Recombinant Silk-Elastinlike Protein Polymer as an Ocular Drug Delivery System

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Statement of Purpose:

We evaluated the potential of genetically engineering protein polymer SELP-47K as an ocular drug delivery system. Specifically, the in vitro cumulative release of ciprofloxacin from SELP-47K films was examined, and the inhibitive effects of released drug on the growth of ciprofloxacin sensitive E. coli 136 were investigated.

Methods:

(1) *Sample Preparation:* The protein polymer SELP-47K was provided by Protein Polymer Technologies, Inc. (San Diego, CA). SELP-47K films were cast from aqueous solution containing ciprofloxacin, and treated using EtOH vapor for 48 hr or MeOH vapor for 24 hr. (2) *Physical stability of SELP-47K films:* The stability of EtOH- and MeOH-treated films was evaluated at 37 °C in 1x PBS containing 0.2 mg/ml NaN_3. The percentage of remaining mass was examined over a time period of 7 days. (3) *Drug release study:* The ciprofloxacin release from both EtOH- and MeOH-treated films was evaluated in 1x PBS at 34°C (ocular temperature). At given times, an aliquot of solution was withdrawn and replaced by an equal volume of fresh PBS. The amount of ciprofloxacin was measured by solution absorbance at a wavelength of 270 nm. (4) *Ciprofloxacin antimicrobial assay:* The antibacterial effectiveness of eluted ciprofloxacin was tested against ciprofloxacin sensitive E. coli 136 and resistant E. coli 132 over a time period of 4 hrs. At predetermined time intervals, the concentration of the bacteria was quantified by absorbance at 600 nm.

Results:

The EtOH-treated SELP-47K films lose 15% mass in the first 48 hrs, but no further loss after 2 days. In contrast, MeOH-treated films are stable in 1x PBS, and show no mass loss in 7 days (Fig. 1). It appears that MeOH treatment induces more stable structures than EtOH treatment does. As shown in Fig. 2, both EtOH- and MeOH-treated films displayed the first-order release kinetics for 108 hrs. The EtOH-treated films released ciprofloxacin at a higher rate than the MeOH-treated films. The release rate constants obtained from curve fitting are 0.08 and 0.0465 hr^{-1} for EtOH- and MeOH-treated films, respectively. After 108 hrs, the cumulative ciprofloxacin release reaches 85% and 70% from the EtOH- and MeOH-treated films, respectively. Likely, the reduced release rate and magnitude of ciprofloxacin from MeOH-treated films is related to their enhanced stability. Upon the release of ciprofloxacin from the drug-eluted SELP-47K films, a complete inhibition of ciprofloxacin sensitive E. coli 136 was observed, comparable to that induced by fresh ciprofloxacin (Fig. 3). For comparison, the ciprofloxacin resistant E. coli 132 exposed to ciprofloxacin continuously grew (data not shown).

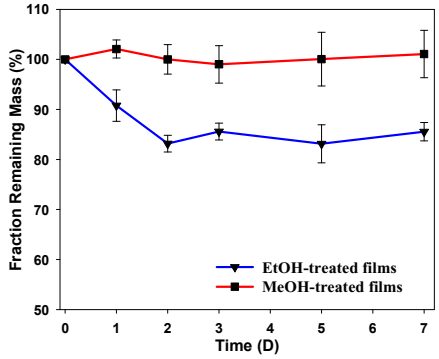

Fig. 1 Mass retention of EtOH-, and MeOH-treated SELP-47K films in 1x PBS.

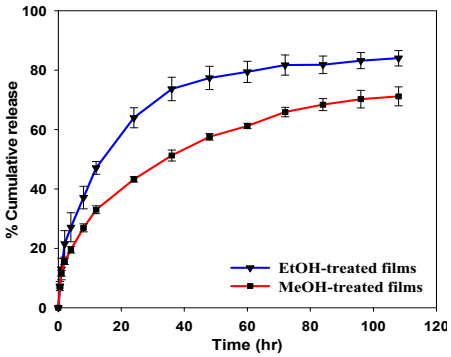

Fig. 2 Cumulative ciprofloxacin released from EtOH- and MeOH-treated SELP-47K films.

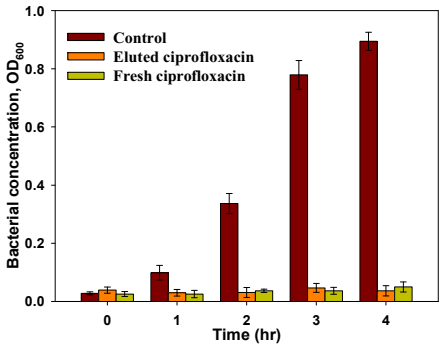

Fig. 3 Growth of ciprofloxacin-sensitive EC 136 in the presence of eluted and fresh ciprofloxacin, and in the absence of ciprofloxacin as a control.

Conclusions:

The antibiotic ciprofloxacin was incorporated into SELP-47K films for ocular drug delivery. Both EtOH- and MeOH treated films showed first-order release kinetics. The released ciprofloxacin from the protein polymer films effectively inhibited growth of bacteria. Thus, the recombinant protein polymer SELP-47K may be a promising material for drug eluting contact lenses.