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Targeted and sustained delivery of hydrocortisone to normal and stratum corneum-removed skin without enhanced skin absorption using a liposome gel

Moon-Kyoung Kim[a], Suk-Jae Chung[b], Min-Hwa Lee[b], Ae-Ri Cho[c], Chang-Koo Shim[b]
[a]Yuhan Research Center, [b]Seoul Nat'l. Univ., [c]Duksung Women's Univ.

Purpose: To determine rate limiting process of percutaneous absorption from liposomes in order to understand whether enhanced drug absorption to the skin or to retarded systemic diffusion of the skin-absorbed drug is responsible for the higher drug concentration in the skin.
Methods: A liposome-gel formulation containing 1% (w/w) hydrocortisone was prepared by blending phosphatidylcholine liposomes of hydrocortisone with Carbopol 934 hydrogel. The liposome-gel was applied topically onto the normal and stratum corneum (SC)-removed skins (3.0 cm^2) of hairless mice at a dose of 1 mg as hydrocortisone. Subsequently, concentrations of hydrocortisone in the skin and various organs were measured.
Results: Judging from hydrocortisone concentration in dosing area, the extent of absorption was reduced in the liposome-gel formulation. However, higher and sustained skin concentrations of hydrocortisone were achieved for the liposome-gel as compared to the ointment. Drug concentration in both viable and deep skin reached its maximum within 0.5 h after application of both formulations to both skin types. Drug concentrations in both skins from the ointment declined with time, while those from the liposome-gel were greatly sustained. The sustainment by the liposome-gel was more remarkable in the viable skin than in the deep skin. Drug concentration in the viable skin could be maintained at a nearly constant level for over 8 h by applying the liposome-gel. As a result, a 5-fold higher viable skin drug concentration was obtained from the liposome-gel than from the ointment at 8 h after the application to the SC-removed skin. However, the plasma concentration of hydrocortisone at 4 h from the liposome-gel was only one-fourth ($p<0.01$) the value from the ointment when the drug was applied to the SC-removed skin, consistent with the lower urinary (one-third, $p<0.05$) and fecal (one-half, $p<0.05$) excretion.
Conclusions: Retarded diffusion of the drug from the skin to the systemic blood stream appears to be a potential factor in the sustained skin concentration of hydrocortisone from the liposome-gel . Interaction of hydrocortisone in the skin with phosphatidylcholine, a component of the liposomes and skin, may well be a factor in retarding the diffusion of the drug in the skin.