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Improvement of mechanical properties of macroporous β-tricalcium phosphate bioceramic scaffolds with uniform and interconnected pore structures

Kaili Lin, Lei Chen, Haiyun Qu, Jianxi Lu, Jiang Chang *

State Key Laboratory of High Performance Ceramics and Superfine Microstructure, Shanghai Institute of Ceramics, Chinese Academy of Sciences, 1295 Dingxi Road, Shanghai 200050, PR China

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Abstract

The biocompatible and degradable macroporous bioceramic scaffolds with high mechanical properties and interconnected porous structures play an important role in hard tissue regeneration and bone tissue engineering applications. In this study, the improvement of mechanical properties of macroporous β-tricalcium phosphate [β-$Ca_3(PO_4)_2$, β-TCP] bioceramic scaffolds with uniform macropore size and interconnected pores were fabricated by impregnation of the synthesized β-TCP nano-powder slurry into polymeric frames. The microstructures, mechanical properties and *in vitro* degradation of the fabricated samples were investigated. For a comparison, β-TCP scaffolds were also fabricated from commercial micro-size powders under the same conditions. The resultant scaffolds showed porosities ~65% with uniform macropore size ranging from 400 to 550 μm and interconnected pore size ~100 μm. The compressive strength of the samples fabricated from nano-size powders reached 10.87 MPa, which was almost twice as high as those fabricated from commercial micro-size powders, and was comparable to the high-end value (2–10 MPa) of human cancellous bone. Furthermore, the degradation of the β-TCP bioceramics fabricated from nano-size powders was apparently lower than those fabricated from commercial micro-size powders, suggesting the possible control of the degradation of the scaffolds by regulating initial powder size. Regarding the excellent mechanical properties and porous structures, the obtained macroporous β-TCP bioceramic scaffolds can be used in hard tissue regeneration and bone tissue engineering applications.

Keywords: C. Mechanical properties; β-Tricalcium phosphate; Scaffolds; Porous structures; Nano-powders; Degradation

1. Introduction

The three-dimensional (3D) macroporous bioceramic scaffolds play an important role in hard tissue regeneration and bone tissue engineering. In tissue repair, these porous scaffolds serve as substrates for migration, proliferation, and differentiation of cells infiltrated from the surrounding tissues followed by the tissue ingrowths into the pores. These processes are affected by pore size, porosity and connectivity, etc. [1,2]. The *in vivo* studies had revealed that the volume of bone ingrowth increased with an increase of pore size. It has also been shown that pore diameters in the range of 150–500 μm can lead directly to mineralize bone [3,4]. Meanwhile, the macropore should be interconnected and the interconnections should be larger than 50 μm in diameter [5]. The well interconnected pore structures can significantly accelerate the vascularization and bone regeneration ability in clinical applications [6,7].

β-Tricalcium phosphate [β-$Ca_3(PO_4)_2$, β-TCP] bioceramics are wildly used for hard tissue regeneration due to their remarkable biocompatibility and their close chemical similarity to biological apatite present in human bones [8,9]. On the other hand, the β-TCP has been proved to be resorbable *in vivo* with new bone ingrowths replacing the implanted β-TCP. This property imparts significant advantage onto β-TCP compared to other biomedical materials, which are not resorbed and replaced by new-formed bone tissues [9,10]. Therefore, β-TCP bioceramics are widely used as bone replacements in the field of oral and plastic surgery and bone tissue engineering scaffolds [11–14].

* Corresponding author. Tel.: +86 21 52412804; fax: +86 21 52413903.
E-mail address: jchang@mail.sic.ac.cn (J. Chang).

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Besides the necessity of biocompatibility and 3D porous structures, the proper mechanical strength is required in order to maintain the shape against the stress during the surgical procedure and recovery. However, the mechanical strength of the scaffolds was usually low due to the high porosity, large macropore size and interconnected structures. The limitation of the scaffold strengths is one of the major challenges in the scaffold fabrication field. Similarly, the poor mechanical properties of β-TCP scaffolds have severely hindered their clinical applications [15–17]. For many years, a number of studies have been focused on the improving of mechanical strength of β-TCP bioceramics [15–20]. Recently, the concept of nano-technology has been applied to fabricate macroporous bioceramic scaffolds with significant improvement of the mechanical properties [15,21].

The aim of the present study was to fabricate the macroporous β-TCP bioceramic scaffolds with improved mechanical properties, and uniform macropore size and interconnected pore structures from nano-powders. Then the influence of the nano-size powders and commercial micro-size powders on the sintering, microstructure, mechanical properties and degradation of the scaffolds was investigated.

2. Materials and methods

2.1. Materials

The commercial micro-size β-TCP powders were obtained from Tomita (Tokushima, Japan). All other chemicals were obtained from China National Medicine Shanghai Chemical Reagent Corporation without further purifications.

2.2. Synthesis of nano-size β-TCP powders

The nano-size β-TCP powders for the present studies were synthesized by the reaction of $Ca(NO_3)_2$ with $(NH_4)_2HPO_4$. Briefly, 1000 mL of 0.4 mol $(NH_4)_2HPO_4$ solution with a pH about 8.0 was vigorously stirred at room temperature, and 1000 mL of 0.6 mol $Ca(NO_3)_2$ with a pH 8.0 was added drop wise over 300–360 min to produce a white precipitate. Throughout the mixing process the pH of the system was maintained at 8.0 ± 0.2 with the adding of ammonia solution. The white precipitate was then stirred for 24 h followed by washing with distilled water, and then washed with 100% ethanol to improve the dispersion characteristics. After washing, the remaining liquid was removed by vacuum filtration, and the precipitate was dried at 80 °C for 24 h. β-TCP was obtained by calcining the powders at 800 °C for 2 h with a heating rate of 5 °C/min.

2.3. Fabrication of macroporous β-TCP bioceramic scaffolds

The macroporous β-TCP bioceramic scaffolds with uniform macropore size and interconnected pores were fabricated by impregnation of β-TCP powder slurry into polymeric frames [22,23]. First, the polymeric frames with diameter 10 mm and height 12 mm were constructed by the polymethylmethacrylate balls (PMMA) in 500–600 μm sizes. The PMMA balls were poured into a metallic mould, and then the acetone was imported as the solvent to dissolve parts of the bodies and induced an overlapping between the individual bodies. This movement leads to the formation of necks between PMMA balls [22,23].

The synthetic nano-sized β-TCP powders and the commercial micro-size β-TCP powders were used as the starting raw materials to prepare the aqueous slurries with a powder concentration of ∼60 wt.%. Slurry defloculation (Darvan C, R.t. Vanderbilt Co.) was added in amount equals to 1.5 wt.% of β-TCP content. A quantity of organic binder (4 wt.% of β-TCP content, Duramax B1001, Rohm and Haas) was added to ensure a consolidation of green material during the polymer frame burnout. After a planetary milling for 1 h, the slurry was poured into plaster mould containing the polymeric frame. The plaster mould ensured the drying of material [22,23]. In the present study, the volume fraction of PMMA frames reached about 70% in the green samples. Therefore, the over-rapid heating rate would release large amounts of gas and generated intensively internal stresses due to the fast differential expansion between the polymer and the ceramic matrix. These phenomena might destruct the ceramic skeleton. To avoid this behaviour, the elimination of the PMMA frames was carried out by a mild thermal treatment at very slow heating rate of ∼0.1 °C/min [22,23]. The residual organic was then eliminated during a heating at 400 °C for 5 h. After this de-binding treatment, samples were sintered at 1100 °C or 1150 °C for 3 h in order to consolidate the ceramics.

2.4. Characterization of β-TCP powders and macroporous scaffolds

The morphology and size of the synthetic and commercially obtained β-TCP powders were observed by field emission transmission electron microscopy (FETEM: JEM-2100F, JEOL, Japan). XRD patterns of the β-TCP powders and scaffolds were characterized by X-ray diffraction (XRD: D/max 2550 V, Rigaku, Japan) with mono-chromated Cu Kα radiation at the scanning rate of 0.2°/min. The chemical composition of the synthesized and commercial β-TCP powders was analyzed by inductively coupled plasma atomic emission spectroscopy (ICP-AES; VISTA AX, Varian Co., USA). The porosity of the sintered samples was determined from the mass and dimensions of the sintered bodies [24,25]. The fracture surfaces of the sintered scaffolds were observed by field emission scanning electron microscope (FESEM: JSE-6700F, JEOL, Japan). The compressive strength of the fabricated samples was measured using a mechanical testing machine (Shimadza AG-5kN, Japan) with a loading rate of 0.5 mm/min. The elastic modulus was obtained automatically by the computer software in the testing machine, and the calculation was performed from the slope of the initial linear