



ORIGINAL ARTICLE

Calcipotriol delivery into the skin as emulgel for effective permeation



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Abstract The objective of this work is to formulate and evaluate an emulgel containing calcipotriol for treatment of psoriasis. Emulgels have emerged as a promising drug delivery system for the delivery of hydrophobic drugs. Isopropyl alcohol and polyethylene glycol have been employed as permeation enhancers. Formulation chart is made with seven formulations, evaluated for physical parameters, drug content, viscosity, thixotropy, spreadability, extrudability, mucoadhesion, diffusion studies, skin irritation test along with short term stability studies. Carbopol is reported to have a direct influence on appearance and viscosity of final formulation. The photomicroscopic evaluations showed the presence of spherical globules in size range of 10–15 μm . Rheograms revealed that all the formulations exhibited pseudoplastic flow. Optimized formulation (F6) had shown $86.42 \pm 2.0\%$ drug release at the end of 8 h study. The release rate through dialysis membrane and rat skin is higher when compared to commercial calcipotriol ointment. Hence it is concluded that calcipotriol can be delivered topically with enhanced penetration properties when formulated as emulgel.

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1. Introduction

Psoriasis is an autoimmune disorder of the skin with relapsing episodes of inflammation and hyperkeratosis (Pradhan et al.,

2013). Like any other dermal disease, psoriasis also challenges the reproducible delivery of drugs into specific layers of diseased skin. Hence, development of an ideal therapy for psoriasis is a great challenge. Multiple approaches have been explored to treat this skin oriented disease using various psoriatic drugs with different modes of action and routes of administration. Many widely used topical agents like ointments, creams, lotions are associated with disadvantages like stability problems, stickiness and lesser spreading coefficient (Gupta et al., 2010). Gels have faster drug release when compared to other semisolid preparations. They have a higher aqueous component that permits greater dissolution of drugs, and also permits easy migration of the drug through

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a vehicle that is essentially a liquid, compared with the ointment or cream base (Khullar et al., 2012). But the major disadvantage is the delivery of hydrophobic drugs. To overcome this limitation emulgels are prepared and with their use even a hydrophobic drug can enjoy the unique properties of gels. When gels and emulsions are used in combination, the dosage forms are referred as emulgel.

Emulgels are emulsions, either of the oil-in water or water-in-oil, which are filled by mixing with a gelling agent. In fact, the presence of a gelling agent in the water phase converts a classical emulsion into an emulgel (Rieger, 1986; Mohamed, 2004). Generally, direct (oil-in-water) system is used to entrap lipophilic drugs whereas hydrophilic drugs are encapsulated in the reverse (water-in oil) system.

Calcipotriol is a vitamin D3 analog, widely used for topical treatment of psoriasis, either alone or in combination with betamethasone. The pharmacological target site is the D-vitamin receptor expressed by keratinocytes present in the lower epidermis, where calcipotriol inhibits proliferation and normalizes differentiation of keratinocytes during psoriasis (Knudsen et al., 2012). In a systematic quantitative review of 37 randomized controlled trials including a total of 6038 patients with moderate plaque psoriasis, the efficacy of calcipotriol is found to be comparable to that of potent corticosteroids after 8 weeks of treatment and better than that of calcitriol, tacalcitol, coal tar, and dithranol (Carrascosa et al., 2009). A major challenge for dermal drug delivery of calcipotriol is its hydrophobic nature and low penetration through impermeable stratum corneum. So to overcome these limitations an emulsion based approach can be used so that even a hydrophobic therapeutic moiety can be successfully incorporated and delivered to the skin. In order to promote its absorption through the skin, penetration enhancing ingredients that temporarily disrupt the skin barrier, fluidize the lipid channels between corneocytes, alter the partitioning of the drug into skin structures can be used.

The present study is undertaken to evaluate the potential of emulgel as a topical vehicle for the delivery of lipophilic calcipotriol in treatment of psoriasis using PEG as permeation enhancer.

2. Materials and Methods

2.1. Materials

Calcipotriol was obtained from Manus Aktteva Biopharma Llp. Ahmedabad. Carbomer homopolymer was obtained from Lubrizol, USA. Cocoyl caprylocaprate (Kollicream3C) and Polyoxyl 20 Cetostearyl Ether (KolliphorCS) were obtained from BASF Corporation, USA. Dialysis membrane having an average flat width 29.31 mm, average diameter of 17.5 mm and a capacity of 2.41 ml/cm (Molecular weight cut off 12,000) was purchased from Himedia labs, Mumbai. Liquid Paraffin was obtained from Symrise Private Limited whereas Propylene Glycol and PEG 400 were obtained from and Sigma Aldrich, Mumbai.

2.2. Preparation of emulgel

Initially the gel base was prepared by adding carbopol into a beaker containing purified water which was previously heated

to 75 °C. In another beaker propylene glycol was taken and the drug was added into it and stirred to completely dissolve the drug. Required amount of PEG was added. Drug dissolved in propylene glycol was added to the carbopol gel base and stirred continuously for 20 min with magnetic stirrer at 800 rpm until homogenous mixture is formed without any lumps. All the oily ingredients Kollicream3C, KolliphorCS20 and Liquid Paraffin were taken in another beaker and heated at 75 °C. Then the oily phase was added to the aqueous phase with continuous stirring (up to 2 h).

The gel was kept aside until it attains 25 °C. At this 25 °C, isopropyl alcohol was added. Strong ammonia was then added to adjust pH to 7.16. Finally English Lavender Fragrance was added and mixed continuously for 10 min (Martin, 1994). The composition and quantities of seven formulations (F1–F7) formulated are given in Table 1. Kollicream3C and KolliphorCS20 were used as emulsifiers. Kollicream3C also functioned as emollient. Propylene glycol and PEG were the permeation enhancers used. To study their influence on drug diffusion, F6 and F7 were designed. In formulation F6 both of them were used at 5% concentration while F7 had only PEG as permeation enhancer.

2.3. Compatibility studies

FT-IR spectroscopy (FT IR- 8400-S, Shimadzu, Japan) was employed to ascertain the compatibility of API with the excipients. The spectra of individual drug and the final formulation containing excipients were compared for confirmation of common peaks.

2.4. Evaluation of emulgel

2.4.1. Photomicroscopy

Optimized batch of the emulgel was viewed under light microscope to study the globular structure in gel base. The emulgel was suitably diluted, mounted on glass slide and viewed by light microscope under magnification of 40×.

2.4.2. Globule size

The globule size obtained was determined using Zetasizer (Malvern Instrument 3000HSA, UK). The sample was suitably diluted and the globule size was measured at 25 °C.

2.4.3. Physical parameters of prepared formulations

All the prepared formulations were visually checked for the color, appearance, homogeneity and phase separation.

2.4.4. Determination of pH

The pH measurements were done using a digital pH meter (Thermo scientific) which was calibrated with standard buffer solutions. The measurements of pH of each system were replicated three times.

2.4.5. Determination of drug content

One gram of formulation was transferred to a 50 ml volumetric flask and was diluted with 100% methanol. Five ml of this solution was further diluted to 25 ml with 100% methanol. The drug content was determined at 264 nm using UV–Vis spectrophotometer.

Table 1 Composition of emulgel formulations.

Quantity in (% w/w)	F1	F2	F3	F4	F5	F6	F7
Calcipotriol	0.05	0.05	0.05	0.05	0.05	0.05	0.05
Carbopol	0.6	0.8	1	1.2	1	1	1
Kollicream3C	3	4	5	3	3	3	3
KolliphorCS	0.05	0.05	0.05	0.05	0.1	0.1	0.1
Liquid paraffin	7.5	7.5	7.5	7.5	7.5	7.5	7.5
Propylene glycol	10	10	10	10	10	5	–
PEG	–	–	–	–	–	5	10
IPA	10	10	10	10	10	10	10
Strong ammonia (Q.S. – pH 7.16)	1.9	1.9	1.9	1.9	2.5	0.9	0.8
Fragrance	0.035	0.035	0.035	0.035	0.035	0.035	0.035
Water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

2.4.6. Determination of viscosity

The viscosity of the prepared formulations was determined at ambient temperature using Brookfield digital viscometer (DV-II + Pro) with spindle no. 96 at 0.1, 0.5, 1 and 1.5 rpm.

2.4.7. Determination of thixotropic characteristics

The formulations were subjected to different rates of shear using GEMINI 200: Rheometer, at constant temperature (25 °C). The measuring system employed was the cone and plate system having 40 mm diameter and 4° angle. The rheogram was constructed by plotting rate of shear against shear stress.

2.4.8. Determination of spreadability

A weighed quantity (350 mg) of emulgel was taken on a glass plate (10 × 5 cm). Another glass plate (10 × 5 cm and 5.8 ± 1 g) was dropped from a distance of 5 cm. The diameter of the circle of spread was measured after 1 min (Rachit et al., 2011). Types of gels based on spreadability are given in Table 2.

2.4.9. Determination of extrudability

The quantity (g/cm²) of emulgel extruded from lacquered aluminum collapsible tube on application of weight (in grams) required to extrude at least 0.5 cm ribbon of emulgel in 10 s was determined (Vijaya et al., 2011). The measurement of extrudability of each formulation was done in triplicates.

$$\text{Extrudability} = \frac{\text{Applied weight to extrude emulgel from tube (g)}}{\text{Area (in cm}^2\text{)}} \quad (1)$$

2.4.10. Bio-adhesive strength measurement

The bioadhesion measurement was performed using a modified balance method (Elahe et al., 2012; Navya et al., 2014)

Table 2 Types of gels based on spreadability (Dignesh et al., 2012).

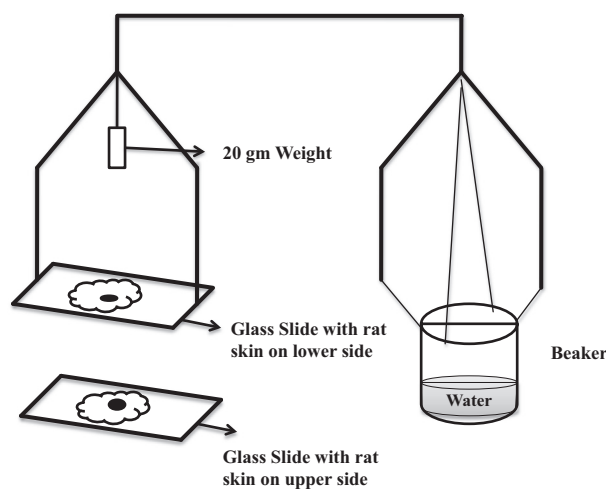
Type of gel	Measurement (in cm)
Fluid gel	More than 2.4
Semi-fluid gel	1.9–2.4
Semi stiff gel	1.9–1.6
Stiff gel	1.6–1.4
Very stiff gel	Less than 1.4

(Fig. 1). The two pans of physical balance were removed. Right side pan was replaced with a 100 ml beaker and on the left side, a glass slide was hanged. For balancing the assembly, a weight of 20 g was hanged on the left side. Another glass slide was placed below the hanged slide. Portions of hairless fresh rat skin were attached with both slides. One gram of gel was placed between two rat skin faces. Little pressure was applied to form bioadhesion bond, and then slowly water was added on right side beaker, till the gel was separated from one face of rat skin attached. Volume of water added was converted to mass. This gave the bioadhesive strength of gel in grams.

2.5. In vitro drug release and permeation studies

2.5.1. In vitro diffusion studies through dialysis membrane

The dialysis membrane was cut to size and boiled in distilled water for 1 h and in absolute alcohol for next 1 h. Finally, it was soaked in pH 7.4 phosphate buffer saline for 24 h. *In vitro* drug release studies were carried out by taking 150–200 mg of emulgel on the dialysis membrane, which was mounted on the Franz diffusion cell. The receptor medium with pH 7.4 phosphate buffer saline was maintained at constant temperature of 37 °C by circulating water bath. The drug release was compared with a marketed product. The release data were fitted

**Figure 1** Schematic diagram illustrating bioadhesion measurement by the modified balance method (Navya et al., 2014).

into various mathematical models using PCP Disso-V2.08 software to know which mathematical model best fits the obtained release profile.

2.5.2. Diffusion through rat skin

The abdominal skin of full thickness was excised from the rats weighing 105–120 g, free from any visible sign of disease. This was mounted in the donor compartment. The emulgel was placed over it and the permeation study was carried out in a similar manner as described for dialysis through membrane (Bharathi et al., 2011). The drug release was compared with that of Calcipotriol ointment (HEXIMAR™).

2.5.3. Skin irritation test

Approval was obtained from the Institutional Animal Ethics Committee before commencement of the study. Guinea pigs (400–500 g) of either sex were used for testing of skin irritation. The animals were maintained on standard animal feed and had free access to water. The animals were kept under standard conditions. They were divided into four groups comprising two animals in each group as

- Group 1: - For control
- Group 2: - Gel base (without drug)
- Group 3: - Prepared test gel
- Group 4: - Calcipotriol ointment

Hair was removed from back of guinea pigs and an area of 4 cm² was marked, Gel was applied (500 mg/guinea pig) twice a day for 7 days and the site was observed for any sensitivity and reaction. The sensitivity was graded as 0, 1, 2, and 3, for no reaction, slight patchy erythema, patchy erythema and severe erythema with or without edema, respectively (Mallikarjuna et al., 2010).

2.5.4. Stability studies of the optimized formulation

The formulations were packed in aluminum collapsible tubes and studies were carried out for 90 days by keeping at 25° + 2 °C and 60 + 5% RH and 40° + 2 °C and 75 + 5% RH Samples were withdrawn on 30th, 60th & 90th day and checked for changes in physical appearance, viscosity, drug content, pH and *in vitro* studies through dialysis membrane.

3. Results and discussion

Seven formulations of calcipotriene emulgel were prepared as indicated in Table 1. From preliminary trails (data not reported) it was found that, when carbopol was used beyond 1.2% the gel base obtained was highly viscous making it unfavorable for use. Similarly at concentrations below 0.6% the viscosity was very poor. Hence carbopol was used in the range of 0.6–1.2% in formulations F1–F4. Based on viscosity, spreadability and extrudability results of F1–F4, 1% carbopol was found to be the best for formulating calcipotriene emulgel. The amount of Kollicream3C to be used as emulsifier was optimized from the formulations F1–F3. When it was used beyond 5% concentration phase separation was reported. No clogging of globules or phase separation was reported when 3%, 4%, 5% Kollicream3C were used. Further, no much difference in the globule size was reported. Hence, the least quantity that

could be employed i.e., 3% was selected in formulating other emulgels. In a similar method, optimum quantity of KolliphorCS was optimized from the globule size of formulations F4 and F5 which had 0.05% and 0.1% of KolliphorCS, respectively. F5 formulation has shown a lower globule size than F4. Hence 0.1% KolliphorCS was optimized for formulating emulgels, F6 and F7.

3.1. Compatibility studies

FT-IR spectra of the individual drug and the emulgel formulation showed no interaction of excipients with the drug and hence it was concluded that the drug is compatible with the excipients used.

3.2. Photomicroscopy

Formulated emulgels exhibited good consistency. The photomicroscopic evaluations (Fig. 2) showed the presence of spherical globules, which indicated formation of emulsion in gel base. This proved the success of the method employed in preparation of emulgel.

3.3. Average globule size

Average globule size measurements are shown in Table 4. The results indicate that globule size of droplet varies from 10 to 15 µm.

3.4. Physical parameters of prepared formulations

The results of various physical parameters evaluated are given in Table 3. Formulation F1 and F2 were fluid due to the presence of low carbopol concentrations. Formulation F4 was thick white in color due to higher carbopol concentration. Formulation F3, F5, F6, F7 which had similar carbopol concentrations were white creamy in appearance. No phase separation was observed in any of the formulated emulgels.

3.5. Drug content and pH evaluation

The drug content of all formulations was within the specified range of 95–105%. It was observed that API was uniformly distributed in all the formulations. pH of all formulation was

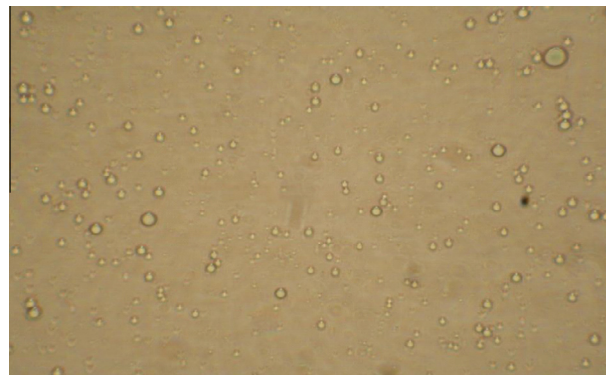


Figure 2 Microphotograph of emulgel (magnification 40×).

Table 3 Physical parameters of prepared emulgels.

Parameters	F1	F2	F3	F4	F5	F6	F7
Color & appearance	White fluid	White fluid	White creamy	Thick white	White creamy	White creamy	White creamy
Homogeneity	Good	Good	Good	Good	Excellent	Excellent	Excellent
Phase separation	No	No	No	No	No	No	No

ranged between pH 6.82–7.10. The results are reported in Table 4.

3.6. Determination of viscosity

The viscosity results helped to study the influence of various formulation parameters on viscosity of the preparations. Formulation F1 and F2 exhibited less viscosity as the carbopol content was very low. F4 formulation showed highest viscosity which could be attributed to the highest concentration of carbopol employed. The influence of emollient concentration could be studied from F5 and F3. F5 which had higher emollient concentration than F3 had higher viscosity. F7 viscosity values were more than that of F6 because of the higher isopropyl alcohol concentration in F6. It was observed from Fig. 3 that with an increase in shear, the viscosity was decreased in all the formulations.

3.7. Determination of thixotropic characteristics

Formulations were subjected to different rates of shear and plot of rate of shear against shearing stress shows thixotropic

behavior of gels with the down curve being shifted to the left of the up curve. As shear is applied flow starts and structure begins to break down as the points of contact are disrupted and polymeric chain aligned, exhibiting shear thinning. Upon removal of stress, structure starts to reform and progressive restoration of consistency. The gels have a lower viscosity at any rate of shear on the down curve than it had on the up curve because of the network structure between neighboring gel chains as well as the entanglements between long polymer chain segments/break down. The area of the loop between the up and down flow curves of a rheogram is a measure of the thixotropic breakdown. In formulation F4 and F7, the area is more, indicating more structural break down. The extent of thixotropy for F3, F5, F6, was low as evidenced by the proximity of the curves. Rheograms revealed that all the formulations exhibited pseudoplastic flow (Fig. 4).

3.8. Determination of spreadability

Emulgels prepared with low concentration of carbopol F1 and F2 belonged to fluid gel category, having more spreadability values. The formulations prepared with higher concentration of carbopol belonged to stiff and semi stiff category and formulation F4 prepared with 1.2 g of carbopol belonged to very stiff category. With an increase in gelling agent concentration in formulation, the spreadability of formulations decreases. The results are reported in Table 5.

3.9. Determination of extrudability

It was found that extrudability of emulgel was a function of concentration of carbopol. Extrudability was decreased with an increase in the concentration of carbopol. In formulation F5, the extrudability was high due to the presence of more emollient concentration. Formulation F3, F6 and F7 exhibited good extrudability. Extrudability was in the order of $F1 > F2 > F5 > F7 > F3 > F6 > F4$. The results are reported in Table 5.

3.10. Bio-adhesive strength measurement

The bio-adhesive strength of various emulgel formulations has been shown in Fig. 5. It was clearly evident that the bio-adhesive strength of emulgel was dependant on the concentration of gelling agent, carbopol. The properties like polymer chain flexibility, ability to form hydrogen bonds and/or the extent of swelling of polymer influence the bio-adhesive strength of the formulation.

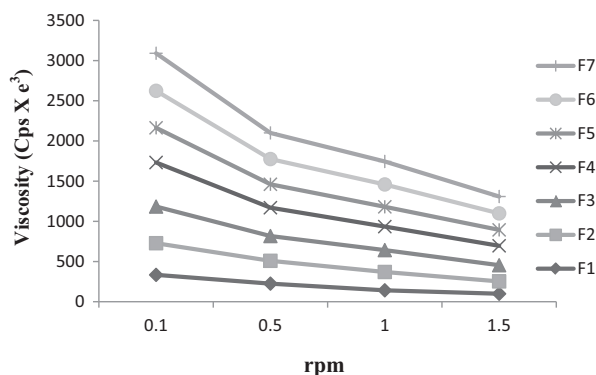
3.11. In vitro drug release studies

Diffusion studies were carried out using Franz type diffusion cell for F3–F7 formulations and for calcipotriol ointment in

Table 4 Globule size, drug content and pH of various formulated emulgels.

Formulation no.	Drug content (%)	pH Mean \pm S.D.*	Globule size (μ m)
F1	98.4 \pm 0.5	7.25 \pm 0.09	10.34 \pm 0.5
F2	98.9 \pm 0.2	7.12 \pm 0.04	11.32 \pm 1.2
F3	99.3 \pm 0.4	7.12 \pm 0.04	11.17 \pm 0.7
F4	98.4 \pm 0.1	6.82 \pm 0.15	15.40 \pm 0.06
F5	97.5 \pm 0.1	7.10 \pm 0.20	10.01 \pm 0.05
F6	99.2 \pm 0.1	7.16 \pm 0.06	11.93 \pm 0.1
F7	99.1 \pm 0.3	7.12 \pm 0.10	10.08 \pm 1.2

* Standard deviation mean "n" = 3.

**Figure 3** Effect of shearing on viscosity of formulations F1–F7.

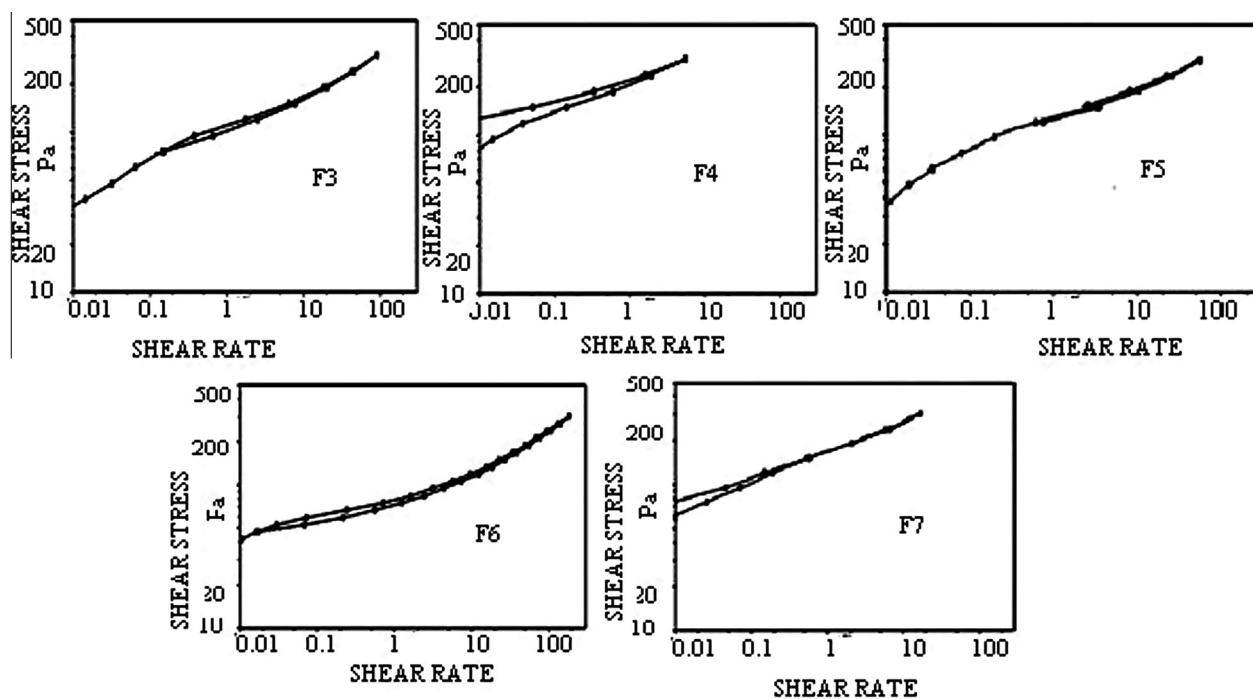


Figure 4 Rheograms of formulations F3–F7 and calcipotriol ointment.

Table 5 Spreadability and extrudability of emulgel formulations.

Formulation	Spreadability (cm) Average \pm S.D.*	Extrudability (g/cm^2) Average \pm S.D.*
F1	2.7 ± 0.05	9.0 ± 0.15
F2	2.3 ± 0.05	6.8 ± 0.21
F3	1.7 ± 0.16	5.4 ± 0.11
F4	1.3 ± 0.18	4.4 ± 0.3
F5	2.1 ± 0.14	5.8 ± 0.25
F6	1.7 ± 0.15	5.3 ± 0.13
F7	1.6 ± 0.17	5.4 ± 0.26

* Standard deviation mean "n" = 3.

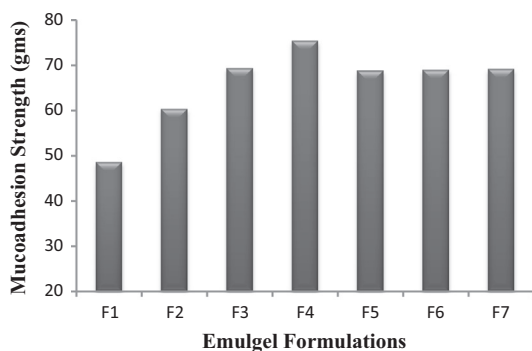


Figure 5 Bioadhesive strength of emulgel formulations.

pH 7.4 phosphate buffer saline solution. F1 and F2 were eliminated from the test due to their poor spreadability and extrudability among all formulations. Release from microemulsion is

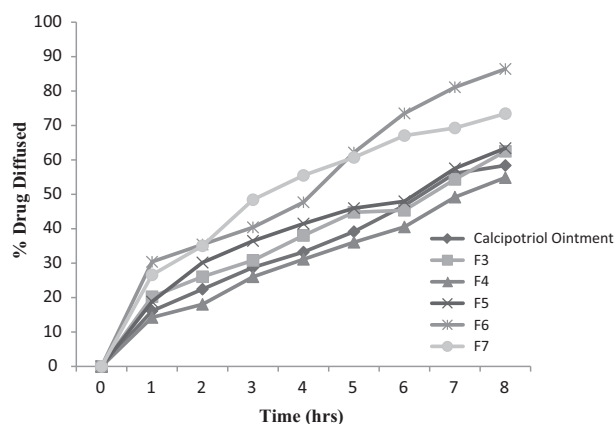


Figure 6 *In vitro* drug diffusion of API from formulations F3–F7 and calcipotriene ointment.

controlled by the interactions between drug and surfactant and/or partitioning of drug between oil and water phase (Pradhan et al., 2013). Percentage drug diffused for 8hr is reported in Fig. 6. The drug release from F4 was very less (lesser even than calcipotriol ointment due to higher concentration of Carbopol). Drug release was in the following order, $F4 < F3 < F5 < F7 < F6$. Presence of two permeation enhancers, PEG and IPA has resulted in the better performance of F6 than F7 which had only PEG. Hence F6 can be considered as the optimized formulation. As stated earlier, PEG could increase the penetration into the skin by binding to water molecules, which could increase the hydration of the SC resulting in enhanced permeation through the SC barrier (Rieger, 1986). The *in vitro* release study data were fitted into various mathematical models to determine the

Table 6 *In vitro* drug diffusion of API from calcipotriol ointment and F6 through rat skin.

Times	Percentage drug diffused Mean \pm S.D.*	
	Calcipotriol ointment	F6
1	7.21 \pm 0.82	13.56 \pm 0.70
2	12.81 \pm 1.45	21.26 \pm 1.05
3	21.69 \pm 1.11	31.18 \pm 0.26
4	23.02 \pm 1.02	37.31 \pm 0.85
5	36.02 \pm 1.02	41.68 \pm 0.86
6	44.71 \pm 0.05	48.73 \pm 1.30
7	48.31 \pm 1.23	56.18 \pm 1.05
8	56.21 \pm 0.42	69.04 \pm 0.23

* Standard deviation mean “n” = 3.

Table 7 Release kinetics of calcipotriol ointment and F6 through rat skin.

Release model		Formulation code	
		Calcipotriol ointment	F6
Zero order	R^2	0.970	0.969
First order	R^2	0.974	0.955
Hixson Crowell	R^2	0.919	0.925
Higuchi	R^2	0.982	0.978
Peppas	R^2	0.924	0.921
	n	0.492	0.502
Best fit model		Higuchi	Higuchi

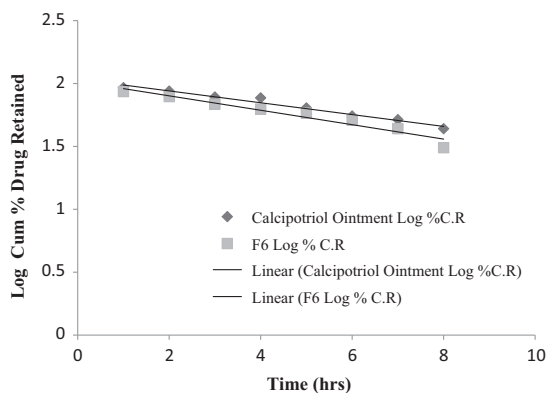


Figure 7 Release kinetics for calcipotriol ointment and F6 through rat skin.

best-fit model. The results indicated that, the best-fit model for all the formulations was Higuchi.

3.12. Drug diffusion through rat skin

The drug release through rat skin was carried out for optimized formulation F6 and the calcipotriol ointment. The drug release was found to be more for formulation F6 than that of the calcipotriol ointment as reported in Table 6. Higuchi plots

Table 8 Flux for formulations F3–F7 and calcipotriol ointment through dialysis membrane.

Formulation no.	Flux (mg/cm ² /h)
F3	1.116
F4	0.993
F5	1.282
F6	1.548
F7	1.340
Calcipotriol ointment	1.067

Table 9 Flux for formulations F3–F7 and calcipotriol ointment through male rat skin.

Formulation no.	Flux (mg/cm ² /h)
F6	1.212
Calcipotriol ointment	0.816

revealed that drug release was by diffusion. Exponent ‘n’ value was less than 0.5, indicating Fickian mechanism of drug release (Table 7). The plots of release kinetics (log% cumulative retained against time) demonstrated that diffusion followed first order kinetics (Fig. 7).

3.13. Determination of flux

Diffusion flux (*J*) measures the amount of substance that will flow through a small area during a small time interval. Flux was obtained from the slope values plotted for amount diffused per unit area against time. Flux of F6 determined through dialysis membrane and skin was higher than marketed ointment (Tables 8 and 9). Incorporation of drug in emulgel base and use of PEG as permeation enhancer were responsible for enhancement of flux.

3.14. Skin irritation test

Skin irritation test was performed on Guinea pigs. Sensitivity or reaction if any were recorded and tabulated as in Table 10. All 4 groups showed value ‘0’, indicating that there are no signs of skin irritation (Fig. 8).

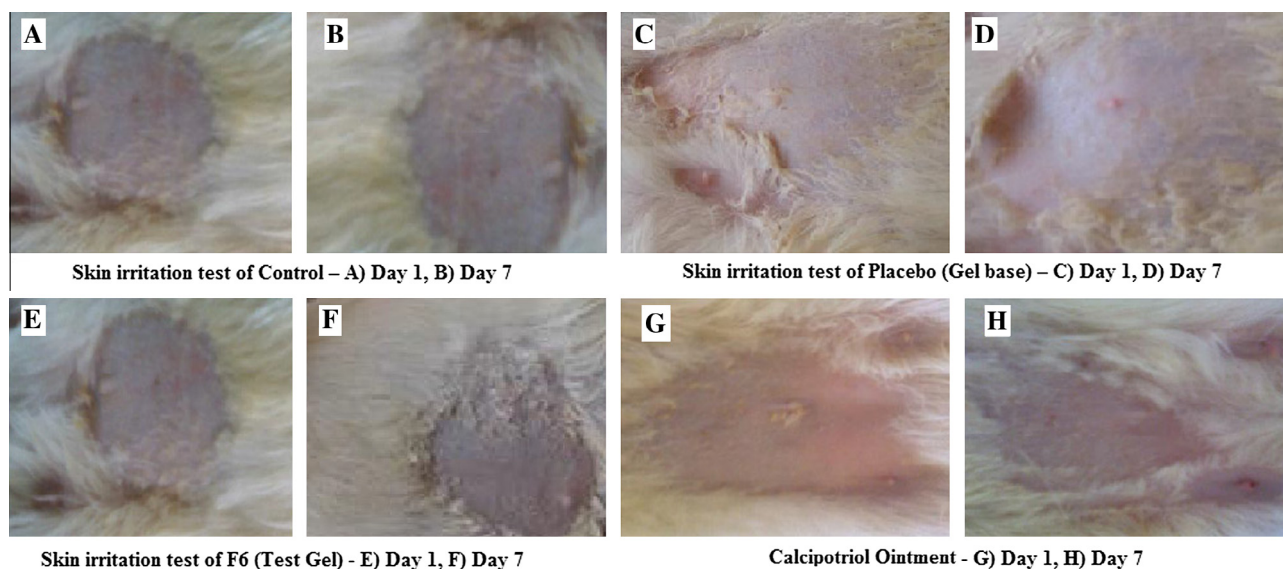
3.15. Stability testing

Accelerated stability studies were performed for Formulation F6 with 25° + 2 °C and 60 + 5% RH and 40° + 2 °C and 75 + 5% RH conditions for 3 months. The samples were analyzed for 1 month, 2 months and 3 months interval for physical appearance, viscosity, drug content, pH and diffusion with dialysis membrane. It was found that there was no phase separation and the drug content, viscosity values were identical to the initial formulation. For both experimental conditions, the drug release through dialysis membrane showed 80.25% and 75.12% in the 3rd month at 25 °C/60% RH and 40 °C/75% RH, respectively.

Table 10 Evaluation gels for skin irritation on guinea pig.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Control	0	0	0	0	0	0	0
Gel base	0	0	0	0	0	0	0
F6	0	0	0	0	0	0	0
Calcipotriol ointment	0	0	0	0	0	0	0

Grades: 0 → no reaction, 1 → slightly patchy erythema, 2 → patchy erythema, 3 → severe erythema with or without edema.

**Figure 8** Images showing the results of *in vivo* skin irritation test.

4. Conclusion

Hence it is concluded that calcipotriol can be delivered topically as emulgel in the local treatment of psoriasis, with required physicochemical, viscosity, spreadability, extrudability, drug release and stability. The topical emulgel showed good drug release and permeation characteristics which is an added advantage. Use of penetration enhancers, PEG and isopropyl alcohol can enhance the penetration of drug through the epidermis than calcipotriol ointment. Incorporation of calcipotriol into gel base enhances the ease of application onto the skin. Further studies on its clinical efficiency have to be carried out. Till-date, calcipotriol gel is not commercially available because the hydrophobic nature of the drug is the greatest hindrance for formulating it as gel. Hence the proposed concept of calcipotriol emulgel can be made available to common man after technology transfer to pharmaceutical industries.

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