TECHNICAL REPORT

MucoLox™

Evaluation of the Safety and Toxicological Profile of MucoLox: Human Oral Mucosa, Nasal Mucosa and Vaginal Mucosa (Part 2/3)

Abstract: Mucoadhesive polymers are delivery systems developed to prolong retention of medication at application sites, such as the nasal mucosa, in order to overcome the short retention time seen with many conventional dosage forms. However, the intimate contact between the mucoadhesive polymer and the nasal mucosa require these delivery systems to be non-toxic and non-irritating. This study was conducted to evaluate the safety and toxicological profile of MucoLox, a mucoadhesive polymer gel, using the EpiAirway™ tissue model, a three-dimensional (3D) model that resembles the human nasal mucosa. Results have demonstrated that MucoLox is potentially as safe as sterile water for injection since cell viability was greater than 100% for MucoLox at various concentrations. MucoLox may therefore be considered a safe mucoadhesive polymer in its ability to prolong contact between the medication and the human nasal mucosa.

Introduction: The nasal cavity is a promising site for drug delivery as it is easily accessible to patients, has a large surface area (due to the presence of microvilli), contains a thin nasal epithelium, and it can bypass first-pass metabolism [1]. However, many conventional dosage forms (e.g. gels, solutions, suspensions) have low residence time (time at site of action) within the nasal cavity as these can be easily expelled from the application site with sneezing, as a result of mucociliary clearance, or by nasal drainage [2].

Mucoadhesive polymers are delivery systems developed to overcome these issues by increasing the adhesion between the polymer and the nasal mucus, inhibiting mucociliary clearance of the medication, and hence prolonging the residence time [1]. Due to the prolonged contact between the delivery system and the application site, it is important to evaluate the toxicity potential of these polymers on the nasal mucosa.

This study was therefore designed to examine the safety and toxicological profile of MucoLox, a proprietary mucoadhesion polymer gel, using the EpiAirway tissue model (MatTek Corporation), a 3-dimensional (3D) model developed to closely resemble the structure and functionality of the human nasal mucosa [3, 4].

Methodology: The EpiAirway tissue model consists of normal human-derived tracheal/bronchial epithelial cells, cultured and differentiated to resemble the pseudostratified epithelium of the nasal mucosa [3] (Figure 1). Following tissue preparation, MucoLox 100%, 10%, and 1% (diluted with sterile water for injection) were applied to tissue samples of the EpiAirway model and incubated for 3 hr at a temperature of 37°C. Sterile water for injection was used in this study as a negative control. After 3 hr of incubation, each tissue sample was rinsed 3 times with Phosphate Buffered Saline (PBS) to remove any residual MucoLox. Afterwards, 300 µL of MTT (3-[4,5-dimethylthiazol-2yl]-2,5-diphenyltetrazolium bromide) solution was applied and the tissue samples were incubated for another period of 3 hr. MTT was used as an indicator of cell viability. Succinate dehydrogenase enzymes within the mitochondria of viable cells have the ability to reduce soluble yellow tetrazonium salt of MTT to an insoluble purple formazan derivative [5].

Following incubation, tissues were rinsed with PBS and immersed in 2 mL of extraction solution. Tissues were then sealed in a plastic bag and soaked overnight at room temperature. Once extraction was completed, extra liquid was decanted and the 200 µL aliquot of the extractant solution was examined using a Molecular Device SpectraMax M5 Microplate Reader to determine the absorbance potential of the extract at 570 nm, a wavelength absorbed by the formazan derivative [5].

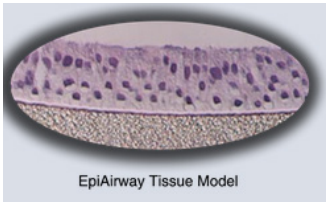

Figure 1. Illustration of the EpiAirway tissue model.

Results and Discussion: The safety and toxicological profile of MucoLox was evaluated by determining the percent absorbancy of the extract (formazan derivative). The greater the percent absorbancy, the greater the amount of MTT reduced by succinate dehydrogenase, and the higher the percent cell viability within the tissue [5]. The percent cell viability for sterile water for injection was 100%. For tissues treated with MucoLox 100%, 10%, and 1%, cell viability after 3 hr of exposure was 103%, 112%, and 104%, respectively (Figure 2). These results demonstrate that MucoLox was not toxic to the tissues of the nasal mucosa as percent viability of the tissues was greater than 100% for all three MucoLox samples.

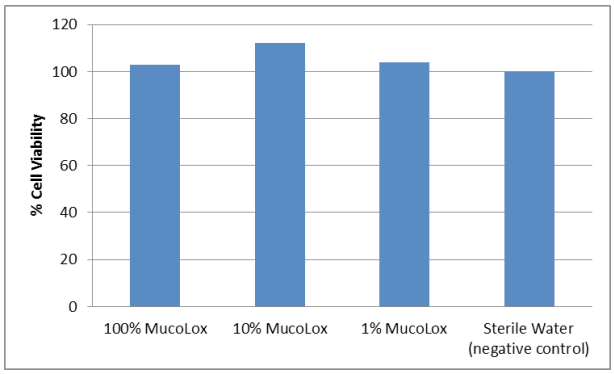

Figure 2. Percent cell viability after 3 hr of exposure to MucoLox 100%, 10%, and 1%; and sterile water (negative control).

In the treatment of local conditions such as rhinitis, congestion and infection, MucoLox can offer prolonged contact within the nasal cavity, despite the regular mucociliary clearance and nasal drainage, in comparison to conventional dosage forms such as solutions and suspensions for nasal delivery.

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The evaluation of the safety and toxicological profile of MucoLox is very important, taking into account the prolonged intimate contact between the delivery system and the nasal mucosa. An ideal mucoadhesive polymer should be non-toxic and non-irritating to the mucosal tissue [2]. Study results have demonstrated that cell viability was greater than 100% for all three concentrations of MucoLox, making it an ideal delivery system with a safety and toxicological profile similar to that of water.

Conclusions: MucoLox has demonstrated to be a safe mucoadhesive polymer that can offer increased retention of medication at the site of action without toxicity concerns. Compounding pharmacists may then safely utilize this mucoadhesive polymer as a delivery system to increase the contact time between the medication and the nasal mucosa, potentially reducing the need for frequent dosing and increasing the effectiveness of each dose administration.

References:

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