Accepted Manuscript

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PII: S0928-0987(18)30105-2

DOI: doi:10.1016/j.ejps.2018.02.028

Reference: PHASCI 4425

To appear in: European Journal of Pharmaceutical Sciences

Received date: 15 December 2017 Revised date: 22 February 2018 Accepted date: 26 February 2018

Please cite this article as: Elena Cutrín Gómez, Soledad Anguiano Igea, José Luis Gómez Amoza, Francisco J. Otero Espinar , Evaluation of the promoting effect of soluble cyclodextrins in drug nail penetration. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Phasci(2017), doi:10.1016/j.ejps.2018.02.028

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ACCEPTED MANUSCRIPT

Evaluation of the promoting effect of soluble cyclodextrins in drug nail penetration

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ABSTRACT

Soluble derivatives of β-cyclodextrin (CD) have a high capacity to solubilise hydrophobic molecules and to interact with proteins and membrane component. As consequence CD derivatives shows a significant activity as drug absorption enhancers through different delivery routes, such as the oral, nasal, ocular or topical route. In this paper, the effect of two CD derivatives -methyl-β-cyclodextrin (MBCD) and hydroxypropyl-β-cyclodextrin (HPB)- on the structure and permeability of the nail plate has been studied using the drug model ciclopirox olamine. Results shows that MBCD and HPB interacting with the nail plate components, modifying their microporous structure and swelling characteristics. The ability of the cyclodextrins to interact with aromatic amino acids and to stabilise and unfold protein structures could be the most likely mechanisms responsible of the nail microstructure modifications. Aditionally CD allow to increase the soluble dose of ciclopirox olamine in aqueous lacquers made with poloxamer and N-acetylcysteine via the formation of high solubility complexes with the drug. Finally the studies of diffusion and penetration obtained using bovine hoof model confirm the enhancing effect of the cyclodextrins on the penetration and accumulation of the drug in the nail structure. Results shows the great potential of the CD for the elaboration of aqueous based nail lacquers containing hidrofobic drugs.

Keywords: nail, nail psoriasis, Cyclodextrins, onychomycosis, porosity, topical drug delivery

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