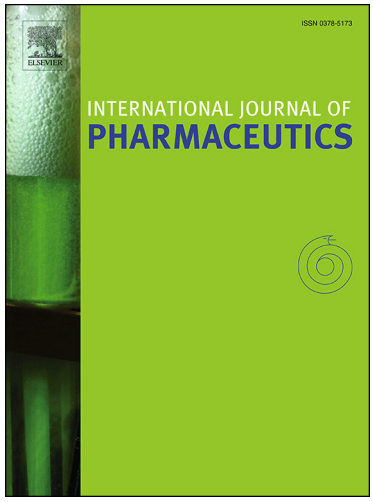
# Accepted Manuscript

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Miguel Paz-Alvarez, Paul D.A. Pudney, Jonathan Hadgraft, Majella E. Lane

PII: S0378-5173(18)30533-7
DOI: https://doi.org/10.1016/j.ijpharm.2018.07.058
Reference: IJP 17674

To appear in: *International Journal of Pharmaceutics*

Received Date: 12 June 2018
Revised Date: 23 July 2018
Accepted Date: 24 July 2018

Please cite this article as: M. Paz-Alvarez, P.D.A. Pudney, J. Hadgraft, M.E. Lane, Topical delivery of climbazole to mammalian skin, *International Journal of Pharmaceutics* (2018), doi: https://doi.org/10.1016/j.ijpharm.2018.07.058

# Topical delivery of climbazole to mammalian skin

Miguel Paz-Alvarez[a,*], Paul D. A. Pudney[b], Jonathan Hadgraft[a], Majella E. Lane[a]

[a]UCL School of Pharmacy. 29-39 Brunswick Square, WC1N 1AX, London, UK

[b] Strategic Science Group , Unilever R&D. Colworth Science Park, MK44 1LQ, Sharnbrook, Bedford, UK

*Corresponding autor. E-mail address: miguel.alvarez.13@ucl.ac.uk (M. Paz-Alvarez), Phone number 07561050836

## Abstract

Dandruff is a common condition, affecting up to half the global population of immunocompetent adults at some time during their lives and it has been highly correlated with the over-expression of the fungus *Malassezia spp.* Climbazole (CBZ) is used as an antifungal and preservative agent in many marketed formulations for the treatment of dandruff. While the efficacy of CBZ *in vitro* and *in vivo* has previously been reported, limited information has been published about the uptake and deposition of CBZ in the skin. Hence, our aim was to investigate the skin permeation of CBZ as well as the influence of various solvents on CBZ skin delivery. Four solvents were selected for the permeability studies of CBZ, namely propylene glycol (PG), octyl salicylate (OSal), Transcutol® P (TC) and polyethylene glycol 200 (PEG). The criteria for selection were based on their wide use as excipients in commercial formulations, their potential to act as skin penetration enhancers and their favourable safety profiles. 1% (w/v) solutions of CBZ were applied under infinite and finite dose conditions using Franz type diffusion cells to human and porcine skin. In line with the topical use of CBZ as an antidandruff agent, comparatively low amounts of CBZ penetrated across the skin barrier (< 1% of the applied dose of CBZ). Finite dose studies resulted in a higher extraction of CBZ from human skin compared with infinite dose studies ($p<0.05$). CBZ was also taken up to a higher extent in porcine skin (> 7-fold) compared with human skin ($p<0.05$). Nevertheless, no statistical differences were observed in the amounts that permeated across the different membranes. These preliminary results confirm the potential of simple formulations of CBZ to target the outer layers of the epidermis. The PG and OSal formulations appear to be promising vehicles for CBZ in terms of overall skin extraction and penetration. Future work will expand the range of vehicles studied and explore the reasons underlying the retention of CBZ in the outer layers of the skin.

## Keywords:

*In vitro*, porcine skin, human skin, finite dose, infinite dose, climbazole