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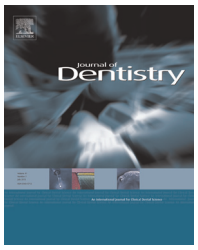

Development of novel self-healing and antibacterial dental composite containing calcium phosphate nanoparticles

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ABSTRACT

Objectives: Fracture and secondary caries are the primary reasons for dental restoration failure. The objective of this study was to develop a self-healing composite to heal cracks, while containing dimethylaminohexadecyl methacrylate (DMAHDM) for antibacterial function and nanoparticles of amorphous calcium phosphate (NACP) for remineralization.

Methods: Microcapsules were synthesized with poly(urea-formaldehyde) (PUF) shells containing triethylene glycol dimethacrylate (TEGDMA) and *N,N*-dihydroxyethyl-*p*-toluidine (DHEPT) as healing liquid. Composite contained 20 mass% of NACP and 35% glass fillers. In addition, composite contained 0%, 2.5%, 5%, 7.5%, or 10% of microcapsules. A single edge V-notched beam method measured fracture toughness (K_{IC}) and self-healing efficiency. A dental plaque microcosm biofilm model was used to test the antibacterial properties.

Results: Incorporation of microcapsules up to 7.5% into the composite did not adversely affect the mechanical properties ($p > 0.1$). Successful self-healing was achieved, with K_{IC} recovery of 65–81% (mean ± sd; $n = 6$) to regain the load-bearing capability after composite fracture. The self-healing DMAHDM-NACP composite displayed a strong antibacterial potency, inhibiting biofilm viability and lactic acid production, and reducing colony-forming units by 3–4 orders of magnitude, compared to control composite without DMAHDM.

Conclusions: A dental composite was developed with triple benefits of self-healing after fracture, antibacterial activity, and remineralization capability for the first time.

Clinical significance: The self-healing, antibacterial and remineralizing composite may be promising for tooth cavity restorations to combat bulk fracture and secondary caries. The method of using triple agents (self-healing microcapsules, DMAHDM, and NACP) may have wide applicability to other dental composites, adhesives, sealants and cements.

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1. Introduction

Q3 Dental composites generally consist of a resin matrix with inorganic filler particles for reinforcement.[1] Composites are widely used in dental practice as filling materials due to their aesthetics and direct-filling capability.[2–4] Extensive efforts have been made to significantly improve the composite properties.[5–8] Nonetheless, composite restorations are still challenged by two main problems: bulk fracture and secondary caries.[9] Studies suggested that fracture was a frequent reason for composite failure, while secondary caries was a common reason for failure after five years of clinical service.[10] Replacing the failed restorations accounts for 50–70% of all restorations performed,[11] hence replacement dentistry represents a significant financial burden.[12] Therefore, it would be highly desirable to develop a new composite with self-healing capability to heal cracks in situ while also possessing a caries-inhibiting capability.

Self-healing polymers were developed to recover the load-bearing capabilities after cracking.[13] Self-healing composite with microcapsules containing a healing agent displayed healing efficacy.[14] The microcapsules had an intact shell encapsulating a healing liquid inside.[15] After incorporation of microcapsules into a polymer matrix, a propagating crack in the matrix would rupture the microcapsules, releasing the healing liquid into the crack planes, thus contacting the catalyst in the matrix, which triggers the polymerization of the healing liquid and autonomously heals the crack.[16] In a previous study,[14] dicyclopentadiene (DCPD) was encapsulated in poly(urea-formaldehyde) (PUF) shells. Grubb's catalyst, a transition metal carbine complex, was incorporated into an epoxy matrix. Polymerization was triggered when a crack ruptured the microspheres, releasing DCPD to react with Grubb's catalyst, achieving a good self-healing efficiency.[14]

A self-healing dental composite was developed by incorporating DCPD-containing microcapsules into a resin containing Grubb's catalyst, in which self-healing achieved a recovery of 57% of the original fracture toughness (K_{IC}) of the composite.[17] The incorporation of microcapsules did not significantly affect the virgin mechanical properties of the composite.[18] Another study developed polyurethane (PU) shell-based nanocapsules containing triethylene glycol dimethacrylate (TEGDMA); however, no initiator or catalyst was described and no healing results were reported.[19] Regarding the use of DCPD and Grubb's catalyst in the oral environment, biocompatibility would be a potential concern.[20] Hence for the use of DCPD and Grubb's catalyst system in dental applications, DCPD toxicity,[21] Grubb's catalyst toxicity, availability and high cost[22] remain as challenges. To date, a self-healing dental composite using a biocompatible healing liquid and catalyst with a demonstrated substantial self-healing efficacy remains to be developed.

Besides the fracture issue, secondary caries is another reason for restoration failures. To combat caries, previous studies developed quaternary ammonium methacrylates (QAMs) to inhibit oral biofilms and reduce acid production.[23,24] Furthermore, previous studies incorporated calcium phosphate (CaP) filler particles in composites for remineralization.[25,26] However, there has been no report on the development of a self-healing dental composite that also possesses antibacterial and remineralization capabilities.

In the present study, self-healing dental composite was developed with microcapsules containing a healing liquid of TEGDMA with *N*,*N*-dihydroxyethyl-*p*-toluidine (DHEPT) as the tertiary amine accelerator. In the resin matrix, benzoyl peroxide (BPO) was incorporated as the self-healing initiator. TEGDMA, DHEPT, and BPO have been used in dental practice with a history of biocompatibility. The objective of this study was to develop a self-healing composite with substantial self-healing efficacy, while also possessing antibacterial and remineralizing capabilities. It was hypothesized that: (1) Self-healing microcapsules containing TEGDMA-DHEPT healing liquid could be synthesized and incorporated into an antibacterial and remineralizing composite without compromising the original mechanical properties of the composite; (2) The recovery of fracture toughness of this composite would be directly proportional to the microcapsule filling level in the composite; (3) The new composite would exhibit an excellent self-healing efficacy and strong antibacterial activities against dental plaque microcosm biofilms.

2. Materials and methods

2.1. Synthesis of self-healing microcapsules

Microcapsules were prepared by in situ polymerization of formaldehyde and urea following a previous study.[27] Briefly, DHEPT (Sigma–Aldrich, St. Louis, MO) at 1% (all mass fractions) was added to TEGDMA monomer (Esstech, Essington, PA). At room temperature, 50 mL of distilled water and 13 mL of a 2.5% aqueous solution of ethylene-maleic anhydride (EMA) copolymer (Sigma–Aldrich) were mixed in a 250 mL round-bottom glass flask.[27] The flask was suspended in a water bath on a hotplate (Isotemp, Fisher Scientific, Pittsburg, PA). The EMA solution was used as a surfactant to form an ''oil-in-water'' emulsion (''oil'' being the TEGDMA-DHEPT). Under agitation by a magnetic stir bar (diameter = 7.8 mm, length = 50 mm, Fisher Scientific) at 300 rpm, the shell-forming material urea (1.25 g), ammonium chloride (0.125 g) and resorcinol (0.125 g) (Sigma–Aldrich) were added into the solution. Resorcinol was added in the reaction of shell formation to enhance the rigidity of the shell.[28] The pH was adjusted to 3.5 via drop-wise addition of 1 M sodium hydroxide solution. Then, the agitation rate was increased to 400 rpm, and 30 mL of the TEGDMA-DHEPT liquid was added into the flask. A stabilized emulsion of fine TEGDMA-DHEPT droplets was formed after 10 min of agitation. Then, 3.15 g of a 37% aqueous solution of formaldehyde (Sigma–Aldrich) was added, and the flask was sealed with aluminium foil to prevent evaporation. The temperature of the water bath was raised to 55 °C and the shell material was isothermally polymerized for 4 h under continuous agitation.[28] In this process, ammonium chloride catalyzed the reaction of urea with formaldehyde to form PUF at the oil–water interface to develop the shell.[28] The microcapsules thus obtained were rinsed with water and acetone repeatedly, vacuum-filtered, and air-dried for 24 h in a hood. The microcapsules were examined by optical microscope (TE2000-S, Nikon, Japan) and their sizes were measured with

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