HUMAN SKIN PERMEATION AND RETENTION OF TWO NOVEL NANOEMULSIONS VERSUS REFERENCE FORMULATION

Fernández Campos, F; Bartes Calsapeu, M; Fabrega Dura, M; Calpena Campmany, AC.
Biopharmaceutical and pharmacokinetics department. University of Barcelona. Spain

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INTRODUCTION

Nystatine (nys) is an antifungical compound effective against mycetes of Candida species.
In comparison to classical dermal formulations, the nanoemulsions are effective vehicles systems for transdermal drug delivery, due to its colloidal structure and its high drug loading.
The aim of this study is to evaluate the permeation and the amounts of nystatine retained in the skin from a topical dosage form

MATERIALS AND METHODS

The nanoemulsions (N1 and N2) were elaborated with Transcutol®, Labrasol®, Plurol oleique®, Labrafac lipophile®, Propylenglycol as excipients in different proportions; dimetilsulfoxide was used as permeation promoter. The nanoemulsions nys concentration was 400µg/mL. Compounds were stirring by ultrasounds under cold.
The particle size, measured by Zeta-Sizer, Malvern Instruments was 45.06nm for N1 and 47.97nm for N2. As reference formulation was used Myscostatin®, not available in the market at present.
Permeation studies (n=6) were carried out with vertical diffusion cell of 2.54cm2 and dermatomed human skin (0.4mm) for a unique donor. Transcutol® was used as receptor phase at 32ºC.
Samples were withdrawn at different time point scheme for 28h and quantified by means a validated HPLC method. The mobile phase was water:ACN (60:40) with 1% acid acetic at 0.8ml/min flow rate and wave length 305nm, a Kromasil® C18 (5µm, 15x4.6cm) column was used. Retention time of nys was 4.1min.
Nys skin extraction was carried out with a mixture of water:ACN (20:80) under sonication for 20 minutes and the percentage of nys skin recovery of the extraction method was also determined.

RESULTS AND DISCUSSION

Permeated amounts of nys after 28h were 1.30µg for N1, 1.40µg for N2 and 3.56µg for reference formulation. The recovery of the skin extraction method was 9.5% and the retained amounts of nys in skin were 26.62, 18.00 and 238.49µg/g/cm2 for N1, N2 and Mycostatin®, respectively. The permeated amounts of nys are not enough to have neither therapeutic nor toxic systemic effects; reported data shows that serum nys concentrations from 4.8 to 24.1µg/mL are well tolerated (1). Although retained skin amounts of Mycostatin® are higher than novel formulations, nanoemulsions reach an effective skin concentration for Candida albicans skin infection treatment. The described MIC for Candida albicans strain ATCC 90028 is 8µg/ml (2). Developed formulations are a promising alternative to Mycostatin®, but further microbiologic studies will be carried out in order to confirm the nanoemulsions efficacy.

BIBLIOGRAFY
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