

〈報 告〉

無限用量にて適用した種々剤形からのカフェインの皮膚透過性と
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2—

用量設定法ガイドライン検討委員会^{1,*}

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**Relationship between Skin Permeation and Concentration of Caffeine 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 2**

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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 difficulty in applying the formulations uniformly. In addition, steady-state skin concentration could not be attained even after several hours of application. In our previous report, 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 with infinite dose (ten to one hundred higher application dose against actual amount of application of personal cosmetic products) in eight research facilities. As the result, the formulation with the highest skin permeation also showed the highest skin concentration. In the present study, the same experiment with the previous report was conducted using a hydrophilic compound, caffeine (CAF). The skin permeation of CAF increased with a decrease in skin electrical resistivity, whereas no relationship was observed in IPMP. Since a large variation of skin permeation of CAF was observed in low skin resistance ($<10 \text{ k}\Omega\text{cm}^2$), the skin having larger than $10 \text{ k}\Omega\text{cm}^2$ skin resistance was used in three facilities in the additional test. The obtained results were consistent among the facilities in the following order of skin permeation (lotion>milk) and corresponded with that of the skin concentration. These results suggest that skin resistance should be considered when a hydrophilic compound is applied in *in vitro* skin permeation test. In addition, the present and the previous results show that 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.

Key words: skin concentration, *in vitro* skin permeation experiment, infinite dose, hydrophilic compound, skin resistance.