Delivery of Alpha-Ketoglutarate from Hyaluronic Acid Hydrogels for Bone Repair Applications

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Research Question

How can the release of alpha-ketoglutarate from polymer microparticles in a hyaluronic acid hydrogel be controlled for increased bone formation?

Background

Approximately 1.6 million people in the United States undergo bone graft surgery every year to treat bone loss.[1] Currently, autograft and allograft bone tissues are the only options for treating bone loss, however, they pose many limitations.[1] Therefore, there is a pressing clinical need to create a novel treatment that will promote bone repair. To accomplish this, the immunomodulating molecule alpha-ketoglutarate (aKG), which stimulates cell metabolism and modulates osteoclast function, can be used. [2] The goal of this project is to create a biomaterial scaffold that will allow control over bone formation through the delivery of aKG in the form of a microparticle.

Experimental Design

To control the release of aKG it was modified into microparticles (MPs). Hydrolytically degradable aKG polymers (paKG) were first created by reacting aKG with 1,10 decanediol (Figure 1).[3] paKG was purified and formed into MPs through a standard oil in water emulsion technique.[3]

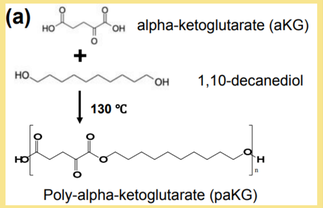


Figure 1: The synthesis of paKG from aKG.[3]

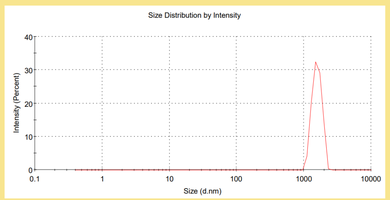


Figure 2: Dynamic Light Scattering (DLS) was run on the MPs showing a size distribution around 1000 nm.

Results

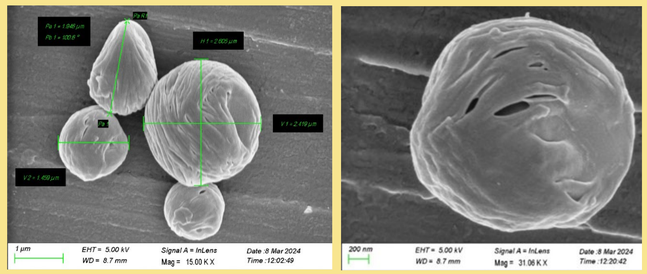
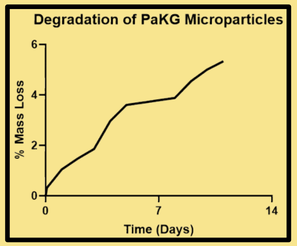


Figure 3: Scanning Electron Microscopy (SEM) was used to visualize the synthesized paKG MPs. The particles are generally the same size, but there is some variance in size.

Figure 4: Degradation of paKG MPs over time at a pH of 7.4. Triplicates with a starting mass of 10 mg were evaluated for the average mass loss over time. The increase in % mass loss over time proves that the particles are degrading.



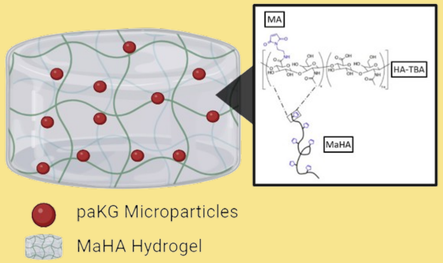
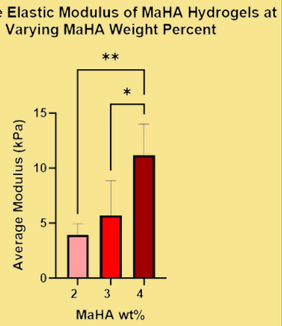


Figure 5: Schematic of the hydrogel paKG MP system. The box to the right depicts the chemical structure of MaHA.

Figure 6: Compression testing was conducted on MaHA hydrogels to determine the average elastic moduli at varying weight percentages (2, 3, 4 wt%). An increase in weight percent results in a higher average elastic modulus.



Results

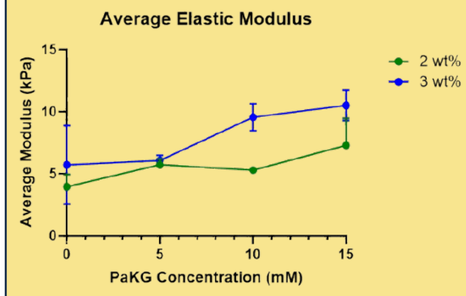


Figure 7: PaKG was added to a 2 and 3 wt% MaHA hydrogel at concentrations of 0, 5, 10, and 15 mM. Compression testing was done to determine how the addition of paKG MPs changed the average modulus. The addition of paKG MPs increased the modulus with an increase in the concentration of MPs.

Conclusions and Future Work

The paKG MPs shape and size distribution were as intended. This is important because the size of the MPs control the release of aKG. The MPs also showed degradation proving aKG can be released from the MPs. MaHA hydrogels at varying weight percents were synthesized showing the versatility in average elastic moduli of MaHA hydrogels. The addition of paKG MPs to MaHA hydrogels saw no impact to the ability of the hydrogels to crosslink. In fact, the addition of paKG MPs at varying concentrations either increased or maintained the modulus. Hydrogels at 4 wt% with paKG at 5, 10, and 15mM will be evaluated for their average elastic moduli. Release kinetics of aKG from hydrogels at different concentrations of paKG will then be evaluated.

Acknowledgments

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References

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Figure 5 was Created with BioRender.com

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