Simvastatin-Releasing Calcium Sulfate and Calcium Phosphate Bioceramics

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Introduction

The capacity to quickly regenerate or augment bone lost as a result of resorption is crucial to restoring proper function and aesthetics. In addition to existing bone grafts, both autologous and allogeneic, a variety of bone graft substitutes are being developed. Calcium sulfate and calcium phosphate ceramics have a lengthy history in dental applications.

Release of bioactive agents and/or the combination of materials to create a stable augmenting platform could be a suitable substitute to the existing gold standard autografts. In this study, release of simvastatin directly loaded into calcium sulfate (CS) and calcium phosphate (CP) implants was investigated. Compression testing was performed to determine effects on mechanical properties of the drug-loaded bioceramics.

Methods

CS slurries were prepared by mixing 1 gram CS powder with 800µL of deionized water (DI). To test the release of a bioactive agent, 10 mg of simvastatin was directly mixed into the CS prior to addition of water. The CS slurry was injected into a Teflon mold and kept at 43°C for 24 hrs.

CP slurries were prepared by combining a mixture of monocalcium phosphate monohydrate and β-tricalcium phosphate with a 1:1 molar ratio with 400 µL of 100 mM sodium citrate to form dicalcium phosphate dihydrate (DCPD). Similar to CS, simvastatin (10-50 mg) was added to the powders prior to mixing with citrate. The DCPD slurry was packed into a mold and a desiccator under vacuum for 24 hr.

All release studies were performed using 4 mL phosphate-buffered saline (PBS) at 37°C. CS and CP samples were mechanically tested on a BOSE ELF 3300 machine. Microcomputed tomography (microCT) was used to evaluate the internal structure of samples during erosion.

Results and Discussion

Fig. 1 shows release profiles for CS and CP samples loaded with the same amount of simvastatin (10 mg per batch). Release rates were approximately 59 and 7 µg/day for CS and CP, respectively. Increasing the amount of simvastatin added to CP resulted in a loading-dependent increase in release rate (*i.e.*, 12 and 26 µg/day for 20 and 50 mg loadings, respectively).

Mechanical testing showed CP to have significantly ($p<0.05$) greater compressive strength (Figure 2) and modulus than did CS. There were no significant differences between CP of different simvastatin loadings. CP eroded much more slowly than CS when incubated in phosphate-buffered saline; CS was gone within 28 days, while CP lasted more than 180 days. Loading did not affect erosion. MicroCT scans showed that CP developed a porous internal structure as it eroded (Figure 3).

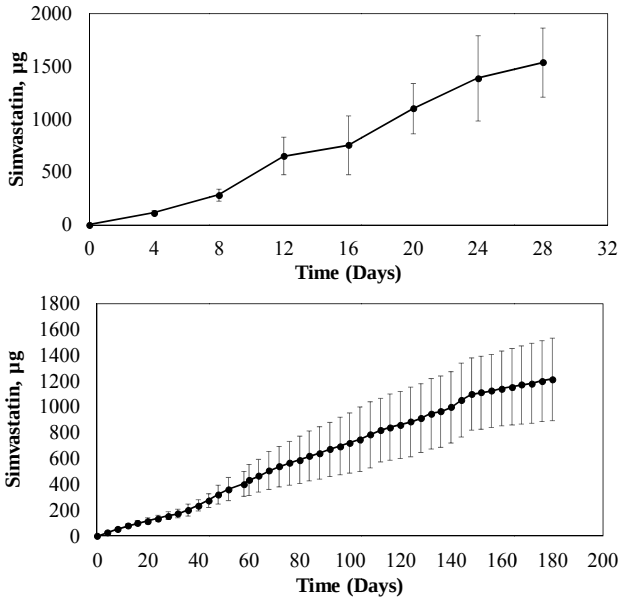

Figure 1: Cumulative release of simvastatin from CS (top) and CP (bottom) samples.

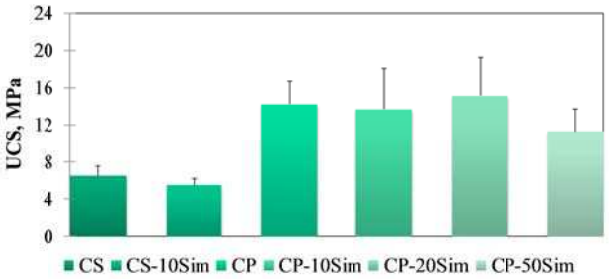

Figure 2: Compressive strength of simvastatin-loaded CS and CP implants.

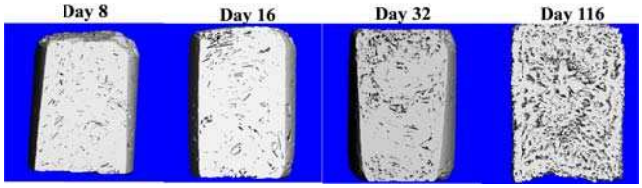

Figure 3: MicroCT cross-sections of CP samples during erosion in PBS.

Conclusion

CS and CP are both proven alternatives to conventional bone grafts, but the use of one over the other will depend on the desired compressive strength, degradation, and drug release when confronted with different sites for bone augmentation.

Acknowledgement

The authors thank Mike McQuinn for his initial work with the CP samples.