

シンポジウムII-1

経皮吸収に影響する諸因子

長村 洋三・石原 勝*

Factors Influencing Skin Penetration of Chemicals

Hiromi OSAMURA & Masaru ISHIHARA*

Factors influencing skin penetration of chemicals are classified as (A) chemicals, (B) skin, (C) contact state and (D) environment.

(A) chemicals: Although the size of molecules or particles, polarity and volatility are factors in skin penetration, the applied amount, concentrations, solubility and vehicles used, influence skin penetration to a greater degree.

With regards to the solubility of chemicals, Overton emphasized the importance of lipid solubility of chemicals permeating the cellular membrane, Treherne, however, reported that in the case of non-electrolytes, chemicals having a ether/water partition coefficient close to 1 possess a greater ability for skin penetration.

In this study, we compared the amount of nicotinic acid, methyl nicotinate and butyl nicotinate which penetrated the separated human epidermis into a saline solution.

It was found that solvents of chemicals greatly influenced the skin penetration of chemicals. When the affinity of chemicals with solvents was too great (i.e., butyl nicotinate in olive oil), the chemical was not readily released by the solvent, and the resultant skin penetration was low.

In the case of water, used as a solvent, the amount of chemical which penetrated the epidermis was greatest for butyl nicotinate, followed by methyl nicotinate.

When olive oil, ethanol or propylene glycol were used as solvents, methyl nicotinate penetrated the epidermal membrane to the greatest degree.

The skin penetration of nicotinic acid was lowest, irrespective of the solvents used.

In *in vitro* tests, the minimal effective concentrations which produced erythema 30 minutes after application were studied. The results of the influence of solvents on each chemical applied in the *in vivo* testing were very similar to those obtained in the *in vitro* tests.

The amount of penetration through separated human epidermis of hydrocortisone, betamethasone, betamethasone 17 valerate and clobetasol 17 propionate in ethanol or propylene glycol was studied.

The amount of each topical corticosteroid which was released from ethanol was greater than that from propylene glycol.

In the case of ethanol solvent, betamethasone 17 valerate penetrated separated human epidermis to a greater degree than any of the other corticosteroids tested.

In *in vivo* tests, the blanching phenomenon of the above mentioned four corticosteroids and also the recently developed hydrocortisone 17 butylate 21 propionate, was studied.

Clobetasol propionate produced the strongest blanching effect, followed by hydrocortisone 17 butylate 21 propionate, betamethasone 17 valerate, and betamethasone. Hydrocortisone was the poorest vasoconstrictor.

While betamethasone 17 valerate exhibited a greater degree of skin penetration, clobetasol 17 propionate produced the greatest topical pharmacological effectiveness, and as such the clinical effectiveness of these topical corticosteroids is based on the latter.

(B) skin: With regards to the skin, animal species, age, region, normal or abnormal skin, the amount of water in the horny layer, etc., will affect the skin penetration of chemicals.

* 東邦大学医学部皮膚科学教室
(東京都大田区大森西6-11-1)

* Department of Dermatology, School of Medicine, Toho University (6-11-1, Omorinishi, Ota-ku, Tokyo)

Ishihara reported that hydrocortisone acetate was more readily released from vehicles to psoriatic lesions, when compared with normal skin. Matsushima et al found that methyl or butyl nicotinate in olive oil penetrated more readily through the hydrated human epidermis than through a non-hydrated epidermis.

(C) contact state: With regards to the contact state, application method (simple application or occlusive dressings), duration of application, site of application, size of application, etc. influence the total amount of skin penetration of chemicals.

(D) environment: Concerning environmental factors, it has been reported by many researchers that ambient temperature or humidity influence the skin penetration of chemicals.

When the skin penetration of chemicals is studied, these various factors must always be taken into account.