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Erodible Film Formulation for Potential Ocular Drug Delivery

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SUMMARY

Drug delivery to the eye has always been an interesting and challenging field in pharmaceutical formulation and drug design. The aim of this research was the formulation development of thin erodible films for potential delivery of lopidine to treat glaucoma. Films were prepared using hyaluronic acid (HA) and hydroxypropyl methylcellulose (HPMC) as polymers, together with glycerol (GLY) as plasticiser. Single layer films were prepared using each polymer individually, as well as in combination to obtain composite thin films. Various combinations and concentrations were optimised to reach the desired transparency, which were then characterised for their physico-chemical and mechanical properties. The following ratios were selected for drug loading: 2% HPMC, 1% HA, 1% composite (HPMC 1:1 HA) and 2% composite (HPMC 1.5:0.5 HA) with all of them containing a ratio of 2:1 polymer to plasticiser.

INTRODUCTION

The estimated number of visually impaired people in the world is 285 million, which is 4% of the global population. The unique anatomy and complicated physiology of the eye and the importance of maintaining visual clarity makes the eye a challenging organ for drug delivery purposes (Patel et al., 2013). Conventional eye drops are not efficient because of their low bioavailability, with only 5% of the dose reaching the site of action within the eye due to splashes during blinking, nasal drainage, small absorptive surface, lipophilicity and low permeability of the corneal epithelium (Addo, 2016). Severe chronic eye conditions such as glaucoma require better drug delivery systems in order to deliver site-specific, controlled drug release with appropriate bioavailability. Therefore, erodible films are required to overcome these limitations of current dosage forms, to ensure controlled release as well as increasing retention time and hence bioavailability.

MATERIALS AND METHODS

Single layer films were prepared using HPMC:GLY and HA:GLY gels in 2:1 ratio of polymer to plasticiser. Composite films were then prepared from gels comprising HPMC:HA:GLY with the same ratio of total polymer to plasticiser. The hydration and gelation of the polymers was carried out at room temperature, and dried in a 40°C oven over night. The films were optimised by characterising for their physico-chemical properties using the following tests: transparency, tensile strength, elastic modulus, swelling capacity, mucoadhesion, attenuated total reflectance Fourier transform infrared (ATR FT-IR), differential scanning calorimetry (DSC) thermogravimetric analysis (TGA) and scanning electron microscopy (SEM). The single polymer films from 1% HA, 2% HPMC gels, composite films from 1% (HPMC 1:1 HA) and 2% (HPMC 1.5:0.5 HA) gels met the desired criteria for drug loading

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RESULTS AND DISCUSSION

Both single polymer and composite films were thoroughly transparent, with digital images of the transparent films taken against a white, black numbered ruler to illustrate film clarity (Figure 1). The transparency was further examined by UV transmission and showed greater than 90% light transmission. The single polymer (1% HA, 2% HPMC) and composite (1% HPMC 1:1 HA; 2% HPMC 1.5:0.5 HA) films had the optimum physical and mechanical properties (Table 1) for ocular drug delivery.

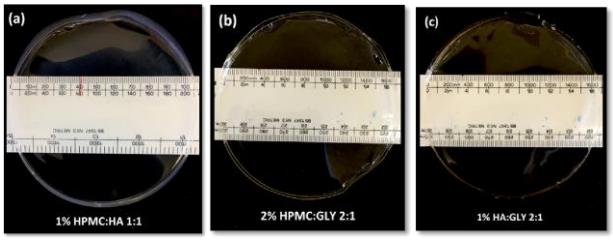

Fig. 1. Transparency of (a) 1% HA:GLY, (b) 2% HPMC:GLY and (c) 1% composite (HPMC 1:1 HA)

The ATR-FTIR results showed possible crosslinking of the polymers in the composite films as new peaks appeared which were not present in the single HA or HPMC films. These peaks include 2994 cm^{-1}, 2827 cm^{-1}, 1288 cm^{-1}, 1265 cm^{-1}, 1240 cm^{-1}, 1214 cm^{-1} and 743 cm^{-1}. Also, the 1645 cm^{-1} peak of HPMC did not appear in the composite films, which is also an indication of chemical interaction. The DSC and TGA results were consistent in terms of water content, melting point and material decomposition. The SEM result showed smooth continuous (non-porous) film surface with negligible number of polymer particles on the surface of the film in the composite films. This is shown by the representative image of the composite film at x50 magnification (figure 2a), as well as the image of the same film at x1800 magnification (figure 2b). This could be due to aggregation of HPMC and HA particles during the hydration process which is even stronger if the polymers are crosslinking.

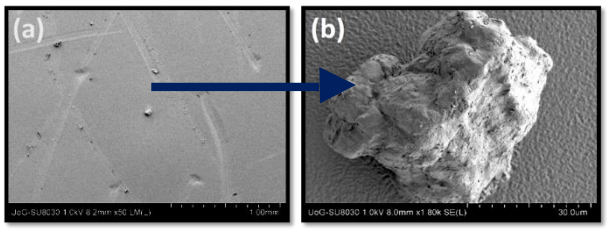

Fig. 2. Representative SEM image of 1% composite (HPMC 1:1 HA); (a) x50 magnification and (b) x1800 magnification showing the small aggregated particle on the film surface.

Table 1. *Tensile strength, elastic modulus, mucoadhesion and swelling results for all the films formulated*

Gels for films (% w/v)	Tensile strength (N/mm^2)	Elastic modulus (mPa)	Peak adhesive force (N)	Swelling capacity (%)
0.5 % HPMC	11.2	19.6	1.9	965.3
1.0% HPMC	25.4	7.7	1.6	360.3
1.5% HPMC	40.9	8.8	1.4	570.7
2.0% HPMC	32.5	9.9	2.1	715.2
1.0% HA	10.1	0.9	2.2	1633.3
1.5% HA	3.7	0.1	2.9	1463.9
1% Composite	14.2	3.5	6.0	931.7
2% Composite	45.7	14.8	3.7	804.3

CONCLUSIONS

Plasticised HA, HPMC and composite films of both polymers possessed ideal physico-chemical properties suitable for ocular delivery. The films containing single polymers, as well as the composite formulation of the two polymers formed transparent, flexible films which can be used for drug loading and thus as potential ocular drug delivery systems. Based on the analytical characterization, the 2% HPMC, 1% HA, 1% composite (HPMC 1:1 HA) and 2% composite (HPMC 1.5:.05 HA) have the required physico-chemical properties required for the drug loading stage.

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