〈シンポジウム〉
「香粧品と経皮吸収—現在と将来」

皮膚に適用した薬物の皮内動態と代謝

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Drug Disposition and Metabolism in Skin after Topical Application

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Abstract

Our recent works were reviewed on the drug disposition and metabolism in the viable cutaneous tissues beneath the stratum corneum. We have developed a new *in situ* experimental system to evaluate disposition of flurbiprofen (FP) as a model drug within skin. A disk-shaped agar gel was implanted in the abdominal region of hairless rats as a drug receptor, and a drug donor cell was subsequently placed above this agar gel. The amount of FP that had migrated from the skin surface to the gel over 10 h was estimated to be 83% of that observed in the gel, and 0.7% of the total penetration into skin. Although most of the FP that had penetrated into the skin was absorbed into the cutaneous vascular system, direct local delivery was also detected. The efficacy of the direct delivery was influenced by addition of vaso-active compounds and penetration-enhancers. Epinephrine and an ethanol-containing enhancer were useful to increase the topical availability and decrease the systemic bioavailability. We also measured simultaneous skin transport and metabolism of ethyl nicotinate (EN) in rats to evaluate the enzymatic barrier of the skin. Metabolic saturation from EN to nicotinic acid (NA) took place in the viable skin at higher EN application. The calculated steady-state fluxes of EN and NA by the differential equations with separately determined permeation and enzymatic parameters were very close to the obtained data. These cutaneous disposition and metabolism of drugs have a great effect on the pharmacological effects of topically applied drugs.

Key words: skin disposition, skin metabolism, topical application, percutaneous absorption, skin penetration.