# Controlled Release of Drugs for Cataract Surgery from an Engineered Hydrogel Device

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## Introduction:

Cataract is the leading cause of treatable blindness worldwide [1], and the population afflicted with cataract is increasing. The primary treatment for cataracts is the surgical removal of the opacified natural lens followed by implantation of a polymeric intraocular lens device. One of the principal complications from the surgery can be intraocular infection. Post-operative infection is a major potential complication which is painful and can lead to permanent blindness. Avoiding infection is addressed in modern surgical practice by extreme attention to cleanliness and the use of antibiotic eyedrops several times a day for up to ten days following lens implantation.

To combat the risk of infection, and to alleviate the challenges of poor patient compliance to frequent application of eye drops, we have developed a surface-coated polymeric hydrogel drug release device that delivers effective levels of antibiotic over an extended period of time within the lens capsule of the globe of the eye[2].

## Materials and Methods:

Copolymer hydrogel, based on a 70:30 solution feed ratio of hydroxyethyl methacrylate,(HEMA), and hydroxypropyl methacrylate (PHMA) were synthesized with 60% monomers dissolved into an equal mixture of solvents of water and ethylene glycol. Tetraethylene glycol dimethacrylate (TEGDMA) was used as a crosslinker. The polymerization was initiated using ammonium persulfate.

Norfloxacin antibiotic was used in an initial series of experiments at the University of Washington. In addition, Inson Medical Systems, Inc., has performed *in vitro* release studies with other commonly used antibiotics including Erythromycin and Ciprofloxacin. In the initial studies the drug was introduced into the monomers prior to polymerization. For the later studies, an immersion of the dried hydrogel bead depot in a high antibiotic concentration aqueous/methanol solution was used for drug loading.

Initially, the polymeric hydrogels were formed into a small bead shape via molding in a glass tube with a suspended wire and then cutting to length. For production efficiencies as this development translates to a medical product, a precision stainless steel multicavity mold has been used. Following hydrogel bead fabrication the antibiotic loaded units are then dried.

In order to prolong the release duration, a hydrophobic barrier coating was added to the surface of the drug loaded bead. The hydroxyl groups of pHEMA and pHPMA were reacted with octadecyl isocyanate (C18-NCO) under an inert atmosphere to yield a covalently bound coating [3]. The coating density was dictated by the reaction time, from 5 min and up to 60 min. The antibiotic release rates were determined by placing the bead in a gently agitated saline reservoirs at 37°C. The drug release was quantified spectrophotometrically using a UV/Vis microplate reader. The pharmaceutical efficiency of the released antibiotic was examined by exposing cultured bacterial bio-films to the released drugs.

The efficacy of the IOL assembly in preventing infections was investigated with a rabbit model. Our *in vivo* model was conducted using New Zealand white rabbits, challenged with bacterial infection. Rabbits underwent IOL implantation with the drug-loaded hydrogels attached, enabling *in-situ* drug delivery without the need for topical eye drops. The remaining rabbits forming the control group had similar IOLs implanted without the hydrogels, and were treated with standard topical antibiotic eye-drops instead. A second phase of this *in vivo* study used a bacterial challenge.

## Results and Discussion

The hydrogel composition pHEMA-pHPMA has been found to be biocompatible and has been long used in biomedical applications.

The drug release profiles demonstrated that the coated hydrogel devices are capable of delivering a clinically relevant dosage of drug *in vitro* over the critical 14 days post-operative time period.

The *in vitro* bacterial culture results showed that the device is capable of delivering drug in quantities capable of having a lethal effect on bacteria. The initial *in vivo* study showed both groups of subjects recovered from surgery without evidence of infection. In the subsequent bacterial challenge study the control subjects (eye drops) all developed fulminate infections and were euthanized after only 3 days. All subjects receiving the therapy beads initially developed infections, and all subjects recovered.

## Conclusions

These results from the hydrogel drug delivery device demonstrate the feasibility of delivering sufficient antibiotic into the eye, as performed in standard cataract surgery.

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References

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