# 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]

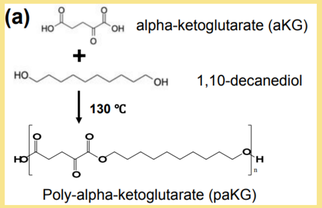



Figure 1: a) The synthesis of paKG from aKG.[3]

## Experimental Design

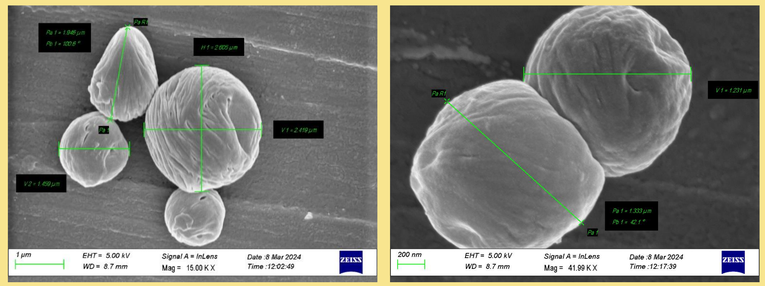
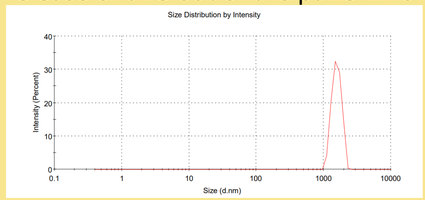


Figure 2: Scanning Electron Microscopy (SEM) was used to visualize the synthesized paKG MPs. The form of the MPs is important as this controls the release of akG out of the paKG MPs

Figure 3: Dynamic Light Scattering (DLS) was run on the MPs confirming that equally sized MPs were formed.



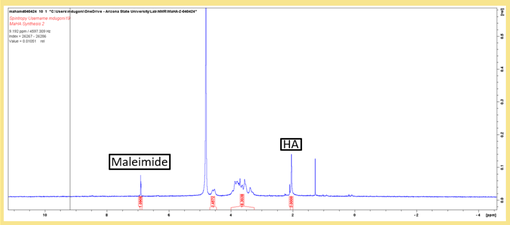




Figure 4: Proton nuclear magnetic resonance ($^1$H NMR) run on Maleimide functionalized hyaluronic acid (MaHA)

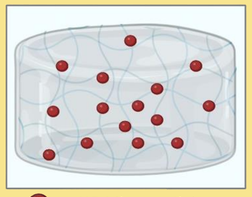



Figure 5: Maleimide functionalized hyaluronic acid (MaHA) hydrogels were used as a delivery vehicle for paKG MPs. HA was chemically modified to enable crosslinking and the aKG particles were incorporated into the HA solution prior to crosslinking.

## Results

The SEM of the MPs visualizes the spherical structure of the MPs, which confirms that paKG was successfully formed into a MP (F2). It was also observed that the microparticles are relatively similar in size, but that there was some variation (F2). The DLS results indicated that the MPs are relatively similar in size distribution (F3). As a delivery system for the MPs maleimide functionalized hyaluronic acid (MaHA) hydrogels were used. Maleimide functionalized hyaluronic acid was successfully synthesized (F4). MaHA hydrogels were successfully synthesized as well (F5).

## Conclusions and Future Work

The MPs shape and size distribution were as intended. This is important because the size of the MPs controls the release of aKG, allowing for the sustained release of aKG from the MP. MaHA being synthesized correctly allow for the creation of MaHA hydrogels to act as a delivery system for the MPs. The MPs will be added to the hydrogels and cell studies will be run to determine the effect of paKG on osteoblasts.

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### References

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[3] Mangal, J. Metabolite release polymers control dendritic cell func. by mod. energy met.
Figure 5 was Created with BioRender.com

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