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A Drug-Eluting Contact Lens

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Abstract

Purpose—To formulate and characterize a drug-eluting contact lens designed to provide extended, controlled release of a drug.

Methods—Prototype contact lenses were created by coating PLGA (poly[lactic-co-glycolic acid]) films containing test compounds with pHEMA (poly[hydroxyethyl methacrylate]) by ultraviolet light polymerization. The films, containing encapsulated fluorescein or ciprofloxacin, were characterized by scanning electron microscopy. Release studies were conducted in phosphate-buffered saline at 37°C with continuous shaking. Ciprofloxacin eluted from the contact lens was studied in an antimicrobial assay to verify antimicrobial effectiveness.

Results—After a brief and minimal initial burst, the prototype contact lenses demonstrated controlled release of the molecules studied, with zero-order release kinetics under infinite sink conditions for over 4 weeks. The rate of drug release was controlled by changing either the ratio of drug to PLGA or the molecular mass of the PLGA used. Both the PLGA and the pHEMA affected release kinetics. Ciprofloxacin released from the contact lenses inhibited ciprofloxacin-sensitive *Staphylococcus aureus* at all time-points tested.

Conclusions—A prototype contact lens for sustained drug release consisting of a thin drug-PLGA film coated with pHEMA could be used as a platform for ocular drug delivery with widespread therapeutic applications.

Topical ophthalmic solutions, or eye drops, are currently the most commonly used method of ocular drug delivery, accounting for approximately 90% of all ophthalmic medications,^{1,2} but they are very inefficient. Eye drops are administered by pulse delivery, which is

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characterized by a transient overdose, followed by a relatively short period of effective therapeutic concentration, and then a prolonged period of an insufficient concentration or underdose. Furthermore, each drop is diluted and washed away by reflex tearing; and the drop is dispersed by blinking, so that only 1% to 7% of the dose delivered from an eye drop is absorbed by the eye.³ The remainder is either flushed onto the patient's cheek or drained through the nasolacrimal system, where the medication is available for systemic absorption,⁴ with potentially toxic side effects. The overdosing of ophthalmic solutions contributes to the ocular and systemic side effects of some ophthalmic drugs.^{5,6} Because of its small surface area and its short contact time with topical drops, the cornea itself only absorbs a fraction of the dose of a drop that is delivered to the surface of the eye.⁷ Moreover, patient compliance can be problematic with ophthalmic drops, especially among the elderly.⁸ The rate of noncompliance in patients with glaucoma is between 24% and 59%,^{8,9} even in long-term users.¹⁰ Simplifying the drug regimen improves compliance,¹¹ but there are few alternatives to eye drops for local delivery of most ophthalmic medications prescribed after surgery.

A sustained release system for ophthalmic drugs could obviate many of these shortcomings. The design criteria for such a system include comfort, biocompatibility, and, ideally, zero-order kinetics (i.e., the release of a constant amount of drug per day), for an extended period. The concept of delivering drugs specifically through a hydrogel (contact lens) was introduced as early as 1960.¹² Ninety-three percent of eye care providers indicate that they would use a drug-eluting contact lens if it was added to their treatment armamentarium,¹³ and 72% of eye care providers have used bandage contact lenses (which protect the cornea and promote re-epithelialization) adjunctively with topical antibiotic drops.¹³

Several researchers have designed contact lenses for drug delivery. However, achieving constant drug release (zero-order kinetics) has been a difficult challenge. The uptake and release of medications from conventional soft contact lenses has been explored.^{14–17} Drugs released by the contact lenses demonstrated nonlinear kinetics: a burst of drug is delivered during the first few hours, followed by declining, subtherapeutic levels of drug release in the subsequent hours. Little, if any, drug is eluted by the second day of use. Research has also focused on the controlled release of medications from delivery systems incorporated into a contact lens' hydrogel material,^{18–22} including copolymerizing the hydrogel, poly(hydroxyethyl methacrylate) (pHEMA), with other monomers in an effort to control the drug's uptake and release properties.²³ Drugs have been released from microemulsions contained in hydrogel prototype lenses.^{18,19,24} "Biomimetic" and molecularly imprinted hydrogels have been used to release medications.^{21,25} Other researchers also investigated the use of molecularly imprinted hydrogel contact lenses for drug delivery.^{26,27} Drug-containing liposomes immobilized onto the surface of contact lenses have also been studied, but demonstrated first-order kinetics.^{28–30} Achieving sustained, long-term drug delivery at the normal physiological temperature, pH, and salinity of the human eye has remained a challenge.

A number of noncontact lens methods have also been explored, but none have achieved these goals. Ocusert (Alza Corp., Palo Alto, CA), which was designed for placement in the cul-de-sac, was the first marketed device to demonstrate zero-order kinetics.³¹ Although now rarely used to treat glaucoma, pilocarpine was once delivered to the eye by Ocusert. It

is no longer commercially available. Collagen shields, which absorb then slowly release a wide variety of medications,³² are most commonly applied after the corneal epithelium is surgically removed. They help to promote corneal re-epithelialization and provide antibiotic prophylaxis.³³ However, they are not widely used by most surgeons because they are not optically clear, they are difficult and uncomfortable to self-insert (typically requiring topical anesthesia by an eye care provider), and they degrade quickly, limiting their use to 1 to 3 days.

In our design of a device that could deliver drugs to the eye with zero-order kinetics, we used a dual polymer system, composed of a polymer film containing the test compounds coated by a transparent polymer that is used in contact lenses. For the former, we used poly(lactic-co-glycolic) acid (PLGA), a biodegradable polymer that is well known for its biocompatibility and its ability to control drug-release kinetics.^{34–37} For the latter, we used pHEMA, which is not biodegradable.^{38,39} Herein, we describe the formulation and characterization of such a drug-eluting contact lens for extended drug zero-order release.

Materials and Methods

PLGAs (65% lactic acid and 35% glycolic acid; Lakeshore Biomaterials, Birmingham, AL) were of 118-kDa (50:50%) and 18-kDa (50:50%) molecular mass (high and low molecular masses, respectively). Ciprofloxacin 0.2% (Cipro IV ready-for-use infusion solutions in 5% dextrose injection) was purchased from Bayer Pharmaceutical Corp. (West Haven, CT). A photoinitiator (Irgacure 2959) was obtained from Ciba Specialty Chemicals Corp. (Tarrytown, NY). Medium grade acrylic resin was obtained from the London Resin Co. (Reading, Berkshire, UK). Ciprofloxacin powder, fluorescein, HEMA and all the other reagents were purchased from Sigma-Aldrich (St. Louis, MO).

Clinical ocular-related *Staphylococcus aureus* strains, obtained from the Massachusetts Eye and Ear Infirmary (MEEI) Clinical Laboratory, were recovered from human cornea, eyelid, and canaliculus infections; the minimal inhibitory concentrations for all bacterial isolates were determined by standard methods (National Committee for Clinical Laboratory Standards [NCCLS]).⁴⁰ MEEI-IB01 is a ciprofloxacin-resistant keratitis strain (minimum inhibitory concentration [MIC] >2 µg/mL). MEEI-IB03, -IB012, and -IB013 are ciprofloxacin-sensitive (MIC < 1 µg/mL) strains.

Solvent Casting of Drug-Polymer Films

To create the drug-polymer film, PLGA was dissolved in 15 mL of ethyl acetate. Fluorescein was added to the solution and mixed to form a fine suspension inside the PLGA solution. Films were created with 118-kDa (high) and 18-kDa (low) molecular mass PLGA polymers and various ratios of PLGA to fluorescein (Table 1). The suspension was poured into a fluoropolymer (Teflon; DuPont, Wilmington, DE) well. The ethyl acetate was removed by evaporation in a fume hood with laminar air flow overnight, then lyophilized for 48 hours. Rings with a 14-mm outer diameter and a 5-mm central aperture, were punched out of the fluorescein-PLGA film. Ciprofloxacin (Sigma-Aldrich) films were also created by solvent casting, as above, using PGLA 65:35 (118-kDa molecular mass) and a 1:1 ratio of medication to PLGA (20 mg ciprofloxacin and 20 mg PLGA).

Coating the Drug-Polymer Film in pHEMA

Drug-PLGA films were coated with pHEMA by ultraviolet (UV) polymerization. The monomer HEMA (11.6 mL) and the cross-linker ethyleneglycol (44 μ L) dimethacrylate (EGDMA) were dissolved in 8.6 mL of deionized water. One hundred microliters of 0.1 g/mL photoinitiator (Irgacure 2959; Ciba) in dimethyl sulfoxide was then added and the resulting solution was degassed under nitrogen for 40 minutes. One hundred sixty microliters of that solution was transferred into a 100- μ m-deep cylindrical rubber mold (16 mm diameter), covered with a glass slide, and placed in a nitrogen-filled plastic bag. The solution was then polymerized with a 305-nm UV lamp for 60 minutes to form the bottom pHEMA layer of the composite contact lens. The drug-PLGA film was manually pressed onto the dried pHEMA gel. They were then placed together into a custom-made cylindrical rubber mold (450 μ m deep by 16 mm in diameter), which was subsequently filled with the HEMA monomer photoinitiator solution and UV polymerized. The resultant contact lens prototype consisted of a thin drug-PLGA film coated on all sides with pHEMA with a total thickness of 450 μ m and a 16 mm outside diameter (Fig. 1).

Crystalline fluorescein without PLGA was also coated in pHEMA. Twenty milligrams of fluorescein was suspended in 15 mL of ethyl acetate and poured into a cylindrical rubber mold with a central 5-mm rubber plug, which had been clamped on top of a 100- μ m-thick preformed pHEMA dehydrated gel. The ethyl acetate was allowed to evaporate overnight in a fume hood, leaving behind a thin layer of fluorescein crystals which occupied the same footprint as the drug-PLGA films prepared in the prototype lenses. The fluorescein was then coated with another layer of pHEMA, as just described, and lyophilized.

Scanning Electron Microscopy

Composite contact lenses were embedded in medium-grade resin (Reading), cross-sectioned with a microtome, and sputter coated with gold-plutonium alloy in a vacuum (Denton Vacuum LLC, Moorestown, NJ). Images were acquired with a scanning electron microscope (model 590; JEOL USA, Inc., Peabody, MA).

Drug Release Studies

Test materials were placed in 15 mL of phosphate-buffered saline (PBS) pH 7.4 inside a 50-mL centrifuge tube and placed in a 37°C incubator with continuous shaking. The PBS was sampled and replaced completely at predetermined intervals. The amount of fluorescein released into the PBS medium was measured by using a UV/VIS spectrophotometer (Molecular Devices, Sunnyvale, CA) at a wavelength of 490 nm. Concentrations and masses of released fluorescein at each kinetic time point were calculated based on a calibration curve prepared with known fluorescein concentrations ($R^2 > 0.99$). Four individual contact lenses were tested for each reported formulation.

The release of fluorescein in the absence of a drug delivery device was tested by suspending 25 mg of free fluorescein powder in 15 mL of PBS. At the same time points at which release from the devices was sampled, the tubes were centrifuged, the supernatants assayed, and the pellets resuspended.

The mass of ciprofloxacin released into the medium was quantified with high-pressure liquid chromatography (HPLC; 110 series; Agilent Technologies, Palo Alto, CA). A dC18 analytical column (4.6×250 mm; particle size $5 \mu\text{m}$; Atlantis; Waters Corp., Milford, MA) was used with a mobile phase mixture composed of 10 mM phosphate buffer (pH 2.1) and acetonitrile. Ratios of acetonitrile to phosphate buffer were increased from 20% to 70% over 8 minutes and then returned to 20% over the next 2 minutes. The flow rate was set at 1 mL/min. The samples were filtered through $0.45\text{-}\mu\text{m}$ syringe filters and $20 \mu\text{L}$ of the samples were injected into the pre-equilibrated column. Ciprofloxacin concentrations were determined with a UV detector set at 275 nm, by correlating the measured peak areas with those measured for a series of ciprofloxacin standards (prepared from Cipro-IV solution; Bayer Pharmaceutical Corp.) freshly prepared for each HPLC run.

Ciprofloxacin Antimicrobial Assay

Ciprofloxacin-containing PBS samples from the release study were tested for antibacterial effectiveness against three clinical test isolates of ciprofloxacin-sensitive *S. aureus* and a ciprofloxacin-resistant *S. aureus*. The resistant strain served as a positive control to assure that the bacterial killing was due to the antibiotic and not to an unknown inhibitory material. All bacteria were grown in antibiotic-free brain heart infusion (BHI)-sucrose-PBS. Release medium without bacteria was used as the negative control.

The bacteria were initially propagated from five large colonies and grown for 2 hours in 3 mL of antibiotic free 10% BHI-0.2% sucrose. The log phase (actively growing) bacterial suspensions were diluted 1:10 by adding 0.01 mL of the bacterial suspension to 0.09 mL of the ciprofloxacin release medium. Samples were incubated at 37°C for 20 hours, after which serial dilutions were plated on nonselective BHI agar without antibiotics at 37°C for 48 hours to allow slow-growing colonies to be recovered. Colonies that did grow were recultured and assessed for ciprofloxacin susceptibility on BHI agar with and without $50 \mu\text{g/mL}$ of ciprofloxacin. Each of the samples was tested in triplicate.

Statistics

Data are presented as the mean $\pm$ SD.

Results

Drug-PLGA Films and pHEMA Coating

The fluorescein-PLGA films (Table 1) composed of high-molecular-mass (118 kDa) PLGA produced thin and flexible films with a uniform appearance. The films made from low-molecular-mass (18 kDa) PLGA were also regular in appearance, but were less flexible and more difficult to remove from the fluoropolymer (Teflon; DuPont) wells. The thickness of the films varied little, measuring between 200 and $250 \mu\text{m}$. Ciprofloxacin-PLGA (1:1 ratio, high [118 kDa] molecular mass) films were also thin and flexible and had an even distribution of ciprofloxacin throughout the film on gross inspection. The ciprofloxacin films measured between 215 and $235 \mu\text{m}$ in thickness. All the films became slightly less pliable after lyophilization.

The drug-PLGA films were easily contained between layers of pHEMA, as described in the Methods section, creating a prototype contact lens. When hydrated, the lenses were flexible and had an optically clear central aperture. Entrapping drug between the pHEMA layers in the absence of a PLGA film was technically difficult and frequently led to the spread of drug into the central optical aperture. A few of the prototype contact lenses containing the films developed bubbles within the pHEMA after 4 weeks of drug release.

Production of lens prototypes where fluorescein powder was deposited alone (i.e., without a polymeric film) was problematic. The powder tended to stray into the optic axis, a problem made worse when the second covering layer of pHEMA was added. In that context, UV polymerization of the second layer was less successful than that of the first layer, forming a tacky, rough, malformed, or incomplete surface.

All devices contained approximately 20 mg of either fluorescein or ciprofloxacin.

Scanning Electron Microscopy

The morphology of sections of the drug-containing PLGA films was studied by scanning electron microscopy. Fluorescein (Fig. 2A) was relatively uniformly dispersed within the PLGA film. In contrast, ciprofloxacin crystals (Fig. 2B) appeared to be concentrated toward one side of the PLGA film—the gravity-dependent (bottom) side during manufacture.

Drug Release

Uncoated fluorescein-PLGA films (PLGA65:35, high [118 kDa] molecular mass) showed drug release with linear kinetics for 10 days, releasing 65% of the fluorescein in the film, with little release thereafter (Fig. 3). Coating of the fluorescein-PLGA films with pHEMA resulted in significantly slower and longer release kinetics, providing more than 4 weeks of release with zero-order kinetics, while releasing 10% of the total fluorescein in the film (Fig. 3A). Release from both devices was significantly slower than the dissolution rate of free fluorescein powder (Fig. 3A). When the drug was entrapped between pHEMA layers without a PLGA film, the release profile was slower than that from drug in the PLGA film but faster than that from drug in a PLGA film coated with pHEMA. There was a greater degree of variability in fluorescein release than was observed when the drug was contained in PLGA surrounded by pHEMA (note the larger coefficient of variation for the former group in Fig. 3A), perhaps because of the surface imperfections that were described earlier. Therefore, both the PLGA film and the pHEMA appeared to be contributing factors in controlling the release of fluorescein from the prototype contact lens.

The pHEMA-coated PLGA film continued to release for at least 100 days (Fig. 3B), at which time 33% of encapsulated fluorescein was released. Release continued to demonstrate the same zero-order kinetics for 60 days and then increased to a higher, but still zero-order release rate. After 100 days of release, the PLGA film within the HEMA layer retained a yellow coloring, indicating that much of the fluorescein was still retained inside the prototype lens.

Varying the ratio of PLGA to drug changed the rate of release of fluorescein from PLGA films coated with pHEMA, while maintaining zero-order kinetics through 4 weeks (Fig. 4). Increasing the proportion of PLGA to fluorescein (keeping the mass of fluorescein constant) slowed the release of fluorescein, as did increasing the molecular mass of the PLGA (Fig. 5). Both modifications maintained near zero-order release kinetics.

Antibacterial prototype contact lenses were fabricated by coating ciprofloxacin-PLGA 65:35 (high [118 kDa] molecular mass) films with pHEMA. They also demonstrated a small initial burst of drug release in the first 24 hours, followed by more than 4 weeks of zero-order kinetics (Fig. 6). After the initial burst, each prototype contact lens released an average mass of 134 μg of ciprofloxacin per day. Over the course of a month, the lenses released 23% of the ciprofloxacin that they initially contained.

Antimicrobial Activity

Ciprofloxacin eluted from the prototype contact lenses had the same HPLC profile as that of commercial ciprofloxacin (Cipro IV; Bayer Pharmaceutical Corp.). We tested the antibacterial effectiveness of ciprofloxacin released from the contact lenses (Table 2) to confirm that it was not impaired by the numerous processing steps to which it had been exposed (ultraviolet light, temperature and pH changes, and interaction with other materials) and by extended presence in solution at 37°C. The release medium was collected from four ciprofloxacin-containing contact lenses (same samples as Fig. 5) on the 28th day of release and tested against *S. aureus* clinical isolates grown in antibiotic-free BHI-sucrose-PBS. In addition, samples were taken from one lens at days 2 and 14 of release. In all cases, the samples represented approximately 16 hours of release of drug. With bacterial inocula of less than 10^5 cells, there was complete inhibition of all three strains of ciprofloxacin-sensitive *S. aureus* (MEEI-IB003, -IB012, and -IB013) by the contact lens release medium (data not shown). Bacterial inocula of 10^6 cells or greater still resulted in complete inhibition of ciprofloxacin-sensitive *S. aureus* at days 2, 15, and 28 of release (Table 2). At the higher bacterial inocula, rare bacterial isolates grew, albeit with very low counts (30 or less, compared with billions in untreated controls), because of the development of resistance to ciprofloxacin.

Discussion

A prototype contact lens was created with a diameter and thickness that are within the range of dimensions found in commercially available contact lenses that released a medication with zero-order kinetics over an extended period. Drug release from the contact lens was significantly influenced by both the drug-PLGA film and by the pHEMA coating.

These prototype contact lenses provided zero-order kinetic drug release for 4 weeks, which is the longest duration for which contact lenses are currently approved. These lenses can clearly provide drug release for much longer periods, a goal that may be of value in the developing world, or in patients who require very extended therapy, as in the context of keratoprotheses, where lenses may be worn for months or years.^{41,42} This study, performed in release conditions with the same pH, salinity, and temperature as the human tear film, compared favorably to previous reports on contact lens drug delivery. The rate of drug

release could be controlled by changing either the ratio of drug to PLGA within the polymer film or by varying the molecular mass of the PLGA. These observations are consistent with the increased barriers to drug diffusion in films containing higher PLGA contents (i.e., a lower loading level of drug)⁴³ or from the better film-forming, high-molecular-mass polymers.⁴⁴ Although PLGA is biodegradable, it is unlikely that degradation of the polymer contributed significantly to the rate of drug release observed during the 4 weeks of release, since 50:50 PLGA typically degrades after 1 to 2 months and 65:35 PLGA after 3 to 4 months.⁴⁵

This drug release study was performed in such a manner that the concentrations of fluorescein and ciprofloxacin were always well below their solubility saturation limits, so that there was no impedance to efflux from the devices. Although one should be cautious when extrapolating in vitro release study results to an in vivo situation, it appears that this drug-eluting contact lens design could continuously deliver a therapeutic concentration of ciprofloxacin to the eye. The prototype contact lenses released 134 μg of ciprofloxacin per day (0.09 μg per minute). The human eye produces 2 to 3 mL of tears each day, equivalent to 1 to 2 μL per minute. If this contact lens released the same amount of drug per minute in an eye producing 3 μL of tears during the same time interval, then the drug would achieve a tear concentration of 31 $\mu\text{g}/\mu\text{L}$. This is well above the MIC₉₀ for ciprofloxacin (2 $\mu\text{g}/\mu\text{L}$) against the most common ocular flora.

Ciprofloxacin showed complete killing of *S. aureus* at inocula of 10⁵ cells. The study demonstrated no change in the bactericidal activity of the ciprofloxacin in the release medium collected at the beginning, middle or end of the 4-week release study (Table 2). In addition, the ciprofloxacin released from all the lenses at the conclusion of the month demonstrated the same bactericidal activity (Table 2). With the use of inocula greater than 10⁶ cells, rare ciprofloxacin-resistant bacteria emerged in all release medium tested. This is consistent with previous reports that more resistance emerges with higher bacterial loads.^{46–48} Therefore, some conditions, such as corneal ulcers with purulent discharge, may require a higher ciprofloxacin concentration than was found in our release medium. However, as already mentioned, a higher drug concentration may very well be obtained in the eye, particularly in the post-contact lens tear lake—the fluid space between the cornea and the contact lens. Ultimately, in vivo studies are needed to confirm the final concentration of ciprofloxacin in a living eye and in the post-contact lens tear lake.

Ciprofloxacin was used here because of its broad-spectrum antibacterial properties and commercial availability, and because it is well studied as a topically applied ophthalmic antibiotic.⁴⁹ Because ciprofloxacin is associated with greater antibacterial resistance and the development of corneal crystal deposits after long-term use,⁵⁰ future studies may employ other fluoroquinolone antibiotics. Medications from other classes of antimicrobials, including antifungals, steroids, and antiallergy and -glaucoma medications, could also be incorporated into the contact lens drug-eluting platform given the flexibility of the film-forming method to incorporate drugs with a range of hydrophobicities and solubilities.

We used PLGA and pHEMA because both have been well studied and are FDA approved for ocular use. pHEMA is a polymer that has been extensively investigated and used by the

contact lens industry since the 1960s.^{38,39} PLGA's safety profile has been well documented, and the U.S. Food and Drug Administration has approved PLGA for use in ocular drug delivery, including its use in intravitreal, subconjunctival, and subconjunctival routes of administration.^{34–37} PLGA has also been incorporated into a device intended for topical drug delivery to the eye. Huang et al.⁵¹ found no ocular irritation from a timolol-PLGA film placed in the inferior fornices of rabbit eyes.

Clearly, there are many aspects of this prototype drug-eluting contact lens that may require optimization before commercialization. Although contact lenses are available that are as thick as 1 mm (and a diameter up to 24 mm; e.g., Precision Sphere; Kontour, Inc., Hercules, CA),⁵² like our prototype, thinner lenses would probably be better for comfort, oxygen diffusion, and other parameters. The polymeric footprint could be modified to improve oxygen diffusion, if that turns out to be a problem. For example, a thin, crescent-shaped film could be incorporated into the superior periphery of a large-diameter contact lens. The thin film would have a negligible effect on oxygen permeability and would be cosmetically undetectable, since it would be covered by the upper lid. We used the contact lens material pHEMA, which has lower oxygen permeability than some of the newer silicon hydrogels that constitute the material for some contact lenses.³⁹ Such materials could also be used for drug-eluting lenses. Finally, the manufacturing process could be optimized in many respects to minimize cost and increase efficiency.

One important concern in contact lens development is shelf life. Conventional contact lenses are often stored for many months at room temperature. It would be expected that the PLGA component of the prototype contact lens described here would degrade substantially and variably during that time. That problem could be circumvented by using a nondegradable polymer. (We used this particular polymer system primarily because of its safety and the fact that its drug-releasing characteristics are extremely well understood.) Even so, drug elution into the liquid storage medium would continue. One way to resolve that problem would be to store the lenses in medium that contains a concentration of drug adequate to stop drug efflux from the lens. Another would be to store the lenses in a dehydrated state, so that there would be no drug efflux, and no polymer degradation. Whether the latter approach would be detrimental to the lens' optical properties remains to be determined.

Conclusions

We have designed a prototype contact lens for sustained drug delivery by incorporating a thin drug-PLGA film into a pHEMA hydrogel, the same polymer used for conventional soft contact lenses. This system of ocular drug delivery showed zero-order release kinetics at therapeutically relevant concentrations for 1 month. The drug release rate can be adjusted by changing the polymer molecular mass and the proportion of medication within the drug-PLGA film. This prototype contact lens design could be used as a platform for ocular drug delivery and may have widespread therapeutic applications.

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Figure 1. Photograph (*left*) and schematic (*right*) of a prototype contact lens made of pHEMA hydrogel coating a PLGA film (in this case with ciprofloxacin) with a 5-mm clear optical aperture.

Figure 2.

Scanning electron micrographs of a fluorescein-PLGA film (**A**) and a ciprofloxacin-PLGA film (**B**). The *top* and *bottom* margins of the figure are the top and bottom of the film, respectively. The ciprofloxacin-PLGA film demonstrated a higher density of ciprofloxacin at the bottom of the film (**B**). Magnification: (**A**) $\times 300$; (**B**) $\times 200$.

Figure 3. (A) 28 days and (B) 100 days. Cumulative release from free fluorescein powder, fluorescein-PLGA films, fluorescein coated with pHEMA and fluorescein-PLGA films coated with pHEMA. Data are the mean $\pm$ SD.

Figure 4.

Cumulative release of fluorescein contained in a pHEMA coatings, without PLGA (fluorescein, no PLGA), or with various proportions of fluorescein to PLGA. The molecular mass of fluorescein per device is constant between groups. Data are the mean $\pm$ SD.

Figure 5. Cumulative release of fluorescein from low (18 kDa)- and high (118 kDa)-molecular-mass PLGA films coated with pHEMA. Data are the mean $\pm$ SD.

Figure 6. Ciprofloxacin release from pHEMA-coated high-molecular-mass (118 kDa) PLGA 65:35 films with a 1:1 ratio of PLGA to ciprofloxacin. Data are the mean $\pm$ SD.

Table 1

Composition of Lens Prototypes

Fluorescein/PLGA Ratio	Fluorescein (mg)	PLGA (mg)	L:G Ratio [*]	PLGA Molecular Mass
2:1	20	10	65:35	118 kDa (high)
1:1	20	20	65:35	118 kDa (high)
1:2	20	40	65:35	118 kDa (high)
1:1	20	20	50:50	118 kDa (high)
1:1	20	20	50:50	18 kDa (low)

Fluorescein-containing PLGA films were created with the same mass of fluorescein and different masses of PLGA, various ratios of lactide to glycolide, and PLGA polymers of high (118 kDa) or low (18 kDa) molecular mass.

* Ratio of lactide to glycolide in PLGA.

Growth of Ciprofloxacin-Resistant and -Susceptible Strains of *S. aureus* after Exposure to Ciprofloxacin Eluted from Four Separate Prototype Contact Lenses

Table 2

<i>S. aureus</i>		Time Point of Ciprofloxacin Release				
Strain	Inoculum	2 Days	14 Days	28 Days	No Ciprofloxacin	
MEEI-IB01 (ciprofloxacin resistant)	8.4×10^6	9.0×10^9	5.0×10^9	$3.0 \times 10^9 - 1.0 \times 10^{10}$	4.0×10^9	
MEEI-IB003 (ciprofloxacin susceptible)	6.6×10^6	0	0	0	2.0×10^9	
MEEI-IB012 (ciprofloxacin susceptible)	8.5×10^6	0	0	0	1.5×10^{10}	
MEEI-IB013 (ciprofloxacin susceptible)	8.0×10^6	0	0	0	8.0×10^9	
No bacteria	0	0	0	0	0	

Data reflect drug released over 16 hours preceding the stated time point and are averages of triplicates of single samples. At 28 days, the data are averages from triplicates of four separate samples.