Ciprofloxacin Release Profiles from Novel Contact Lens Materials

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Introduction

- Soft contact lenses were first proposed as a vehicle for ophthalmic drug delivery by Sedlacek in 1965. The aim is for the lens to provide slow drug release to the ocular surface, to increase bioavailability and penetration of the drug through the cornea. [1-4]
- Silicone hydrogel (SH) contact lenses have an advantage over conventional soft contact lenses in that they are able to transmit more oxygen so that the SH lenses are better suited for longer wear. This characteristic is important as a patient may need to wear their therapeutic lenses continuously for up to two weeks.[2]
- Ciprofloxacin (CP) is a broad-spectrum antibiotic available as an ophthalmic solution or ointment. It kills bacteria by inhibiting DNA synthesis and is effective against both gram-positive and gram-negative bacteria.[5]
- Molecular imprinting, a technique adapted from chromatography, is designed to specifically remove components from solutions. By polymerizing the materials in the presence of "templates", molecular memory is created within the material. The memory can potentially retard the movement of the template out of the material, leading to extended release times.[6]

Purpose

The purpose of this study was to evaluate molecular imprinting techniques as an avenue in the creation of novel contact lens materials for ciprofloxacin drug delivery. Uptake and release kinetics of created materials were then compared to non-imprinted materials.

Materials & Methods

Solution Preparation

A 3 mg/ml ciprofloxacin solution (Sigma, Oakville, ON) was prepared in a modified phosphate buffered saline solution (PBS) containing glucose and urea. The pH was adjusted to approximately pH 4.0 with hydrochloric acid to ensure complete solubility of ciprofloxacin. Linear standard curves were created from the stock drug solution to convert fluorescence readings into concentrations. Amber vials were used throughout the experiment to minimize light exposure to the drug, which is light sensitive.

Materials

Two soft lens materials (pHEMA[a]; pHEMA TRIS[b];) were prepared with and without hyaluronic acid of 132 kDa molecular weight. Molecular imprinting was performed by dissolving ciprofloxacin powder (1% by weight) into the samples before polymerization. Hydrogel discs were punched out from a sheet of material with a uniform diameter of 7.5 mm and a dry weight range from 0.0205 g to 0.0312 g.

Uptake Kinetics

At room temperature, four discs of a given lens type were rehydrated in artificial tear solution for 24 hours and then placed in a solution of 0.3% ciprofloxacin for one week. Aliquots of the solutions were removed at specified time points and measured on a Hitachi F4500 Fluorescence Spectrophotometer at 274 excitation and 419 emission wavelengths.

Release Kinetics

The lens discs from the uptake phase were transferred into the PBS after surface residual drug solution was removed with a brief rinse in PBS. To approximate in-eye conditions, the lens discs were incubated in a 34°C shaking water bath. At specified time points over 2 weeks, aliquots of the solutions were taken out and measured as in the uptake kinetics.

Results–Uptake Kinetics

Figure 1. Uptake during first 5 hours into pHEMA and Ciprofloxacin Imprinted pHEMA-TRIS

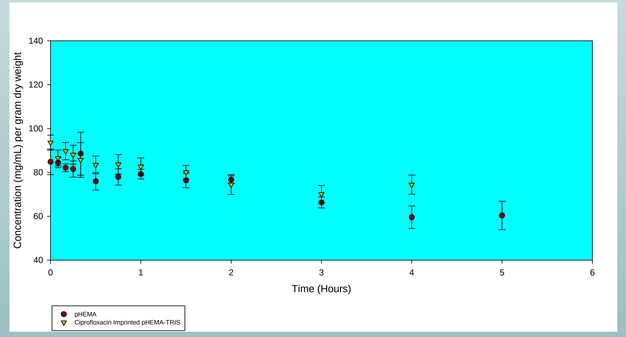


Figure 2. Uptake during first 5 hours into pHEMA-HA and Ciprofloxacin Imprinted pHEMA-TRIS-HA

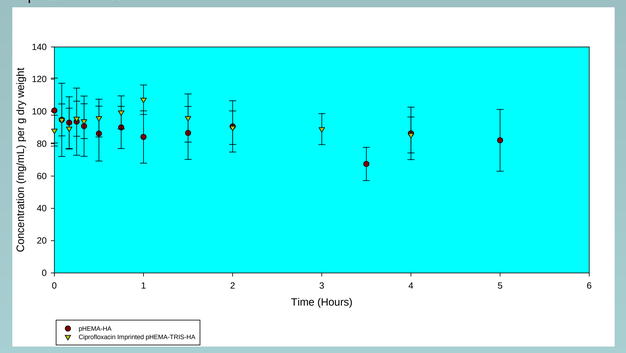
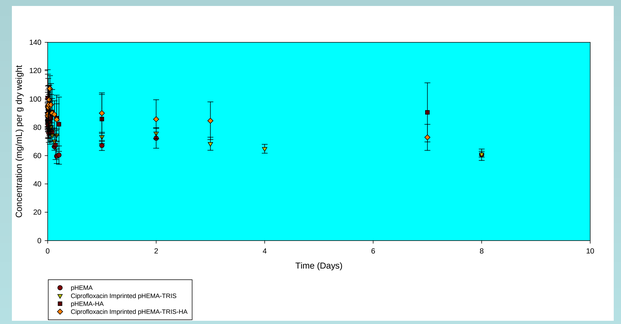


Figure 3. Uptake over 1 week into pHEMA, pHEMA-HA and Ciprofloxacin Imprinted pHEMA-TRIS and pHEMA-TRIS-HA



Results–Release Kinetics

Figure 4. Release during first 5 hours from pHEMA, and Ciprofloxacin Imprinted pHEMA-TRIS

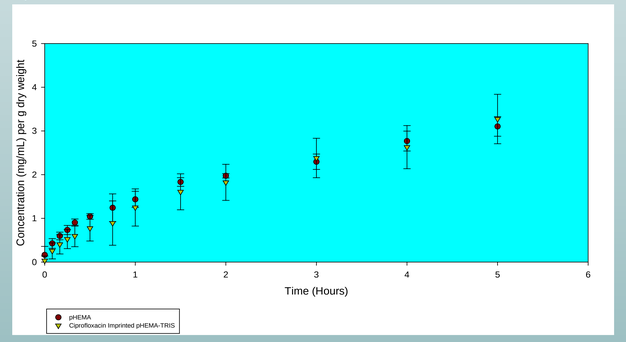


Figure 5. Release during first 5 hours from pHEMA-HA and Ciprofloxacin Imprinted pHEMA-TRIS-HA

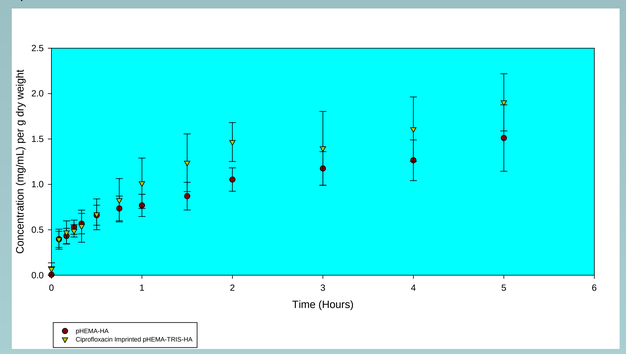
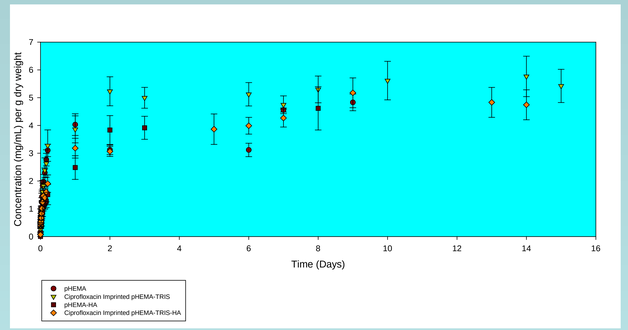


Figure 6. Release over 2 weeks from pHEMA, pHEMA-HA, and Ciprofloxacin Imprinted pHEMA-TRIS and pHEMA-TRIS-HA



Results– Total CP Released

Table 1 . Total mg of ciprofloxacin release from different lens types

Material	mg/lens mean ± SD
pHEMA	0.288 ± 0.013
pHEMA-HA	0.234 ± 0.025
Ciprofloxacin Imprinted pHEMA TRIS	0.328± 0.035
Ciprofloxacin Imprinted pHEMA-TRIS-HA	0.268 ± 0.019

Conclusions

- Molecular imprinting techniques can be successfully used to extend the release profiles of drugs from contact lens materials.
- Further refinements are needed to optimize both drug release and contact lens properties to create a viable combination device.

References

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Notes

a. pHEMA; poly(2-hydroxyethyl methacrylate)
b. pHEMA TRIS; pHema and Methacryloxypropyltris (trimethylsiloxy)silane (TRIS)

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