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〈報　　告〉

無限用量にて適用した種々剤形からのイソプロピルメチルフェノールの皮膚透過性と皮膚内濃度の関係について
—ヒト長期投与（安全性）試験の用量設定法ガイドライン策定のための検証結果　その1—

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Relationship between Skin Permeation and Concentration of Isopropyl Methyl Phenol Obtained *in Vitro* Skin Permeation Experiments after Application of Various Formulations with an Infinite Dose: Verification Result for Utilization to Dose Setting Method Guideline for Human Long-Duration Trials (Safety), Part 1

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Abstract

The skin concentration of topically applied cosmetic active ingredients is very important for evaluating cosmetics. However, a large variation is often observed in finite dose experiments due to the evaporation of volatile components in the formulation and difficulties for applying formulation uniformly. In addition, steady-state skin concentration could not be attained even after several hours of application. In this verification report, we conducted *in vitro* skin permeation experiment with an infinite dose to confirm whether formulation with the highest skin permeation would also show the highest skin concentration. Three formulations, lotion, milk, and cream, and the mixture of these formulations containing isopropyl methyl phenol (IPMP) as a model ingredient were applied to excised human skin in eight research facilities. The present experiment was conducted with receptor solution containing 1.0% of Brij 98 in order to increase solubility of IPMP in the receptor fluid without changing skin integrity. The obtained results were consistent among the facilities in the following order of skin permeation (lotion＞milk＞cream≅the mixture) and corresponded with that of the skin concentration. This result showed that evaluation of topical formulations with *in vitro* skin permeation experiment with an infinite dose could identify the formulation which exhibited the highest steady-state skin concentration of cosmetic active ingredients. In addition, experiment with mixture formulation might reveal changes in skin permeability associated with changes in thermodynamic activity of IPMP after co-application of several formulations on the skin.

Key words: skin concentration, skin permeation, *in vitro* skin permeation experiment, infinite dose, finite dose.