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# Content and Transdermal Delivery of Clobetasol 17-Propionate from Commercial Creams and Ointments

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## ABSTRACT

Semisolid creams and ointments containing 0.05% w/w clobetasol 17-propionate (CP) as active ingredient are categorized as super-potent topical dermatological corticosteroids. The objective of the study was to evaluate the content and transdermal delivery of CP from eleven commercial dosage forms, including three ointments and eight creams. It was found that the CP content of the ointments ranged from 77.5 to 96.1% of the labeled amount, and that of the creams ranged from 84.0 to 105.6%. *In vitro* transdermal flux of CP through nude mouse skin ranged from 0.156 to 0.270 $\mu g/cm^2/h$ for ointments, and 0.100 to 0.521 $\mu g/cm^2/h$ for creams. Total amount of CP penetrated in 8 h ranged from 1.03 to 1.75 $\mu g$ for ointments, and 0.67 to 2.95 $\mu g$ for creams. Lag time to reach steady-state of delivery ranged from 1.48 to 1.63 h for ointments, and 1.53 to 3.19 h for creams. In comparison with the brand name products, transdermal flux of CP from the generic ointments was 57.7% and 83.5% of Dermovate ointment, and that from the generic creams ranged from 19.2 to 94.8% of Dermovate cream. The results demonstrated that commercial 0.05% CP creams and ointments were highly variable in the transdermal delivery of CP, which may influence their bioavailability and clinical efficacy.

Key words: clobetasol 17-propionate, content, transdermal delivery, topical, semisolid

## INTRODUCTION

Topical corticosteroids are the most frequently prescribed of all dermatologic products[1]. According to a survey, corticosteroids constituted approximately one fourth of the 120 topical dermatologic products prescribed in the clinics and hospitals in Taiwan[2]. The most potent glucocorticoid for topical use is clobetasol 17-propionate, which is about 1000 times more potent than hydrocortisone[3]. Both Temovate creams and ointments containing 0.05% clobetasol 17-propionate (CP) as active ingredient are categorized as super-potent class I topical dermatological corticosteroids[3,4]. It is well-known that drug release and skin penetration are greatly influenced by formulations, which in turn may determine their bioavailability and clinical efficacy[5]. In the prior studies, we have demonstrated that topical bioavailability of salicylic acid varied substantially among different formulations[6]. It has been shown in various studies[e.g., 7,8] using vasoconstrictor assay, that large differences existed between generic and trade name formulations containing the same steroid in the same concentration in different vehicles. Moreover, by varying vehicles, betamethasone dipropionate have been formulated into four potency classes[3]. Furthermore, studies have shown that CP formulated in various cream bases released the drug and penetrated skin at different rates, causing various degrees of skin blanching response[9,10].

More than twenty generic formulations containing 0.05% w/w CP have been listed to be commercially marketed in Taiwan[11], which raised that the concern that significant differences may exist in their drug release and skin penetration, and hence their therapeutic effectiveness. In the following, we report the content and *in vitro* transdermal delivery of CP from eleven commercial dosage forms, including three ointments and eight creams, available in pharmacy stores. It is the goal of this study to evaluate the differences in the percutaneous absorption of CP among commercial formulations using *in vitro* methodology.

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## MATERIALS AND METHODS

### I. *Materials*

Clobetasol 17-propionate (CP) of greater than 99% purity, p-phenylphenol, betamethasone dipropionate, and phosphate buffered saline (PBS) were purchased from Sigma Chemical Co. (St. Louis, MO, USA). HPLC grade acetonitrile was obtained from BDH Laboratory Supplies (Poole, England). Hydrophilic Ointment USP was obtained from China Chemical & Pharmaceutical Co., Ltd. Dermovate ointment and cream were gifts from GlaxoWellcome (Pty) Ltd. Generic formulations containing 0.05% w/w CP as active ingredient were purchased from pharmacy stores located in southern Taiwan, including two ointments and seven creams. Eight of the products were marketed by local pharmaceutical manufacturers, and the other was imported. The two generic ointments were coded as products B, C, and the creams as products E to K randomly. The three ointments appeared semi-translucent, and the creams have typical, creamy-white appearance. Gross examinations of those products revealed no visually perceivable particulate matter.

II. *Content Determinations*

The procedures to extract CP from ointment were modified from Patel *et al*. [12]. Briefly, approximately 200 mg of each formulation, equivalent to 0.1 mg of CP, were accurately weighed into a 50-mL centrifuge tube. Thirty mL of methanol-water mixture (80:20, v/v) were added to the tube. The tube was then placed in a 60˚C water bath for 2 min, and the formulation was dispersed into solution with the aid of vigorous shaking. After cooling with ice for 20 min, the dispersion was centrifuged. The supernatant was decanted into a 100-mL volumetric flask. Extraction was repeated two more times. Adequate volume of methanol-water mixture was then added to make 100 mL and obtain a final concentration of approximately 1 $\mu$g/mL of CP. Samples were submitted to the following high-performance liquid chromatography (HPLC) for CP quantitation, and CP content in the formulations was expressed as percentage of the labeled amount. The recovery of CP from the ointment base was estimated by adding 100 $\mu$L of 1 mg/mL CP standard solution in methanol to 200 mg of white petrolatum. Methanol was then evaporated under air stream, and the ointment was melted in a 60˚C water bath and extracted as described above. Recovery was calculated to be 100.8 ± 2.9% (n = 5).

For the cream, approximately 200 mg of each formulation, equivalent to 0.1 mg of CP, were accurately weighed into a 50-mL centrifuge tube, and dispersed in 10 mL of water with the aid of vigorous shaking. The dispersion was extracted with 5 mL of chloroform three times. The combined chloroform extract was evaporated to dryness and brought into 100 mL of methanol:water (80:20, v/v) mixture to a final concentration of approximately 1 $\mu$g/mL of CP. The recovery of CP from the cream bases was estimated by adding 100 $\mu$L of 1 mg/mL CP standard solution in methanol to 200 mg of Hydrophilic Ointment USP followed by the extraction procedures described above. Recovery was calculated to be 97.6 ± 1.3% (n = 4).

III. *In Vitro Skin Penetration Studies*

The experiments were conducted in accordance with the guidelines for the care and use of laboratory animals in research and teaching (National Science Council, Republic of China). Freshly prepared full thickness skin obtained from 8 to 12 weeks old female nude mouse (strain BALB/c-nu) was used in all the experiments. The animals were maintained on a standard mouse chow diet, and water ad libitum. Transepidermal water loss (TEWL) levels on both flanks were measured using Tewameter TM210 (Courage & Khazaka, Köln, Germany) following the guidelines[13] before the anesthetized animals were sacrificed by cervical dislocation. Adhering subcutaneous fat on the dermal side was carefully removed from the skin's surface.

Penetration studies were performed using flow-through diffusion cells (Laboratory Glass Apparatus, Berkeley, CA, USA) with a diffusion area of 1 $cm^2$ and a receiver volume of 3.6 mL, as previously described[14]. After the skin was mounted on a diffusion cell with dermal side down and a medium consisting of freshly prepared isotonic pH 7.4 PBS:ethanol (70:30, v/v)[9] was pumped through the receiver compartment at a flow rate of 3 - 4 mL/h using a peristaltic pump (Ismatec, Glattbrug-Zürich, Switzerland), approximately 400 mg of each formulation was applied uniformly to the skin surface and the upper donor cell was sealed with parafilm. Preliminary testing demonstrated that the cumulative amount - time profiles were similar among doses of 300, 400 and 500 mg, and an infinite dose condition has been approximated under the experimental conditions. The receptor fluid was stirred at 700 rpm with a small Teflon-coated magnet and collected at one hour intervals for eight hours using a Retriever IV fraction collector (ISCO, Lincoln, NE, USA). The receiver compartment was maintained at a constant temperature of 37˚C in a circulating water bath. CP content in the collected fractions was quantitated using the following HPLC methods.

Transdermal flux of CP from different formulations was calculated from the quasisteady-state slope of the cumulative amount penetrated in the receiver fluid versus time profiles. Only terminal data points with correlation coefficients greater than 0.99 were included in data analysis. Lag time of penetration was then deduced from the intercept of steady-state extrapolation to the time axis.

IV. *Analytical Methods*

CP content in the various samples was identified chromatographically by HPLC methods modified from Weigmann *et al*.[15] and Fang *et al*.[9]. The HPLC system consisted of a system controller (model 600E, Waters Co., Milford, MA) and an autosampler (Waters model 700 Satellite WISP) on a C18 reverse phase column (Lichrospher® 100 RP-18 5 $\mu$m, 12.5 cm × 4.0 mm, Merck KGaA, Darmstadt, Germany) using a 1 mL/min flow rate of mobile phase of acetonitrile-water (50:50, v/v). A UV detector with tunable wavelength (Waters model 486) set at 240 nm was used to detect CP. The retention times were about 10 min, 4.5 min, and 12 min for CP and the internal standards, either p-phenylphenol or betamethasone dipropionate, respectively. To avoid interferences in the HPLC chromatogram from unknown ingredients present in different dosage forms, betamethasone dipropionate was used as internal standard in determining CP content in the dosage forms, while p-phenylphenol was used in the samples from skin penetration studies. Preliminary tests with methylparaben, propylparaben, butylparaben, and benzoic acid didn't interfere with CP and the internal standards in the chromatographic analysis. Drug concentration in the samples was determined from CP standard curves generated with the pure compound. The standard curve was linear for the peak-area ratio of CP to the internal standard in CP concentration ranges of 0.025 to 5 $\mu$g/mL. The limit of quantitation was determined to be 3.75 ng. The intra- and inter-day reproducibility of the HPLC assay is shown in Table 1.

*Journal of Food and Drug Analysis, Vol. 10, No. 1, 2002*

**Table 1.** Intra- and inter-day assay reproducibility of CP (n = 6 each)

| CP | Intra-day | | Inter-day | |
|---|---|---|---|---|
| Concentration ($\mu$g/mL) | Accuracy (RE, %) | Precision (CV, %) | Accuracy (RE, %) | Precision (CV, %) |
| 0.1 | 11.93 | 4.96 | 13.09 | 6.42 |
| 0.2 | 3.60 | 1.97 | 4.95 | 3.80 |
| 0.5 | -1.95 | 2.04 | -2.79 | 2.13 |
| 1 | -2.10 | 0.39 | -3.27 | 1.73 |
| 2 | 0.58 | 0.17 | 0.28 | 1.20 |

## RESULTS AND DISCUSSION

### I. *CP Content in Commercial Dosage Forms*

As summarized in Table 2, CP content of the ointments ranged from 77.5 to 96.1% of the labeled amount, and that of the creams ranged from 84.0 to 105.6%. CP content of ointment B and cream I fell beyond the common pharmacopeial specification of 90 to 110%. In addition, even with the small sample size of 3 to 5 replicates, it appeared that both generic ointment formulations were not as uniform as Dermovate, with greater variations in their CP content. However, not only the generic creams E and F, but also Dermovate cream varied significantly in their content uniformity. The phenomenon of dosage disuniformity has been demonstrated in commercial hydrocortisone ointments and suggested a large number of drug agglomerates existing in the topical products[16]. The greater variations in uniformity of cream formulations could be explained by the highly lipophilic features of CP (log $K_{O/W}$ = 3.83)[17], which might have increased the difficulties in drug distribution in o/w creams than in petrolatum ointments during manufacturing process. The aspect of dosage uniformity and presence of drug agglomerates in topical products would require further investigation.

### II. *In Vitro Transdermal Delivery of CP*

The data were plotted as cumulative amount of CP collected in the receiver fractions as a function of time for the eleven formulations, as shown in Figure 1. *In vitro* skin penetration characteristics including transdermal flux, lag time, and total amount penetrated in 8 h for the eleven formulations

**Table 2.** CP content in 0.05% w/w commercial creams and ointments

| Formulation type | product ID | % of labeled amount (mean ± SD) | N |
|---|---|---|---|
| Ointment | A[a] | 96.1 ± 0.5 | 3 |
| | B | 77.5 ± 4.1 | 5 |
| | C | 95.2 ± 8.5 | 5 |
| Cream | D[a] | 98.5 ± 10.8 | 3 |
| | E | 95.5 ± 19.6 | 5 |
| | F | 95.6 ± 15.5 | 3 |
| | G | 97.8 [b] | 2 |
| | H | 98.5 [b] | 2 |
| | I | 84.0 ± 2.8 | 4 |
| | J | 105.6 ± 8.0 | 4 |
| | K | 97.5 [b] | 2 |

[a] A, D:Dermovate.

[b] average of two samples.

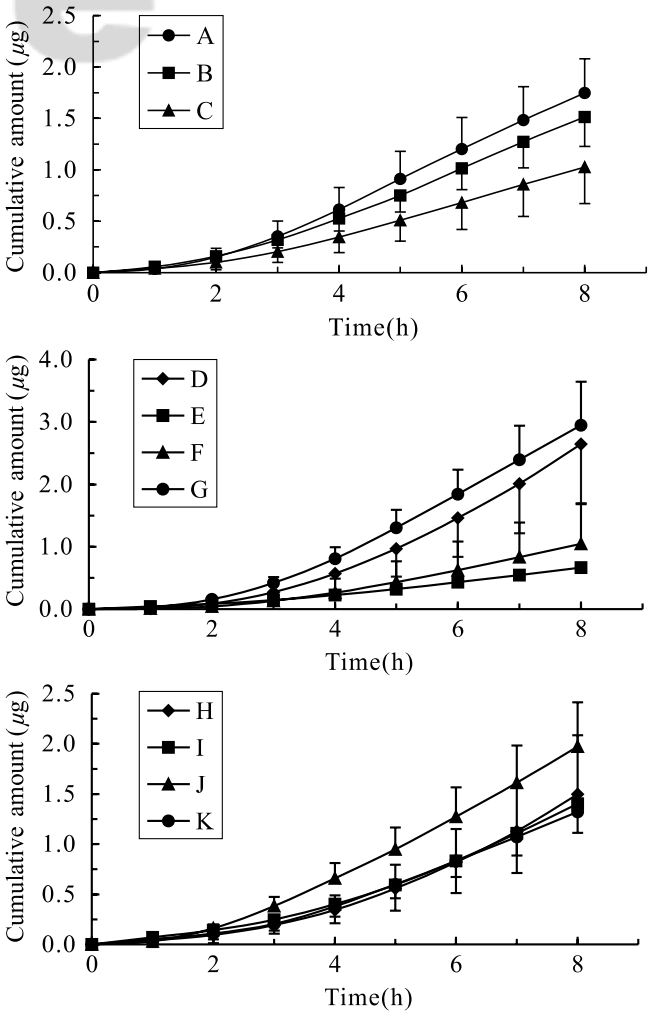


**Figure 1.** Cumulative amount of CP penetrated through nude mouse skin as a function of time from commercial 0.05% w/w ointments and creams. A: Dermovate ointment; B&C: generic ointments; D: Dermovate cream; E to K: generic creams.

are summarized in Table 3. Transdermal flux of CP through nude mouse skin varied from 0.156 to 0.270 $\mu$g/cm$^2$/h for ointments, and 0.100 to 0.521 $\mu$g/cm$^2$/h for creams. Total amount of CP penetrated in 8 h ranged from 1.03 to 1.75 $\mu$g for ointments, and 0.67 to 2.95 $\mu$g for creams. Lag time to reach quasisteady-state of delivery ranged from 1.48 to 1.63 h for ointments, and 1.53 to 3.19 h for creams. In comparison with the brand name product, Dermovate, transdermal flux of CP from the generic ointments B and C was 83.5% and 57.7% of Dermovate ointment, respectively, and that from the seven generic creams ranged from 19.2 to 94.8% of Dermovate cream. The variations in total amount penetrated in 8 h among different formulations appeared to parallel their transdermal CP flux. The greatest transdermal flux of CP for ointments and creams were both from Dermovate, indicating highest efficiency from the brand name formulations in transdermal drug delivery. Furthermore, it appeared that cream was more efficient in CP delivery through nude mouse skin than the ointment for Dermovate. The result is consistent with the findings shown by Harding *et al.*[18] and Smith *et*

**Table 3.** *In vitro* transdermal delivery of CP from 0.05% commercial ointments and creams through nude mouse skin

| Formulation type | product ID | flux ($\mu$g/cm$^2$/h) | ratio** | lag time (h) | ratio** | total amount penetrated in 8 h ($\mu$g/cm$^2$) | ratio** | N |
|---|---|---|---|---|---|---|---|---|
| Ointment | A* | 0.270 ± 0.041 | 1.00 ± 0.15 | 1.63 ± 0.52 | 1.00 ± 0.32 | 1.75 ± 0.33 | 1.00 ± 0.19 | 12 |
| | B | 0.226 ± 0.038$^b$ | 0.84 ± 0.14 | 1.48 ± 0.24$^a$ | 0.91 ± 0.15 | 1.52 ± 0.29$^a$ | 0.87 ± 0.16 | 6 |
| | C | 0.156 ± 0.053$^e$ | 0.58 ± 0.19 | 1.56 ± 0.75$^a$ | 0.96 ± 0.46 | 1.03 ± 0.36$^e$ | 0.59 ± 0.20 | 6 |
| Cream | D* | 0.521 ± 0.135 | 1.00 ± 0.26 | 3.19 ± 0.75 | 1.00 ± 0.24 | 2.65 ± 0.95 | 1.00 ± 0.36 | 7 |
| | E | 0.100 ± 0.008$^e$ | 0.19 ± 0.02 | 1.57 ± 0.39$^d$ | 0.49 ± 0.12 | 0.67 ± 0.05$^e$ | 0.25 ± 0.02 | 5 |
| | F | 0.188 ± 0.091$^e$ | 0.36 ± 0.18 | 2.86 ± 0.69$^a$ | 0.90 ± 0.22 | 1.04 ± 0.64$^d$ | 0.39 ± 0.24 | 7 |
| | G | 0.494 ± 0.121$^a$ | 0.95 ± 0.23 | 2.12 ± 0.65$^b$ | 0.66 ± 0.21 | 2.95 ± 0.70$^a$ | 1.11 ± 0.26 | 5 |
| | H | 0.294 ± 0.119$^c$ | 0.57 ± 0.23 | 3.06 ± 0.60$^a$ | 0.97 ± 0.18 | 1.50 ± 0.59$^b$ | 0.57 ± 0.22 | 6 |
| | I | 0.240 ± 0.061$^d$ | 0.46 ± 0.12 | 2.37 ± 0.28$^b$ | 0.74 ± 0.09 | 1.40 ± 0.39$^b$ | 0.53 ± 0.15 | 5 |
| | J | 0.291 ± 0.063$^c$ | 0.56 ± 0.12 | 1.53 ± 0.20$^e$ | 0.48 ± 0.06 | 1.97 ± 0.44$^a$ | 0.75 ± 0.17 | 5 |
| | K | 0.218 ± 0.033$^e$ | 0.42 ± 0.06 | 2.10 ± 0.29$^b$ | 0.66 ± 0.09 | 1.32 ± 0.21$^b$ | 0.50 ± 0.08 | 5 |

*A, D: Dermovate; $^a$ $p > 0.05$, $^b$ $p < 0.05$, $^c$ $p < 0.01$, $^d$ $p < 0.005$, and $^e$ $p < 0.001$ in comparison with Dermovate.
**Ratio was calculated as the data from generic products divided by the data from Dermovate.
Data represent mean ± SD.

**Table 4.** Transdermal delivery of CP from commercial dosage forms normalized to 100% of labeled content

| Formulation type | product ID | flux ($\mu$g/cm$^2$/h) | ratio$^b$ | total amount penetrated in 8 h ($\mu$g/cm$^2$) | ratio$^b$ |
|---|---|---|---|---|---|
| Ointment | A$^a$ | 0.281 | 1.00 | 1.82 | 1.00 |
| | B | 0.292 | 1.04 | 1.96 | 1.08 |
| | C | 0.164 | 0.58 | 1.08 | 0.59 |
| Cream | D$^a$ | 0.529 | 1.00 | 2.69 | 1.00 |
| | E | 0.105 | 0.20 | 0.70 | 0.26 |
| | F | 0.197 | 0.37 | 1.09 | 0.41 |
| | G | 0.505 | 0.95 | 3.02 | 1.10 |
| | H | 0.298 | 0.56 | 1.52 | 0.57 |
| | I | 0.286 | 0.54 | 1.67 | 0.62 |
| | J | 0.296 | 0.56 | 1.88 | 0.70 |
| | K | 0.224 | 0.42 | 1.35 | 0.50 |

$^a$ A, D: Dermovate.
$^b$ Ratio was calculated as the data from generic products divided by the data from Dermovate.

*al.*[19], that Dermovate and Betnovate cream formulations were slightly more potent than their corresponding ointment formulations in inducing vasoconstrictor responses. As the actual vehicle compositions of Dermovate formulations are unavailable to us, we speculate that the emulsifiers and cosolvents, such as glyceryl monostearate, glyceryl stearate and PEG 100 stearate, contained in the cream may have enhanced the skin permeability of CP[20], in comparison with the petrolatum-based ointment. Among the generic creams, the largest deviation from Dermovate cream observed was from cream E, showing a five-fold reduction in transdermal CP flux and a four-fold decrease in total penetration in 8 h.

The mechanisms in deviation of drug delivery from Dermovate may vary among generic formulations. To dissect the influences of both driving force and formulation factors, transdermal delivery of CP from each dosage form was normalized to 100% of its labeled content, listed in Table 4. As seen in both Tables 3 and 4, transdermal flux and total delivery in 8 h of ointment B have been elevated from 84 to 104% and 87 to 108% of Dermovate ointment after data normalization, respectively, suggesting that the driving force is the determinant in its lower transdermal delivery relative to Dermovate. However, for other generic formulations except cream I, the differences in transdermal CP flux could not be explained by their CP content, indicating predominant influences from formulation factors other than drug content. Cream I delivered CP at a 46% rate of Dermovate, which could only be partly attributed to its CP content (85% relative to Dermovate). Its transdermal delivery remained as low as 54% (flux) and 62% (8 h delivery) of Dermovate after data normalization, suggesting major influences from other formulation factors. As vehicle compositions of these formulations were proprietary information of their manufacturers, we were unable to explain how they influence CP delivery at this point. Whether the differences in transdermal delivery of CP will reflect their *in vivo* bioavailability is currently under investigation.

### III. *Effect of Skin Barrier Function on the Transdermal Delivery of CP*

As shown in Figure 2, no correlation between transdermal flux of CP from Dermovate ointment and skin barrier function, as indicated by TEWL levels up to 15 g/m$^2$/h, was observed ($R^2 = 0.03$). With a log $K_{O/W}$ value of 3.83 for CP, the result was consistent with our previous findings[14] that

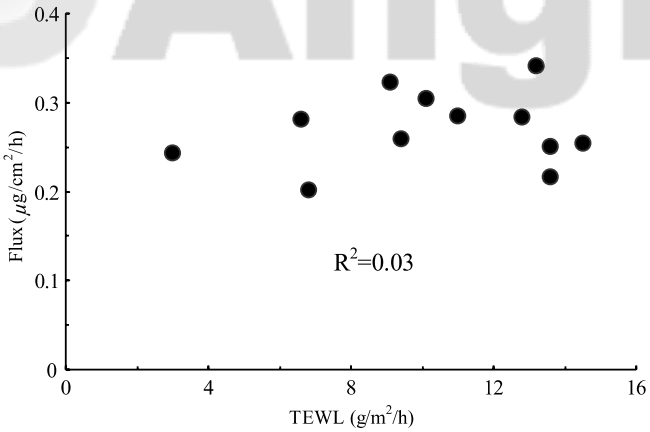


**Figure 2.** Transdermal flux of CP from Dermovate ointment versus TEWL levels of nude mouse skin membrane.

permeability barrier disruption didn't alter percutaneous absorption of highly lipophilic drugs, even when formulated in ointment forms.

In conclusion, commercial 0.05% w/w CP creams and ointments were highly variable in the transdermal delivery of CP *in vitro*, with the generic products delivering CP at slower rates than Dermovate, which may impact their bioavailability and clinical efficacy. The differences in transdermal delivery rate were mainly attributed to their formulations. Further studies should be conducted to verify their bioavailability *in vivo*.

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## REFERENCES

1. Baumann, L. and Kerdel, F. 1999. Topical glucocorticosteroids. In "Dermatology in General Medicine". 5th ed. vol. 2, pp. 2713-2717. Freedberg, I. M., Eisen, A. Z., Wolff, K., Austen, K. F., Goldsmith, L. A., Katz, S. I. and Fitzpatrick, T. B. ed. MacGraw-Hill. New York, U. S. A.
2. Liao, C. C. 1997. Report on the Survey of Pharmaceutical Products Prescribed in Hospitals and Clinics. pp. 37-42. Chang Gung Memorial Hospital. Taipei, Taiwan.
3. Stoughton, R. B. and Cornell, R. C. 1993. Corticosteroids. In "Dermatology in General Medicine". 4th ed. vol. 2, pp. 2846-2850. Fitzpatrick, T. B., Eisen, A. Z., Wolff, K., Freedberg, I. M. and Austen, K. F. ed. MacGraw-Hill. New York, U. S. A.
4. Guzzo, C. A., Lazarus, G. S. and Werth, V. P. 1996. Dermatological pharmacology. In "Goodman and Gilman's The Pharmacological Basis of Therapeutics". 9th ed. pp. 1593-1616. Hardman, J. G., Limbird, L. E., Molinoff, P. B., Ruddon, R. W. and Gilman, A. G. ed. McGraw-Hill. New York, U. S. A.
5. Caron, D., Queille-Roussel, C., Shah, V. P. and Schaefer, H. 1990. Correlation between the drug penetration and the blanching effect of topically applied hydrocortisone creams in human being. J. Am. Acad. Dermatol. 23: 458-462.
6. Tsai, J. C., Chuang, S. A., Hsu, M. Y. and Sheu, H. M. 1999. Distribution of salicylic acid in human stratum corneum following topical application *in vivo*: a comparison of six different formulations. Intl. J. Pharm. 188: 145-153.
7. Woodford, R. and Barry, B. W. 1974. Bioavailability and activity of betamethasone 17-benzoate in gel and cream formulations: comparisons with proprietary topical corticosteroid preparations in the vasoconstrictor assay. Curr. Ther. Res. Clin. Exp. 16: 338-345.
8. Stoughton, R. B. 1987. Are generic formulations equivalent to trade name topical glucocorticoids? Arch. Dermatol. 123:1312-1314.
9. Fang, J. Y., Shen, K. , Huang, Y. B., Wu, P. C. and Tsai, Y. H. 1998. Topical application of clobetasol 17-propionate from various cream bases by using Wistar rat as an animal model. Kaohsiung J. Med. Sci. 14: 286-293.
10. Fang, J. Y., Shen, K. L., Huang, Y. B., Wu, P. C. and Tsai, Y. H. 1999. Evaluation of topical application of clobetasol 17-propionate from various cream bases. Drug Dev. Ind. Pharm. 25: 7-14.
11. Tsai, C. Y. 1999. Handbook of Common Drugs. pp. 1352-1363. Xing-Lin. Taipei, Taiwan.
12. Patel, A. G., Patel, R. B. and Patel, M. R. 1990. Liquid chromatographic determination of clobetasone-17-butyrate in ointments. J. Assoc. Off. Anal. Chem. 73: 893-895.
13. Pinnagoda, J., Tupker, R. A., Agner, T. and Serup, J. 1990. Guidelines for transepidermal water loss (TEWL) measurement. Contact Dermatitis 22: 164-178.
14. Tsai, J. C., Sheu, H. M., Hung, P. L. and Cheng, C. L. 2001. Effect of barrier disruption by acetone treatment on the permeability of compounds with various lipophilicities: implications for the permeability of compromised skin. J. Pharm. Sci. 90: 1242-1253.
15. Weigmann, H. J., Lademann, J., Pelchrzim, R. V., Sterry, W., Hagemeister, T., Molzahn, R., Schaefer, M., Lindscheid, M., Schaefer, H. and Shah, V. P. 1999. Bioavailability of clobetasol propionate - Quantification of drug concentrations in the stratum corneum by dermatopharmacokinetics using tape-stripping. Skin Pharmacol. Appl. Skin. Physiol. 12: 46-53.
16. Orr, N. A., Hill, E. A. and Smith, J. F. 1980. Dosage uniformity in hydrocortisone ointment B.P. J. Pharm. Pharmacol. 32: 766-772.
17. Craig, P. N. 1990. Drug compendium. In "Comprehensive Medicinal Chemistry". Vol. 6, p. 395. Hansch, C., Sammes, P. G. and Taylor, J. B. ed. Pergamon Press. New York, U. S. A.
18. Harding, S. M., Sohail, S. and Busse, M. J. 1985. Percutaneous absorption of clobetasol propionate from novel ointment and cream formulations. Clin. Exp. Dermatol. 10: 13-21.

19. Smith, E. W., Meyer, E. and Haigh, J. M. 1990. Blanching activities of betamethasone formulations. Arzneim.-Forsch. 40: 618-621.

20. Williams, A. C. and Barry, B. W. 1992. Skin absorption enhancers. Crit. Rev. Ther. Drug Carrier Sys. 9: 305-353.

# 市售氯貝他索丙酸乳軟膏製劑之含量測定與穿皮速率研究

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## 摘　要

氯貝他索丙酸（Clobetasol 17-propionate, CP）乳軟膏製劑是外用皮質類固醇中效價最強的藥品，本研究之目的在評估市售11種含0.05% clobetasol 17-propionate的外用製劑（包括3種軟膏和8種乳膏）的含量及體外穿皮速率。含量測定結果得3種軟膏的CP含量在標示量的77.5 - 96.1%之間，而8種乳膏的含量則在標示量的84.5-105.6%之間。體外裸鼠皮滲透試驗結果得軟膏的穿皮速率介於0.156與0.270 $\mu g/cm^2/h$之間，而乳膏則為0.100-0.521 $\mu g/cm^2/h$；8小時總穿透量在軟膏為1.03 - 1.75 $\mu g/cm^2$，乳膏則為0.67 - 2.95 $\mu g/cm^2$；其滯留時間在軟膏為介於1.48和1.63小時間，乳膏則在1.53 - 3.19小時間。如與商品名製劑比較，兩種學名軟膏的穿皮速率分別為Dermovate軟膏的57.7%和83.5%，而學名乳膏的穿皮速率則為Dermovate乳膏的19.2-94.8%。研究結果顯示市售0.05%CP乳軟膏製劑的穿皮速率差距差大，可能嚴重影響這些製劑的生體可用率和臨床療效。

**關鍵詞**：氯貝他索丙酸，含量，穿皮速率，外用，半固體