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| **Development of a Drug-Eluting Composite for Reducing Post-Surgical Inflammation and Fibrosis in Glaucoma** |
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| **Background:** Glaucoma is often associated with disrupted aqueous humour drainage in the eye. This leads to elevated intraocular pressure (IOP) that causes permanent damage to the optic nerve resulting in progressive vision loss. The gold standard surgery to treat glaucoma is trabeculectomy followed by application of the anti-metabolite Mitomycin C (MMC). However, a 1-year failure rate of 9%, rising to 23% by year 5 due to post-operative inflammation, angiogenesis, and fibrosis results in unacceptable numbers of patients requiring repeat surgeries or losing their sight entirely. Currently, MMC and post-surgery patient administered corticosteroid eye drops are used to address this. However, they are limited by cost, side-effects and poor patient compliance. To this end, we have developed a Decorin (Dec)--modified hyaluronic acid (HyA) hydrogel-polycaprolactone (PCL) composite drug-eluting device to eliminate complications and remove the need for drops. |
| **Methods:** Prednisolone or dexamethasone loaded PCL was 3D printed and characterized in terms mechanical properties. Dec-HyA hydrogels were chemically crosslinked, freeze-dried and assessed for percentage crosslinking, swelling speed, and degradation. The drug-loaded PCL mesh was surrounded by Dec-loaded HyA hydrogel to make the final device. Drug release was assessed for 1-12 weeks depending on the drug. Anti-fibrotic effect was studied using primary rabbit conjunctival fibroblasts (RconF) stimulated with TGF-β *in vitro*. Finally, device safety and efficacy were assessed *in vivo* using a 28-day trabeculectomy study on New Zealand white Rabbits. |
| **Results:** It was found that mechanical properties can be tuned by mesh dimensions and drug loading. HyA hydrogels were capable of rapid swelling with full hydration in less than 30 minutes and stability up to 4 weeks. Release of drug from mesh-gel composites were found to exhibit a biphasic release with initial burst release followed by more gradual release*. In vitro* analysis revealed that anti-fibrotic effect was dose-dependent for both dexamethasone and prednisolone and that 1% loading resulted to the best performance. Moreover, a significant reduction in collagen deposition was observed at 1 week with a decrease of up to 35% versus controls with prednisolone. The *in vivo* studies revealed that all devices were retained and well tolerated with minimal fibrotic encapsulation. The optimized device showed significant reductions in IOP at day 28 and comparable safety and efficacy to the standard of care, even without the use of Mitomycin C (MMC). |
| **Conclusions:** Our study presents promising results regarding the efficacy and safety of the optimized device, both *in vitro* and *in vivo*. These findings demonstrate a compelling therapeutic option for mitigating fibrosis and improving patient outcomes in glaucoma. This technology now forms the basis of a spin-out company with the goal of progressing to clinical trials. |