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Development of high-viscosity, two-paste bioactive bone cements

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Abstract

Self-curing two-paste bone cements have been developed using methacrylate monomers with a view to formulate cements with low polymerization exotherm, low shrinkage, better mechanical properties, and improved adhesion to bone and implant surfaces. The monomers include bis-phenol A glycidyl dimethacrylate (bis-GMA), urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEGDMA) as a viscosity modifier. Two-paste systems were formulated containing 60% by weight of a bioactive ceramic, hydroxyapatite. A methacroyloxy silane (A174) was used as a coupling agent due to its higher water stability in comparison to other aminosilanes to silanate the hydroxyapatite particles prior to composite formulation. A comparison of the FT-infrared spectrum of hydroxyapatite and silanated hydroxyapatite showed the presence of the carbonyl groups ($\sim 1720\,\mathrm{cm}^{-1}$), –C = C–($\sim 1630\,\mathrm{cm}^{-1}$) and Si–O– ($1300$–$1250\,\mathrm{cm}^{-1}$) which indicated the availability of silane groups on the filler surface. Two methods of mixing were effected to form the bone cement: firstly by mixing in an open bowl and secondly by extruding the two pastes by an auto-mixing tip using a gun to dispense the pastes. Both types of cements yielded low polymerization exotherms with good mechanical properties; however, the lower viscosity of UDMA allowed better extrusion and handling properties. A biologically active apatite layer formed on the bone cement surface within a short period after its immersion in simulated body fluid, demonstrating in vitro bioactivity of the composite. This preliminary data thus suggests that UDMA is a viable alternative to bis-GMA as a polymerizable matrix in the formation of bone cements.

Keywords: Orthopaedic bone cements; Hydroxypatite; Composites; Mechanical properties

1. Introduction

Poly(methylmethacrylate) (PMMA) bone cement is extensively used in orthopaedic surgery as an anchoring agent in hip and knee replacements, to repair skull defects and spinal surgery. The main application of PMMA bone cement is as a grouting agent in cemented joint replacement surgery to help in the transfer of service loads and immediate immobilization of the prosthesis. Commercial acrylic bone cements consist of prepolymerized PMMA beads and polymerizable monomer, methyl methacrylate. The cement is known to perform adequately given the range of its properties; however, it is beset with some well-known disadvantages such as its high polymerization exotherm, shrinkage, brittle nature and release of unreacted monomer. The cement is also not adhesive to bone, and particulate debris generated due to wear plays a role in the inflammatory response. PMMA is well tolerated in the body but lacks any adhesion to bone. Although it is known to perform adequately in cemented arthroplasties and other surgical procedures, there has been an effort both by industry and academia to overcome some of the disadvantages associated with PMMA-based bone cements [1–3]. The major improvements that have had an impact clinically are the improved mixing and dispensing techniques; however, the composition has remained virtually unchanged.

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Recently, novel bone cements are being investigated to overcome the disadvantages of conventional PMMA cement, one of which is the lack of adhesion to bone and lowering of polymerization exotherm. Bioactive bone cements, including calcium phosphate cements and polymeric cements with bioactive fillers [4], have been reported as alternatives to acrylic bone cements. Calcium phosphate cements, however, are resorbable and have insufficient load-bearing properties; thus the rationale of the inclusion of a bioactive phase in a polymeric matrix to form a composite is attractive due to its bone bonding ability and combination of properties of the different phases. Polymer composites comprising of bioactive fillers are recently being investigated as viable alternatives to PMMA bone cements [5,6]. Bioactive fillers such as AW glass ceramic, β-TCP and hydroxyapatite have been used to develop bone cements with bis-phenol A glycidyl methacrylate (bis-GMA) as the monomer, which have been reported to exhibit bone bonding properties [5,6]. High molecular weight PMMA polymers reinforced with bioactive beads of $MgO–CaO–SiO_2–P_2O_5–CaF_2$ have also been recently reported to enhance the properties and osteoconductivity of the PMMA cement [7,8]. Bis-GMA has been used as a polymerizable component in bioactive bone cements due to its known use in dentistry, its chemical structure and low polymerization exotherm. These composites are also superior in strength and additionally have the ability to bond to living bone. However, bis-GMA has been lately implicated with oestrogen-mimicking activity and reports suggest that bis-phenol A, a precursor of bis-GMA, and bis-phenol A dimethacrylate are both oestrogenic, which are able to leach from the sealants applied to the teeth into saliva [9,10].

In this study we report bone cements with a bioactive component using organic monomers that are large and rigid in structure and are expected to lower the net polymerization shrinkage in comparison to PMMA. The present study reports the development of a two-paste bioactive bone cement containing hydroxyapatite with two different organic monomers, namely bis-GMA and urethane dimethacrylate (UDMA) along with a viscosity modifier triethylene glycol dimethacrylate (TEGDMA). The organic matrix influences the properties of the cement, such as amount of unreacted monomer, fluid uptake and mechanical properties. The feasibility of UDMA as a functional monomer was investigated. Furthermore, two methods of mixing and dispensation were studied, one involving hand mixing of the requisite amount of the two pastes in an open bowl, and in the second case, the pastes were extruded using a cement gun, with an auto-mixing tip to allow mixing of the two pastes as used for elastomeric impression materials with the two pastes being stored in opaque cartridges. The effect of the mixing and dispensing methods on the cement properties is reported. The polymerization exotherms and mechanical properties such as ultimate compressive strength and diametral tensile strengths were measured for each type of cement, and the effect of the two different monomers and mixing methods are reported. The ability of in vitro calcification in simulated body fluids of the composites was studied using scanning electron microscopy methods and energy dispersive X-ray analysis (EDAX).

2. Materials and methods

UDMA, bis-GMA were procured from EssTech, USA, TEGDMA, benzoyl peroxide and N,N-dimethyl -ptoluidine were purchased from Sigma-Aldrich and were used without further purification. Hydroxyapatite (HAp, Plasma Biotal, UK) with an average particle size of 7 μm was silanated using gamma methacroyloxy trimethyl silane using a 70:30 acetone–water solution as described elsewhere [11].

UDMA/TEGDMA–HA composite: Resin composites composed of UDMA (25% by wt), TEGDMA (15% by wt), benzoyl peroxide (1.5% by weight of the total monomer content), N,N-dimethyl *p*-toluidine (tertiary amine; in equimolar ratio to benzoyl peroxide) and HAp particles (60% by wt) were prepared. The resin monomers were mixed with the peroxide or the amine to which the silanated HAp filler was added in small parts to ensure complete wetting of the particulate HAp to yield the two pastes. Similar pastes were prepared using bis-GMA/TEGDMA and cements were made by using both dispensing methods. Self-curing was effected by adding equal amounts of each paste, by simple hand mixing of the two pastes in an open bowl. In a second method referred to as the extrusion method, preweighed pastes (one containing the amine and the other the peroxide) were placed individually in the cartridges (Fig. 3a) and kept closed during storage. The gun (3 M –ESPE) (Fig. 3a) was used to extrude the cement through a mixing tip (Fig. 3c) that allowed the pastes to come into contact due to the geometry of the mixing tip.

Setting time and peak curing temperature: The two pastes, mixed by either method, were poured into a Teflon mould and the time–temperature profile was recorded. The time was recorded at the start of mixing. Setting time was defined as the period midway between the start of mixing and the time when the maximum temperature was reached [12]. A PMMA-based commercial bone cement, CMW1RO, was used as the control group.

Mechanical testing: Compressive and diametral tensile tests were carried out using cylindrical specimens of 4 mm diameter × 6 mm height. The cement pastes were mixed either by hand spatulation or extruded through the auto-mix tip and placed in steel cylindrical moulds to produce specimens for diametral and compressive