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Original Research Article

Comparative assessment of cutaneous delivery of clobetasol propionate from two topical cream formulations using an *in vitro* Franz diffusion model

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ABSTRACT

Background: The therapeutic effectiveness of topical corticosteroids depends on their ability to achieve adequate skin retention while minimizing systemic absorption. This study compared the cutaneous delivery characteristics of two clobetasol propionate 0.05% cream formulations, clobetasol 0.05% cream and clobetasol 0.05% cream (innovator), using an in vitro Franz diffusion model.
Methods: Comparative skin permeation studies were conducted using excised swine skin mounted on Franz diffusion cells in accordance with OECD Test Guideline 428. A 100 mg dose of each formulation was applied to the skin surface and receptor fluid samples were collected over 12 hours. Clobetasol propionate concentrations were quantified using a validated HPLC method. Drug permeation, skin retention and surface residue were determined.
Results: Both formulations exhibited low transdermal permeation and substantial skin retention. At 12 hours, cumulative permeation was 2.52% for clobetasol 0.05% cream and 2.85% for clobetasol 0.05% cream (innovator). Skin retention was 59.25% and 52.67%, respectively, while the remaining drug was estimated as surface residue. Although minor differences in permeation kinetics were observed, the overall distribution profiles of clobetasol propionate were comparable between the two formulations.
Conclusions: Clobetasol 0.05% cream and clobetasol 0.05% cream (innovator) demonstrated comparable cutaneous delivery characteristics, with high skin retention and minimal transdermal permeation. The findings indicate that both formulations effectively localize clobetasol propionate within the skin, supporting their suitability for topical treatment of inflammatory dermatoses.

Keywords: Clobetasol propionate, Franz diffusion cell, Skin permeation, Skin retention, Topical corticosteroid

INTRODUCTION

The therapeutic performance of a topical dermatological product is determined not only by the potency of the active ingredient but also by its ability to distribute appropriately within the skin following application.[1,2] For topical corticosteroids, optimal treatment outcomes are achieved when sufficient quantities of the drug are retained within the epidermal and dermal tissues, where the inflammatory process occurs, while minimizing drug passage beyond the skin. Clobetasol propionate is a super-potent corticosteroid extensively used in the treatment of corticosteroid-responsive dermatoses, including psoriasis, eczema and chronic inflammatory skin conditions.[3] Although products containing the same concentration of active ingredient may be therapeutically equivalent, differences in formulation composition can influence drug release, skin uptake and tissue retention.[4,5]

Therefore, characterization of dermal delivery behavior is an important component in the evaluation of topical corticosteroid formulations.

Understanding the disposition of a topically applied drug requires assessment of three key parameters: the fraction that penetrates through the skin, the fraction retained within skin tissues and the fraction remaining on the skin surface following application. Together, these parameters provide insight into the extent of local drug availability and the potential for systemic exposure.[5]

In vitro permeation studies employing Franz diffusion cells are widely used to investigate these characteristics under controlled experimental conditions.[5,6] Swine skin has been recognized as a suitable surrogate for human skin due to similarities in morphology, lipid composition and permeability properties.[7,8] Consequently, the Franz diffusion cell model using excised swine skin has become a standard approach for comparative evaluation of topical formulations.

The present study aimed to compare the skin permeation and retention characteristics of two clobetasol propionate 0.05% cream formulations, Clobetasol 0.05% Cream and Clobetasol 0.05% Cream (Innovator), using excised swine skin mounted on Franz diffusion cells.

METHODS

Materials

Two topical cream formulations containing clobetasol propionate (0.05% w/w) were evaluated in this study. Clobetasol 0.05% cream (sample code: SRC/AB/25/12/03) and clobetasol 0.05% cream (innovator) (Sample Code: SRC/AB/25/12/04) were supplied by the study sponsor and stored according to the manufacturer's recommendations until use.

Study design and ethical considerations

The present study was an experimental, comparative in vitro skin permeation study conducted using a Franz diffusion cell model. The study was carried out at KET's scientific research centre, animal biotechnology and biochemistry division, Mumbai, India.

Excised full-thickness dorsal skin obtained from domestic swine (Sus scrofa) was used as the biological membrane. Skin samples were selected based on predefined suitability criteria, including intact surface morphology and absence of visible cuts, abrasions, lesions or other defects. Skin samples showing visible damage or abnormalities were excluded from the study.

As the present investigation was an in vitro laboratory study and did not involve human participants, patient selection, patient recruitment and hospital-based clinical procedures were not applicable. No human subjects or patient-derived samples were used. The porcine skin was obtained as excised tissue from an appropriate source and no animals were specifically subjected to experimental dosing for the purpose of this study. The collection and handling of animal-derived tissue were performed in accordance with applicable institutional procedures and ethical requirements.

In vitro skin permeation study

Comparative skin permeation studies were performed using Franz diffusion cells in accordance with OECD test guideline 428 for in vitro skin absorption.[5] Full-thickness dorsal skin obtained from domestic swine (Sus scrofa) was selected as the diffusion membrane because of its close resemblance to human skin with respect to barrier properties and permeability characteristics.[7,8]

The skin was mounted between the donor and receptor compartments of the diffusion cells, providing an effective diffusion area of 1.36 cm^2. The receptor chamber was filled with phosphate buffer supplemented with 20% ethanol and 0.5% Tween 20 to maintain sink conditions throughout the study.[5] The receptor medium was maintained at 35±1°C and continuously stirred using magnetic stir bars at 150 rpm. Following an equilibration period of approximately one hour, 100 mg of each cream formulation was applied evenly onto the exposed skin surface in the donor compartment. Based on the product strength, the applied dose contained 0.05 mg of clobetasol propionate.

Validation of the Franz diffusion system

The Franz diffusion system was validated for its suitability for comparative in vitro skin permeation studies based on assessment of membrane integrity, temperature control, receptor-medium homogeneity, maintenance of sink conditions, absence of leakage and consistency of the sampling procedure. Prior to mounting, the skin membranes were visually inspected to ensure the absence of cuts, tears, lesions or other visible defects. During the experiment, the diffusion cells were monitored for leakage, air bubbles at the skin-receptor interface and other abnormalities that could potentially affect drug permeation. Cells showing visible membrane damage or leakage were considered unsuitable for evaluation.

Sample collection and quantification

Aliquots of receptor fluid were withdrawn at 0.5, 1, 2, 4, 6, 8, 10 and 12 hours after application. Following each collection, an equivalent volume of fresh receptor medium maintained at the same temperature was added to the receptor compartment to ensure a constant volume and preserve sink conditions. At the end of the 12 hours exposure period, residual formulation remaining on the skin surface was recovered for analysis. Drug retained within the skin was subsequently calculated by mass

balance to establish the overall distribution of clobetasol propionate between the receptor phase, skin surface and skin tissue. The concentration of clobetasol propionate in all collected samples was determined using a validated high-performance liquid chromatography (HPLC) method.

High-performance liquid chromatography method

Clobetasol propionate was quantified using a validated HPLC method in accordance with USP <621>.[9] Chromatographic separation was performed on a C18 analytical column (250×4.6 mm, 5 µm particle size) using a mobile phase comprising Orthophosphoric Acid solution and Acetonitrile in a 50:50 (v/v) ratio. The mobile phase was delivered at a flow rate of 1.0 ml/min. An injection volume of 20 µl was used for analysis and detection was carried out at 240 nm using a UV detector.

Data evaluation

Dermal delivery characteristics were assessed by determining cumulative permeation, surface residue and skin retention after 12 hours of exposure. The cumulative permeated fraction was calculated from the total amount of clobetasol propionate recovered in the receptor compartment and expressed as a percentage of the applied dose,

% Permeation= (Amount recovered in receptor fluid) / (Applied dose)×100

The amount of drug remaining on the skin surface after completion of the experiment was expressed as the unabsorbed fraction:

% Surface Residue= (Drug recovered from skin surface)/(Applied dose)×100

The percentage of drug retained within the skin was estimated by mass balance using the relationship:

% Skin Retention= (Applied dose–(Receptor amount+Surface residue)/Applied dose×100

Statistical analysis

All experiments were performed in duplicate and the results are presented as mean values of the duplicate determinations. Cumulative permeation, surface residue and skin retention were evaluated using descriptive analysis. The two formulations were compared at corresponding sampling time points and at 12 hours based on their numerical values and overall drug-distribution profiles.

Because the study included duplicate determinations only, no formal inferential statistical analysis was performed. The findings were therefore interpreted descriptively, with emphasis on the comparative permeation and skin-retention profiles of the two formulations.

RESULTS

In vitro permeation of clobetasol

The cumulative permeation of clobetasol from clobetasol 0.05% cream (SRC/AB/25/12/03) and clobetasol 0.05% cream (innovator) (SRC/AB/25/12/04) across the skin membrane was evaluated over a period of 12 hours (Tables 1–3). For Clop cream, clobetasol was first detected at 2 hours, with a cumulative permeated amount of 0.00018 mg (0.36%). The cumulative permeation increased progressively to 0.00126 mg (2.52%) at 12 hours. No drug permeation was detected during the first hour of the study.

For clobetasol 0.05% cream (innovator), clobetasol permeation remained below the detection limit up to 2 hours. Drug permeation was first detected at 4 hours, reaching 0.000195 mg (0.39%) and increased to 0.001424 mg (2.85%) at 12 hours. Comparison of the percentage cumulative permeation profiles showed that clobetasol 0.05% cream exhibited earlier detectable permeation than clobetasol 0.05% Cream (Innovator). Up to 8 hours, clobetasol 0.05% cream demonstrated slightly higher permeation values (1.10% vs. 0.93% at 8 hours). However, at later time points, clobetasol 0.05% cream (innovator) showed little more cumulative permeation, reaching 2.44% and 2.85% at 10 hours and 12 hours, respectively, compared with 1.96% and 2.52% for clobetasol 0.05% cream.

Distribution of clobetasol at 12 hours

The distribution of clobetasol among the permeated, skin-retained and unabsorbed fractions was determined after 12 hours of application (Tables 4–6). For Clop cream, of the total clobetasol content present in the 100 mg formulation sample (0.05000 mg), 0.00126 mg (2.52%) permeated through the skin. A further 0.01912 mg (38.23%) remained on the skin surface, while 0.02962 mg (59.25%) was retained within the skin. For clobetasol 0.05% cream (innovator), 0.00143 mg (2.86%) of clobetasol permeated through the skin after 12 hours. The amount remaining on the skin surface was 0.02223 mg (44.46%), whereas 0.02634 mg (52.67%) was retained within the skin.

Overall, both formulations exhibited low transdermal permeation (<3%) and substantial skin retention (>50%) after 12 hours. Clobetasol 0.05% cream showed slightly more skin retention (59.25%) and lower surface residue (38.23%) compared with clobetasol 0.05% cream (innovator), whereas clobetasol 0.05% cream (innovator) demonstrated slightly greater cumulative permeation (2.85% vs. 2.52%).

Table 1: Cumulative amount of clobetasol permeated over time from clobetasol 0.05% cream (SRC/AB/25/12/03).

Clobetasol 0.05% Cream (SRC/AB/25/12/03)		
	Clobetasol	
Time	Amount Permeated (mg)	Amount Permeated (%)
30 min	BDL	BDL
1 hour	BDL	BDL
2 hours	0.00018	0.36
4 hours	0.00027	0.54
6 hours	0.00037	0.74
8 hours	0.00055	1.1
10 hours	0.00098	1.96
12 hours	0.00126	2.52

*BDL: Below Detection Limit.

Table 2: Cumulative amount of clobetasol permeated over time from clobetasol 0.05% cream (innovator) (SRC/AB/25/12/04).

Clobetasol 0.05% cream (innovator) (SRC/AB/25/12/04)		
	Clobetasol	
Time	Amount permeated (mg)	Amount permeated (%)
30 min	BDL	BDL
1 hour	BDL	BDL
2 hours	BDL	BDL
4 hours	0.000195	0.39
6 hours	0.000289	0.58
8 hours	0.000465	0.93
10 hours	0.001221	2.44
12 hours	0.001424	2.85

*BDL: Below Detection Limit.

Table 3: Comparative percentage permeated of clobetasol 0.05% cream and clobetasol 0.05% cream (innovator) at different time points.

Time	Clobetasol (% amount permeated)	
	Clobetasol 0.05% Cream (SRC/AB/25/12/03)	Clobetasol 0.05% cream (innovator) (SRC/AB/25/12/04)
30 min	BDL	BDL
1 hours	BDL	BDL
2 hours	0.36	BDL
4 hours	0.54	0.39
6 hours	0.74	0.58
8 hours	1.10	0.93
10 hours	1.96	2.44
12 hours	2.52	2.85

Table 4: Distribution of clobetasol in clobetasol 0.05% cream at 12 hours (permeated, unabsorbed and retained fractions).

Clobetasol 0.05% Cream (SRC/AB/25/12/03)		
Parameter (at 12 hours)	Clobetasol	
	mg	%
Amount present in 100 mg sample	0.05000	100
Cumulative drug permeated (% permeated)	0.00126	2.52
Drug remaining on skin surface (% unabsorbed)	0.01912	38.23
Drug retained in skin (% skin retention)	0.02962	59.25

Table 5: Distribution of clobetasol in clobetasol 0.05% cream (innovator)at 12 hours (permeated, unabsorbed and retained fractions).

Clobetasol 0.05% Cream (Innovator)(SRC/AB/25/12/04)		
Parameter (at 12 hours)	**Clobetasol**	
	mg	**%**
Amount present in 100 mg sample	0.05000	100
Cumulative drug permeated (% permeated)	0.00143	2.85
Drug remaining on skin surface (% unabsorbed)	0.02223	44.46
Drug retained in skin (% skin retention)	0.02634	52.67

Table 6: Percentage distribution of clobetasol at 12 hours in clobetasol 0.05% cream and clobetasol 0.05% cream (innovator) (permeated, unabsorbed and skin retained fractions).

Parameter (at 12 hours)	Clobetasol	
	Clop cream	**Clobetasol 0.05% Cream (Innovator)**
Cumulative drug permeated (% permeated)	2.52	2.85
Drug remaining on skin surface (% unabsorbed)	38.23	44.46
Drug retained in skin (% skin retention)	59.25	52.67

DISCUSSION

The present study compared the cutaneous delivery characteristics of two clobetasol propionate 0.05% cream formulations using an in vitro Franz diffusion model with excised swine skin. Both formulations demonstrated a similar pattern of drug disposition, characterized by low transdermal permeation, substantial skin retention and measurable residual drug on the skin surface after 12 hours. Such a distribution profile is consistent with the intended pharmacokinetic behavior of topical corticosteroids, where effective local delivery with minimal systemic absorption is desirable.[1-4] The cumulative permeation results showed that less than 3% of the applied clobetasol propionate permeated across the skin during the 12 hours. Although detectable permeation occurred at slightly different time points, the overall permeation profiles of the two formulations were comparable. Small variations in the onset of permeation are expected for semisolid formulations because formulation attributes such as vehicle composition, rheological properties and excipient interactions can influence the initial release of drug without substantially altering its overall dermal delivery.[1,2,10]

A notable finding of the present investigation was the high proportion of drug retained within the skin, with more than half of the applied clobetasol propionate remaining in the skin after 12 hours for both formulations. Clobetasol propionate is a highly lipophilic corticosteroid and its affinity for the lipid-rich stratum corneum promotes drug partitioning into the epidermis, where it can act as a reservoir for sustained local delivery.[2,4,9] Retention of corticosteroids within the epidermal and dermal tissues is considered an important determinant of therapeutic activity because these layers represent the principal sites of inflammatory skin disorders.[3,4]

The observed permeation behavior is consistent with previous reports describing topical corticosteroid delivery using Franz diffusion systems. Trommer and Neubert reported that highly lipophilic corticosteroids generally exhibit limited transdermal permeation while preferentially accumulating within the skin, with formulation composition influencing the rate of drug release more than the ultimate extent of skin localization.[11] Similarly, Hadgraft described the stratum corneum as an effective reservoir for lipophilic molecules, thereby restricting systemic transport while facilitating localized drug availability within the skin.[2] The high skin retention and low receptor-phase recovery observed in the present study are therefore consistent with the established permeation characteristics of potent topical corticosteroids.

Both formulations also showed measurable quantities of drug remaining on the skin surface after completion of the study. Residual drug following finite-dose application has been widely reported in vitro permeation studies and reflects the dynamic equilibrium between formulation, skin partitioning and permeation during the exposure period rather than incomplete formulation performance.[5,6,12] Together with the retained fraction, the surface residue contributes to the overall mass balance and provides a comprehensive assessment of drug disposition following topical application.

Comparison of the overall drug distribution demonstrated that the two formulations exhibited comparable cutaneous delivery characteristics. The cumulative permeation, skin retention and surface residue values showed only minimal differences between the formulations, resulting in essentially similar distribution profiles after 12 hours of application. These findings suggest that both formulations provide comparable localization of clobetasol propionate within the skin while maintaining

limited transdermal permeation, an important characteristic for topical corticosteroid therapy. The experimental model employed in the present study further supports the relevance of the findings. Excised swine skin is widely accepted as an appropriate surrogate for human skin because of its comparable structural organization, lipid composition and permeability characteristics.[7,8] Moreover, the Franz diffusion methodology recommended in OECD Test Guideline 428 remains the standard in vitro approach for comparative evaluation of topical formulations, enabling reproducible assessment of drug permeation and skin retention under controlled laboratory conditions.[5,6]

Overall, the findings of the present study are in agreement with the established understanding of topical corticosteroid disposition reported in the literature and demonstrate that both clobetasol 0.05% cream and clobetasol 0.05% cream (innovator) exhibit comparable cutaneous delivery characteristics. The combination of low transdermal permeation and high skin retention observed for both formulations supports effective localization of clobetasol propionate within the skin, consistent with the intended therapeutic objective of topical corticosteroid treatment.

CONCLUSION

The present in vitro Franz diffusion study demonstrated that clobetasol 0.05% cream and clobetasol 0.05% cream (innovator) exhibited comparable cutaneous delivery characteristics for clobetasol propionate. Both formulations showed low transdermal permeation and high skin retention after 12 hours, indicating effective localization of the drug within the skin while limiting systemic passage. Although minor differences were observed in the permeation and retention profiles, the overall distribution of clobetasol between the permeated, retained and surface-residual fractions was similar for both products. These findings suggest that both formulations provide comparable dermal delivery performance and are suitable for achieving the intended local therapeutic effect of clobetasol propionate.

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REFERENCES

1. Benson HAE. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv. 2005; 2(1):23–33.
2. Hadgraft J. Skin, the final frontier. Int J Pharm. 2001; 224(1–2):1–18.
3. Wolverton SE. Comprehensive Dermatologic Drug Therapy. 4th ed. Philadelphia: Elsevier. 2020.
4. Shah VP, Elkins JS, Williams RL. Evaluation of in vitro release test methods for topical drug products. Pharm Dev Technol. 1998; 3(3):299–306.
5. Organisation for Economic Co-operation and Development (OECD). OECD Guideline for the Testing of Chemicals No. 428: Skin Absorption: In Vitro Method. Paris: OECD Publishing. 2004.
6. Franz TJ. The finite dose technique as a valid in vitro model for the study of percutaneous absorption in man. Curr Probl Dermatol. 1978;7:58–68.
7. Simon GA, Maibach HI. The pig as an experimental animal model of percutaneous permeation in man. Skin Pharmacol Appl Skin Physiol. 2000; 13(5):229–34.
8. Dick IP, Scott RC. Pig ear skin as an in vitro model for human skin permeability. J Pharm Pharmacol. 1992; 44(8):640–5.
9. United States Pharmacopeia (USP). General Chapter <621> Chromatography. In: United States Pharmacopeia and National Formulary (USP–NF). Rockville (MD): United States Pharmacopeial Convention.
10. Barry BW. Dermatological formulations: percutaneous absorption. New York: Marcel Dekker. 1983.
11. Trommer H, Neubert RHH. Overcoming the stratum corneum: the modulation of skin penetration. Skin Pharmacol Physiol. 2006; 19(2):106–21.
12. Lodén M. Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. Am J Clin Dermatol. 2003; 4(11):771–88.

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