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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 CaF₂ nanoparticles into dental resin to develop stress-bearing, F-releasing nanocomposite. CaF₂ 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% of CaF₂ 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% CaF₂ had a cumulative F release of 2.34 ± 0.26 mmol/L at 10 weeks. The initial F release rate was 2 μg/(h·cm²), and the sustained release rate after 10 weeks was 0.29 μg/(h·cm²). 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.

Keywords

dental nanocomposite; CaF₂ nanoparticles; fluoride release; stress-bearing; tooth caries

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

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all operative work [4], and replacement dentistry costs about \$5 billion/year in the U. S. [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 (PO₄) 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 (CaF₂) nanoparticles and demonstrated the efficacy of the CaF₂ 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 CaF₂ nanoparticles into dental resins to develop stress-bearing nanocomposites with fluoride release.

The objectives of the present study were to develop stress-bearing dental nanocomposites for tooth cavity restorations with caries-inhibiting capability. Three hypotheses were tested: (1) Resin composite containing the CaF₂ nanoparticles would have sustained release of high levels of fluoride; (2) Composite containing both CaF₂ nanoparticles and calcium phosphate nanoparticles would release not only F but also Ca and PO₄ 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 CaF₂ nanoparticles

The CaF₂ 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, NH₄F 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 NH₄F led to the formation of CaF₂ and NH₄OH: $\text{Ca(OH)}_2 + \text{NH}_4\text{F} \rightarrow \text{CaF}_2 + \text{NH}_3\uparrow + \text{H}_2\text{O}\uparrow$. The CaF₂ 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 ($\alpha\text{-Si}_3\text{N}_4$, 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 [4648]. 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% npropylamine. 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 hrs.

The purpose of the second group was to determine the mechanical properties of the composite containing whiskers and CaF₂ and DCPA nanoparticles. A potential benefit for this composite is to release both F, Ca and PO₄ ions to promote the formation of fluorapatite, which is more resistant to acid attacks and caries than hydroxyapatite. The filler mass fractions were: 25% whiskers, 20% CaF₂, 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% CaF₂ 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 CaF₂, 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 CaF₂ and DCPA nanoparticles for F, Ca and PO₄ 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 mm³/mL. This compared to a specimen volume per solution of approximately 3.0 mm³/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 hours [38], 600 hours [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 PO₄ 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 PO₄ concentrations via spectrophotometric methods (DMS-80 UV-visible, Varian, Palo Alto, CA) following previous studies [33,38,39].

One-way ANOVA was performed to detect the significant effects of the variables. Tukey's multiple comparison test was used to compare the measured data at a p value of 0.05.

3. Results

Fig. 1A shows a typical TEM micrograph of the CaF₂ nanoparticles. Fig. 1B at a higher magnification shows that the particles exhibited numerous spherical protuberances on the surfaces, suggesting that they were formed during the spray drying process through the fusion of much smaller particles. XRD analysis in Fig. 1C shows that the powder was indeed CaF₂. This demonstrated the feasibility of synthesizing CaF₂ nanoparticles using the two-liquid nozzle spray-drying approach. Compared to its highly crystalline macro counterpart, the CaF₂ nanopowder had broader peaks, indicating that the CaF₂ was in a relatively poorly-crystalline phase.

The BET measurement for the CaF₂ powder yielded a specific surface area $A = 35.5 \text{ m}^2/\text{g}$. With the density of CaF₂ $\rho = 3.18 \text{ g/cm}^3$, the CaF₂ particle diameter $d = 6/(A\rho) = 53 \text{ nm}$. In addition, four random TEM pictures were taken of the CaF₂, and the sizes of 200 particles were measured by magnification. The smallest particle size thus measured was 15 nm; the largest was 335 nm. Hence the CaF₂ particle size ranged from 15 nm to 335 nm. The CaF₂ median (50th percentile) particle size was 56 nm. Histogram of the CaF₂ particle size distribution is shown in Fig. 2.

Fig. 3A plots the flexural strength of the first group of specimens. NCF denotes nanoparticles of CaF₂, and WHI denotes whiskers. Increasing the CaF₂ content (NCF), and hence decreasing the whisker content (WHI), significantly decreased the composite strength (one-way ANOVA at 0.05). The flexural strength (mean \pm sd; n = 6) for the composite with 0% NCF and 65% WHI was $(145 \pm 9) \text{ MPa}$, significantly higher than $(110 \pm 11) \text{ MPa}$ for the composite with 30% NCF and 35% WHI, and $(93 \pm 5) \text{ MPa}$ for the composite with 40% NCF and 25% WHI (Tukey's multiple comparison at 0.05). The strengths of the CaF₂ composites were not significantly different from the $(108 \pm 19) \text{ MPa}$ of the commercial hybrid composite ($p > 0.1$).

In Fig. 3B, the elastic modulus of the composite with 40% NCF and 25% WHI was $(13.6 \pm 1.3) \text{ GPa}$, significantly lower than $(16.8 \pm 0.8) \text{ GPa}$ of the composite with 0% NCF and 65% WHI ($p < 0.05$). The CaF₂ composites had moduli that were not significantly different from the $(11.6 \pm 2.6) \text{ GPa}$ of the commercial hybrid composite control ($p > 0.1$).

The second group of specimens, containing 25% whiskers, 20% CaF₂ and 20% DCPA, had a flexural strength (mean \pm sd; n = 6) of $(100 \pm 7) \text{ MPa}$ and elastic modulus of $(14.6 \pm 1.2) \text{ GPa}$. These values are not significantly different from the $(93 \pm 5) \text{ MP}$, and $(13.6 \pm 1.3) \text{ GPa}$, of the composite with 25% whiskers and 40% CaF₂ ($p > 0.1$). This indicates that as long as the composite contained the same amount of whiskers (25%), whether the nanoparticles were CaF₂ or DCPA did not significantly change the composite mechanical properties.

Fig. 4 plots the results from the third group. The F release for the composite containing 25% whiskers, 20% CaF₂ and 20% DCPA was plotted vs. time. The cumulative F release (mean \pm sd; n = 3) was $(0.15 \pm 0.03) \text{ mmol/L}$ at 1 day; it increased to $(0.68 \pm 0.11) \text{ mmol/L}$ at 1 week, and $(2.34 \pm 0.26) \text{ mmol/L}$ at 10 weeks ($p < 0.05$). The corresponding F release rate per hour per specimen surface area was calculated from the data in Fig. 4 and plotted in Fig. 5. The

initial F release rate reached $1.94 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$; it decreased to a level of about $0.5 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ after 500 hours, and further decreased to about $0.29 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ after 1680 hours (10 weeks).

The Ca and PO_4 ion releases are plotted in Fig. 6. The PO_4 ion release increased rapidly from 1 day to about 2 weeks, after which it plateaued, reaching a steady-state concentration of about 1.75 mmol/L. The corresponding Ca ion release was low (at 0.03 mmol/L).

4. Discussion

4.1 Fluoride release from nanocomposite

The F release from the nanocomposite was near the high end of values reported previously. In one study [14], the initial F release rate was approximately $2.9 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for a glass ionomer (Ketac-Fil), $0.4 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for another glass ionomer (Fuji II), and $0.4 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for a resin-modified glass ionomer (Vitremer) (estimated from Fig. 1 of Ref. 14). Another study examined the F release of a resin filled with a commercial CaF_2 powder which was ground to yield particle sizes of $0.04\text{--}3.0 \mu\text{m}$ [17]. The F release was measured at pH of 6 and 4. Decreasing the pH significantly increased the F release. At a CaF_2 filler mass fraction of 23% in the resin, the initial F release rate was $1.6 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ at a pH of 4, and $0.6 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ at a pH of 6 [17]. In the present study, at a slightly lower filler mass fraction of 20% of CaF_2 nanoparticles, the initial F release rate was $1.94 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ at a pH of 7.4. This release rate was higher than the $0.6\text{--}1.6 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ of the previous study.

The sustained (or longer-term) F release rate (at 50 days) was reported to be approximately $0.1 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for Ketac-Fil, $0.03 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for Fuji II, and $0.04 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ for Vitremer (calculated from Table 4 in Ref. 14). In another study [17], for the resin filled with 23% by mass of a commercial CaF_2 powder, the F release rate at 70 days (1680 hours) was similar to that at 2000 hours (83 days); both were approximately $0.05 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ [17]. The nanocomposite of the present study had a much higher F release rate of $0.29 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ after 70 days.

The reason for the relatively high F release from the nanocomposite was likely the small size and hence the high surface area of the nanoparticles. Traditional particles can be reduced in size by grinding or ball milling. However, it is difficult to reduce the median particle size to much smaller than $1 \mu\text{m}$. For example, in a recent study on Ca and PO_4 releasing composites, a commercial DCPA powder of $12\text{-}\mu\text{m}$ particle size was ball-milled for 24 hours, reducing the median particle size to $0.88 \mu\text{m}$ [44]; further grinding did not significantly reduce the particle size. In that study [44], the PO_4 release was 3 mmol/L for the nanocomposite containing DCPA particles of 112 nm; it was 2-fold that of the composite containing the $0.88\text{-}\mu\text{m}$ DCPA, and 3-fold that of the composite containing $12\text{-}\mu\text{m}$ DCPA. The high release of the nanocomposite was correlated to the high particle surface area of the DCPA nanopowder ($18.6 \text{m}^2/\text{g}$), compared to the $2.3 \text{m}^2/\text{g}$ for the $0.88\text{-}\mu\text{m}$ DCPA, and $0.19 \text{m}^2/\text{g}$ for the $12\text{-}\mu\text{m}$ DCPA [44].

In the present study, the CaF_2 had a surface area of $35.5 \text{m}^2/\text{g}$. While a previous study used a traditional commercial CaF_2 powder and did not report a median particle size [17], for the purpose of illustration, assume it was $1 \mu\text{m}$. With a density of CaF_2 being $\rho = 3.18 \text{g}/\text{cm}^3$, this yields a specific surface area of $1.9 \text{m}^2/\text{g}$ for the traditional CaF_2 powder. Hence the CaF_2 nanoparticles had a surface area that was nearly 20-fold higher than the traditional CaF_2 particles. This likely contributed to the high and sustained release of F ions from the nanocomposite.

4.2 Mechanical properties of nanocomposite

Achieving a high F release at a relatively low CaF_2 filler level (20%) made room for reinforcement fillers in the same resin. The nanocomposite with high F release had a flexural

strength of 121 MPa; that with both F release and Ca and PO₄ release had a flexural strength of 100 MPa (Table 2). These values matched the 108 MPa for the stress-bearing, non-releasing composite (TPH). For comparison, a previous study reported a diametral tensile strength of 15 MPa for Ketac, and 40 MPa for Vitremer [14]. Flexural strengths for Ketac and Vitremer are listed in Table 2, measured in the same laboratory using the same method as for the nanocomposites. Therefore, the method of combining the nanoparticles with reinforcing fillers resulted in composites that had high levels of sustained ion release and high mechanical properties. Considering that secondary caries and restoration fracture are the two major problems in restorative dentistry, the CaF₂ nanocomposite may be promising to produce restorations with a combination of stress-bearing and caries-inhibiting capabilities. Further in vitro and in vivo studies are needed to investigate and realize this potential.

While the present study did not include a water-aging experiment, a previous study immersed Ca and PO₄ releasing DCPA-whisker nanocomposites for 56 days in water [42]. The composite strength decreased by approximately 20% compared to specimens without immersion. For a composite containing 30% DCPA and 30% whiskers, the strength decreased from about 120 MPa to 100 MPa at 56-day [42]. This represented a smaller decrease compared to other releasing composites. For example, a previous composite using micron-sized DCPA had a biaxial flexural strength of 40–60 MPa before immersion [33]; the strength decreased to 10–20 MPa after a 90-day immersion [49]. The strength of an amorphous calcium phosphate composite decreased to 40 MPa after 11 days of immersion [38]. One reason that the nanocomposite strength was higher than previous Ca-PO₄ composites was that the nanocomposite relied on the reinforcing fillers that were stable in water, not the releasing fillers, for strength. However, a long-term water-aging study is needed for the CaF₂ composite. In addition, the whisker-reinforced composites are whitish in color but relatively opaque, and may be useful in stress-bearing posterior restorations with F, Ca and PO₄ ion release. Further studies are needed to improve the esthetics and develop photo-activated nanocomposites for anterior restorations.

4.3 Ca and PO₄ ion release from nanocomposite

Regarding PO₄ ion release, previous Ca-PO₄ composites released PO₄ to concentrations of 0.1–0.7 mmol/L measured using a similar method as that of the present study [33,38]. These composites were shown to effectively remineralize tooth lesions in vitro [33,38,39]. The nanocomposite in Fig. 6 released PO₄ to a higher concentration of 1.75 mmol/L. This was likely because the DCPA nanopowder had a high surface area of 18.6 m²/g [43]. In a previous study [33], the traditional DCPA particle size, *d*, was 1.1 μm and the tetracalcium phosphate (TTCP) particle size was 16 μm. The density, *ρ*, is 2.89 g/cm³ for DCPA and 3.07 g/cm³ for TTCP. Hence the specific surface area $A = 6/(\rho d) = 1.9 \text{ m}^2/\text{g}$ for DCPA, and $A = 0.12 \text{ m}^2/\text{g}$ for TTCP. Hence the DCPA nanopowder had a surface area that was 1–2 orders of magnitude higher than the traditional particles. In Fig. 6, the Ca ion release was minimal. This was possibly because there was precipitation of fluoroapatite (FAp) as a result of the release of Ca, PO₄ and F ions. The formation of one FAp, Ca₅(PO₄)₃F, consumes one F ion, three PO₄, but five Ca ions. Hence this would reduce the Ca concentration much more than the F and PO₄ concentrations. The fact that the formation of one FAp consumes one F ion but three PO₄ ions may also explain why the PO₄ concentration reached a plateau (Fig. 6), while the F concentration still increased steadily (Fig. 4). Since FAp has a relatively low energy state with very limited solubility, it is possible that the Ca ions were used up by FAp precipitation as soon as they were released. Further studies are needed to understand the FAp precipitation due to ion release from the nanocomposite. In situ studies are also needed to examine whether FAp could be formed in the tooth structure near the composite restoration to render the enamel and dentin more resistant to subsequent acid attacks.

5. Conclusions

Dental resin composite containing CaF₂ nanoparticles was developed for the first time. The composite released fluoride ions that matched or exceeded reported releases from traditional glass ionomer and resin-modified glass ionomer materials. The strength and elastic modulus of the nanocomposite matched those of a commercial stress-bearing, non-releasing composite. The composite mechanical properties and ion release could be tailored via changing the nanoparticle filler level and reinforcing filler level. Nanocomposite capable of releasing fluoride, phosphate and calcium ions for precipitation of fluoroapatite and inhibition of caries were formulated with good mechanical properties. These composites with high strength and ion release may be promising for restorations that can reduce secondary caries and restoration fracture, two common problems facing restorative dentistry.

Acknowledgments

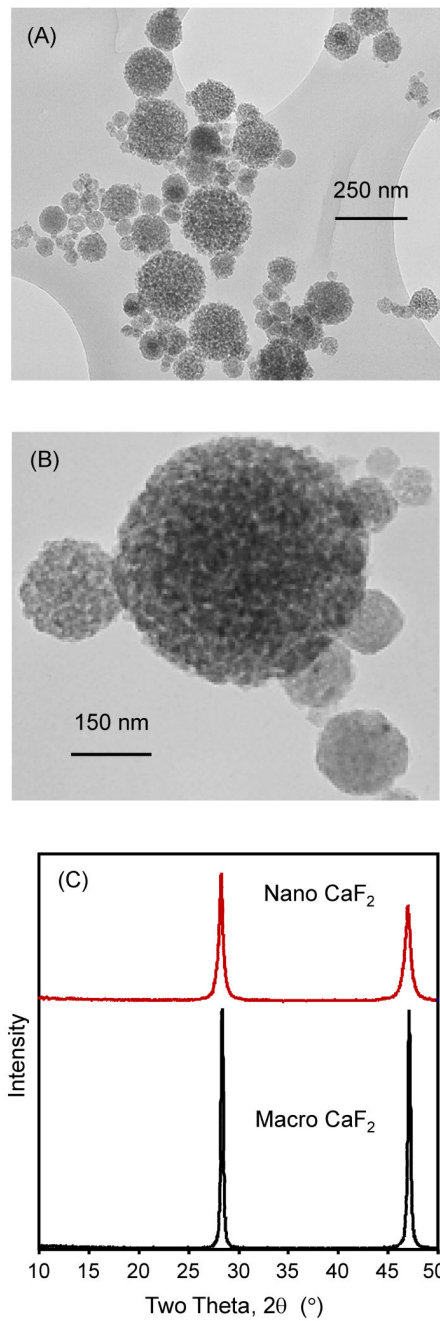
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REFERENCES

1. Sarrett DC. Clinical challenges and the relevance of materials testing for posterior composite restorations. *Dent Mater* 2005;21:9–20. [PubMed: 15680997]
2. Sakaguchi RL. Review of the current status and challenges for dental posterior restorative composites: clinical, chemistry, and physical behavior considerations. *Dent Mater* 2005;21:3–6. [PubMed: 15680996]
3. Mjör IA, Moorhead JE, Dahl JE. Reasons for replacement of restorations in permanent teeth in general dental practice. *International Dent J* 2000;50:361–366.
4. CDC (Center for Disease Control). 2005 Dec. www.cdc.gov/OralHealth/factsheets
5. Jokstad A, Bayne S, Blunck U, Tyas M, Wilson N. Quality of dental restorations. FDI Commission Projects 2-95. *International Dent J* 2001;51:117–158.
6. Benelli EM, Serra MC, Rodrigues AL Jr, Cury JA. In situ anticariogenic potential of glass ionomer cement. *Caries Res* 1993;27:280–284. [PubMed: 8402802]
7. Souto M, Donly KJ. Caries inhibition of glass ionomers. *Am J Dent* 1994;7:122–124. [PubMed: 8054186]
8. Hsu CYS, Donly KJ, Drake DR, Wefel JS. Effects of aged fluoride-containing restorative materials on recurrent root caries. *J Dent Res* 1998;77:418–425. [PubMed: 9465175]
9. Tyas MJ, Burrow MF. Clinical evaluation of a resin-modified glass ionomer adhesive system - results at 5 years. *Operative Dent* 2002;27:438–441.
10. Kielbassa AM, Schulte-Monting J, García-Godoy F, Meyer-Lueckel H. Initial in situ secondary caries formation: Effect of various fluoride-containing restorative materials. *Oper Dent* 2003;28:765–772. [PubMed: 14653292]
11. Weigand A, Buchalla W, Attin T. Review on fluoride-releasing restorative materials – fluoride release and uptake characteristics, antibacterial activity and influence on caries formation. *Dent Mater* 2007;23:343–362. [PubMed: 16616773]
12. Mathis RS, Ferracane JL. Properties of a glass-ionomer/resin-composite hybrid material. *Dent Mater* 1989;5:355–358. [PubMed: 2638281]
13. Mitra SB, Kedrowski BL. Long-term mechanical properties of glass ionomers. *Dent Mater* 1994;10:78–82. [PubMed: 7758852]
14. Glasspoole EA, Erickson RL, Davidson CL. A fluoride-releasing composite for dental applications. *Dent Mater* 2001;17:127–133. [PubMed: 11163382]

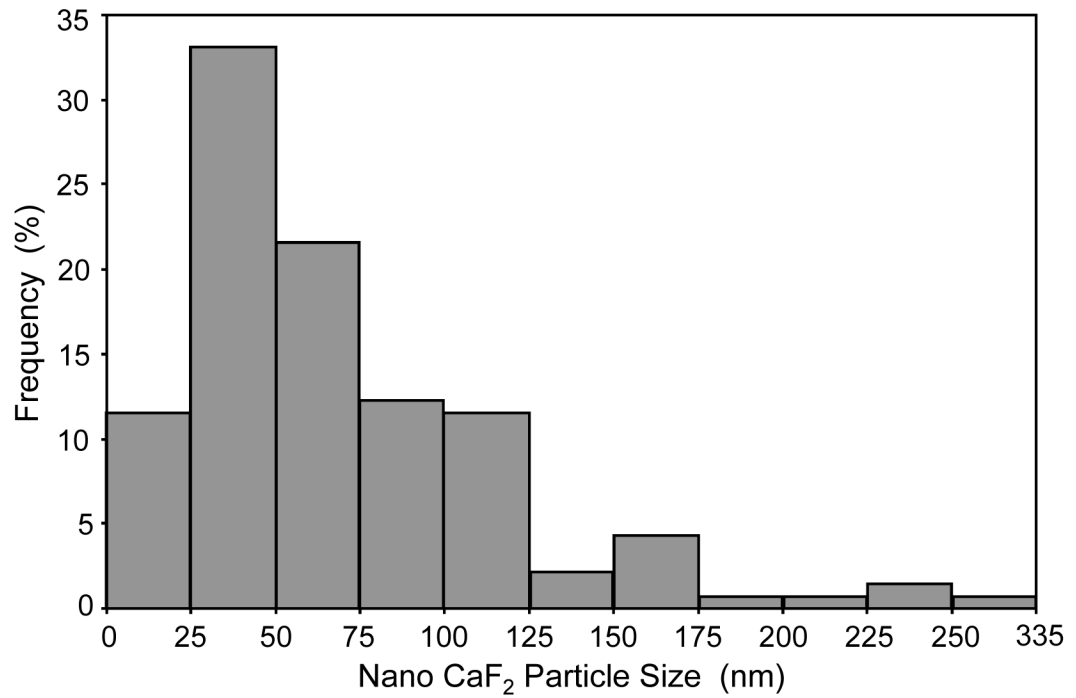
15. Asmussen E, Peutzfeldt A. Long-term fluoride release from a glass ionomer cement, a compomer, and from experimental resin composites. *Acta Odontol Scand* 2002;60:93–97. [PubMed: 12020121]
16. Itota T, Carrick TE, Yoshiyama M, McCabe JF. Fluoride release and recharge in giomer, compomer and resin composite. *Dent Mater* 2004;20:789–795. [PubMed: 15451233]
17. Anusavice KJ, Zhang NZ, Shen C. Effect of CaF₂ content on rate of fluoride release from filled resins. *J Dent Res* 2005;84:440–444. [PubMed: 15840780]
18. Diaz-Arnold AM, Holmes DC, Wistrom DW, Swift EJ Jr. Short-term fluoride release/uptake of glass ionomer restoratives. *Dent Mater* 1995;11:96–101. [PubMed: 8621041]
19. Wilson, AD.; McLean, JW. *Glass-ionomer cement*. Chicago: Quintessence Pub Co; 1988.
20. Sidhu SK, Sherriff M, Watson TF. The effects of maturity and dehydration shrinkage on resin-modified glass ionomer restorations. *J Dent Res* 1997;76:1495–1501. [PubMed: 9240386]
21. Ellakuria J, Triana R, Minguez N, Soler I, Ibaseta G, García-Godoy F. Effect of one-year water storage on the surface microhardness of resin-modified versus conventional glass-ionomer cements. *Dent Mater* 2003;19:286–290. [PubMed: 12686292]
22. Ten Cate JM. Review on fluoride, with special emphasis on calcium fluoride mechanisms in caries prevention. *Eur J Oral Sci* 1997;105:461–465. [PubMed: 9395110]
23. Xu HHK, Eichmiller FC, Antonucci JM, Schumacher GE, Ives LK. Dental resin composites containing whiskers and precured glass ionomer particles. *Dent Mater* 2000;16:356–363. [PubMed: 10915897]
24. Xu HHK, Eichmiller FC, Antonucci JM, Flaim GM. Single-crystalline ceramic whisker-reinforced carboxylic acid-resin composites with fluoride release. *Oper Dent* 2000;25:90–97. [PubMed: 11203805]
25. Carey CM, Spencer M, Gove RJ, Eichmiller FC. Fluoride release from a resin-modified glass ionomer in a continuous-flow system: Effect of pH. *J Dent Res* 2003;82:829–832. [PubMed: 14514765]
26. Xu X, Burgess JO. Compressive strength, fluoride release and recharge of fluoride-releasing materials. *Biomaterials* 2003;24:2451–2461. [PubMed: 12695072]
27. Tyas MJ. Clinical evaluation of glass-ionomer cement restorations. *J Applied Oral Sci* 2006;14:10–13.
28. Goldberg AJ, Burstone CJ, Hadjinikolaou I, Jancar J. Screening of matrices and fibers for reinforced thermoplastics intended for dental applications. *J Biomed Mater Res* 1994;28:167–173. [PubMed: 8207027]
29. Bayne SC, Thompson JY, Swift EJ Jr, Stamatides P, Wilkerson M. A characterization of first-generation flowable composites. *J Am Dent Assoc* 1998;129:567–577. [PubMed: 9601169]
30. Chan DC, Titus HW, Chung KH, Dixon H, Wellinghoff ST, Rawls HR. Radiopacity of tantalum oxide nanoparticle filled resins. *Dent Mater* 1999;15:219–222. [PubMed: 10551087]
31. Lim BS, Ferracane JL, Sakaguchi RL, Condon JR. Reduction of polymerization contraction stress for dental composites by two-step light-activation. *Dent Mater* 2002;18:436–444. [PubMed: 12098572]
32. Drummond JL, Bapna MS. Static and cyclic loading of fiber-reinforced dental resin. *Dent Mater* 2003;19:226–231. [PubMed: 12628435]
33. Dickens SH, Flaim GM, Takagi S. Mechanical properties and biochemical activity of remineralizing resin-based Ca-PO₄ cements. *Dent Mater* 2003;19:558–566. [PubMed: 12837405]
34. Lu H, Stansbury JW, Bowman CN. Impact of curing protocol on conversion and shrinkage stress. *J Dent Res* 2005;84:822–826. [PubMed: 16109991]
35. Hench LL. *Bioceramics*. *J Am Ceram Soc* 1998;81:1705–1728.
36. Ducheyne P, Qiu Q. Bioactive ceramics: the effect of surface reactivity on bone formation and bone cell function. *Biomaterials* 1999;20:2287–2303. [PubMed: 10614935]
37. Pilliar RM, Filiaggi MJ, Wells JD, Grynbas MD, Kandel RA. Porous calcium polyphosphate scaffolds for bone substitute applications – in vitro characterization. *Biomaterials* 2001;22:963–972. [PubMed: 11311015]
38. Skrtic D, Antonucci JM, Eanes ED. Improved properties of amorphous calcium phosphate fillers in remineralizing resin composites. *Dent Mater* 1996;12:295–301. [PubMed: 9170997]

39. Skrtic D, Antonucci JM, Eanes ED, Eichmiller FC, Schumacher GE. Physiological evaluation of bioactive polymeric composites based on hybrid amorphous calcium phosphates. *J Biomed Mater Res* 2000;53B:381–391. [PubMed: 10898879]
40. Chow LC, Sun L, Hockey B. Properties of nanostructured hydroxyapatite prepared by a spray drying technique. *J Res NIST* 2004;109:543–551.
41. Xu, HHK.; Sun, L.; Takagi, S.; Chow, LC. Dental releasing materials. U. S. Patent. Application No. 11/138,182. 2005 May 26. filed
42. Xu HHK, Sun L, Weir MD, Antonucci JM, Takagi S, Chow LC, Peltz M. Nano DCPA-whisker composites with high strength and Ca and PO₄ release. *J Dent Res* 2006;85:722–727. [PubMed: 16861289]
43. Xu HHK, Weir MD, Sun L, Takagi S, Chow LC. Effect of calcium phosphate nanoparticles on Ca-PO₄ composites. *J Dent Res* 2007;86:378–383. [PubMed: 17384036]
44. Xu HHK, Weir MD, Sun L. Dental nanocomposites with Ca-PO₄ release: Effects of reinforcement, dicalcium phosphate particle size and silanization. *Dental Materials* 2007;23:1482–1491. [PubMed: 17339048]
45. Sun L, Chow LC. Preparation and properties of nano-sized calcium fluoride for dental applications. *Dent Mater* 2008;24:111–116. [PubMed: 17481724]
46. Xu HHK, Eichmiller FC, Smith DT, Schumacher GE, Giuseppetti AA, Antonucci JM. Effect of thermal cycling on whisker-reinforced dental resin composites. *J Mater Sci: Mater in Med* 2002;13:875–883. [PubMed: 15348553]
47. Xu HHK. Long-term water aging of whisker-reinforced polymer-matrix composites. *J Dent Res* 2003;82:48–52. [PubMed: 12508045]
48. Xu HHK, Quinn JB, Giuseppetti AA. Wear and mechanical properties of nano-silica-fused whisker composites. *J Dent Res* 2004;83:930–935. [PubMed: 15557400]
49. Dickens SH, Flaim GM, Floyd CJE. Effect of resin composition on mechanical and physical properties of calcium phosphate filled bonding systems. *Polymer Preprints* 2004;45:329–330.



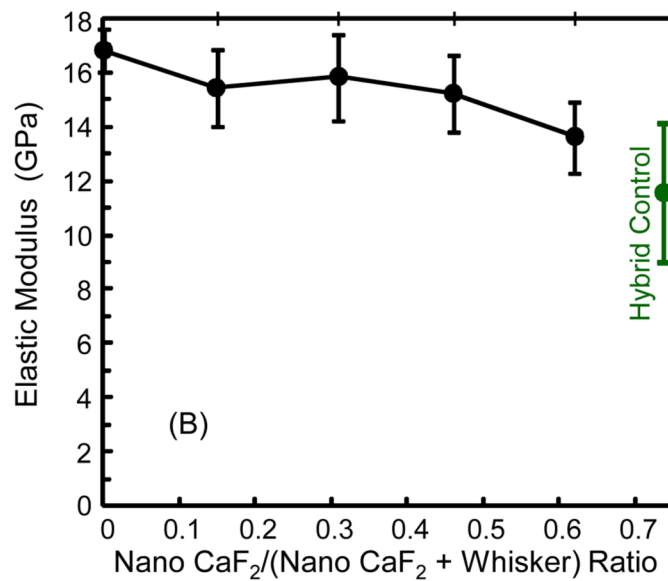
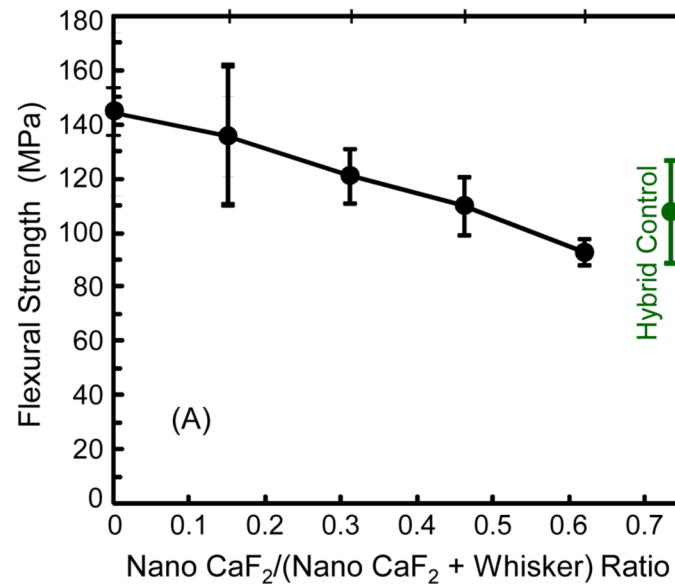
[1].

(A) TEM micrograph of CaF_2 nanoparticles. (B) Higher magnification shows that the particles had numerous spherical protuberances on the surfaces, suggesting that they were formed during the spray drying process through the fusion of much smaller particles. (C) XRD patterns show that the nanoparticles were CaF_2 , albeit with a relatively lower crystallinity than the known pattern of traditional CaF_2 macroparticles.

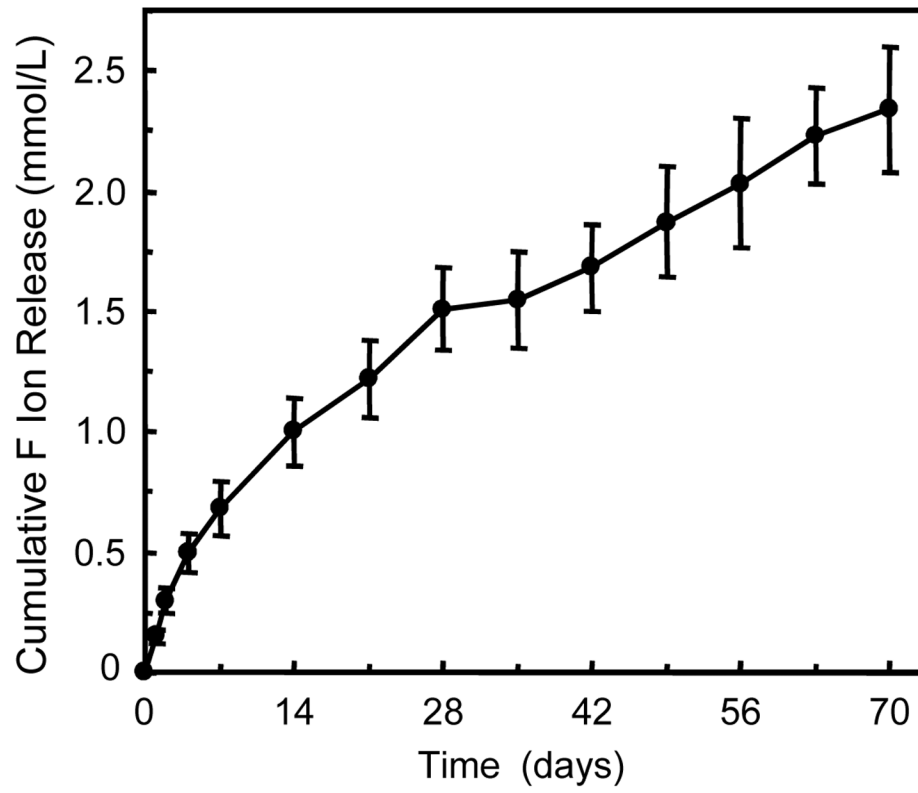


[2]. Histogram of CaF₂ nanoparticle size distribution, obtained via measuring the sizes of 200 particles on TEM pictures. The particle size ranged from 15 nm to 335 nm, with a median (50th percentile) of 56 nm. BET surface area measurement yielded a specific surface area of 35.5 m²/g, and a calculated CaF₂ particle diameter of 53 nm.

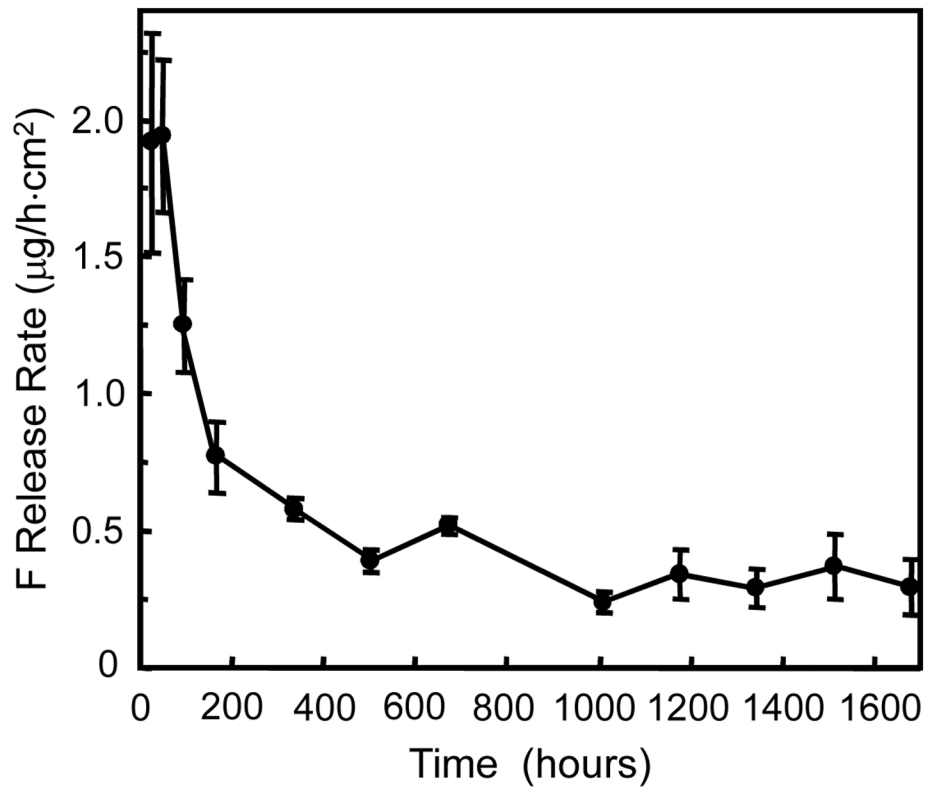
NCF: 0%	10%	20%	30%	40%
WHI: 65%	55%	35%	35%	25%



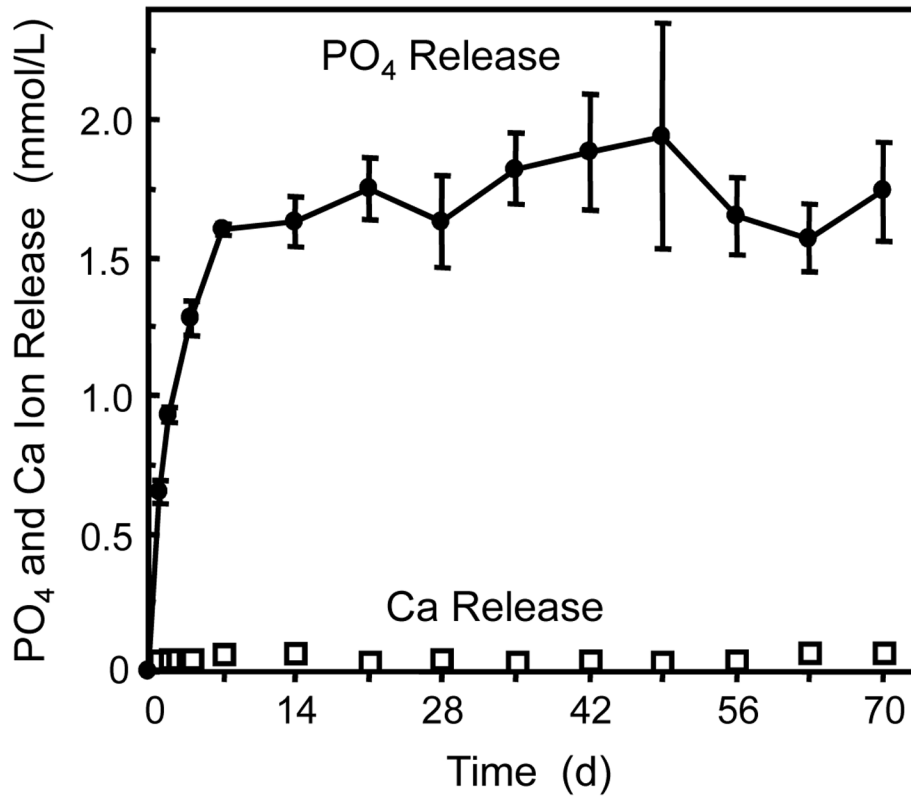
[3]. (A) Flexural strength, and (B) elastic modulus, of dental resin composite containing CaF₂ nanoparticles. At the top, NCF denotes nanoparticles of CaF₂, and WHI denotes whiskers. The x-axis denotes the corresponding CaF₂/(CaF₂ + whisker) mass ratio, where “0” means all whiskers and no CaF₂. Each value is the mean of six measurements with the error bar showing one standard deviation (mean ± sd; n = 6).



[4]. Cumulative fluoride ion (F) release from the nanocomposite containing 25% whiskers, 20% CaF₂ and 20% DCPA nanofiller mass fractions. Each value is mean \pm sd; n = 3.



[5]. Rate of fluoride release per hour per specimen surface area ($\mu\text{g}/\text{h}\cdot\text{cm}^2$) from nanocomposite containing mass fractions of 25% whiskers, 20% CaF_2 and 20% DCPA. Each value is mean \pm sd; $n = 3$. The initial release rate was nearly $2 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$. It decreased to $0.50 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ after 500 hours, and $0.29 \mu\text{g}/(\text{h}\cdot\text{cm}^2)$ after 1680 hours (10 weeks).



[6]. Ca and PO₄ ion release from the nanocomposite containing 25% whiskers, 20% CaF₂ and 20% DCPA nanoparticles. Each value is mean ± sd; n = 3

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%

Table 2F, PO₄ and Ca ion release and strength of several restorative materials*

	F ion release rate (long-term) ($\mu\text{g}/\text{h}\cdot\text{cm}^2$)	PO₄ ion release (mmol/L)	Ca ion release (mmol/L)	Flexural strength (MPa)
Nanocomposite with 20% CaF ₂ , 20% DCPA, and 25% whiskers	0.29 ± 0.10 (after 70 days)	1.74 ± 0.19	0.03 ± 0.01	100 ± 7
TPH hybrid composite	0	0	0	108 ± 19
Ketac-Fil [14]	0.1 (50 d)			54 ± 6 [24]
Vitremer [14]	0.04 (50 d)			60 ± 6 [24]
Resin filled with 23% traditional CaF ₂ particles [17]	0.05 (70 d)			Not reported

* For Ketac-Fil and Vitremer, the sustained (or long-term) F release rate was calculated from Table 4 in Ref. 14. For the resin filled with 23% of a commercial CaF₂ powder, the F release rate was estimated from Fig. 1B in Ref. 17. When the composite contained 20% CaF₂ nanopowder and 45% whiskers, its flexural strength was increased to 121 ± 10 MPa.