

Macroporous Calcium Phosphate Scaffolds derived from Freeze Drying

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Statement of Purpose: Three dimensional (3D) interconnective macroporous scaffolds are highly desirable in orthopedics and tissue engineering. Calcium phosphates, such as beta-tricalcium phosphate (β -TCP), are one of the most favorable resorbable materials that are used as scaffolds to support bone tissue regeneration [1]. Many processes have been reported for preparing macroporous structures, typically, by using replica, sacrificial templates, and direct foaming [2]. In the present study interconnective macroporous scaffolds composed of calcium phosphates were fabricated by freeze drying and evaluated by micro CT and density measurements for porosity, and x-ray diffraction for crystallinity. We expect an interconnective macroporous biodegradable calcium phosphate scaffold will serve as a favor template for osteoblasts to adhere and migrate, thereby enhancing bone tissue in-growth and regeneration.

Methods: Beta-TCP slurry was prepared by mixing β -TCP powders (TAL materials Inc, Ann Arbor, MI), carboxymethyl cellulose (CMC) and water at designed ratios (1:1.5 to 1:5). The slurry mixture was then cast into proper molds and frozen down to -18°C for 4 hours; Then they were freeze- dried by using a freeze dryer (Labconco corp., Kansas, MO). The dried body was calcified at 1200°C using a furnace (Thermolyne, Barnstead International, Dubuque, IO). 3D structures were observed using a micro-CT scanner (MicroCAT, Imtek Inc., San Diego, CA). Crystalline phases were analyzed using an Advance D8 x-ray diffractometer (Bruker AXS, Madison, WI). Porosity of the scaffolds was estimated by comparing the apparent and theoretical densities of beta-TCP.

Results/Discussion: In the micro-CT images, all samples displayed similar 3D architectures (Fig.1), described as interconnected macro-scale, laminated structures. The ceramics layers were approximately 150 microns thick while the space between two neighboring layers were approximately 450 microns. Fig 1B shows the 2D assembled pattern of the laminated structures. The micropores on the macroporous walls were observed to be regulated by the ratio of CMC.

All scaffolds exhibited beta-TCP and hydroxyapatite (HA) crystalline peaks via XRD analyses. HA peak intensities increase with CMC in the starting composition.

The scaffold porosity ranged from 75% to 92% according to the solid/water ratio in the starting compositions. The porosity of the scaffolds was influenced by the solid/water ratio of the starting

composition. A higher concentration of water resulted in a higher porosity ($p < 0.05$ when the solid/water ratios change from 1:1.5 to 1:5). In addition, the increasing percentage of CMC in the starting composition significantly reduced the porosity of the scaffolds ($p < 0.05$) due to the bigger shrinkage.

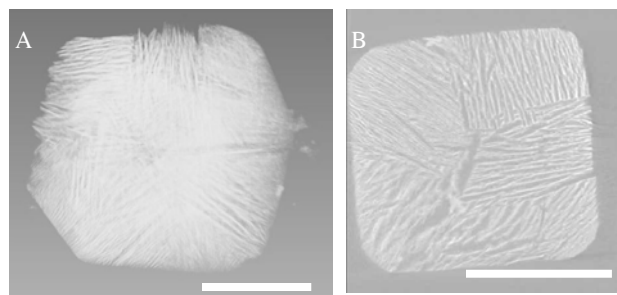


Fig 1. Representative micro CT images of scaffolds, A. 3D images; B. 2D image. Scale bars: 1mm

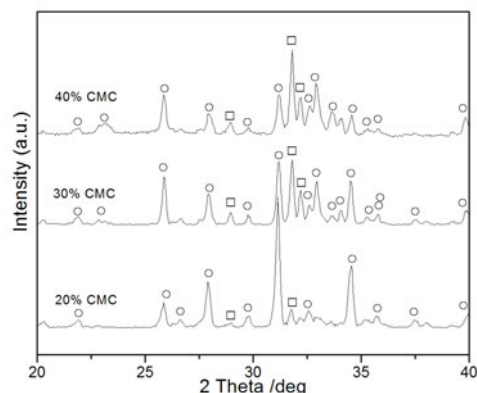


Fig 2. TF-XRD patterns for scaffolds which were derived from 10% to 40% CMC starting compositions. \circ : beta-TCP, \square :HA

Conclusions: The interconnective macroporous calcium phosphate scaffolds were successfully fabricated using a freeze-dry method. The scaffolds exhibited laminated structures, where the ceramic layer was about 150 microns thick while the pores between two neighboring layers was approximately 450 microns. The dominate crystalline phase was beta-TCP, but hydroxyapatite phase was detected and its percentage increased with the increase of CMC in the starting composition. The scaffold porosity increased from 75% to 92% as solid to water ratio in the starting slurry composition decreased.

References:

- [1] Hutmacher DW. J Biomater Sci Polymer Edn. 2001;12:107-124.
- [2] Studart AR, et al. J Am Ceram Soc, 2006, 89; 6: 1771-1789.