Development of Mucoadhesive Films with Increased Residence Time for Treatment of Local Disorders

S.K. Ramineni[1], L.L. Cunningham, Jr.[2], T.D. Dziubla[3], and D.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]Chemical and Materials Engineering, University of Kentucky, Lexington, USA

Introduction

Oral mucosal delivery has gained prominence in the last two decades because the rich vasculature of the tissue enables rapid delivery and avoidance of first pass metabolism. Although commercial mucoadhesive systems are used for systemic delivery, they are not currently available for treatment of local conditions. Disorders, such as oral dysplastic lesions and mucositis, as well as tissue regeneration may require extended drug release and protection from the dynamic oral cavity. Literature review of developed mucoadhesive films shows that most release drug for only 4 to 6 hours (J Control Rel 99:73, 2004; Int J Pharm 307:318, 2006; J Biomed Mater Res A, 89:1063, 2009; Pharm Dev & Technol 14:199, 2009). Hence, the aim of the current research was to slow erosion and increase the residence time of mucoadhesive films previously developed for oral dysplastic lesions by incorporating a hydrophobic polymer.

Methods

Films were made from a blend of polyvinylpyrrolidone (PVP) carboxymethylcellulose (CMC). To adjust properties, a hydrophobic polymer, Eudragit RL-PO was incorporated. RL-PO was added to the PVP:CMC films in two ratios (5% and 20% w/w). An immune response modifier, imiquimod, solubilized in 3:7 [methanol:acetate buffer (100 mM, pH4.0)] was added to the aqueous polymer solution with or without RL-PO solubilized in methanol.

Swelling profiles of samples from different films loaded with increasing RL-PO amounts were analyzed. Films loaded with 20% RL-PO were selected from this experiment and further tested for their release profiles and *ex vivo* mucoadhesion time.

Bilayered (films with a poly(ethylene-co-vinyl acetate) backing layer) film samples were adhered to the mucosal surface of pre-hydrated porcine buccal tissue attached to a glass slide with cyanoacrylate glue. The glass slide was moved up and down into 700 mL of simulated saliva at a rate of 18 cycles/min. The time at which the backing layer was completely detached from the tissue was recorded as the *ex vivo* mucoadhesion time. In addition, thicker (0.39 mm) films were also prepared and compared with the thinner (normal; 0.30 mm) films to assess the effect of thickness.

Results and Discussion

Increased content of RL-PO (more than 20% (w/w) of PVP and CMC) resulted in formation of thick slurry with poor handling properties in terms of homogeneity and the casting process. The swelling index (Fig. 1) of films loaded with 20% RL-PO was significantly different ($p<0.05$) from that of the original films after 180 minutes and from 5% RL-PO films after 240 minutes. Unlike the other film types, 20% RL-PO films did not erode with time and stayed intact in the absence of physical agitation.

Imiquimod release profiles (Fig. 2) showed that incorporation of RL-PO (20% w/w) into PVP:CMC increased the duration of release drug from 4 to 10 hours. The initial burst was observed to be similar to that for the straight PVP:CMC films, except that it was followed by an extended period of sustained release.

Although incorporation of RL-PO did not significantly affect the *ex vivo* mucoadhesion time of normal films, a 70% increase was observed for thicker films.

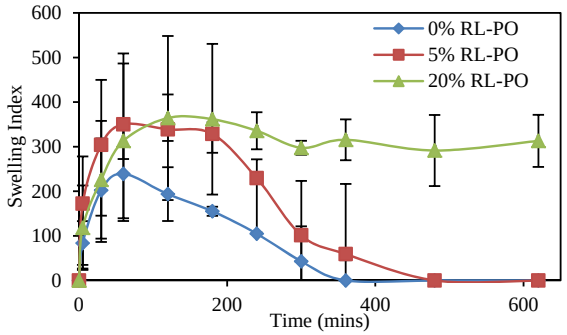

Figure 1. Swelling profiles of PVP:CMC films with increasing amounts of RL-PO.

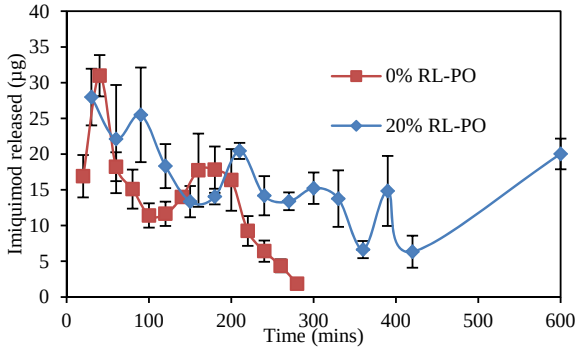

Figure 2. Imiquimod release from straight PVP:CMC films and those containing 20% w/w RL-PO.

Conclusions

Incorporation of a hydrophobic component into mucoadhesive films composed of hydrophilic polymers increases the duration of controlled drug release by decreasing the rate of erosion. Current studies also showed that the hydrophobic polymer did not decrease adhesivenss, and indeed it increased the residence time in the case of thicker films.

Acknowledgement

This work was supported by the NIH/NIDCR (DE019645).