CAP-Pluronic Film Based Multiple Drug Delivery System

Sharath kumar C. Sundararaj[1], Mark V. Thomas[2], Thomas D. Dziubla[3] and David A. Puleo[1]

[1] Center for Biomedical Engineering, University of Kentucky, Lexington, KY, USA
[2] College of Dentistry, University of Kentucky, Lexington, KY, USA
[3] Department of Chemical and Materials Engineering, University of Kentucky, Lexington, KY, USA

Statement of Purpose

Physiological processes in the human body work based on complex cascades of events involving multiple typesof cells and biomolecules. A defect or dysfunction in an organ or tissue will thus require more than one factor to be addressed for optimally treating it. This often creates the need for multiple drugs to be administered for treating a particular condition. The main aim of this research is to develop a multiple drug delivery coating/film system based on a cellulose acetate phthalate -Pluronic F-127 (CAPP) association polymer.CAPP association polymers are biodegradable by surface erosion, which makes their drug release kinetics easier to control.This CAPP association polymer system can be applied as multiple layers of coatingon an implant to deliver multiple drugs in the required temporal sequence.

Methods

CAPP films were prepared by dissolving CAP and Pluronic in the ratio of 70:30 in acetone. This polymer solutionalong with 5wt%of drugwas cast in Teflon dishes,and the films were obtained by solvent evaporation at 4 °C. Metronidazole (antibiotic to fight bacterial infection) and ketoprofen (anti-inflammatory to fight the inflammation that occurs due to infection) were the first drugs loaded in the CAPP films. Multilayered films were made bycoatingalternating layers of blank and drug-loaded CAPP on top of eachother in the required sequence.Two types of multilayered films were fabricated. One comprised alternating layers of same drug (metronidazole) to achieve intermittent drug release. The other type of multilayered film consisted of alternate layers of different drugs (metronidazole and ketoprofen) toachieve sequential release of more than one drug in a particularorder. Both the single and multilayered drug-loaded films were pressed ontoa polystyrene substrateto simulate an implant and enable unidirectional drug release.The drug-loaded filmswere degraded in phosphate buffer saline (PBS) at 37 °C. The release samples were collected and replaced with fresh PBS at regular time intervals.The release samples were analyzed for the concentration of metronidazole by measuring UV absorbance at 318 nm. The concentration of the ketroprofen releasedwas determined using HPLC. The measured release concentrations of the drugs were used to construct drug release profiles.

Resultsand Discussion

The releaseprofilefrom single layer CAPP filmswith metronidazole or ketoprofen showed zero-order release of drug over the course of polymer degradation indicating surface erosion-based release of drug.The cumulative release of the single layer films also showed a linear drug release pattern that was expected. The multilayered films with alternating metronidazole and blank layer showed intermittent release of metronidazole (Figure 1). Similarly,the multilayeredcoatings with alternating layers of different drugs showed sequential release of metronidazole and ketoprofen (Figure 2).This shows the ability of the device to release more than one type of drug in the required temporal sequence.

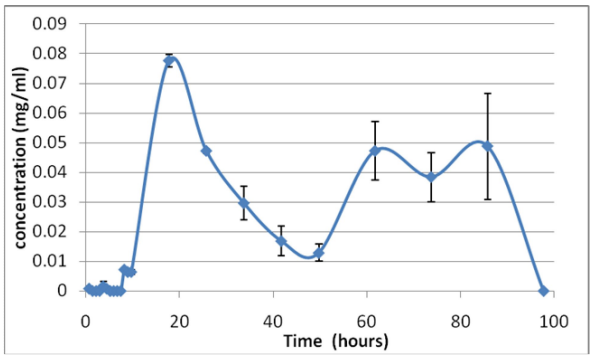

Figure 1.Intermittent release of metronidazole from multilayered CAPP.

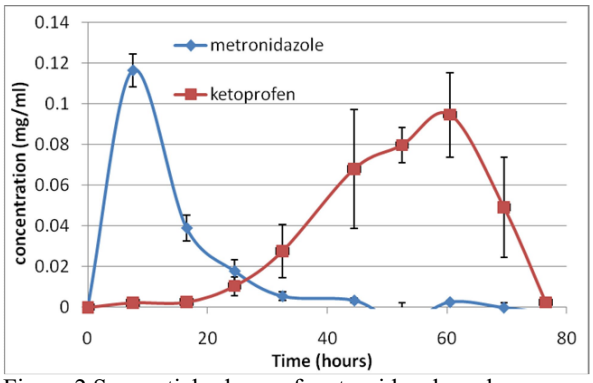

Figure 2.Sequential release of metronidazole and ketoprofen from multilayered CAPP devices.

Conclusion

The primary aim of this research,to obtain surface erosion-based release of drugs from CAPP films,has been achieved. Intermittent release of the same drug and sequential release of more than one drug was demonstrated. CAPPcoated in the form ofmultilayered filmswill serve as a model for development of bioerodible materials for delivering different drugs for treatment of pathophysiologicalconditions in which temporal control of drug delivery is required.

Acknowledgements

This research was supported by the NIH (DE019645).