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Pharmaceutical Research
Publisher: Springer Science+Business Media B.V., Formerly Kluwer Academic Publishers B.V.
ISSN: 0724-8741 (Paper) 1573-904X (Online)
DOI: 10.1023/A:1020319329145
Issue: Volume 19, Number 9
Date: September 2002
Pages: 1381 - 1386
Effects of Calcium Modulation on Percutaneous Absorption of a Model Drug

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Abstract Purpose. To investigate the effect of modulation of the calcium gradient in the skin on the percutaneous absorption of nicotinic acid (NA).
Methods. A skin model with an altered calcium gradient was produced by pretreatment with A23187 (25 mgrg/ml). The immunohistochemistry was used to evaluate the change in phosphoprotein Elk-1. ATR-FTIR spectroscopy was employed to investigate the changes in lipid conformation in the skin. The permeation profiles of the model drug were studied and the distribution profile of the model drug in the skin layer was evaluated using the cryostat micro-sectioning method.
Results. The immunohistochemistry demonstrated that modulation of the calcium gradient increased phosphorylated Elk-1 in the dermis. The FTIR study showed a shift of the asymmetric stretch peak, implying an increase in lipid fluidity in the epidermis. The amount of NA permeated through the A23187-pretreated skin was significantly lower than that of the control (2.2714 ± 0.6040 vs. 3.1895 ± 0.2456 mgrg/cm2/h). The Cryostat micro-sectioning study showed that there are concentration gradients of the model drug across the skin layers with a higher gradient in the control than in the A23187-pretreated skin.
Conclusions. The alteration in the calcium gradient significantly decreased the permeation rate of a hydrophilic drug, such as nicotinic acid.