PHYSICO-CHEMICAL APPROACH FOR PREDICTION OF THE SKIN CONCENTRATION OF TOPICALLY APPLIED DRUGS

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ABSTRACT

Transdermal formulations are expected to exhibit a biological efficacy of drugs or active substances, as well as pleasant skin feel. In addition, their safety guarantee is important, so that researchers in this field should consider not only the efficacy but also adequate skin concentrations to verify the safety of topically applied substances. ICCR (International Cooperation on Cosmetics Regulation) established international frameworks for the regulation of cosmetics and cosmetic-like drugs (quasi-drug products), and the international harmonization of the frameworks has been discussed from 2007. Since several countries have quite different regulations, regulation based sciences are presently necessary in the international frameworks. In the present study, we predicted the skin concentration of topically applied substances with the skin permeation parameters obtained from in vitro skin permeation studies. Skin concentration was also predicted with physicochemical parameters such as octanol-water partition coefficient or solubility parameter of substances. Full-thickness or stratum corneum-striped abdominal skin was excised from hairless rats and set in Franz type diffusion cells to continuously measure the skin permeation of several compounds. The excised skin was withdrawn after the permeation experiments to observe the skin concentration of compounds. Furthermore, theoretical skin concentration of the compounds was calculated both from the permeation parameters and octanol-water partition coefficient (ClogP) of the compounds. ClogP was calculated by Chem Draw Ultra (Cambridge Soft Corp.). Skin is histologically divided into two membranes, stratum corneum and viable epidermis/dermis. Theoretical skin concentrations calculated not only from the full-thickness skin and stripped skin permeation parameters but also from ClogP well corresponded to the observed values. Establishment of detail and precise relationship between skin concentration and permeation parameters or physicochemical properties using much more substances will lead to better estimation of skin concentration of substances. This in silico approach to determine skin concentration would useful to assure the efficacy and safety of topically applied substances.
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