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Original article

Preparation and characterization of a novel injectable strontium-containing calcium phosphate cement with collagen

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ABSTRACT

Purpose: To develop a novel injectable strontium-containing calcium phosphate cement with collagen.
Methods: A novel calcium phosphate bone cement (CPC) was prepared with the addition of strontium element, collagenI, and modified starch; the injectability, solidification time, microstructure, phase composition, compressive strength, anti-collapsibility and histological properties of material were evaluated.
Results: The results showed that the material could be injected with an excellent performance; the modified starch significantly improved the anti-washout property of cement; with the liquid to solid ratio of 0.3, the largest compressive strength of cement was obtained (48.0 MPa ± 2.3 MPa); histological examination of repair tissue showed that the bone was repaired after 16 weeks; the degradation of cement was consistent with the new bone growth.
Conclusion: A novel injectable collagen-strontium-containing CPC with excellent compressive strength and suitable setting time was prepared, with addition of modified starch. The CPC showed a good anti-washout property and the degradation time of the cement met with the new bone growing. This material is supposed to be used in orthopedic and maxillofacial surgery for bone defects.

1. Introduction

Calcium phosphate bone cement (CPC) is an excellent human hard tissue repairing material, and its application promoted a higher level of bone repairing.[1,2] Since being presented by Brown and Chow in 1986, CPC has been the focus of increasing attention. But some issues of CPC are needed to be improved[3]: First, due to the different composition and microstructure, there is a great difference in the physical, chemical, biological and mechanical performance between CPC and bone tissue; The organization and cell affinity of CPC material is not ideal for the clinical application; Second, the degradation speed of CPC can not satisfy the new bone tissue growth; Third, CPC is easily washed away by the bleeding of the surgical area[4–6]; Fourth, the injection quantity of CPC is poor, which makes CPC can not be widely used in percutaneous injection operation. These deficiencies greatly limit its wide application in clinical orthopedics. In order to increase the physical, chemical and biological properties of the CPC, the different additives have been used in CPC, including the curing accelerator, plasticizer, anti-water/blood solvent, porogen, compressing intensity enhancer, biological active substances and drug compound.

In the present study, a novel CPC material was prepared with addition of strontium element, collagenI, and modified starch. The injectability, solidification time, microstructure, phase composition, compressive strength, anti-collapsibility and histological properties of material were characterized.

2. Materials and methods

2.1. Experimental method

The Sr-CPC with Sr/(Sr + Ca) ratio of 5% was used in the experiment (supplied by South China University of Technology Materials Science and Engineering).[1] The Sr-CPC was composed of the partial crystallization of calcium phosphate and anhydrous dicalcium phosphate with the weight ratio of 1:1 adding 0.5% modified starch; type I collagen was dissolved in deionized water, which was used as the liquid phase for CPC. The liquid phase and the cement powders were mixed in a mortar to obtain a paste, and

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the paste was molded at 24–26 °C and 40–50% humidity. The cement specimens were stored in an incubator at 37 °C and 97% humidity. After setting for 24 h, the physical and chemical properties of material were tested.

2.2. Phase and microstructure characterization

The as-prepared samples were analyzed using X-ray diffraction analysis (X'Pert Pro, PANalytical, Netherlands).

2.3. Setting time

Setting times of the cement were measured according to the international standard ISO 9917 for dental water-based cement. Ninety seconds after the end of mixing the CPC powders and liquid, the indenter (300 g + 5 g in mass, 1 mm + 0.05 mm in diameter of the needle) was carefully lowered vertically onto the surface of the cement and allowed to remain there for 5 s. Initial setting occurred when a 1-mm needle penetrated 25 mm into cement paste as original time. Final setting occurred when there was no visible penetration as final time. Each specimen was repeated six times and the average value was calculated.

2.4. Compressive strength test

Steel cylindrical molds with an inner diameter of 6 mm and a height of 12 mm were used to prepare cement columns for compressive tests. The cement specimens were stored in an incubator at 37 °C and 97% humidity for 24 h. Then the samples were ready for mechanical tests. The compressive strength of the columns was measured using a universal material testing machine (Instron 5567, Instron, Britain). Each measurement was repeated 6 times and the average value was calculated.

2.5. The injectability test

The injectability of the CPC was tested with a syringe of 14.5 mm inner diameter, which was fit with a needle of 1.6 mm inner diameter. With different liquid/powder ratios (mass ratio: 0.3, 0.4, 0.5, and 0.6), the as-prepared paste was poured into the syringe. A 5 kg compressive load was then mounted vertically on the top of the plunger for 2 min. The entire process took about 4 min, which was much shorter than the initial and final setting time. The mass of the paste before and after injection was measured, and the injectability was calculated according to following equation. Each test was performed six times and the average value was calculated.

$$\text{Injectability}(\%) = (\text{Mass expelled from the syringe}/\text{Total mass before injection}) \times 100\%$$

2.6. Anti-washout test

The obtained cement columns were immersed in the deionized water, and put in shaker at 37 °C, 180 r/min rate of shaking. Pictures at 0, 5, 15, 30 min were taken to observe the turbidity level of water.

2.7. Histological examination

In the animal experiment, the bone cement was embedded into the back muscle of the rabbit; and the rabbit was sacrificed after 2 weeks. The samples were fixed in 4% paraformaldehyde, decalcified in 10% EDTA and embedded in paraffin. The samples were stained with hematoxylin-eosin (H&E) to observe the presence of fibroblasts, fibrous connective tissue, inflammatory cell infiltration, as well as newly formed vessels.

The bone cement was embedded into the defect of the rabbit's distal femur (about 1 cm × 1 cm). The rabbits were sacrificed at weeks 4, 8, 12 and 16. The distal part of each femur was removed, fixed in 4% paraformaldehyde, decalcified in 10% EDTA and embedded in paraffin. Then sections were cut from the middle of each sample, stained with hematoxylin-eosin and then evaluated

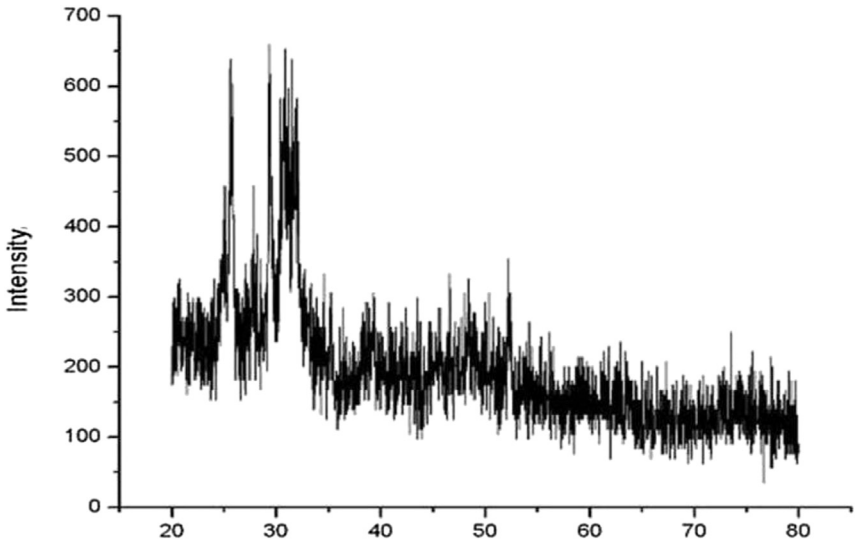

Fig. 1. X-ray diffraction patterns of cement revealed that the hydration product of cement was poorly crystallized hydroxyapatite.