composites [25,27]. The NACP nanocomposite was "smart" and can rapidly neutralize lactic acid solutions at a cariogenic pH of 4 and increase the pH to a safe level of above 6 [29]. The NACP nanocomposite successfully remineralized enamel lesions in vitro, achieving a remineralization that was 4-fold that of a commercial fluoride-releasing composite [30]. In a human in situ model, the NACP nanocomposite inhibited secondary caries at the enamel-restoration margins in vivo, reducing the enamel mineral loss at the margins to 1/3 of the mineral loss associated with a control composite without NACP [31].

However, a major drawback of CaP composites is that the Ca and P ion release lasts for only weeks to months, and then the ion release is diminished over time. Previous studies measured Ca and P ion release from composites to at most a couple of months [21,23,27,30,32]. However, clinicians and patients would expect the composite restoration to be effective in vivo for much longer than a few months (e.g., for 10 or 20 years). Therefore, it would be highly desirable for the CaP composite to be able to recharge and re-release Ca and P ions, thereby to release Ca and P ions indefinitely and provide long-term caries-inhibition capability. However, literature and patent searches revealed no report on rechargeable calcium phosphate dental composites and resins.

Therefore, the objectives of this study were to develop rechargeable calcium phosphate dental composite for the first time, and to investigate the effects of different resin matrices on the CaP recharge and re-release efficacy. A previous NACP nanocomposite using bisphenol A diglycidyl methacrylate (BisGMA)-based matrix with high levels of Ca and P ion release and good mechanical properties served as a control [22,27]. Two new NACP nanocomposites were synthesized. One contained pyromellitic glycerol dimethacrylate (PMGDM) and ethoxylated bisphenol A dimethacrylate (EBPADMA) at a mass ratio of 1:1. The other contained Bis[2-(methacryloyloxy)ethyl] phosphate (BisMEP). PMGDM and BisMEP were selected because both are acidic adhesive monomers [33–35], and may chelate with calcium and phosphate ions from a recharge solution to achieve the recharge capability. The following hypotheses were tested: (1) rechargeable calcium phosphate composites can be developed and the recharge efficacy will depend on matrix resin type; (2) the re-release of Ca and P ions from the NACP nanocomposite will be maintained over time and not decrease with increasing the number of recharge/re-release cycles; (3) the rechargeable NACP nanocomposite will possess mechanical properties matching or exceeding commercial control fluoride-rechargeable restorative materials.

2. Materials and methods

2.1. NACP nanocomposite fabrication

NACP [$Ca_3(PO_4)_2$] were synthesized via a spry-drying technique as previously described [27,30]. Briefly, calcium carbonate and dicalcium phosphate anhydrous were dissolved into an acetic acid solution. The concentrations of Ca and P ions were 8 mmol/L and 5.333 mmol/L, respectively. The solution was sprayed into a heated chamber to evaporate the water and volatile acid. The dried particles were collected by an electrostatic precipitator. This yielded NACP with a mean particle size of 116 nm [27,30]. As a co-filler, barium boroaluminosilicate glass particles with a median size of 1.4 μm (Caulk/Dentsply, Milford, DE) were silanized with 4% 3-methacryloxypropyltrimethoxysilane and 2% n-propylamine as previously described [27,30].

Three types of matrix resins were prepared to fabricate the NACP nanocomposite. For type 1, a resin of BisGMA and triethylene glycol dimethacrylate (TEGDMA) (Esstech, Essington,

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