Variables Affecting Delivery of Glycopyrronium Tosylate Through Human Skin In Vitro

Francesco Caserta¹, Jon Leon¹, Hans Hofland²
MedPharm, Durham, NC; Dermira, Inc., Menlo Park, CA

Introduction

- Hyperhidrosis is a medical condition characterized by excessive sweating beyond what is required for normal thermoregulation, and can involve multiple areas including the axilla, palms, soles, or craniofacial region
- Glycopyrronium tosylate (GT) is a topical anticholinergic recently approved by the US Food and Drug Administration for the treatment of primary axillary hyperhidrosis in patients 18 years of glycopyrronium cloth 2.4% for topical use
- In vivo permeation models can be a powerful tool to gain insights on drug absorption (flux) profiles under varying conditions and to optimize clinical trial design

Objective

- To determine using in vitro skin penetration studies how GT delivery through human skin is impacted by varying conditions including occlusion, wash-off, and skin thickness

Methods

- Across all experiments:
  - Human skin was dermatomed to a thickness of approximately 0.5 mm and mounted into flow-through diffusion cells (MedFlux-HT)
- GT solution was applied at 1mg/cm² for 5 minutes and allowed to dry

Results - Occlusion

- Human abdominal skin was obtained from 4 donors after abdominoplasty
- Two methods of occlusion were used: 1) possible was pressed on the surface of the donor compartment, which leaves a small closed-off column of air above the skin; 2) Saran wrap was placed down in the top of the surface of the skin
- Non-occluded skin was used as control
- The receiving fluid was collected over 12 hours, and the GT flux was assessed using liquid chromatography with tandem mass spectrometry (LC/MS/MS)

Occlusion

- Occluded flux was calculated: C(occluded)/C(not-occluded)
- During this exposure period the skin was either occluded using the saran wrap method or not occluded
- Each bar represents the mean and standard error of 4 replicates per donor

Results - Wash-off and Exposure Time

- All wash-off techniques were effective; however, washing with hand soap was the most effective method (99.5% removal of GT from skin surface) while use of water alone was the least effective method (99.8% removal) (Figure 3)
- In general, similar delivery of GT was observed through palmar vs abdominal skin and for male vs female skin (Figure 2)

Results - Skin Thickness / Anatomical Sites

- In these in vitro studies, wash-off, occlusion and skin thickness substantially influenced GT delivery
- Occlusion increased GT delivery (flux) by 7-10 fold
- A 90% decrease in flux was observed after washing, independent of how long GT was left on the skin (5, 15, or 60 min) (Figure 3)
- Across all experiments:
  - The amount of GT delivered through human skin was reduced by 95% after washing. This reduction appeared independent of the length of time the product was left on the skin before washing; however, in one of the 4 donors (Donor 3) there appears to be a benefit of washing the product on the skin before washing (Figure 3)

CONCLUSIONS

- It should be noted that the in vitro skin penetration studies summarized here involved a single dose of GT; skin delivery of GT upon clinical application was not assessed in these studies
- These data underscore the importance of characterizing skin flux under clinical conditions and will inform future hyperhidrosis clinical trial designs with topical agents

REFERENCES

4. Detailed information about the experimental protocols, materials and methods used for this study are available in the online supplementary material:

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Author Disclosures

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