How Different Drugs Affect the Properties, Degradation, and Release Profiles of Drug Delivery Films

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Statement of Purpose

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 degradable polymer for drug delivery. CAP-Pluronic films are typically rigid and unable to conform to varying geometries that may be needed for dental, wound healing, or other applications. In previous work, plasticizers were added to impart flexibility. The objective of the present studies was to investigate effects of plasticizers in combination with drug on drug release, mechanical properties, and degradation.

Methods

Films were prepared using solvent evaporation casting. The CAP and Pluronic were combined in a 70:30 weight ratio. Plasticizer [triethyl citrate (TEC) or tributyl citrate (TBC)] was added at a 0, 10, or 20 wt%. The same molar amount of either antioxidant drug, quercetin, or anti-fibrotic drug, pirfenidone, were included in the mixture, and then all components were dissolved in 8 ml acetone, sonicated, and cast in Teflon dishes. The dishes were left in a 10ºC refrigerator during the evaporation of acetone. Mechanical properties were determined according to ASTM D1708. Film erosion was measured by incubating samples in phosphate-buffered saline (PBS) on an orbital plate shaker at 37ºC. Aliquots were taken every hour and later analyzed using high performance liquid chromatography (HPLC) to determine drug release profiles.

Results

The elongation before failure is related to the flexibility of a material. Increasing plasticizer content increased the elongation. Drug was also shown to act as a plasticizer. For the same molar concentration, quercetin-loaded films had twice as much or greater the elongation than films loaded with pirfenidone (Figure 1). As elongation increased, the ultimate tensile strength and modulus decreased (not shown).

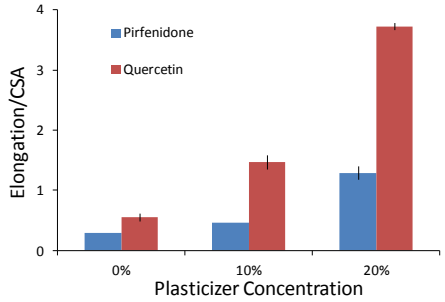

Figure 1. Effect of drug and plasticizer (TEC) concentration on elongation.

Plasticizer concentration did not significantly affect the rate of film erosion. Quercetin-loaded films had a more linear drug release and erosion compared to those with pirfenidone (Figure 2).

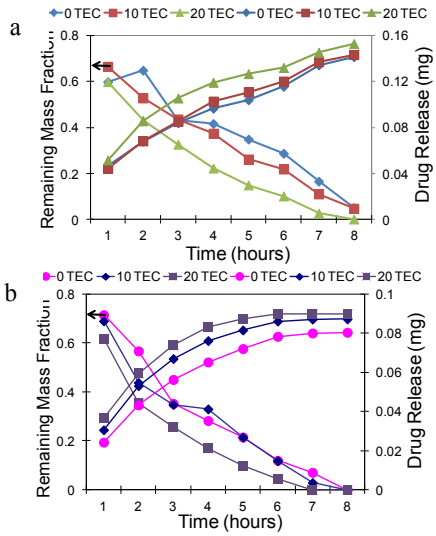

Figure 2. Degradation and cumulative release profiles for TEC-plasticized films loaded with (a) quercetin and (b) pirfenidone.

Discussion

Quercetin plasticized the CAP-Pluronic films to a greater degree than did pirfenidone. Quercetin has a MW 1.63 times larger than pirfenidone and may separate the polymer chains more than pirfenidone. The larger separation could allow the chains to slide past each other more easily, resulting in higher elongations and lower ultimate tensile strengths and moduli. Pirfenidone-loaded films had a biphasic release. The rates of erosion and release were the same for the first half of mass loss, suggesting erosion-based release, followed by an increased drug release rate compared to erosion, suggesting that diffusion was a factor. Because pirfenidone is a smaller, more hydrophilic molecule than quercetin it may leach out of the system creating pores and ultimately causing the biphasic release, whereas the hydrophobic quercetin does not leach as quickly.

Conclusions

Mechanical properties, erosion, and drug release can be tailored by changing the plasticizer content and choice of drug, causing CAP-Pluronic films to be an appealing system for a flexible drug delivery film.

Acknowledgements

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