Tailored Properties of Bilayered Calcium Sulfate and Calcium Phosphate Bone Graft Substitutes

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Introduction

Bone augmentation, commonly employed for maxillofacial applications, is the build-up of new bone on an already compromised bony surface using a grafting material to restore proper function and aesthetics. Release of bioactive agents and/or the combination of materials to create a stable augmenting platform could be a suitable substitute to existing gold standard autografts. Synthetic bilayered implants are being developed that will act as 'tenting' barriers to soft tissue infiltration, while also stimulating osteogenesis. In this study, the release of simvastatin directly loaded into calcium sulfate (CS) bilayered implants was investigated. Compression testing was performed to determine effects on the strength of simvastatin loaded bilayer CS implants and implants with a combination of CS and calcium phosphate (CP).

Methods

Bilayered CS implant posts were produced according to Fig.1a. CS slurries were prepared by mixing 1 gram CS powder with 800µL of deionized water (DI). To create cores, prepared CS slurry was injected into a Teflon mold and kept at 43°C for 24 hrs. Finished cores were suspended on a peg to center in a larger mold that allowed for a CS mixture to be injected, completely surrounding the CS core. To test the release of a bioactive agent from different CS layers, 20 mg of simvastatin was directly mixed into 1g of CS and combined with 800 µL DI and used to produce either the shell only (SSBC), core only (BSSC), or both (SSSC). All release studies were performed in 4 mL phosphate-buffered saline (PBS) at 37°C. To enhance mechanical stability, dicalcium phosphate dihydrate (DCPD) was added to the CS bilayered implants (Fig. 1b). CP slurries were prepared by combining 1 g DCPD (a mixture of monocalcium phosphate monohydrate and β-tricalcium phosphate with a 1:1 molar ratio) powder and 400 µL of 100 mM sodium citrate. Cores with either CS or DCPD slurries were packed into a mold and kept in either a 43°C oven or a desiccator under vacuum for 24 hr, respectively. Finished cores were inserted in a larger mold that allowed for a slurry mixture to be packed around the cores. Final samples consisted of CP blanks, CP-shell/CS-core, and CS-shell/CP-core. All CS and CP samples were mechanically tested on a BOSE ELF 3300 machine.

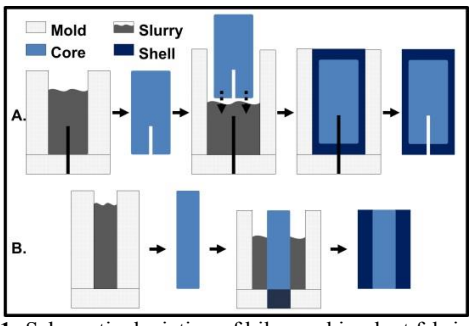

Figure 1: Schematic depiction of bilayered implant fabrication.

Results and Discussion

Fig. 2 displays the results for compression testing of both CS with simvastatin and CP/CS implant samples. CP blanks had double the strength of CS blanks and were stronger than all other samples ($p<0.001$). CP shell only samples were significantly stronger than CS blanks ($p<0.001$). Incorporation of simvastatin in the CS matrix of the bilayered implants did not significantly affect the overall strength when compared to monolithic (no layer) CS samples.

Fig. 3 shows the cumulative release of simvastatin from bilayered implants. Simvastatin loaded into the shell was released in a sustained manner during the first 16 d of the study. The majority of drug loaded into the core was released after day 16, during which the core was exposed due to dissolution of the CS shell. When summed together, these two plots equaled the total amount of drug released from the entire implant.

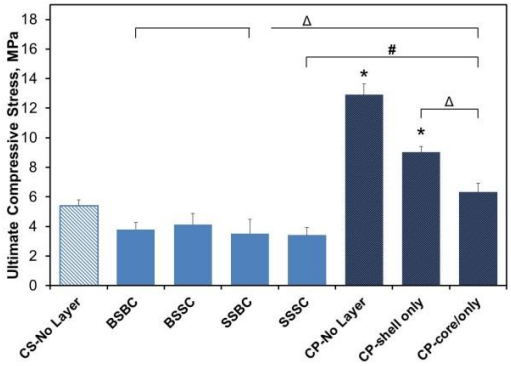

Figure 2: Compressive strength of bilayered, simvastatin-loaded CS implants and bilayered CS/CP implants. (*) $p<0.001$; (#) $p<0.01$; (Δ) $p<0.05$.

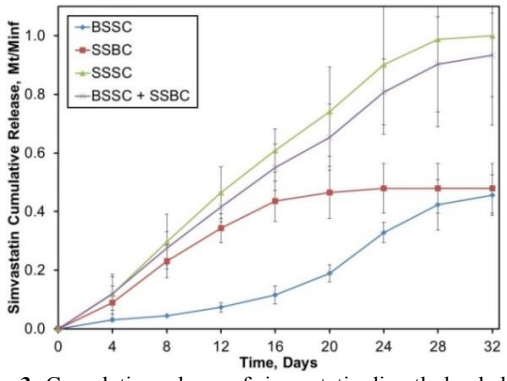

Figure 3: Cumulative release of simvastatin directly loaded into different components of bilayered implants.

Conclusion

With the addition of sustained release of a bioactive agent or calcium phosphate to enhance the mechanical stability, this customizable CS/CP implant system can be useful for developing bone graft substitutes.

Acknowledgement

This research was funded in part by the NIH (DE019645). MWM was supported by a Student Research Fellowship from the UK College of Dentistry.