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Development of a multifunctional adhesive system for prevention of root caries and secondary caries

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ABSTRACT

Objectives. The objectives of this study were to: (1) develop a novel adhesive for prevention of tooth root caries and secondary caries by possessing a combination of protein-repellent, antibacterial, and remineralization capabilities for the first time; and (2) investigate the effects of 2-methacryloyloxyethyl phosphorylcholine (MPC), dimethylaminohexadecyl methacrylate (DMAHDM), and nanoparticles of amorphous calcium phosphate (NACP) on dentin bond strength, protein-repellent properties, and dental plaque microcosm biofilm response.

Methods. MPC, DMAHDM and NACP were added into Scotchbond Multi-Purpose primer and adhesive. Dentin shear bond strengths were measured. Adhesive coating thickness, surface texture and dentin–adhesive interfacial structure were examined. Protein adsorption onto adhesive resin surface was determined by the micro bicinchoninic acid method. A human saliva microcosm biofilm model was used to investigate biofilm metabolic activity, colony-forming unit (CFU) counts, and lactic acid production.

Results. The resin with 7.5% MPC + 5% DMAHDM + 30% NACP did not adversely affect dentin shear bond strength ($p > 0.1$). The resin with 7.5% MPC + 5% DMAHDM + 30% NACP produced a coating on root dentin with a thickness of approximately 70 μm and completely sealed all the dentinal tubules. The resin with 7.5% MPC + 5% DMAHDM + 30% NACP had 95% reduction in protein adsorption, compared to SBMP control ($p < 0.05$). The resin with 7.5% MPC + 5% DMAHDM + 30% NACP was strongly antibacterial, with biofilm CFU being four orders of magnitude lower than that of SBMP control.

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Significance The novel multifunctional adhesive with strong protein-repellent, antibacterial and remineralization properties is promising to coat tooth roots to prevent root caries and secondary caries. The combined use of MPC, DMAHDM and NACP may have wide applicability to bonding agents, cements, sealants and composites to inhibit caries.

1. Introduction

The prevalence and severity of tooth root caries increases with aging, and this is a growing public health issue due to the rapid increase in the elderly population coupled with substantial increases in tooth retention in seniors [1]. Gingival recession due to aging, periodontal disease or traumatic tooth-brushing habits can increase the susceptibility to root caries [1]. In addition, low salivary flow in seniors and patients with dry mouths further contribute to biofilm and plaque buildup and the occurrence of root caries [2]. Indeed, root caries occurrence in the United States was reported to increase rapidly with aging, from 7% among young people, to 56% in seniors (≥75 years of age) [3]. In addition, secondary caries has been suggested in previous studies as a primary reason for dental restoration failures [4,5]. The replacement of the failed restorations accounts for 50–70% of all restorations performed [6]. The annual cost for tooth cavity restorations was approximately $46 billion in 2005 in the United States [7]. Hence, dental caries is a significant burden, and it is highly desirable to develop effective methods to prevent root caries and secondary caries.

Dental plaque formation is a prerequisite for the occurrence of root caries and secondary caries [8,9]. Dental plaque are aggregates of microorganisms, which are formed due to the attachment of bacteria to tooth surface and to each other in the oral environment [9]. Once the tooth root surface or resin restoration surface are exposed in the oral cavity, they are coated with a salivary pellicle that comprises a layer of selectively adsorbed salivary proteins that mediate the binding of microorganisms [8,9]. The adherence of bacteria to the salivary pellicle is an initial step in biofilm formation [8,9]. Therefore, inhibiting protein adsorption and bacterial adherence is a promising approach for suppressing plaque formation and preventing root caries and secondary caries.

The prevention of root caries have been attempted by the daily usage of fluoride solutions or toothpastes [10], professional application of fluoride gel/varnishes [11], or the use of chlorhexidine solutions/varnishes [12]. However, these treatments are temporary and success depends on the compliance of patients [13]. Efficient and simple single-visit methods to prevent root caries are currently not available [14]. Recently, coating of tooth root surface with adhesives was investigated as a preventive treatment against root caries, as it provides a strong physical barrier with the formation of a hybridized layer [14–17]. Besides coating tooth roots, adhesives are also used to bond composite in tooth cavities. However, while composites are the principal material for cavity restorations due to their excellent aesthetics and direct-filling capability [4,5,18–20], resins *in vivo* tend to accumulate more plaque than other restorative materials [21]. Furthermore, microgaps can be observed at the tooth-restoration interfaces [19,22]. Microleakage can occur and biofilms at the restoration margins can produce acids and cause secondary caries [4,5]. While adhesive compositions and bonding procedures have been improved [23,24], further improvements could be achieved by developing a protein-repellent and antibacterial bonding agent to combat biofilms at the tooth-restoration margins. To date, a dentin adhesive that possesses a combination of protein-repellent and antibacterial capabilities has not been reported.

Quaternary ammonium methacrylates (QAMs) were incorporated into adhesives [25–28]. Antibacterial adhesives reduced biofilm viability and acid production. The antibacterial activity increased when the alkyl chain length (CL) was increased from 5 to 16 [29]. Dentin adhesive containing a new monomer dimethylaminohexadecyl methacrylate (DMAHDM) with CL of 16 had the strongest antibacterial activity [30].

2-Methacryloyloxyethyl phosphorylcholine (MPC), a methacrylate with a phospholipid polar group in the side chain, is one of the most common biocompatible and hydrophilic biomedical polymers [31,32]. It has been shown that hydrophilic material surfaces are more resistant to protein adsorption than hydrophobic surfaces [33]. The MPC polymer coating rendered the surfaces extremely hydrophilic and prevented the adsorption of proteins [31,32]. Recently, MPC was incorporated into dentin bonding agents and composites, achieving a strong protein-repellent capability [34,35]. It would be highly desirable to combine MPC with DMAHDM to develop a novel dental adhesive with a combination of protein-repellent and antibacterial capabilities, in order to repel protein and inhibit bacteria attachment, thereby preventing root caries and secondary caries.

Exposure of root dentin after gingival recession is common among seniors because the thin cementum can be lost due to tooth-brushing or biofilm acids [36]. Dentin differs from enamel due to the smaller mineral crystallites with a higher carbonate content [37]. Moreover, dentin mineral is more soluble than enamel mineral [37]. Demineralization on tooth root is approximately twice as rapid as that of enamel [38]. Therefore, it is beneficial for the adhesive that is used to coat tooth roots to also possess remineralization capability. Calcium phosphate (CaP) composites released supersaturating levels of calcium (Ca) and phosphate (P) ions and remineralized tooth lesions *in vitro* [39]. Recently, nanoparticles of amorphous calcium phosphate (NACP) with a size of 116 nm were synthesized via a spray-drying technique and filled into composites and adhesives [40–44]. These nanocomposites achieved Ca and P ion release similar to those of traditional CaP composites, while possessing much better mechanical properties [40,41].