Effect of Plasticizers and Drug-Loading on the Properties of Drug Delivery Films

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Statement of Purpose

Chronic inflammation and unconstrained wound healing can cause contracted fibrotic scar tissue with functional and aesthetic consequences. Theoretically, the well timed and sequenced release of drugs can permit regenerative control, thereby preventing excessive scarring. Films composed of 70:30 wt% cellulose acetate phthalate (CAP) and Pluronic F-127 have been proven to be an erosion controlled system, making them an attractive combination for this application. However, CAP-Pluronic films are typically rigid structures that are unable to conform to the varying geometries of wound sites. In order to impart flexibility, the effects of plasticizers on mechanical properties and erosion kinetics of CAP-Pluronic films were studied. The effects of drug in addition to plasticizers on the mechanical and degradation properties of the films were also studied.

Methods

The CAP, Pluronic, plasticizer [triethyl citrate (TEC) or tributyl citrate (TBC)], and anti-inflammatory drug (ketoprofen) were dissolved in acetone, sonicated, and cast in Teflon dishes layer by layer. The dishes were left on the lab bench to speed up the evaporation of acetone. Erosion was measured during destructive degradation tests in phosphate-buffered saline (PBS). Tensile testing measured the mechanical properties caused by the plasticizers and drug. Mechanical samples that were degraded first were left in PBS for 2 hours, dried, and then tensile tested.

Results

The TEC films degraded slightly faster than TBC but not significantly. As the plasticizer concentration increased, degradation rates and mass loss after 16 hours increased (Figure 1). Adding ketoprofen increased the rate of degradation. The mechanical testing showed that dry TEC films had lower moduli (Figure 2) and ultimate tensile strengths (UTS) than TBC films. The TEC films elongated much more than did the TBC films.

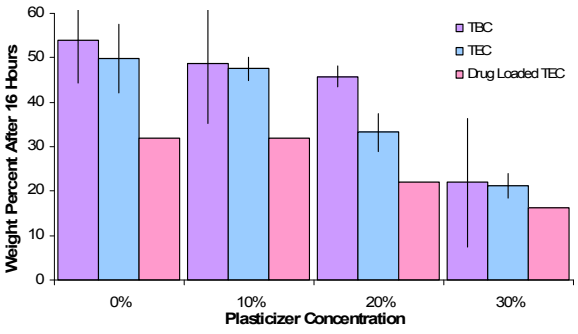

Figure 1. Weight percentage of TBC and TEC films remaining after 16 hours of degradation.

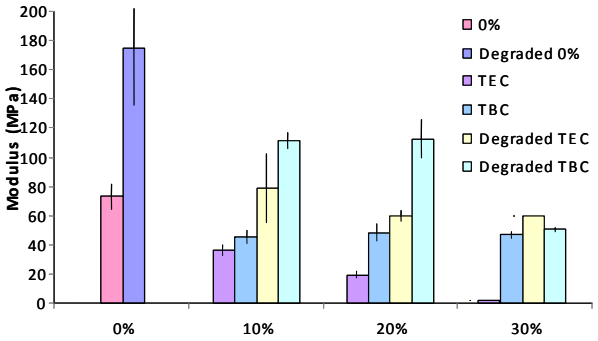

Figure 2. Moduli of TBC and TEC films.

Degradation increased the UTS greatly. After 2 hours, plasticizer had no significant effect on the % elongation in any of the samples tested. The addition of plasticizer and ketoprofen into the films caused them to have an even lower modulus and UTS than with plasticizers alone. Also, incorporation of ketoprofen into plasticized films caused them to degrade faster than they otherwise would.

Discussion

Leaching of plasticizer from the films during degradation changed their mechanical properties. For the same weight %, TEC had greater effect (i.e., lower modulus and higher % elongation) than TBC. More TEC molecules were present in films causing a higher degree of plasticization. TBC films remained more plasticized after degradation than did TEC films. TBC molecules are larger and more hydrophobic than TEC and therefore take longer to leach out of films. Ketoprofen behaved as a plasticizer in the CAP-Pluronic system. The addition of ketoprofen into the plasticized films resulted in lower mechanical strength and faster degradation. Thus, including ketoprofen into the system requires less plasticizer for the same mechanical effect.

Conclusions

Degradation and mechanical properties of CAP-Pluronic films can be varied by the type and amount of plasticizer and the addition of drugs, thereby making this system tunable in its behavior for different applications, including use as a bioerodible drug delivery film.

Acknowledgements

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