Journal of Dentistry 45 (2016) 32–38

Contents lists available at ScienceDirect

Journal of Dentistry

journal homepage: www.intl.elsevierhealth.com/journals/jden

Ion release, fluoride charge of and adhesion of an orthodontic cement paste containing microcapsules

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ARTICLE INFO

Article history:
Received 5 October 2015
Received in revised form 24 November 2015
Accepted 30 November 2015

Keywords:
Bioactive
Fluoride
Calcium
Phosphate
Recharge
Orthodontic cement
Composites
Bioactive
Ion release

ABSTRACT

Objectives: Dental materials capable of releasing calcium, phosphate and fluoride are of great interest for remineralization. Microencapsulated aqueous solutions of these ions in orthodontic cement demonstrate slow, sustained release by passive diffusion through a permeable membrane without the need for dissolution or etching of fillers. The potential to charge a dental material formulated with microencapsulated water with fluoride by toothbrushing with over the counter toothpaste and the effect of microcapsules on cement adhesion to enamel was determined.
Methods: Orthodontic cements that contained microcapsules with water and controls without microcapsules were brushed with over-the-counter toothpaste and fluoride release was measured. Adhesion measurements were performed loading orthodontic brackets to failure. Cements that contained microencapsulated solutions of 5.0 M $Ca(NO_3)_2$, 0.8 M NaF, 6.0 M K_2HPO_4 or a mixture of all three were prepared. Ion release profiles were measured as a function of time.
Results: A greater fluoride charge and re-release from toothbrushing was demonstrated compared to a control with no microcapsules. Adhesion of an orthodontic cement that contained microencapsulated remineralizing agents was 8.5 ± 2.5 MPa compared to the control without microcapsules which was of 8.3 ± 1.7 MPa. Sustained release of fluoride, calcium and phosphate ions from cement formulated with microencapsulated remineralizing agents was demonstrated.
Conclusions: Orthodontic cements with microcapsules show a release of bioavailable fluoride, calcium, and phosphate ions near the tooth surface while having the ability to charge with fluoride and not effect the adhesion of the material to enamel. Incorporation of microcapsules in dental materials is promising for promoting remineralization.

1. Introduction

Orthodontic cements and other organic composites are commonly used in dental restoratives due to the ease of use and aesthetic quality the patient desires. These materials function to help straighten teeth and restore proper tooth function upon enamel loss. However, secondary caries continue to form. Undesired side effects of orthodontic cements are white spot lesions, a form of demineralization [1–3]. If demineralization of the tooth enamel continues around the orthodontic bracket then an opaque square shaped lesion develops called a white spot lesion. Reviews show that exposure to fluoride ions on the demineralized tooth structure will assist in the treatment of white spot lesions after an orthodontic procedure [4–6].

A recent review has extensively covered approaches to enamel remineralization [7]. Fluoride ions, in the presence of hydroxyapatite may promote the formation of fluorapatite ($Ca_{10}(PO_4)_6F_2$) [8–10]. Fluorapatite has a lower solubility product (K_{SP}) than hydroxyapatite and the critical pH for dissolution of the mineral is lower [11]. As a result, fluoride has been introduced into drinking water, mouth rinses and toothpastes. Brushing with fluoridated toothpaste may help with the remineralization process by removing bacteria from the immediate surface of the tooth and exposing the demineralized enamel to fluoride ions, possibly forming fluorapatite. A review has been published showing other dental materials besides toothpaste that release fluoride ions to promote the formation of fluorapatite [12]. Most materials contain

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http://dx.doi.org/10.1016/j.jdent.2015.11.009
0300-5712/

an initial burst of fluoride ions when the material is first placed and a slow release over the course of the following day [13].

After fluoride ions are present in the oral environment the limiting factor in remineralization may be the concentration of calcium and phosphate ions [14,15]. Several approaches have attempted to address the release of calcium and phosphate ions in the oral environment as well as fluoride ions. Some studies have reported that increased levels of calcium in the plaque increase the ability of the plaque to retain fluoride, thereby extending the potential time of fluoride availability in the oral environment [16]. Several other approaches to promote remineralization of enamel are bioactive glass systems, unstabilized and stabilized amorphous calcium phosphate systems, and calcium orthophosphates [17–29]. In many cases the source of a bioactivity is from some form of bioactive glass (BAG) [30,31]. One example is a material that utilizes casein phosphopeptide amorphous calcium phosphate (CPP-ACP), which releases calcium and phosphate ions near the enamel surface to promote mineral formation [32,33]. CPP-ACP uses a milk derived protein that can stabilize calcium, phosphate and fluoride ions into a more available amorphous complex while binding adjacent to the tooth to allow the ions to reach subsurface enamel lesions [34]. CPP-ACP transform from an amorphous phase to a crystalline phase of hydroxyapatite. Recently CPP-ACPs have been used with zirconia for a slower release of calcium and phosphate ions [35].

Despite the use of fluoride, calcium and phosphate ions, demineralization remains a challenge in oral healthcare. Regardless of the deficiencies of the quantification of fluoride uptake into the enamel, reviews of materials such as glass ionomers and resin based materials show the ability to release fluoride ions initially and recharge to release fluoride ions again to continue the promotion of fluorapatite formation on the enamel [31]. All of these materials, when incorporated directly near the tooth improve remineralization in some form [36–38]. The ion-releasing agents require the dissolution or etching of the mineral fillers in order to release remineralizing ions. As a result, it would be ideal to innovate a filler material that can release fluoride, calcium and phosphate ions in their bioavailable forms adjacent to the enamel without dissolution of the dental material for remineralization. The ability to recharge ion releasing dental materials with fluoride is also of great interest [39].

A novel approach to promote remineralization through bioactive fillers has been reported. This approach incorporated microcapsules that could be loaded into any type of dental material and are capable of releasing fluoride, calcium and phosphate in a bioavailable form. Davidson, et al. showed microcapsules composed out of different polymers were able to release bioavailable forms of calcium, phosphate, and fluoride ions through a semipermeable membrane. The membranes used showed a difference of permeability and the potential to control the rate of ion release [40]. Falbo, et al. extended this work by incorporating these microcapsules into rosin varnishes and resin glazes [41]. The study showed some of the key variables of controlling ion release rates over extended periods of time.

In this study, several orthodontic cement paste formulations were prepared with and without microcapsules. Initially, the ability of a non-fluoridated composite orthodontic cement paste formulated with microcapsules that had only water contained within the shell was studied. This was done to determine if the microcapsules promoted fluoride charge in the oral environment from a simple, over the counter toothpaste. This sample was compared to a control cement with no microcapsules formulated within. This was accomplished by cycling forty brushing cycles with toothpaste on both of these samples and then checked for the subsequent rerelease of fluoride ions from these cements over time. From there, the release of fluoride, calcium and phosphate ions from orthodontic cement pastes formulated with microcapsules containing these remineralizing ions was established. Finally, incorporating microcapsules into orthodontic cement paste and how the adhesion was affected of the orthodontic bracket to the tooth was examined. This study demonstrates the potential for an orthodontic cement that can release calcium, phosphate and fluoride, be charged with greater fluoride levels by simple toothbrushing while maintaining the working standard for adhesion to the enamel surface.

2. Materials and methods

2.1. Prepolymer synthesis

Microcapsules were prepared with a polyurethane shell via a prepolymer synthesis in an inert environment at 70 °C. [40] A cyclohexanone solvent was used to react ethylene glycol (Fisher, New Jersey) with isophorone diisocyanate (Sigma–Aldrich, Steinheim) and left overnight. The prepolymer was then dried by vacuum.

2.2. Microcapsule synthesis

The prepolymer, after being dried was added to an emulsifying agent and methyl benzoate (Acros Organics, New Jersey). Aqueous salt solutions of 6.0 M potassium phosphate dibasic (Fisher Scientific, New Jersey), 5.0 M calcium nitrate tetrahydrate (Alfa Aesar, Massachusetts) and 0.8 M sodium fluoride (MP Biomedicals, Ohio) were prepared. These were introduced to the prepolymer during synthesis after having prepared a reverse emulsion [40].

When the prepolymer oil solution is agitated and the aqueous salt solution is introduced a reverse emulsion forms. The oil solution was agitated in a custom made reactor at 70 °C. while the aqueous salt solution was added slowly. The reaction was then quenched using ethylene glycol to drive the reaction to the desired product. These microcapsules were centrifuged in a Fisher Centrific 288 centrifuge using a diluent, rinsed and prepared for formulation into the orthodontic cements.

2.3. Orthodontic cement formulations

This study included different formulations of orthodontic cements. An orthodontic cement formulation was formulated with microcapsules containing 7 w/w% nanopure water. Nanopure water was generated by a Thermo Scientific Barnstead filtration system. There was only water within the microcapsules of this formulation to unambiguously determine the source of fluoride for use in the charging experiment. Three custom manufactured formulations were obtained from BJM Laboratories (Or Yehuda). These formulations were acrylate-based composites that contained standard boroaluminosilicate glass fillers. The first of these were formulated to incorporate 5 w/w% of microcapsules that contained 0.8 M sodium fluoride aqueous salt solution. The second formulation consisted of microcapsules containing a mixture of 2 w/w% 0.8 M sodium fluoride, 2 w/w% 5.0 M calcium nitrate tetrahydrate and 1 w/w% 6.0 M potassium phosphate dibasic aqueous salt solutions (2/2/1), all the ions needed for remineralization. The third formulation was prepared as a control in which no microcapsules were added.

Two more formulations were prepared in lab for ion release studies by adding microcapsules into the formulation containing no microcapsules to complement the BJM manufactured formulations. The first formulation included microcapsules containing 3 w/w% 6.0 M potassium phosphate dibasic aqueous salt solution. The second formulation included microcapsules containing 3 w/w % 5.0 M calcium nitrate tetrahydrate aqueous salt solution.