Hydrogels for Sustained Drug Release with Intraocular Lens Implantation for Cataract Surgery

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Statement of Purpose: Cataract is the leading cause of treatable blindness worldwide and the population afflicted by cataract is increasing globally [1]. Post-operative infection is a major concern resulting from suboptimal sterile operating conditions and scarce availability of post-operative medication, leading to bacterial growth and bio-film formation that blocks the vision pathway, causing repeated blindness [2]. We aim to develop a novel drug delivery system that allows sustained sufficient antibiotic level during the post-operative recovery period for cataract surgery. The development concludes a simple polymeric drug depot, releasing the antibiotic over the critical period post-implantation and up to four weeks. The proof of concept was made using both *in-vitro* and *in-vivo* experiment, performs adequate drug release profile and even overcoming bacteria challenged implants [3].

Methods: Poly(hydroxyethyl-methacrylate) (pHEMA) hydrogel was used as a drug depot, containing Norfloxacin antibiotics as a drug model [4]. The sustained drug-release was achieved using subsequent surface modification of the pHEMA. The hydroxyl groups were reacted with octadecyl-isocyanate, forming hydrophobic mono-layer coating. The surface coating was optimized to allow sustained release over a period of four weeks. The device was examined *in-vitro* for the detection of the antibiotic release patterns using spectrophotometry. The antibiotic function of the device was then further examined *in-vitro* using a silicone biofilm model. *In-vivo* feasibility was investigated using rabbits model. The control group of rabbits underwent standard cataract surgery with intraocular lens (IOL) implant and post-operative topical antibiotic and steroid. The experimental group received the polymeric device inserted on the standard three-piece IOL at the time of surgery and received only topical steroids post-operatively. In order to examine the antibiotic effectiveness *in-vivo*, the experimental group was also challenged with Staphylococcus epidermidis bacteremia in concentration as high as 10^7/ml in 30µl bolus. *In-vivo* antibiotics levels were sampled from the anterior chamber for up to 30 days and the infection was tracked visually and *ex-vivo*. Clinical outcomes of both groups were also evaluated.

Results and Discussion: Our *in-vitro* data demonstrate that the pattern of antibiotic release can be achieved by optimization of the surface coating. The *in-vivo* results demonstrated sustained sufficient antibiotic concentration (above the minimum inhibitory concentration (MIC) for most common bacteria related to endophthalmitis) for more than four weeks. Minimum toxicity was observed *in-vivo*. Both groups of animals recovered from surgery without evidence of infection.

Conclusions: The initial findings of the polymeric drug delivery device demonstrate the feasibility of delivering sufficient antibiotic in the anterior chamber for the critical post-operative period in a rabbit model. The device is simple to produce and may help alleviate the potential post-surgical infections.

References

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