Bioactive bone cement microspheres by rapid hydroxyapatite (HA) coating

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Statement of Purpose: Bioactive porous ceramic fillers have been used in defective bones since they are advantageous in bone ingrowth which stems from interconnected micro spacing built among fillers. In particular, microsphere-type bone cement fillers have gained increasing attention because of relatively simple fabrication, faster resorption rate, and easy incorporation of bioactive molecules as compared to heat treated ceramics [1]. However, bone cement microspheres, composed of α-TCP, requires long incubation time in simulated body fluid (SBF) solution for the conversion into hydroxyapatite (HA) for mechanical and chemical stability [2]. Therefore, in this study, we introduce the rapid hydroxyapatite coating to the bone cement microspheres via the composite microsphere system, achieving significant reduction of the incubation time to a few hours, yet enhancing bioactivity.

Methods: Bone cement powders were prepared as the 2:3 mixture of α-tricalcium phosphate (α-TCP) and tetracalcium phosphate (TTCP). As the hardening liquid of bone cement, 1M sodium phosphate solution with 10 wt% citric acid was used. The cement paste was obtained by mixing 1 g cement powder and 0.5 ml hardening liquid for 30sec and then was immediately emulsified in olive oil for 10 min. While the obtained microspheres were immersed in 10x SBF for 2 hrs, the container kept rotating in a ball milling machine at 40rpm. The morphology and composition of all samples were assessed by SEM and XRD. Chemical stability before and after immersion in SBF solution was tested. MC3T3-E1 cell line was used for in vitro cell tests.

Results: Bone cement microspheres were found to have the average size of 180~250 µm. After immersion in SBF solution, needle-like apatite coating layer with 3~5 µm thickness was formed on the surface of the microspheres, resulted from Ca/P precipitation in 10x SBF solution (Fig. 1). As-prepared microspheres, composed of α-TCP and TTCP, were often found to lose TTCP faster than α-TCP under physiological conditions because of 10x higher dissolution rate than that of α-TCP, however, TTCP still remained underneath the apatite coating layer even after 2 week-immersion in 1x SBF solution (Fig. 2). As a result, HA coating layer not only successfully protected the internal microspheres from degradation, increasing chemical stability in the body, but also induced additional HA deposition as nucleus sites in SBF solution. Cells on HA-coated microspheres appeared more proliferated as compared to bare microspheres because of its biomimetic chemical composition and moderate dissolution rate (Fig. 3A). In particular, surface coverage of cells on HA-coated microspheres was found to reach ~50% after 5-day culture (Fig. 3B).

Conclusions: Calcium phosphate composite microspheres were successfully fabricated in oil emulsion and coated with HA for a few hours in concentrated SBF solution. The chemical stability and biocompatibility of the coated microspheres were significantly enhanced. This shortened fabrication process using composite microspheres was remarkably efficient, having great potential for commercial usage.

References:

Figure 1. (A) Surface and (B) cross-section images of HA-coated microsphere

Figure 2. XRD patterns of microspheres with HA-coating layer (A) before and (b) after the dissolution test for 2 weeks. (▼: α-TCP, ▽: β-TCP, ◆: TTCP, ★: HA)

Figure 3. (A) The viability of cells cultured up to 10 days on bare and coated microspheres. (n=3, *: p <0.01) and (B) SEM image of cells on a HA-coated microsphere after 5-day culture.