

Skin penetration enhancement and mechanism by multi-component lipophilic systems

Kenji Sugibayashi

Faculty of Pharmaceutical Sciences, Josai University

Utility and action mechanism of a multi-component lipophilic skin-penetration enhancer, L-lactic acid-ethanolisopropyl myristate (IPM) system (LEI system) were investigated. Silicone fluid, IPM, ethanol-IPM (EI) system, and L-lactic acid-IPM (LI) system were used for comparison with the LEI system. Rank order of the permeation of a model compound, ketotifen (KT) through excised hairless rat skin was silicone fluid < IPM < LI system << EI system < LEI system. Addition of ethanol in the lipophilic vehicles markedly increased the permeation of L-lactic acid as well as KF. Enormous effect by IPM on the ethanol permeation was found from a skin permeation experiment where the systems were applied on the dermis surface (not the stratum corneum surface). These results suggest that the penetration-enhancing effect of the LEI system is complicatedly related to the effects by each component in the system. The KT permeation through two artificial membranes, silicone membrane and porous polypropylene membrane was then measured for further understanding the mechanism of the LEI system. Although both membrane permeations were increased by ethanol, the ethanol effect on the polypropylene membrane permeation was much greater than the silicone one. Addition of L-lactic acid promoted the KT permeation through the polypropylene membrane. These results using artificial membranes suggest that the LEI system acts on the lipophilic domain in the skin barrier and that the solvent drag of KT by ethanol is one of the enhancement mechanism by the LEI system. The skin permeation experiments were finally done using nine drugs. This data pointed out that ethanol increased the skin permeation of ethanol-soluble drugs and that the addition of L-lactic acid was useful to increase basic drugs containing amino groups but acidic drugs containing carboxyl groups.