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A facile fabrication of porous PMMA as a potential bone substitute

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ABSTRACT

This study is aimed to develop porous poly(methyl methacrylate) (PMMA) as a potential bone substitute via a facile fabrication method. Composites consisting of water-soluble chitosan oligosaccharide (CSO) and PMMA were prepared by combining freeze-drying with radical polymerization. Open porous PMMA with controlled porosities were obtained after the CSO was extracted gradually from the composites. The CSO aqueous solutions with different concentrations were frozen and then freeze-dried to obtain interconnected porous framework. Methyl methacrylate with initiators and a crosslink agent was introduced into the porous framework and polymerized, resulting in two-continuous phase composites. The mechanical properties of the initial composites and porous materials after immersion in PBS for 8 weeks were investigated. Dynamic mechanical analysis was conducted to study the mechanical strength of the composite, compared with bulk PMMA. Porosity and morphology of porous PMMA were studied using the liquid displacement method and scanning electron microscopy, respectively. Thermogravimetric analysis indicated that composite exhibited better thermal stability than bulk PMMA. The composites became porous materials after extracting bioactive CSO component. The mechanical properties of porous materials were closer to those of cancellous bone. The generation of pores using CSO seems to be a promising method to prepare porous PMMA as a potential bone substitute.

1. Introduction

Poly(methyl methacrylate) (PMMA) and its derivatives have been successfully used in orthopedic surgeries such as bone filler or vertebroplasty [1,2]. However, the disadvantages of PMMA as a biomaterial, such as its insufficient adhesion to bone surface [3], monomer toxicity [4] and high exothermic reaction temperature [5], cannot be ignored. Researchers have tried solving these problems by adding hydroxyapatite (HA) powder reinforcement [6], bone particles [7,8] and growth hormones [9]. The bioactivity and adhesion of PMMA-based materials have been improved through these modifications.

Another significant issue of PMMA is the mechanical property. The Young's modulus of commonly used bone substitute materials based on bulk PMMA (2–3 GPa) is much higher than that of cancellous bone (5–800 MPa [10]). An increased fracture risk has been demonstrated for the adjacent vertebral bodies after reinforcement [11,12]. It is desirable to fabricate PMMA with low Young's modulus suitable for bone substitute. Fabricating porous materials with controlled modulus and porosity is a feasible solution. The earliest research on porous bone cements with a lower bulk modulus was conducted by De Wijin, who introduced non-miscible phases [13]. Klawitter et al. fabricated and characterized porous-rooted PMMA with two different porous root structures as dental implants, the large pore size intended to accept bone tissue ingrowth and a fine pore size intended to accept fibrous tissue ingrowth [14]. Nathanson et al. investigated the histologic response to porous PMMA implant materials and none of the implants was rejected or caused chronic inflammation [15]. Van Mullen et al. proposed the incorporation of carboxymethyl cellulose as biodegradable component to acrylic bone cement of formulations to create porous cement after the degradable phase leached during time [16]. Tricalcium phosphate as a powder or as an aqueous dispersion modified PMMA porous bone cement was fabricated by Beruto et al. [17]. Liu et al. investigated four types of porous implant materials and found that porous PMMA was biocompatible but possessed less osteogenic potential than hydroxyapatite [18]. Espigares et al. fabricated partially degradable and bioactive acrylic bone cements based on corn starch/cellulose acetate blends and ceramic fillers hydroxylapatite [19]. Bruens et al. prepared porous PMMA as bone substitute in the craniofacial area by using carboxymethyl cellulose gel [20]. Employing a commonly used porogen leaching technique, Shimko et al. fabricated highly porous PMMA scaffold with controllable elastic modulus and permeability for use in tissue grafting and tissue engineering applications [21]. Boger et al. prepared low modulus PMMA bone cement for osteoporotic bone by mixing

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commercially available PMMA cement and sodium hyaluronate polymer solution [22]. In this research, we fabricated porous PMMA by adding bioactive chitosan oligosaccharide (CSO) as a framework or porogen.

Chitosan, the deacetylated derivative of chitin, composed of β-(1,4)-2-amine-2-deoxy-D-glucopyranose units and small amount of N-acetyl-D-glucosamine residues, has been utilized in biomedical field due to its excellent biocompatibility, biodegradability and antibacterial activity. Chitosan powder or nanoparticles have been incorporated into bone cement aiming to improve its properties [6,23]. However, poor solubility in physiology conditions makes chitosan difficult to use in food and biomedical applications. Recently, researchers have become interested in partially hydrolyzed chitosan and chitosan oligosaccharide (CSO). CSO is readily soluble in water due to its shorter chain lengths and free amino groups in D-glucosamine units. CSO, like chitosan, has positive charges which allow it to bind strongly to negatively charges and had some properties including biological activity, non-toxicity, biodegradability and biocompatibility. Previous work has demonstrated that CSO possesses versatile functional properties such as antitumor activity [24], antimicrobial activity [25] and free radical scavenging activity [26,27]. Recent interest has focused on chitosan oligosaccharides as a bone-inducing substance for use as bone graft material [28]. Li et al. found that low molecular weight chitosan (LMWC) inhibited osteoclast formation and the resorbing activity of osteoclasts, as a result, LMWC prevented decreases in bone density after ovariectomy [29]. Iwata et al. also demonstrated that chitosan oligosaccharides prevented a decrease in cancellous bone mass, which suggested that chitosan oligosaccharides might be useful in preventing bone loss associated with postmenopausal osteoporosis [28].

The purpose of the present study was to develop porous PMMA as a potential bone substitute material derived from CSO/PMMA composites. Chitosan oligosaccharide as a bone-inducing biopolymer was utilized as a framework or porogen. The mechanical properties and thermal stability of composites were characterized. Due to the water-solubility of chitosan oligosaccharide, the CSO component dissolved gradually from the composites and left the PMMA as interconnected porous material with an appropriate compression modulus and strength, which would be an ideal bone substitute.

2. Experimental

2.1. Materials

Chitosan oligosaccharide (molecular weight of 3000 g/mol, about 85% deacetylated) was purchased from Zhejiang Golden-Shell Biochemical Co., Ltd. (Zhejiang, China). Methyl methacrylate (MMA, Tianjin Fuchen Chemical Co.) was purified by vacuum distillation. Triethyleneglycol dimethacrylate (TEGDMA) was kindly supplied by Sartomer Company (Guangzhou, China) and used without further purification. Benzoyl peroxide (BPO) and N,N-bis(2-hydroxyethyl)-p-toluidine (BHET) were obtained from Xilong Chemical Co., Ltd. (Shantou, China) and Fluka Chemical Co., respectively. Benzoyl peroxide was purified by fractional precipitation from a chloroform solution, using methanol as precipitant.

2.2. Preparation of CSO/PMMA composites

The fabrication process of CSO/PMMA composites and porous PMMA is illustrated in Fig. 1. First, the cylinder chitosan oligosaccharide frames were fabricated via a freeze-drying method. Chitosan oligosaccharide solutions with different concentrations were prepared by dissolving CSO in deionized water. The solutions were placed into cylinder molds, maintained at −40 °C for 24 h, and then lyophilized in a freeze-dryer until dried. Secondly, two kinds of methyl methacrylate solution were prepared: one MMA solution containing 0.5 wt.% BPO as an initiator while the other containing 0.5 wt.% BHET as a co-initiator and 5 wt.% TEGDMA as a crosslink agent. Finally, two kinds of MMA solutions were mixed in a 1/1 weight ratio and injected into the dried porous CSO framework quickly. Radical polymerization of MMA and TEGDMA took placed in a porous framework at room temperature. After 48 h, columned CSO/PMMA composites with different weight ratios were obtained. For comparison, bulk PMMA without chitosan oligosaccharide was also prepared at the same condition. CSO could be extracted gradually from the composites through immersion in water, leaving the PMMA component as an interconnected porous material. Table 1 illustrates the sample codes and their compositions.

2.3. Mechanical compression testing

The compression modulus and compression strength of bulk PMMA and CSO/PMMA composites were determined using an Instron 4505 mechanical tester (Instron, High Wycombe, England) with a 10 kN load cell. The specimens were circular discs of 8 mm in diameter and 12 mm in thickness. The crosshead speed of the Instron tester was set at 5 mm/min and the load was applied until a 30% reduction in specimen height was achieved. Five samples were tested for each composition. To analyze the long term mechanical properties of various samples, they were immersed in PBS (pH = 7.4) 8 weeks, and their compression modulus and compression strength were compared with the initial compression modulus and compression strength determined at the beginning of the experiment.

2.4. Dynamic mechanical analysis

The dynamic mechanical thermal analysis of the materials in the form of circular discs (diameter = 8 mm, thickness = 4 mm) was carried out with a dynamic mechanical analyzer (NETZSCH DMA 242C, Germany), operating in the compression mode. The scans were performed on samples maintained under a nitrogen atmosphere at frequency of 1 Hz, temperature range of −50 to 300 °C with 5 °C/min heat rate.

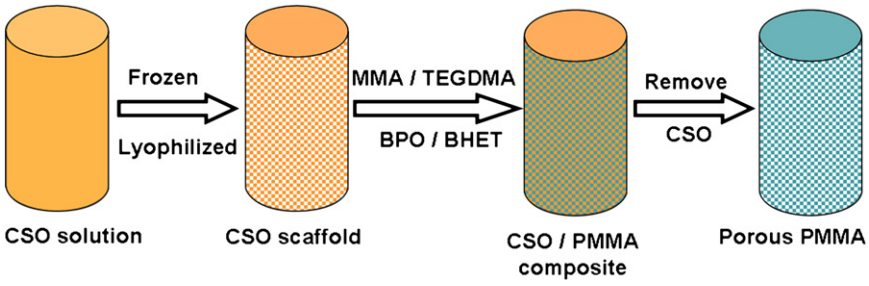

Fig. 1. Schematic illustration for preparation of CSO/PMMA composites.