

Research Article

Porous Strontium-Containing Ceramic Granules as Bone Graft Substitutes

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Abstract We have synthesized calcium phosphate-based, strontium (Sr) containing, porous ceramic granules for use as bone graft substitutes. The granules with a particle size between 1 and 2 mm and a (macro)-pore size around 200–500 μm were mixed with a fibrin sealant to form a moldable composite material. The starting material with Sr contents between 0 and 100% Sr were precipitated from Ca/Sr solutions with appropriate Ca/Sr ratios, and ammonium phosphate solution using a published protocol with slight variations. A selection of the resulting powders was calcined, milled, mixed with urea as porogen and compacted into disks. These disks were fractured to result in raw granules, which were then sintered at high temperature. In preparation for in vivo implantation, the granules were mixed with fibrin sealant (Artiss™, Baxter) to create a cohesive, moldable composite material that can be used as a bone graft substitute.

Keywords strontium; calcium phosphate granules; porous; bone graft substitute; fibrin

1 Introduction

Synthetic bone graft substitute materials have gained widespread use in a wide range of orthopedic procedures. Some of the reasons for their use include the fact that no autologous bone graft has to be harvested, the availability of material of consistent quality, and the fact that no risk for pathogen transmission exists. These materials have been shown to have a bone forming capacity that is at least comparable to bone autograft harvested from the patient's iliac crest.

In an effort to create bone graft substitutes that show increased radio-opacity for better visibility of graft placement in minimally invasive procedures, we have created a series of ceramic materials containing strontium (Sr) in addition to calcium as the cation in apatite ceramics, ranging from fine powders as fillers for injectable formulations to granular materials. These materials were made with strontium contents ranging from 0 to 100 atom %

in an attempt to adjust the radio-opacity of these materials for various indications.

In this paper we report on the synthesis and manufacturing of macroporous Sr-substituted ceramic granules that are intended for combination with Baxter's fibrin sealant to create a cohesive, moldable composite material that can be used as a bone graft substitute.

2 Materials and methods

Different ceramic powders with varying Sr contents (0–100 atom % Sr) were prepared according to and adapted from a solution precipitation method described by Kim et al. 2004 [1]. The precipitate was dried under vacuum, calcined and then milled in a planetary ball mill. A selection of the resulting powders (0, 25 and 80% Sr) was mixed with urea and uniaxially compressed into disks. These disks were fractured into granules of the approximate size, and from these granules the size fraction between 1 and 2 mm was collected by sieving. The granules were subjected to careful heating to remove the porogen, and then sintered at various temperatures. Final Sr contents of the precipitates were measured by ICP-OES (inductively coupled plasma optical emission spectrometry) and verified by EDX (Energy dispersive X-ray spectroscopy). The granules were macroscopically tested for stability after sintering, and imaged using a Hitachi TM-1000 scanning electron microscope.

For making the fibrin – ceramic composite that can ultimately be implanted into the bony defect, 3,5 g of the ceramic granules were filled into a custom syringe with removable threaded front end. The granules were hydrated with 1 ml of water, and then 2 ml of Artiss™ fibrin sealant were injected.

3 Results and discussion

The strontium content of the precipitated powders, as measured with ICP-OES and EDX was very close to the stoichiometric ratio between the two ions in the feed solution

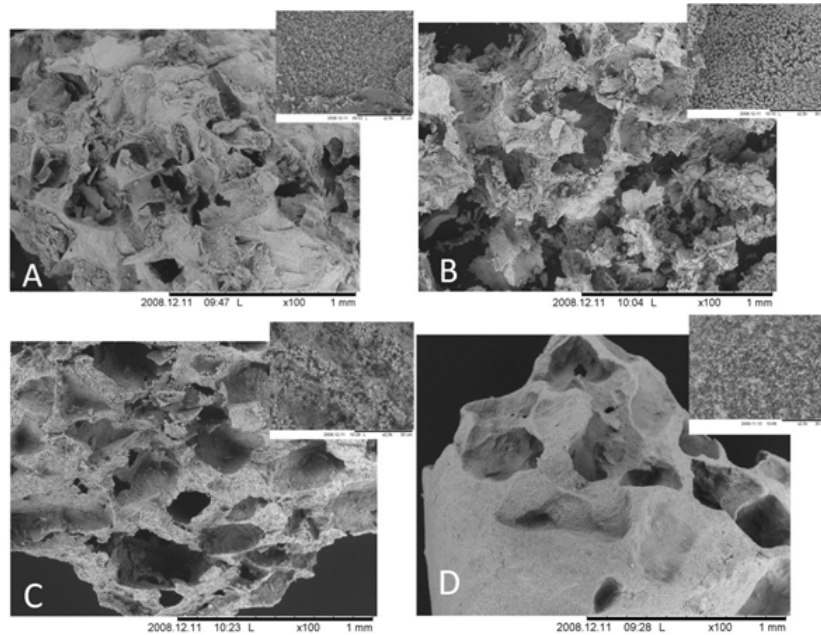


Figure 1: (A) 0% Sr calcium phosphate particles at 100x and 2,5 kx (inset); (B) 25% Sr calcium phosphate particles at 100x and 2,5 kx (inset); (C) 80% Sr calcium phosphate particles at 100x and 2,5 kx (inset); (D) TricOs MBCP particles at 100x and 2,0 kx (inset).

before precipitation. This is a clear indication that Ca^{2+} and Sr^{2+} precipitate stoichiometrically under the chosen condition. Therefore Ca/Sr phosphate powders with any desired Sr/Ca ration can be produced with this method.

Mixing the resulting powders after calcination with urea resulted in a raw material which allowed uniaxial compression into disks without further processing. These disks were stable enough for further handling, and when fractured resulted in irregular granules of about the right grain size for further processing. The removal of the porogen by careful treatment at moderate heat resulted in granules with macropores that corresponded in size with the grain size of the porogen (Figure 1).

Sintering the green body granules at high temperature yielded granules that were mechanically stable.

These could be mixed with solutions of fibrinogen and thrombin inside of a custom syringe with a threaded removable front end. During injection the two solutions mix, and the reaction between fibrinogen and thrombin forms a fibrin clot in and around the granules. This holds the granules together and yields a moldable composite material for implantation in a bony defect site.

4 Conclusions

We have created macro-porous ceramic granules with varying degree of Sr substitution. For application into bony voids, these granules can be mixed with fibrin to form a cohesive, moldable composite material.

References

- [1] H. W. Kim, Y. H. Koh, Y. M. Kong, J. G. Kang, and H. E. Kim, *Strontium substituted calcium phosphate biphasic ceramics obtained by a powder precipitation method*, J Mater Sci Mater Med, 15 (2004), 1129–1134.