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Strength and fluoride release characteristics of a calcium fluoride based dental nanocomposite

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ABSTRACT

Secondary caries and restoration fracture remain the two most common problems in restorative dentistry. Release of fluoride ions (F) could be a substantial benefit because F could enrich neighboring enamel or dentin to combat caries. The objective of this study was to incorporate novel CaF_2 nanoparticles into dental resin to develop stress-bearing, F-releasing nanocomposite. CaF_2 nanoparticles, prepared in our laboratories for the first time, were combined with reinforcing whisker fillers in a resin. Flexural strength (mean ± sd; $n = 6$) was 110 ± 11 MPa for the composite containing 30% CaF_2 and 35% whiskers by mass. It matched the 108 ± 19 MPa of a stress-bearing, non-releasing commercial composite (Tukey's at 0.05). The composite containing 20% CaF_2 had a cumulative F release of 2.34 ± 0.26 mmol/L at 10 weeks. The initial F release rate was 2 μg/(h cm^2), and the sustained release rate after 10 weeks was 0.29 μg/(h cm^2). These values exceeded the reported releases of traditional and resin-modified glass ionomer materials. In summary, nanocomposites were developed with relatively high strength as well as sustained release of fluoride ions, a combination not available in current materials. These strong and F-releasing composites may yield restorations that can reduce the occurrence of both secondary caries and restoration fracture.

1. Introduction

Secondary (or recurrent) caries and restoration fracture remain the two most common problems in restorative dentistry [1,2]. Caries at the restoration margins is a frequent reason for replacement of existing restorations [3]. Restoration replacement accounts for about 70% of all operative work [4], and replacement dentistry costs about $5 billion/year in the United States [5]. There is evidence that the sustained release of fluoride ions (F) could be a substantial benefit for a dental restoration because the fluoride could enrich neighboring enamel or dentin to combat secondary caries [6–11]. Fluoride-releasing restorative materials include glass ionomers, resin-modified glass ionomers, compomers, and resin composites [11–17]. These materials have received much attention due to their release of fluoride, the uptake of fluoride into cavity walls and plaque, and the enhanced reprecipitation of calcium and phosphate promoted by the fluoride release [6,9,10,13,18]. However, the inferior mechanical properties of glass ionomer and resin-modified glass ionomer materials have limited their use [13,19–21]. It was predicted that "the most intractable problem is likely to be lack of strength and toughness" [19]. The addition of a resin in the matrix did not significantly reduce the problems of glass ionomer materials [20]. When traditional and resin-modified glass ionomer materials were immersed in water for 12 months [21], it was found that the addition of resins to glass ionomer did not improve microhardness. Therefore, extensive studies have been undertaken to understand and further improve the performance of F-releasing restorative materials [11,14,22–27].

Resin composites have been developed for tooth cavity restorations [28–34]. Calcium phosphate-based biomaterials are important for hard tissue repair due to their excellent biocompatibility and bioactivity [35–40]. Recently, nanoparticles of calcium phosphates were synthesized and incorporated into dental resins for the first time [40–44]. To address the two problems of secondary caries and restoration fracture, the nanoparticles and reinforcing whiskers were combined to develop stress-bearing, caries-inhibiting composites. These nanocomposites released supersaturating levels of calcium (Ca) and phosphate (PO_4) ions requisite for remineralization to occur, while possessing mechanical properties that matched commercial stress-bearing, non-releasing composites [41–44]. Our previous studies investigated the effects of nanoparticle to whisker ratio [42], filler level [43], and particle size and silanization [44]. A recent study synthesized calcium fluoride (CaF_2) nanoparticles and demonstrated the

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efficacy of the CaF_2 rinse as a labile F reservoir for the reduction of dentin permeability [45]. However, there has been no study on the incorporation of the new CaF_2 nanoparticles into dental resins to develop stress-bearing nanocomposites with fluoride release.

The objective of the present study was to develop stress-bearing dental nanocomposites for tooth cavity restorations with caries-inhibiting capability. Three hypotheses were tested: (1) resin composite containing the CaF_2 nanoparticles would have sustained release of high levels of fluoride; (2) composite containing both CaF_2 nanoparticles and calcium phosphate nanoparticles would release not only F but also Ca and PO_4 ions; (3) composite containing both nanoparticles and reinforcing fillers would have high levels of ion release as well as high mechanical properties.

2. Materials and methods

2.1. Preparation of CaF_2 nanoparticles

The CaF_2 nanopowder was prepared using a spray-drying system that was described in recent studies [40,42,45]. Briefly, a two-liquid nozzle (ViscoMist, Lechler, St. Charles, IL) was employed to allow two solutions to be mixed at the time of atomization. A calcium solution (calcium hydroxide, $Ca(OH)_2$ at 2 mmol/L) and a fluoride solution (ammonium fluoride, NH_4F at 4 mmol/L), prepared using reagent grade chemicals, were simultaneously fed to the nozzle. The feed rate was 10 mL/min and the solution was atomized into a heated air stream of approximately 70 °C within a glass column (VM770-48, VM Glass, Vineland, NJ) having dimensions of 15 cm × 15 cm × 122 cm. The reaction of $Ca(OH)_2$ and NH_4F led to the formation of CaF_2 and NH_4OH: $Ca(OH)_2{+}NH_4F \rightarrow CaF_2 + NH_3\uparrow + H_2O\uparrow$. The CaF_2 nanoparticles suspended in the flow were trapped in the electrostatic precipitator (MistBuster, Air Quality Engineering, Minneapolis, MN) and collected at the end of the process. The NH_4OH was removed as NH_3 and H_2O vapors with the air flow.

2.2. Preparation of DCPA nanoparticles

Nanoparticles of dicalcium phosphate anhydrous (DCPA, $CaHPO_4$) were prepared via the same spray-drying method. A single solution was prepared by dissolving 1.088 g of a traditional DCPA powder (J.T. Baker, Phillipsburg, NJ) in 1 L of an acetic acid at 16 mmol/L concentration to obtain a Ca and PO_4 ionic concentration of 8 mmol/L [42]. The solution was sprayed through the nozzle into the heated column, and the dried nanoparticles of DCPA were collected by the electrostatic precipitator.

2.3. Characterization of nanoparticles

The microstructure of the nanoparticles was examined using Transmission Electron Microscopy (TEM) (3010 HREM, JEOL, Peabody, MA). The TEM sample was prepared by depositing particles onto a holey carbon film-coated copper grid from a well-sonicated dilute suspension in acetone to minimize agglomeration. The phase of the nanopowders was determined by powder X-ray diffraction (XRD) (DMAX 2200, Rigaku Denki, Woodlands, TX). Multipoint BET particle surface area analyses were performed (AUTOSORB-1, Quantachrome Instruments, Boynton Beach, FL) with ultra high purity nitrogen as the adsorbate gas and liquid nitrogen as the cryogen. The samples were dried in air overnight at 110 °C before the measurement.

2.4. Preparation of whiskers fused with silica nanoparticles

As a co-filler, silicon nitride whiskers were used to improve the mechanical properties of the composite. The whiskers were obtained from a commercial source (α-Si_3N_4, Nanostructured and Amorphous Materials, Los Alamos, NM). The whiskers were examined using a scanning electron microscope (SEM, 5300, JEOL, Peabody, MA). The average whisker length of 100 randomly-selected whiskers was measured to be 14 μm, with a range of 3–55 μm. The average whisker diameter was 0.5 μm, with a range of 0.1–2.0 μm. The whiskers were mixed with silica (Aerosil-OX50, Degussa, Ridgefield, NJ) having a diameter of about 40 nm, at a whisker:silica mass ratio of 5:1 [46–48]. The mixture was heated at 800 °C for 30 min to fuse the silica onto the whiskers. The silica roughened the whisker surfaces and enhanced the silanization efficacy with improved retention in the resin. The powder was silanized with 4% 3-methacryloxypropyltrimethoxysilane and 2% *n*-propylamine. These fillers are referred to as "whiskers".

2.5. Resin composite fabrication

A monomer consisting of 48.975% Bis-GMA (bisphenol glycidyl dimethacrylate), 48.975% TEGDMA (triethylene glycol dimethacrylate), 0.05% 2,6-di-*tert*-butyl-4-methylphenol, and 2% benzoyl peroxide formed part I, the initiator, of a two-part chemically-activated resin [42–44]. Part II, the accelerator resin, consisted of 49.5% Bis-GMA, 49.5% TEGDMA, and 1.0% *N*,*N*-dihydroxyethyl-*p*-toluidine.

Three groups of specimens were fabricated. The purpose of the first group was to examine the effect of CaF_2/whisker ratio on mechanical properties of CaF_2–whisker composite. The total filler included the CaF_2 particles and the whiskers. The filler levels are listed in Table 1. The total filler level was fixed at 65% by mass because the fillers and resin could be readily mixed into a cohesive paste. In Table 1, the minimum whisker level was 25% because preliminary studies showed that this was required for the composite to have a strength comparable to that of commercial hybrid composite. This is because one purpose of this study was to develop F-releasing composite that can match the mechanical properties of commercial stress-bearing, non-releasing composite. The fillers were mixed with resin part I to form the initiator paste. The accelerator paste consisted of the same amount of fillers mixed with resin part II. Equal masses of the two pastes were blended and filled into a mold of 2 mm × 2 mm × 25 mm. Specimens were incubated at 37 °C for 24 h.

The purpose of the second group was to determine the mechanical properties of the composite containing whiskers and CaF_2 and DCPA nanoparticles. A potential benefit for this composite is to release F, Ca and PO_4 ions to promote the formation of fluoroapatite, which is more resistant to acid attacks and caries than hydroxyapatite. The filler mass fractions were: 25% whiskers, 20% CaF_2, and 20% DCPA. They were selected because preliminary studies showed that 25% of whiskers were needed to have good mechanical properties, and the composite containing 20% CaF_2 and 20% DCPA released significant levels of ions.

The purpose of the third group was to measure the ion release for the nanocomposite. The release was measured from the composite containing 25% of whiskers, 20% of CaF_2, and 20% of DCPA (with a total filler level of 65% by mass). The method for the ion release measurement is described in Section 2.7.

A hybrid composite (TPH, Caulk/Dentsply, Milford, DE) was used as a control for mechanical properties. It consisted of barium glass and fumed silica with a mean size of about 0.8 μm, at 78% filler level by mass in a urethane-modified Bis-GMA-TEGDMA resin. The specimens were photo-cured (Triad-2000, Dentsply, York, PA) for 1 min on each open side of the specimen. This is a typical hybrid composite with no ion release, and is clinically used in both anterior and posterior restorations.

2.6. Flexural testing

Flexural strength and elastic modulus were measured using a three-point flexural test at a crosshead-speed of 1 mm/min with a 10-mm span on a computer-controlled Universal Testing Machine (5500R, MTS, Cary, NC). Flexural strength was calculated: $S = 3P_{max}L/(2bh^2)$, where P_{max} is the maximum load, L is span, b is specimen width, and h is specimen thickness. Elastic modulus was calculated by: $E = (P/d)\ (L^3/[4bh^3])$, where load P divided by the corresponding displacement d is the slope of the load-displacement curve in the linear elastic region.

2.7. Measurement of ion release

Specimens of the third group were used for ion release measurement because the composite contained both CaF_2 and DCPA nanoparticles for F, Ca and PO_4 release, and the composite had good mechanical properties. To measure F release, a NaCl solution (133 mmol/L) buffered with 50 mmol/L HEPES ($pH = 7.4$; 37 °C) was used to immerse the specimens. Following previous studies [42–44], three specimens of 2 mm × 2 mm × 12 mm were immersed in 50 mL solution, yielding a specimen volume/solution of 2.9 mm^3/mL. This compared to a specimen volume per solution of approximately 3.0 mm^3/mL in a previous study [38]. The concentrations of F released from the specimens were measured vs. immersion time: 1 day (d), 2 d, 4 d, 7 d, 14 d, 21 d, 28 d, 35 d, 42 d, 49 d, 56 d, 63 d, and 70 d. The duration of 10 weeks was within the range of previous studies from 250 h [38], 600 h [39], to 100 days [14] and 16 weeks [17]. At each time period, aliquots of 0.5 mL were removed and replaced by fresh solution. The amount of F release was measured with a combination of a fluoride ion selective electrode and a reference electrode (Orion, Cambridge, MA). The collected solutions were first diluted to a concentration within the ranges of measurement and then combined with equal volume of total ionic strength adjustment buffer (TISAB) solution (Fisher, Fair lawn, NJ). Fluoride standard solutions ranging from 1×10^{-6} to 1×10^{-3} mol/L were measured to form a calibration curve, which was used to determine the F concentration.

To measure Ca and PO_4 ion release, the same specimens in the same solution were used. At each of the same time periods stated above, aliquots of 0.5 mL were removed and replaced by fresh solution. The aliquots were analyzed for Ca and PO_4 concentrations via spectrophotometric methods (DMS-80 UV-visible, Varian, Palo Alto, CA) following previous studies [33,38,39].

Table 1
Filler level mass fractions (%) in the resin composite

CaF_2 nanoparticles	0%	10%	20%	30%	40%
Whiskers	65%	55%	45%	35%	25%
Total fillers	65%	65%	65%	65%	65%