The Release 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 (MP).

Experimental Design

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

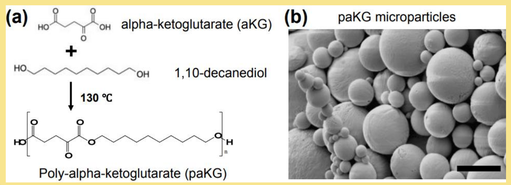

Figure 1: a) The synthesis of paKG from aKG. b) Scanning electron microscopy (SEM) image of paKG MPs.[3]

Experimental Design

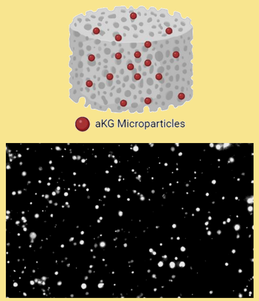

Figure 2: Hyaluronic acid (HA) hydrogels were used as a delivery vehicle for paKG MPs (top). HA was chemically modified to enable photo-crosslinking and the aKG particles were incorporated into the HA solution prior to crosslinking. MPs were visualized using a fluorescent dye (bottom).

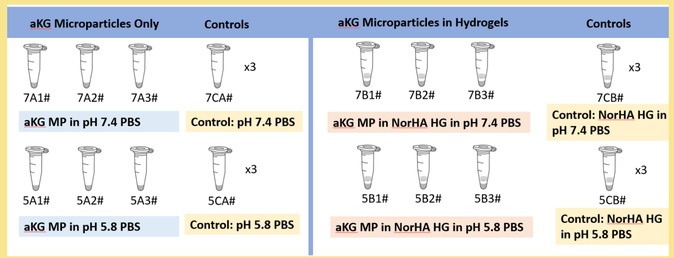

Figure 3: We evaluated the release kinetics for 10 mg of paKG MPs alone and encapsulated within HA hydrogels at a pH of 7.4 and 5.8.

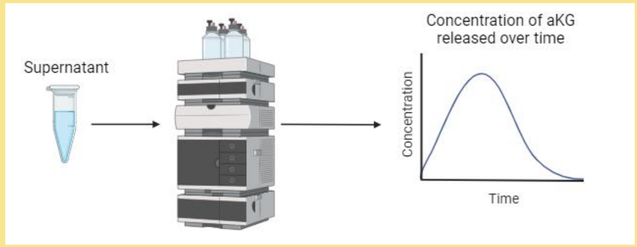

Figure 4: Release supernatant was collected over a 4-week period. High-performance liquid chromatography (HPLC) will be used to determine the concentration of aKG in the supernatant at various time points across the 4-week period.

Results

When we created our hydrogels with 10 mg of paKG MPs they did not crosslink into a hydrogel. Nonetheless, we were able to successfully start the release studies for paKG MPs alone and buffer only controls. We believe that our hydrogels were not crosslinking because the MPs inhibit UV light penetration and the photo-crosslinking reaction needed to form hydrogels. We are currently troubleshooting methods to solve this challenge and encapsulate paKG MPs within our hydrogels at a sufficient concentration to perform the release studies.

Check back in Spring 2024 for release data!

Conclusions and Future Work

The next step for this project is to run release studies at pHs of 7.4 and 5.8 with the paKG MP in our newly designed hydrogels. From there we plan to run 4-week release studies varying the concentration and sizes of MPs to determine their impacts on the release of aKG. This work is part of my honors thesis and will be continued in the spring of 2024.

Acknowledgments

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References

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Figure 2 & 4 were Created with BioRender.com

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