Poster #

Evaluation of the Mucosal Retention Properties of Mucoadhesive Polymers Using a 3D Model of the Human Oral Mucosa

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Purpose

The aim of this study is to assess the mucoadhesive properties of a proprietary mucoadhesive polymer gel, in comparison to a mucoadhesive reference product, using the EpiOral model (MatTek Corporation), a highly differentiated three-dimensional (3D) model of the human oral mucosa. The oral mucosa is an ideal target for drug delivery due to the ability of medications to bypass first-pass metabolism, avoid gastrointestinal degradation, and achieve more rapid onset of action[1]. Within the oral mucosa lies the buccal mucosa, which is highly vascularized, has low levels of enzymatic activity, and is fairly immobile, making it a suitable site for both local and systemic delivery of medication[2]. However, a disadvantage to buccal delivery is the low residence time (time at site of action) of the medication. Mucoadhesive polymers are delivery systems designed to prolong retention of medication at application sites, such as mucosal tissue, in order to overcome the short retention time seen with conventional dosage forms[3].

Methods

The EpiOral (ORL-200) tissue model comprises of normal human-derived non-keratinized oral epithelial cells, cultured and differentiated to resemble the native buccal tissue of the human oral mucosa[4]. The reference product and Mucoadhesive Polymer Gel were labeled with appropriate quantities of sodium fluorescein using 1% NaFl stock solution. A 100 µL of each fluorescently labeled sample was applied to the apical surface of the EpiOral tissues (2 tissues for each sample) and incubated at intervals of 5, 10, 30, 40 min, 1, 2, and 5 hr. Two EpiOral tissues were left untreated to serve as a negative control. After each allotted incubation interval, tissue samples were removed and rinsed 3 times by immersing in 10 mL of Dulbecco's phosphate-buffered saline. In order to ensure that any loss of NaFl would be due to washing rather than leakage through the EpiOral tissues, culture supernatant was also collected and measured for NaFl content using a fluorescent plate reader. For each incubation and washing cycle, images were acquired for each EpiOral tissue using an Olympus FV1000 confocal microscope. Through the images of the gel retention, mucoadhesive properties of the samples were then analyzed and compared.

Results

For the EpiOral tissue treated with the reference product, the NaFl-labeled sample was washed out after 5 min of incubation (Figure 1). This is evident by the absence of the fluorescein dye (green fluorescence) above the tissue area on the images captured following washing. For the tissue treated with NaFl-labeled Mucoadhesive Polymer Gel, the dye was retained on the apical surface of the tissue for up to 40 min (Figure 2). There was limited sample retention (faint green fluorescence) noted at 1 and 2 hr following application. The absence of NaFl in the culture supernatant was also confirmed to show that there is no leakage of NaFl from tissues. Rather, the loss of fluorescent dye is from washing. Results show that the Mucoadhesive Polymer Gel was superior to the reference product in terms of mucoadhesive properties as the duration in which the Mucoadhesive Polymer Gel was retained on the surface of the tissue was approximately 24 times longer than that of the reference product.

A major barrier to buccal delivery of medication is the short residence time at the application site due to the surfaces of the cheeks being constantly washed with saliva, causing loss of medication[3].Optimal mucoadhesive properties exhibited by Mucoadhesive Polymer Gel are ideal features sought after by many compounding pharmacists. The increased mucoadhesion allows for prolonged retention of active ingredients at the affected site, facilitating the treatment process.

Conclusions

The longer mucosal retention potential seen with Mucoadhesive Polymer Gel offers an advantage over the reference product in allowing for prolonged contact between the mucosal tissue and the delivery system. This can help maintain the active ingredient at the site of action, potentially reducing the need for frequent dosing and increasing the effectiveness of each dose administration.

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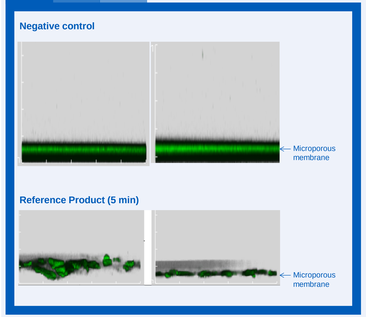

Figure 1. Reference product disappearance from the top of the tissue after 5 min of incubation and washing.

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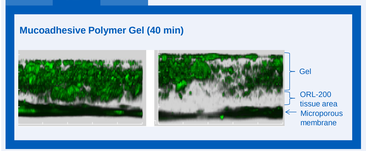

Figure 2. Mucoadhesive Polymer Gel retention following 40 min of incubation and washing.

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