Drug Delivery from Calcium Sulfate/Hydrogel Space-Making Composites

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Introduction

For dental implants to be successful, the jawbone needs to have a sufficient amount of bone to anchor the implant. Sometimes a loss of bone or narrow ridge is caused by periodontal disease, trauma, or birth defects. Bone augmentation is performed to build up these defects to achieve a desired platform for implant attachment.

Calcium sulfate (CS)-based composites are being developed that will act as a 'tenting' barrier to soft tissue infiltration, while allowing the delivery of osteogenic agents from embedded poly(β-amino ester) biodegradable hydrogel particles to promote bone regeneration. These enhancements could improve CS's osteogenic properties and ability to be developed as a bioactive-delivery vehicle enriching augmentation. In this study the degradation of composites, the morphology of embedded biodegradable hydrogel particles, and the composites' release of lysozyme as a model protein were studied.

Methods

The composites consisted of calcium sulfate hemihydrate as the structural matrix and varying amounts of All-1.4 hydrogel (HG) particles [*Adv. Mater.* 18:2614, 2006] as the delivery component. CS control samples were produced by mixing 1g of CS powder with 1000µL of deionized (DI) water. The mixture was injected into a mold. The mold could yield up to 46 samples when completely filled with an average diameter of 4.66 mm and a height of about 6.70 mm. The loaded mold was placed in a 43ºC oven for 24 hrs to set.

CS samples with varying amounts of HG (1 and 10 wt%) were also produced. For a 1 wt% mixture, 0.01g HG was combined with 0.98g CS powder and 1200µL DI. The mixture was loaded into a mold and left to set in a 43ºC oven for 24 hrs. Samples with 10 wt% HG consisted of 0.1 g HG, 0.8 g CS, and 1400 µL DI water.

Destructive degradation testing was performed to understand degradation profiles of the composites. MicroCT imaging was used to determine distribution trends of HG particles throughout the CS matrix. Release of lysozyme protein from composites was tested for sustained delivery profiles.

Results and Discussion

Shown in Fig. 1, samples degraded very consistently to one another via surface erosion, suggesting the amount of HG particles did not have a significant effect on the degradation rate. The HG loading-independence of composite degradation rate may allow for tuning to provide long enough protection from soft tissue infiltration while also adding sustained delivery of a sufficient amount of drug-loaded HG particles to stimulate bone formation.

MicroCT images showed a uniform distribution of hydrogel particles within the CS matrix. These results provide confidence for reproduction from sample to sample, as well as consistent release of HG particles as the composites degrade.

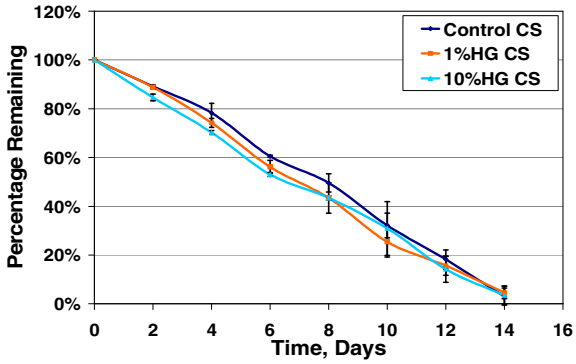

Figure 1: Mass loss of CS only (control) and CS-hydrogel composites. Hydrogel particle size: 150-250µm.

Fig. 2 shows the cumulative release of lysozyme from composite pellets. The 10%HG loaded with 286µg (0.37% of total mass) and the 1%HG loaded with 30.7µg (0.037% of total mass) demonstrated a trend close to a controlled, zero-order release. The 1%HG samples also released their predicted total loading. However, 10%HG total protein amount was less than the predicted value of 286 µg.

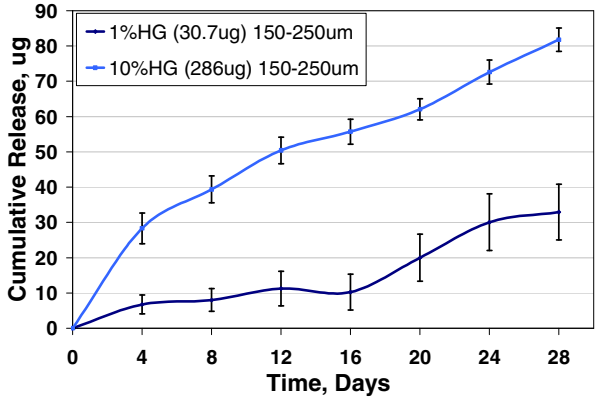

Figure 2: Composites' release of lysozyme protein.

Conclusion

CS composites containing biodegradable hydrogel particles for delivering osteogenic biomolecules can be useful for bone augmentation. The incorporation of HG particles in CS had little effect on degradation, thus providing a suitable composite for promoting controlled release of drug. Composite release studies showed promising results for sustained release of protein. Further release studies will investigate altering the drug loading in hydrogel particles needed to optimize the delivery capabilities of the composites.

Acknowledgement

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