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

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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™, 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 & Toxicologicological 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 μL of MTT solution (3-[4,5-dimethylthiazol-2-yl]-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 μL 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.
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.
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?

Please send correspondence to:

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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)
References