Citrate Modified Hydroxyapatite for Orthopedic Tissue Engineering

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**Background**

- Hydroxyapatite and Citrate have been determined to be 65 and 6 wt.\% respectively of native bone tissue
- Carboxyl groups in citrate interact with calcium atoms within the HA crystal lattice during HA growth and become strongly bound along specific crystal faces
- Oxa bound, citrate inhibits further growth of HA crystals on these faces which helps to regulate crystal size
- It is hypothesized that by adding Citrate during HA synthesis, citrate/nano HA complexes can be created that will better match native HA morphology

**Citrate HA Synthesis**

- Solutions of .1 M Calcium Nitrate, and .9 M Ammonium Hydrogen Phosphate, and differing concentrations of citric acid (0, 5, 15, 30, 60 mM) were prepared with a pH of 10
- Solutions were heated to 95°C
- Citric acid solution was combined with Calcium Nitrate and Ammonium Hydrogen Phosphate was added by dropwise addition from drip funnel
- Reaction was maintained at 95°C and stirred for 24 hours

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\text{Ca(NO}_3\text{)}_2 \cdot 2\text{H}_2\text{O} + \text{NH}_4\text{H}_2\text{PO}_4 + \text{NH}_3\text{OH} \rightarrow \\
\text{Ca}_10\text{(PO}_4\text{)}_6\text{(OH)}_2 + \text{NH}_4\text{PO}_4 + \text{H}_2\text{O}
\]

**POC/HA Composite Fabrication**

- POC is a synthetic biomaterial being researched to simulate the native composition of bone when composit with HA
- It is hypothesized that the addition of Citrate HA to the polymer will increase the mechanical strength and improve cellular interactions
- Poly[1,8-octanediol-co-citric acid] (POC) polymer was synthesized through a condensation reaction of citric acid and octanediol

**Mechanical Testing**

- Citrate HA was mixed at 50 wt.% into the POC polymer to form composites
- Composites were molded into cylinders and crosslinked for mechanical testing

**Conclusions**

- Citrate HA with up to 60 mM citrate concentration was able to be successfully synthesized
- Higher concentrations of Citrate HA composites have shown similar mechanical strength to micro HA, currently being used in our composites, and native bone (100-230 MPa)
- In future testing, the synthesis of Citrate HA will be modified to improve the mechanical strength by increasing the ability of HA to disperse within composites
- Testing the effects of Citrate HA and Citrate HA composites on cell proliferation and osteogenic differentiation in vitro