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PRETREATED EFFECT OF ETHANOL ON THE SKIN PERMEATION OF DRUGS

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ABSTRACT

Ethanol (EtOH) is used as a skin permeation enhancer as well as a skin disinfectant and a poorly-soluble drug solubilizer. However, little information is found on the pretreated effect of EtOH on the skin permeation of drugs. In this study, deuterium oxide (D₂O, molecular weight; 20), isosorbide mononitrate (ISMN, molecular weight; 191), isosorbide dinitrate (ISDN, molecular weight; 236), calcein sodium (CA-Na, molecular weight; 668) and fluorescein isothiocyanate-dextran (FD-4, molecular weight; 3300-4400) were selected as model drugs and the pretreated effect of EtOH was determined on their skin permeations. Yucatan micropig (YMP) skin was mounted in the Franz-type diffusion cells and different concentrations (0, 20, 40, 60, 80 and 99.5 v/v %) of EtOH solution were applied the stratum corneum side of skin for 12 h. After removal of the EtOH solution, each model drug solution was applied on the stratum corneum side and periodically sampling was performed to determine the skin permeation. In addition, electric resistance of skin membrane was measured immediately after the skin permeation experiment

Constant skin permeabilities of D₂O and ISDN were observed independents of EtOH concentration. On the other hand, skin permeabilities of ISMN, CA and FD-4 were increased by pretreatment with low concentration of EtOH, whereas they were decreased by pretreatment with high concentration of EtOH (>80 %). Although skin permeabilities of CA and FD-4 were dramatically decreased with 99.5 % EtOH pretreatment, ion transports confirmed by electric resistance through skin were almost constant at any EtOH concentrations. These results suggested that pretreatment with EtOH would affect skin permeation of drugs and the effects were highly dependent on the physicochemical properties of penetrants. Furthermore, the decreased skin permeabilities of CA and FD-4 by high concentration of EtOH suggests that high concentration of EtOH might affect lipid structure in the stratum corneum.

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