Development of Novel Citrate Based Membranes for Periosteum Regeneration

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The periosteum is a multilayered membrane found between the outer cortical region and the surrounding skeletal muscle tissue of all bones in the body except for areas around joints. The outer layer consists of an elastic extracellular matrix and contains a large amount of blood vessels that perfuse the bone tissue, while the inner layer is composed of a stiffer matrix containing abundant osteogenic stem cells that also serves to create a barrier between fibrous tissue and the bone. The critical contribution of periosteum to bone regeneration along with the high instance of its destruction during reparative surgery indicates that the development of a synthetic replacement is critical to improving orthopedic tissue regeneration. Dr. Yang’s lab has previously developed a range of biodegradable polymers based on citric acid, including poly(1,8-octanediol-co-citrate) (POC). In order to replicate the inner layer of the periosteum, POC modified with calcium ions will be cast on top of the outer layer. The abundant carboxyl and hydroxyl groups present on the POC polymer chain are capable of forming ionic bonds with cations. This incorporated, divalent calcium forms ionic crosslinks between polymer chains, which results in a stiffer, less elastic mechanical character similar to the natural periosteum inner layer. Additionally, incorporation of calcium will improve the formation of bone minerals on the inner surface and can aid in stem cell differentiation towards an osteogenic phenotype.

**MECHANICAL**

- **Figure 1**: POC CaCl2 Dry & Hydrated (A) Tensile Stress & (B) Tensile Strain
- **Figure 2**: POC CaCitrate Dry & Hydrated (A) Tensile Stress & (B) Tensile Strain
- **Figure 3**: Varying Crosslinking Time (ºC - days) POC CaCl2 - (A) Tensile Stress & (B) Tensile Strain

**PHYSICAL PROPERTIES**

- **Figure 4**: Varying Citric Acid to Octanediol Ratio POC CaCl2 - (A) Tensile Stress & (B) Tensile Strain
- **Figure 5**: Sol Content after 1 week in DI Water – (A) POC CaCl2 & (B) POC CaCitrate
- **Figure 6**: Sol Content after 1 week in Dioxane – (A) POC CaCl2 & (B) POC CaCitrate
- **Figure 7**: Swelling Ratio after 2 weeks – (A) POC CaCl2 & (B) POC CaCitrate

**CONCLUSION**

- Calcium incorporation increases mechanical strength of POC films in both dry and hydrated conditions
- Found a direct correlation between calcium content and mechanical strength
- Incorporating calcium improves cytotoxicity of POC films
- Calcium doped films display mineralization potential in vitro
- Future studies will focus on: Determining the osteogenic potential of calcium doped POC Testing antibacterial and hemostat potential of calcium doped POC Combining calcium doped POC with a 3D printed vascular layer (acting as outer layer for replication of periosteum)