

Evaluation of the Mucosal Retention Properties and Toxicological Profiles of a Mucoadhesive Polymer Gel

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- B.S. in Chemistry. 2002. Morehead State University.
- Doctor of Pharmacy. 2006. University of Kentucky College of Pharmacy.
- Practiced 8 years in a compounding pharmacy preparing sterile and non-sterile medications
- Consultant Pharmacist at Professional Compounding Centers of America

Oral Mucosa

- Targeted to:
 - Bypass first pass metabolism
 - Avoid gastrointestinal degradation
 - Achieve a more rapid onset of action

Buccal Mucosa

- Non-keratinized epithelial cells of the inner cheeks
 - Highly vascularized
 - Low enzymatic activity
 - Fairly immobile

Challenges for Buccal Delivery

- Low residence time
 - Continuous secretion of saliva causing swallowing
 - Food intake
 - Movement of the tongue
- Mucoadhesive polymers adhere to mucosal lining of the cheeks and increase residence time

Mucolox™

- Water
- Isomalt
- Pullulan
- Glycerin
- Poloxamer 407
- Tamarindus Indica Seed Polysaccharide
- Sodium Hyaluronate
- Zea Mays (Corn) Starch
- Simethicone
- Carbomer
- Sodium Benzoate
- Potassium Sorbate
- Disodium EDTA

MucoLox™ , also referred to as Mucoadhesive Polymer Gel, is a proprietary gel designed to improve mucoadhesion and prolong retention of medications at application sites within the oral mucosa.

Evaluation of Mucosal Retention

- Compare the retention of MucoLox™ to that of a mucoadhesive commercial reference product.
- EpiOral Model (MatTek Corporation)
 - EpiOral (ORL-200): human derived, non-keratinized oral epithelial cells

Methodology

- MucoLox™ and the reference product were labeled with sodium fluorescein
- 100 uL sample of each product applied to the apical layer of the EpiOral tissues
- Incubated at intervals of 5, 10, 30, 40 min, 1, 2, and 5 hr

Methodology

- Samples rinsed 3 times in Dulbecco's Phosphate-Buffered Saline
- Loss of NaFl only from the sample validated by collection of supernatant
- Images acquired by Olympus FV1000 confocal microscope

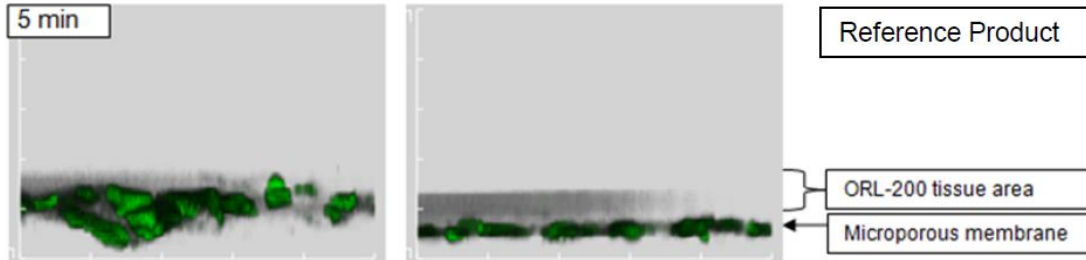


Figure 1: Showing disappearance of the reference product after 5 min of incubation and washing

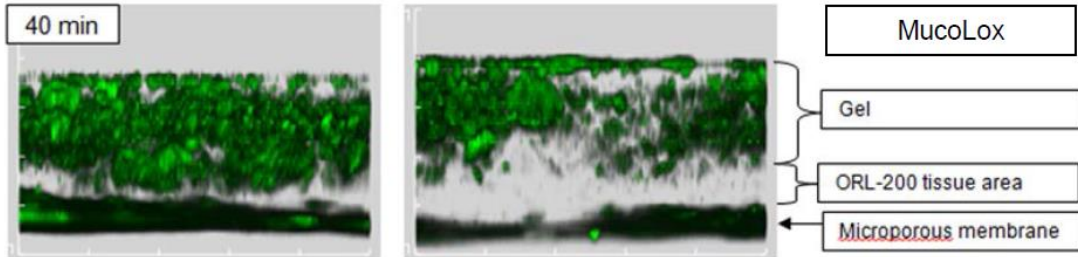


Figure 2: Showing gel retention following 40 min of incubation and washing.

Safety & Toxicological Profile

- Oral Human Mucosa evaluated with the EpiOral Model
- Tissue exposed to distilled water (negative control)
- 40 uL of Mucolox™ diluted to 50% and 1% Triton X-100 applied to the samples
- Incubated at 37° C for intervals of 1, 4.5, and 20 hr

Human Oral Mucosa Evaluation

- Samples rinsed twice with phosphate buffer saline
- 300 μ L of MTT solution (3-[4,5-dimethylthiazol-2yl]-2,5-diphenyltetrazolium bromide) applied and incubated for 3 hours
- 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

Human Oral Mucosa Evaluation

- Samples immersed in 2mL of extraction solution, sealed in plastic bag, stored at room temperature overnight
- 200 μ L aliquot of each extract was evaluated using a Molecular Device SpectraMax[®] M5 Microplate Reader
- This device quantifies the absorbance potential of the samples at 570 nm, a wavelength absorbed by reduced MTT

Human Oral Mucosa

- The greater the percent absorbancy, the greater the amount of MTT reduced by succinate dehydrogenase within the extract, and the higher the percent cell viability within the tissue
- Mean percent cell viabilities were calculated

Human Oral Mucosa

- For tissues treated with MucoLox™ 50%, mean percent viabilities were 97%, 98%, and 85% following 1, 4.5, and 20 hr of exposure, respectively.
- For tissues treated with Triton X-100 1%, mean percent viabilities were 117%, 30%, and 6% following 1, 4.5, and 20 hr of exposure, respectively.

Human Oral Mucosa

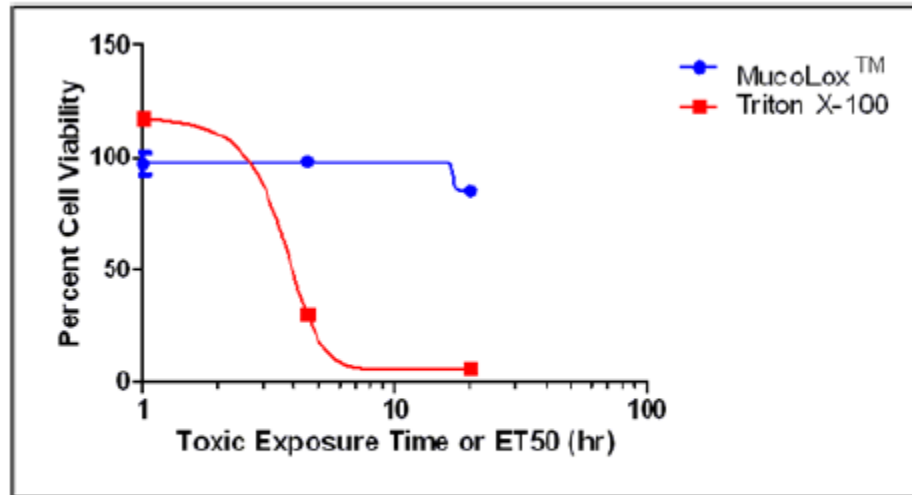


Figure 2. Mean percent cell viability of MucoLox and Triton X-100.

Human Nasal Mucosa

- EpiAirway- normal human-derived tracheal/bronchial epithelial cells, cultured and differentiated to resemble the pseudostratified epithelium of the nasal mucosa
- Mucolox™ 100%, 10%, and 1% diluted with sterile water applied to tissues vs sterile water as the negative control.

Human Nasal Mucosa

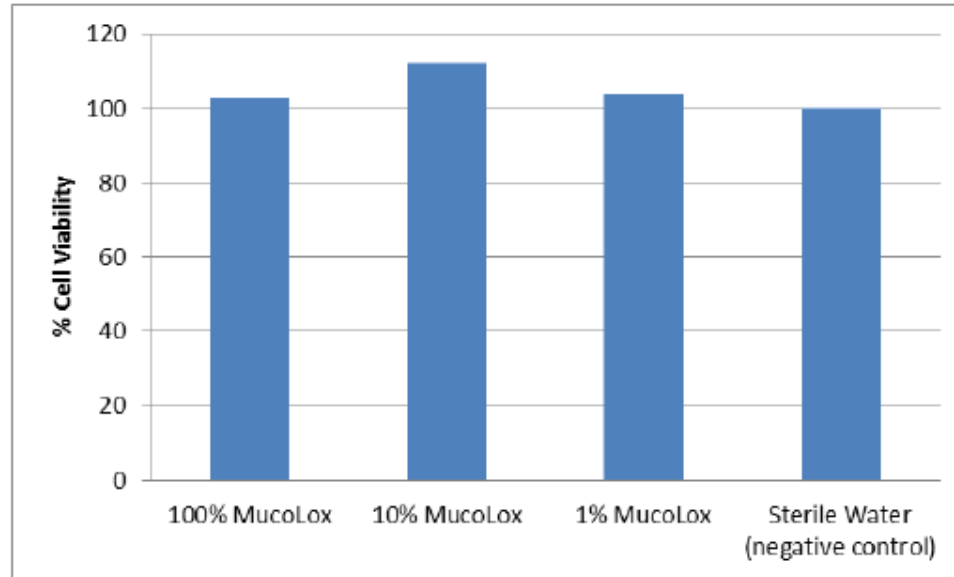


Figure 2. *Percent cell viability after 3 hr of exposure to MucoLox 100%, 10%, and 1%; and sterile water (negative control).*

Human Vaginal Tissue

- EpiVaginal™
- Multilayered tissue produced from human-derived vaginal-ectocervical epithelial cells (Figure 1).
 - Composed of basal layer and multiple non-cornified layers
 - Highly differentiated to resemble the growth and morphological characteristics of the human vaginal mucosa

Human Vaginal Tissue

- Mucolox™ 100% compared to Triton X-100 1% (positive control)
- Percent cell viabilities for the tissue treated with MucoLox™ were 87%, 78%, and 79% following exposure at 1, 4.5, and 20 hr, respectively
- Triton X-100 percent cell viabilities were 97% and 26% at 45 min and 2 hr of exposure, respectively

Human Vaginal Tissue

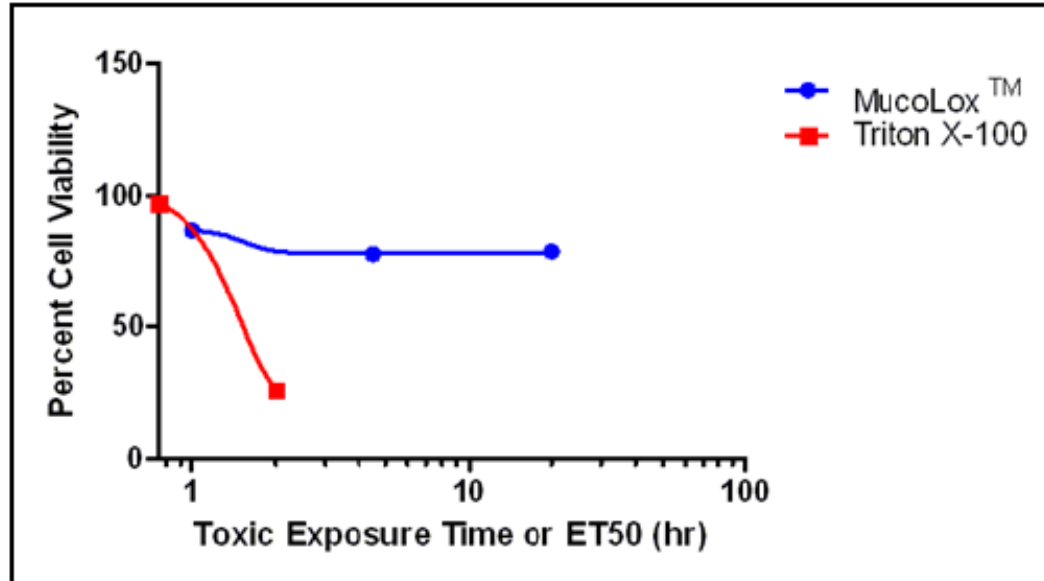


Figure 2. *Toxicological profiles of MucoLox and Triton X-100.*

Questions?

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References

- Assessment of the Mucoadhesive Properties of MucoLox™ Using a 3D Model of the Human Oral Mucosa
- Evaluation of the Safety and Toxicological Profile of MucoLox™: Human Oral Mucosa, Nasal Mucosa and Vaginal Mucosa (Part 1/3)
- Evaluation of the Safety and Toxicological Profile of MucoLox™: Human Oral Mucosa, Nasal Mucosa and Vaginal Mucosa (Part 2/3)
- Evaluation of the Safety and Toxicological Profile of MucoLox™: Human Oral Mucosa, Nasal Mucosa and Vaginal Mucosa (Part 3/3)

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