Reinforcement of Calcium Phosphate Cement Using Silk Fibroin (SF) and Self-assembled SF-Hydroxyapatite Complex

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Statement of Purpose: Vertebral augmentation through minimally invasive surgeries including vertebroplasty and Kyphoplasty has been widely used to treat vertebral compression fractures caused by osteoporosis, multiple myeloma, and osteolytic metastases. As a biodegradable material, calcium phosphate cement (CPC) may achieve orchestrated cement resorption and new bone formation to restore vertebral body without the potential risks of poly(methyl methacrylate) bone cement, the most commonly used filling material in such surgeries. However, the mechanical strength of CPCs is generally insufficient to provide adequate vertebral augmentation. In this study, we aim to develop a novel mechanically adequate CPC using silk fibroin (SF) and self-assembled SF-hydroxyapatite (HAP) complex as reinforcing components.

Methods: ***Preparation of SF-HAP complex***. Calcium hydroxide, phosphoric acid, and SF solution were reacted with pH being 9.0~11.0 for 3 hr to obtain SF-HAP complex. ***Preparation of CPCs***. A combination of 75% α-tricalcium phosphate, 20% tetra calcium phosphate, and 5% dicalcium phosphate anhydrous were manually mixed with water until a CPC pallet was molded. SF solution or a combination of SF-HAP complex and SF solution were used respectively to prepare CPC/SF or CPC/SF/SF-HAP composites. The liquid-to-powder ratio was kept at 0.3 ml/g. ***Characterizations of CPCs***. The cements were analyzed using FTIR, XRD, and SEM, respectively. Their compressive strengths were measured using a mechanical testing system. The reported data is the average of 6 measurements.

Results: In the FTIR spectrum of reaction product, peaks at 1640, 1531, and 1237/cm correspond to characteristic β-sheet structures of SF. Peaks at 1093, 1031, 961, 602 and 567/cm come from phosphate group (**Fig. 1A**). The XRD spectrum shows similar pattern as HAP, implying that HAP was formed in the presence of SF (**Fig. 1B**). This was further revealed by SEM imaging, which shows needle-like crystals, typical morphology of HAP (**Fig. 2A**). These results indicate that self-assembled SF-HAP complex has been obtained. When SF and SF-HAP were supplemented into CPC, the microstructure of CPC was markedly altered, including reduction of flake-like crystals and increase of needle-like crystals (**Fig. 2B-D**). Consequently, the compressive strength of CPC was improved (**Fig. 3**). While addition of SF only slightly enhanced CPC (10% increase of strength), supplementation of 1%-3% SF-HAP to CPC/SF dramatically reinforced CPC, with a strength increase of up to 50%. The reinforcing effect of SF-HAP deteriorated when it exceeded 3%.

Conclusions: We have successfully developed a new type of CPC derived from a composite of CPC, SF and self-assembled SF-HAP complex. The compressive strength of this cement was far higher than the trabecular bone of human vertebral body and close to cortical bone, which is ideal for vertebral augmentation. The reinforcing effect of SF-HAP complex might be resulted from the formation of hierarchic, multi-scale microstructures which contain a combination of flake-like crystals and needle-like crystals in the CPC/SF composite.

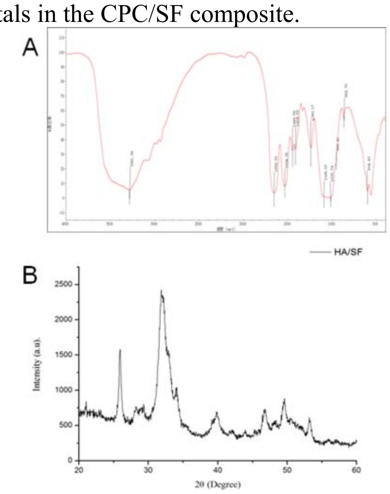

Figure 1. Characterizations of SF-HAP complex. (A) FTIR spectrum; (B) XRD spectrum.

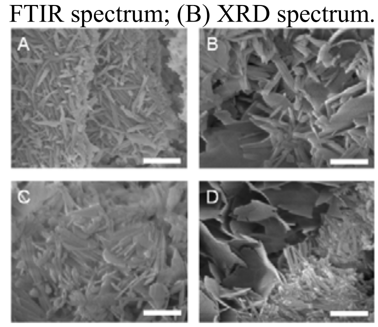

Figure 2. SEM images of SF-HAP complex (A), CPC (B), CPC/SF (C), and CPC/SF/SF-HAP(3%) (D), respectively. Scale bars, 500 nm.

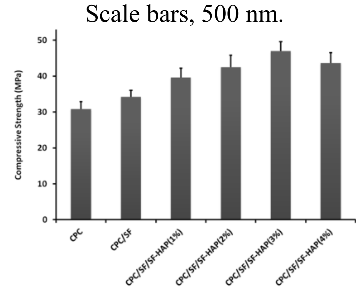

Figure 3. Compressive strengths of CPC, CPC/SF, and CPC/SF/SF-HAP of various SF-HAP contents.

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