PROSPECTS
IN PHARMACEUTICAL SCIENCES

Prospects in Pharmaceutical Sciences, -
https://prospects.wum.edu.pl/

Original Article

COMPARATIVE IN VITRO AND IN VIVO EVALUATIONS OF NIOSOMAL GEL VS. CONVENTIONAL GEL PREPARATIONS FOR THE TREATMENT OF PSORIASIS

Megha Shyam Matlapudi[1], Anka Rao Areti*[1], Yukti Jaiswal[2], Veeresh Bantal[2]

[1] *Department of Pharmacy, K L College of Pharmacy, Koneru Lakshmaiah Educational Foundation, Green Fields, Vaddeswaram, Guntur, Andhra Pradesh, India.*

[2] *Department of Pharmacology, G. Pulla Reddy College of Pharmacy, Mehdipatnam, Hyderabad, Telangana, India.*

* Correspondence, e-mail: ankarao@kluniversity.in

Received: date / Revised: / Accepted: date / Published: date

ABSTRACT

Psoriasis is a chronic inflammatory skin disease marked by excessive keratinocyte proliferation and immune dysregulation. While corticosteroids like Desonide are commonly used to alleviate symptoms, their limited skin permeability and potential systemic side effects restrict long-term use. This study aimed to develop and compare a novel niosomal gel formulation of Desonide (DG6) with a conventional Desonide gel (DG8), assessing their physicochemical properties, skin permeation, drug release behavior, and therapeutic efficacy in an imiquimod-induced mouse model of psoriasis. DES-loaded niosomes were prepared via the thin-film hydration technique and characterized for particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, and morphology. Niosomes were incorporated into a carbomer-based gel to create DG6. Comparative evaluations of DG6 and DG8 were conducted using rheology studies, in vitro release, ex vivo skin permeation, and in vivo efficacy assessments, including PASI scoring, stratum corneum hydration, transepidermal water loss (TEWL), spleen index, and histopathological analyses. DG6 exhibited controlled and sustained drug release, higher skin deposition (192.3 ± 55.1 µg vs. 140.9 ± 51.7 µg for DG8), and significantly lower PASI scores in vivo (3.8 ± 1.0 vs. 6.4 ± 1.1). Histological evaluations showed notable restoration of normal skin architecture with DG6 treatment, with reduced epidermal hyperplasia, parakeratosis, and inflammatory cell infiltration. Rheological studies confirmed favorable spreadability and mechanical strength comparable to a marketed formulation. The niosomal gel formulation demonstrated superior skin localization, therapeutic efficacy, and barrier restoration over the conventional gel. These findings underscore the potential of niosomal systems in enhancing topical corticosteroid therapy for psoriasis.

KEYWORDS: Desonide Niosomal Gel, Psoriasis, Skin Permeation, In vivo assessment

1. Introduction

Psoriasis is a chronic, immune-mediated dermatological chronic disorder affecting the global population. It significantly diminishes patients' quality of life and is considered one of the most prevailing skin disorders [1]. Psoriasis is characterized by hyperproliferation and abnormal differentiation of keratinocytes, accompanied by excessive inflammation, infiltration of immune cells, and increased turnover of the epidermis. Clinically, psoriasis manifests as erythematous plaques covered with silvery scales, often associated with itching, pain, and psychological distress [2]. The pathophysiology of psoriasis is complex, involving dysregulated interactions between the innate and adaptive immune systems, especially overexpression of pro-inflammatory cytokines such as TNF-α, IL-17, and IL-23. Despite extensive research, psoriasis remains a challenging condition to treat due to its chronic, relapsing nature and the limitations of current therapies [3].

Topical corticosteroids remain the mainstay for treating mild-to-moderate psoriasis. Among them, Desonide (DES), a low-potency corticosteroid, is frequently employed owing to its relatively favorable safety profile. DES is available in the market as topical gel, cream, ointment, foam, lotion used for the treatment of inflammatory and pruritic manifestation of corticosteroid dermatoses, mild to moderate atopic dermatitis and to treat redness, swelling itching and discomfort due to various skin conditions, including psoriasis [4]. However, the therapeutic efficacy of DES is often compromised due to its systemic exposure and less action at the affected site [5]. In addition, long-term use of topical corticosteroids can lead to significant adverse effects, including dermal atrophy, telangiectasia, and suppression of local immune responses [6]. To overcomes these adverse effects, DES was previously formulated into microemulsion based gel [7], nanoemulgel system [8], ethosomes [9], nanocapsule systems [10], nanocapsule hydrogels [11] for investigation on various skin inflammation conditions (especially atopic dermatitis and psoriasis). Corticosteroids are considered first line drugs for chronic inflammation conditions. However, the elaborate side effects due to long term usage and steroid withdrawal symptoms are un-warranted for the patient well being and quality of life. These challenges underscore the urgent need for innovative topical drug delivery systems that not only enhance drug bioavailability at the site of action but also minimize systemic absorption and associated side effects of corticosteroids [5,10,12].

Nanocarrier-based drug delivery systems, such as niosomes, have emerged as promising tools to overcome these limitations. Niosomes are self-assembled vesicles composed of non-ionic surfactants and cholesterol, capable of encapsulating both hydrophilic and lipophilic drugs. Due to their amphiphilic nature, niosomes can traverse the skin barrier more efficiently, providing sustained drug release, enhanced cutaneous localization, and improved pharmacological outcomes. Unlike liposomes, niosomes offer superior stability, lower production cost, and ease of scale-up, making them suitable for clinical translation in dermatological applications [13]. DES loaded into niosomes was not investigated previously.

This study was designed to develop and evaluate a niosomal gel formulation of DES for topical treatment of psoriasis. DES loaded niosomes were prepared using the thin-film hydration method and incorporated into a carbomer gel base. The formulation was characterized for particle size, zeta potential, entrapment efficiency, drug release, morphology, rheological behavior, in vitro drug release from gel and ex vivo skin deposition studies. Furthermore, the therapeutic potential of the niosomal gel was assessed using an imiquimod-induced mice model of psoriasis - a widely accepted model that mimics the pathological features of human disease. A conventional DES gel served as the comparator for the study. The goal was to demonstrate whether niosomal encapsulation of DES could offer enhanced skin deposition, prolonged drug release, and improved therapeutic effect. These characterisitics ultimately contributing to the development of a more effective and patient-friendly topical corticosteroid therapy for psoriasis.

2. Materials and Methods

2.1. Materials

Desonide (DES) was used as the active pharmaceutical ingredient. The non-ionic surfactant Span 80, Cholesterol which serves as a stabilizing agent in the niosome formulation were from Croda. Solvents including chloroform, methanol, dimethylformamide, ethanol and other solvents of AR grade were used. All materials were provided by Orbicular Pharmaceutical Technologies Pvt. Ltd.

2.2. Drug and excipient compatibility studies

Attenuated Total Reflectance Infrared (ATR-IR) spectroscopy was employed to evaluate the compatibility between DES and selected excipients, namely Cholesterol, Span 80, and Carbomer 974P. Physical mixtures of DES with each excipient were prepared in a 1:1 (w/w) ratio to simulate potential interactions. Additionally, a placebo mixture comprising all excipients (except DES) was prepared as control. All samples were initially analyzed and a set of samples was subjected to accelerated stress conditions at 50°C for 2 weeks, to evaluate thermal stability and possible interaction of the drug with excipients. ATR-IR was performed using an Alpha II spectrometer (Bruker) equipped with ZnSe prism. Approximately 150–200 mg of each sample was placed on the sample holder. Spectral data were recorded in transmittance mode over a wavenumber range of 4000–500 cm^{-1} with a resolution of 4 cm^{-1}. A background scan of air was recorded prior to sample analysis to eliminate environmental interference. All spectra were acquired using identical instrumental settings for consistency across samples. The spectral profiles were analyzed to detect any

shifts, disappearance, or emergence of characteristic peaks, which could indicate potential drug–excipient interactions [14].

2.3. Determination of DES by HPLC

High pressure liquid chromatography (HPLC) method (Shimadzu LC-20AD) was employed to determine the chemical assay of DES in the niosomes and gel formulations. This is a modified method adapted from USP monograph of DES. DES was extracted from the sample with the use of Methanol as diluent. The sample preparation was then centrifuged to collect the supernatant and filtered using 0.45µ PVDF filter. Hypersil ODS C18 column (150 mm x 4.6 mm, 5µ) was used with 0.1% formic acid and Acetonitrile as mobile phases for gradient elution. Filtrate was collected to inject into the HPLC system (Shimadzu LC-20AD) at 0.8 mL/min and detected using UV-visible detector at 254 nm at 25°C.

2.4. Preparation of DES niosomes

DES niosomes were formulated using thin film hydration method [15]. Span 80, cholesterol and DES were dissolved in chloroform. The above mixture was added to a round-bottom flask and subjected to rotary evaporation at 60°±5°C under vaccum, leaving a thin lipid film on the inner wall of the flask. After evaporation of solvents, the formed thin lipid layer was rehydrated with pH 7.4 Phosphate buffer under rotation at 60°±5°C. Then, the hydrated preparation was sonicated to obtain niosomal dispersion. The niosomal disperion was washed with de-ionized water and refrigerated at 4°C for further assessments. The niosomes were ealier optimized in our previous studies by Box-Behnken Design, and the optimized formulation was used in these studies for niosomal formulation evaluations [16].

2.5. Evaluation of DES niosomes

The DES niosomes were characterized to determine the particle size, PDI, zeta potential, entrapment efficiency and morphology. Particle size and polydisperse index (PDI) were determined by Litesizer (Anton-Paar GmbH). Zeta potential was determined by Litesizer (Anton-Paar GmbH) using Omega cuvette with an equilibration time of 60 seconds [17]. All measurements were done at 25°C in triplicate. The entrapment efficiency of DES was evaluated by centrifugation method. An accurately measured quantity of the niosomal suspension was centrifuged for 30 minutes at 15,000 rpm and the free drug in the supernatant was determined by HPLC [18]. The size and shape of the niosomes were determined by Transmission Electron Microscopic analysis (TEM). The TEM analysis was carried out on Thermo Scientific™ Talos L120C TEM at a voltage range of 20-120 kV present at Jamia Hamdard University, New Delhi. The niosomal dispersion was placed on a carbon-coated copper grid stained with a 1% phosphotungstic acid solution to increase the contrast at the time of TEM examination. The images present the characteristics such as size, shape and surface characteristics of the niosomal particles [19]. Drug release from optimal DES niosomes was evaluated by dialysis bag method. A dialysis bag (12-14 kDa) was sealed at both ends containing DES niosomal dispersion and exposed to 100 mL of phosphate buffer (pH 7.4) containing 45% Isopropyl alcohol at 32°±0.5°C with continuous agitation at 100 rpm [18]. Aliquots of the receptor media were collected at predetermined intervals to calculated the drug release of DES.

2.6. Preparation of DES niosomal gel

The niosomal gel was prepared by dissolving edetate disodium, propyl gallate, glycerin and phenoxyethanol as preservative in purified water. Carbomer 974P was dispersed in the above solution using homogenizer. DES niosomal dispersion was added under stirring. pH was adjusted at 7±0.5 using triethanolamine and stirred for uniformity [19]. The prepared niosomal gel 0.05% (DG6) was filled into lami tubes and sealed. Similarly, conventional gel 0.05% (DG8) was also prepared using DES.

2.7. Evaluations of gels

The physical characteristics of the DG6 and DG8 were assessed by checking the overall visual appearance, pH (Hanna Instruments) and drug loading of gels (Shimadzu LC-20AD) of the formulations. Rheological paramters (flow curve and yield stress), drug release of DES from gels, skin permeation of DES from gels and in vivo assessments were also performed.

2.7.1. Rheology of DES gels

The rheological properties of the gel formulations were evaluated using a Modular Compact Rheometer (MCR 302, Anton Paar). Flow behavior was assessed by applying a variable shear rate ranging from 0.001 s^{-1} to 1000 s^{-1} in rotational mode. Yield stress was determined using oscillatory mode with a variable shear strain from 0.01% to 100% at a constant angular frequency of 1.6 Hz. Viscosity was measured under a constant shear rate in rotational mode at 150 s^{-1}. All measurements were conducted at a controlled temperature of 25±0.5°C using a PP25/S measuring system with a gap setting of 0.2 mm [15]. A marketed formulation, Omnigel® (Diclofenac diethylamine topical gel, Cipla), was used as reference for comparative analysis.

2.7.2. Drug release of DES from gel

Immersion cell apparatus was employed to evaluate the in vitro release profile of DES from the gel formulations. Approximately 1 g of the gel was enclosed in a dialysis membrane (12–14 kDa) and immersed in 200 mL of receptor medium consisting of 0.9% saline solution with 25% Ethanol. The receptor fluid was maintained at 32 ± 0.5°C under stirring at 30 rpm. Sink conditions were maintained, as the solubility of DES in the receptor medium exceeded 3X times the required concentration

[20,21]. At predetermined time intervals, aliquots were withdrawn from the receptor compartment and replaced with an equal volume of fresh medium to maintain equilibration.

2.7.3. Skin deposition of DES from gels

Ex vivo skin permeation studies were performed using a vertical diffusion cell apparatus (Logan instruments) on excised pig's ear skin obtained from the local slaughter house. The receptor compartment was filled with 10 mL of phosphate buffer (pH 7.4) at 32 ± 0.5°C to simulate physiological conditions. Stirring at 400 rpm was done to ensure uniform mixing and promote stable diffusion conditions [17,21]. Permeation of DES across the skin was assessed at a 24-hour time point by collecting samples from the receptor fluid.

2.7.4. Stability studies of DES niosomal Gel

Stability studies were performed on DG6 at accelerated condition (40°C and 75% RH) and real time condition (25°C and 60% RH) as per ICH stability guidelines. The gel was packed in Aluminum backed laminate tubes and sealed to prevent leakage. The stability loaded niosomal gel was evaluated for visual observation, pH, viscosity, and drug content by HPLC at 1,3 and 6 months time points.

2.7.5. Comparative in vivo assessment of DES gels

In vivo studies were conducted to compare the therapeutic efficacy of DG6 with DG8 using an Imiquimod-induced psoriasis model on Swiss Albino mice. The study protocol was approved by the Institutional Animal Ethics Committee (IAEC) under approval number GPRCP/IAEC-2/28/12/2023/PCL/AE-13 and conducted at the animal house facility of G. Pulla Reddy College of Pharmacy, Hyderabad. The animals were randomly allocated into four groups (n = 6): Normal Control (NC), Imiquimod Control (IMQ), treatment groups (DG6 and DG8).

To induce psoriasis-like skin inflammation, 5% Imiquimod cream was applied topically to the shaved dorsal region of mice (excluding the NC group) once daily in the morning for three consecutive days. From fourth day, Imiquimod cream was applied followed by the treatment after 2 hours for the next 7 days [22]. DG6 group received the DES niosomal gel, and DG8 group received the DES gel.

Throughout the study, mice were monitored for morphological changes associated with psoriatic symptoms. Clinical assessment included Psoriasis Area and Severity Index (PASI) scoring, measurement of stratum corneum moisture content using a MoistureMeterSC (Delfin Technologies), and evaluation of transepidermal water loss (TEWL) using a Vapometer (Delfin Technologies). On 8th day, animals weight was measured and then euthanized to collect dorsal skin from the treatment/experimental area and the spleen. The collected spleen samples were wiped clean and splee weights were measured. The skin samples were preserved in 10% formalin solution for histological assessments [22].

3. Results and Discussion

3.1. Drug and excipient compatibility studies

ATR-IR spectra of DES and the physical mixtures with cholesterol, span 80, carbomer 974P and placebo are presented in Fig. 1. The characteristic absorption bands for DES (Fig. 1a) were identified at 3490 cm^{-1} (N-H stretching), 3360 cm^{-1} (O-H stretching), 2950 cm^{-1} (asymmetric stretching of CH_3), 2920 cm^{-1} (asymmetric stretching of CH_2), and 2870 cm^{-1} (symmetric stretching of CH and CH_2). Additionally, notable peaks appeared at 1700 cm^{-1} (C=O stretching of carboxylic acids), 1650 cm^{-1} (amide band), 1610 cm^{-1} (aromatic C=C stretching), 1400-1500 cm^{-1} (C-H bending), and within the range of 1100-1270 cm^{-1} (C-O stretching) [10].

Following exposure to a temperature of 50°C for 2 weeks, DES spectrum (Fig. 1d) retained all key absorption bands, indicating thermal stability. Similarly, in the DES-excipients mixture spectrum (Fig. 1b), the characteristic peaks of DES remained evident, suggesting the functional groups of DES were unaltered by the presence of the excipients. These peaks were not observed in the placebo spectrum (Fig. 1c), as expected due to the absence of DES. Furthermore, the spectrum of DES-excipient mixture after thermal treatment (Fig. 1e) continued to show all major DES peaks, implying that no significant physicochemical interactions or degradation had occurred. The thermally treated placebo spectrum (Fig. 1f) also showed no noticeable changes, supporting the conclusion that DES is compatible with cholesterol, span 80, and carbomer 974P under the tested conditions.

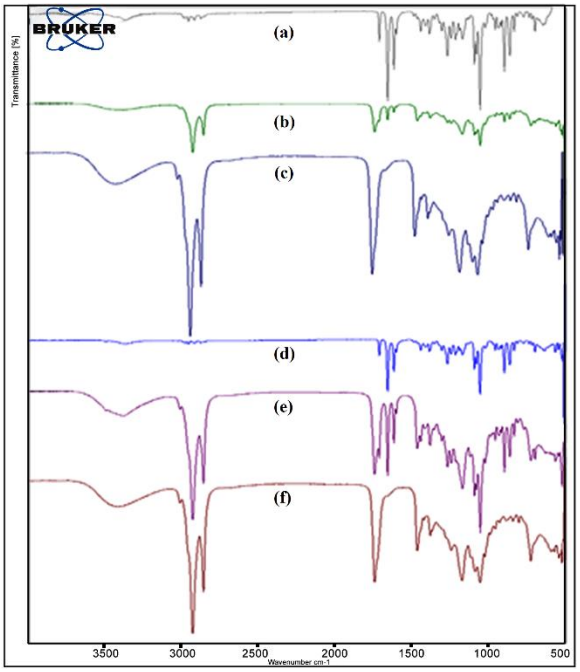

Fig 1. IR spectrum of DES and key excipients. (a) DES. (b) Active mixture of DES, Cholesterol, Span80, Carbomer 974P. (c) Placebo mixture of Cholesterol, Span80, Carbomer 974P. (d) DES at 50°C after 2weeks. (e) Active mixture of DES, Cholesterol, Span80, Carbomer 974P at

50°C after 2 weeks. (f) Placebo mixture of Cholesterol, Span 80, Carbomer 974P

3.2. Determination of DES by HPLC

Drug content analysis was performed using high-performance liquid chromatography (HPLC), with niosomes and gel formulations along with DES standard. The analytical procedure was adapted from Desonide USP monograph, with modifications to the sample preparation. No major interference peaks were observed, confirming the selectivity and reliability of the method. The DES standard exhibited a retention time of approximately 12.1 minutes, which matched the retention time observed for the DES in the sample. Thus, indicating that the method is suitable for accurate quantification of DES in sample. The overlay of DES standard and sample chromatographs is presented in Fig. 2.

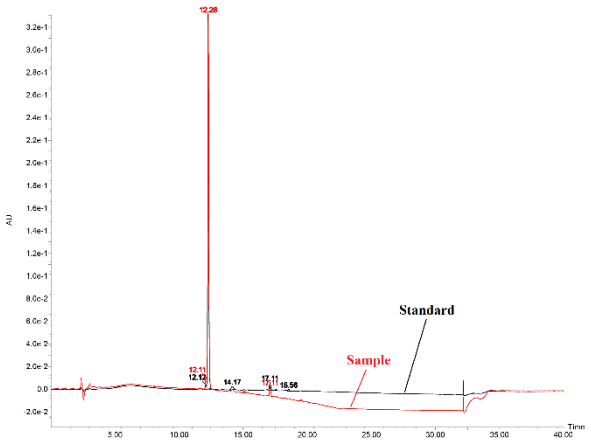

Fig 2. HPLC chromatograms overlay of DES standard and sample

3.3. Preparation and evaluation of DES niosomes

DES niosomes were prepared by thin film hydration technique. Optimization was performed using Box-Behenken Desing (BBD) in our earlier study [16]. The desing space for Cholesterol levels was 80 to 100 mg and Span 80 was 10 – 20 mg/mL. The exprerimental runs were evaluated for vesicle size, entrapment efficiency and polydispersive index (PDI) as responses. The interplay of cholesterol level and span 80 were evident. The higher levels of cholesterol yielded high entrapment and slow drug release, but vesicle size was greater than 200 nm. Whereas, higher levels of span 80 yielded smaller vesicles size and low entrapment resulting in faster drug release. An optimal levels of cholesterol and Span 80 were selected by the BBD desing (DesignExpert® software). It was observed that the optimized levels of Cholesterol was 95.29 mg, Span 80 was 10.76 mg/mL with sonication time as 3.71 min. In this study, DES niosomes were prepared using thin film hydration technique with the finalized parameters to yield optimized niosmes, which were further evaluated. The vesicle size of the optimize niosomes was found to be 180.23±11.8 nm (Fig. 3a), entrapment efficiency was found to be 75.92±3.1%, PDI was found to be 0.42±0.09 and zeta potential was found to be 34.73±2.51 mV (Fig. 3b). Surface morphology by TEM showed spherical shape of the niosomes with smooth surface and uniform distribution (Fig. 3c). Drug release of optimal DES niosomes showed a sustained drug release profile for about 10h, as witnessed in the Fig. 3d indicating the modified release mechanism of niosomes. The drug release was mathamethically modelled using zero order, first order, Korsmeyer-Peppas, Higuchi and Hixon-Crowell models [23].

Kinetic modeling of drug release is essential for understanding the underlying mechanisms governing drug dissolution and release behavior. It involves establishing a relationship between the experimental drug release data and various mathematical models. In the current study, the release of DES from niosomal formulations was evaluated by fitting the in vitro release profiles to various kinetic models, including zero-order, first-order, Higuchi, Korsmeyer–Peppas, and Hixson–Crowell models [23]. The zero-order model suggests a constant drug release rate that is independent of drug concentration, whereas the first-order model indicates that the release rate is proportional to the remaining drug concentration in the dissolution medium. The Higuchi model describes a diffusion-controlled release process. The Korsmeyer-Peppas model, based on Fickian diffusion, is used to analyze the drug release mechanism further, where the diffusional exponent (n) provides insight into the type of release mechanism. A value of $n \leq 0.45$ indicates Fickian diffusion, while $n > 0.45$ suggests an anomalous (non-Fickian) transport mechanism involving both diffusion and erosion. If $n > 0.89$, this indicates super case II trasport indicating rapid drug release due polymer changes. The Hixson–Crowell model accounts for changes in the surface area and diameter of drug particles during dissolution, providing additional understanding of release dynamics.[24]

The model equations are described:

Zero order model is equation is given as $C_0 - C_t = K_0 t$

where C_t is the amount of drug released at time t, C_0 is the initial concentration of the drug at initial, K_0 is the zero-order rate constant.

First order model is given as $\log C = \log C_0 - K_1 t/2.303$

where C_0 is the initial concentration of the drug, C is the %of drug remaining at time t, and K_1 is the first order rate equation expressed in per unit time.

The Korsmeyer-Peppas model is given as $F = M_t/M = K_m t^n$

where F is a fraction of drug released at time t, M_t is the amount of drug released at time t, M is the total amount of drug in dosage form, K_m is the release rate constant and n is the release exponent.

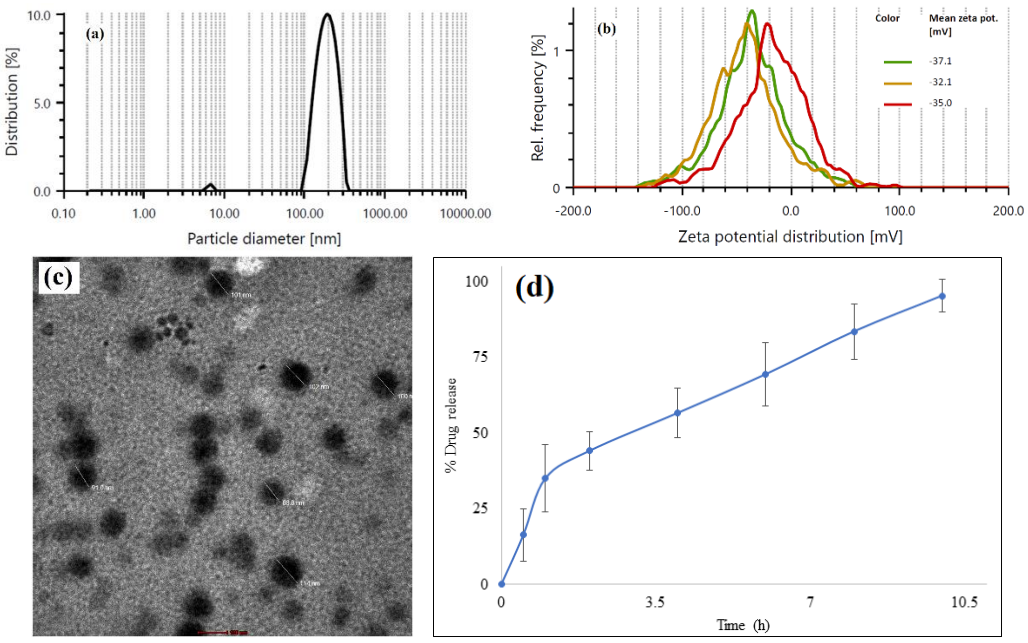

Fig 3. Evaluation of Optimized DES niosomes. (a) Particle size distribution, (b) Zeta-potential, (c) TEM photomicrograph, (d) Drug release from DES niosomes

Hixon-Crowell's model is given as $Q_0^{1/3} - Q_t^{1/3} = KHt$

where Q_0 is the initial amount of drug in the niosomes, Q_t is the remaining amount of drug in the niosomes at time t, and KH is the Hixson-Crowell release constant.

Higuchi's model is given as $Q = K_H t^{1/2}$

where Q is cumulative amount of drug release at time t and K_H is Higuchi constant

It was observed that the Higuchi model with the regression coefficient R^2 of 0.990 was the best fit drug release mathematical model, indicating diffusion driven drug release. The second best model was found to be Korsmeyer-Peppas model (R^2 of 0.985) with non-fickian or anamolous transportation (n > 0.45). This indicates the drug release is driven by diffusion coupled with erosion mechanism. These finding were inline with previous studies where Higuchi driven drug release was observed from the niosomes [25]. The summary of the release kinetics is presented in the table 1.

Table 1. Drug release kinetics modeling for release of DES from niosomes for the optimized formulation

Drug release kinetic model					
Zero order	**First order**	**Korsmeyer-Peppas**		**Hixson-Crowell**	**Higuchi**
R^2	R^2	R^2	n	R^2	R^2
0.922	0.914	0.985	0.50	0.971	0.990

3.4. Preparation and evaluations of gels

The optimized DES niosomes were used to prepare the DG6 gel. Where as DES was used to prepare the conventional gel DG8. Table 2 provides the primary evaluation of DG6 and DG8 gels.

Table 2. Physico-checmial assessment of DG6 and DG8

Trial code	pH	Viscosity (Pa.s)	Drug content (%)
DG6	7.41 (±0.07)	1867.23 (±161.9)	97.3% (±0.1)
DG8	7.51 (±0.14)	1894.86 (±180.2)	98.5% (±0.9)

Values reported as mean (±SD), n=3

3.4.1. Rheology of DES gels

The rheological profiles of the DES-based gel formulations DG6 and DG8 were evaluated and compared with a commercially available topical product, Omnigel®. The flow behavior of both DG6 and DG8 was found to be comparable to that of Omnigel® (Fig. 4a), suggesting similar flow properties. Additionally, yield stress measurements revealed values of 91.4 ± 6.9 Pa for DG6, 77.14 ± 9.8 Pa for DG8, and 73.11 ± 10.7 Pa for Omnigel® (Fig. 4b), indicating that the DES formulations exhibit similar mechanical force requirement to initiate flow of the gel. These findings suggest favorable rheological and

spreadability properties critical for patient compliance during topical administration. The dynamic viscosity of the formulations was also assessed for DG6 and DG8 exhibiting viscosities of 1867.23 ± 161.9 Pa·s and 1894.86 ± 180.2 Pa·s respectively (Table 1). These values fall within an acceptable range for topical gel formulations, further supporting their suitability for dermal application [15].

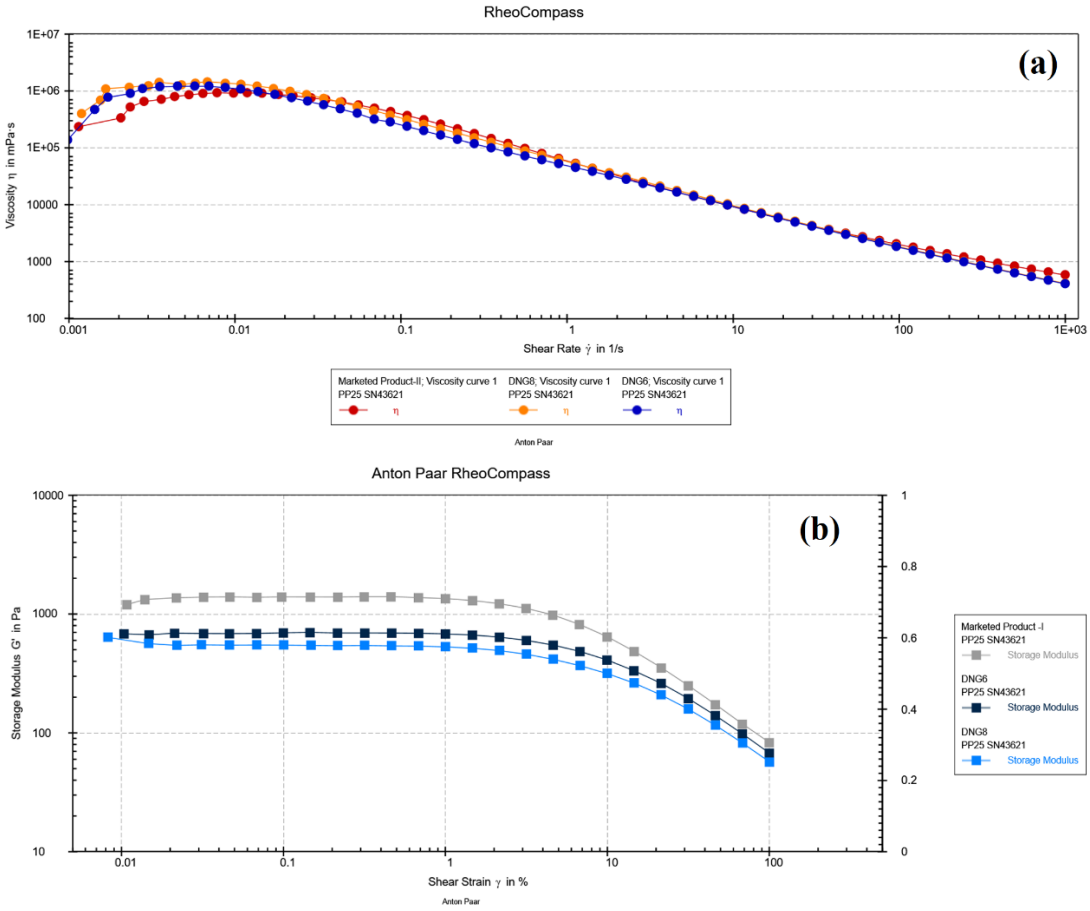

Fig 4. Rheology of DES niosomal gel and DES conventional gel. (a) Flow curve comparison of DG6, DG8 and Marketed product. (b) Yield stress comparison of DG6, DG8 and Marketed product

3.4.2. Drug release of DES from gels

The in vitro release behaviour of DES from DG6 and DG8 formulations was investigated using an immersion cell diffusion apparatus. The cumulative drug release at predefined time intervals was quantified and is presented in Fig. 5. The niosomal gel formulation (DG6) exhibited a controlled release profile, with 88.4% ± 10.2% of the drug released over a period of 6 hours. In contrast, the conventional gel formulation (DG8) showed a faster and more immediate release, with 97.9% ± 13.1% of DES released within 3 hours (Fig. 5). This distinct difference in release kinetics highlights the sustained-release capability of the niosomal system. The niosomal gel displayed a linear and prolonged release profile which is a characteristic of sustained release drug delivery system.

The diffusion flux, calculated from the slope of the cumulative drug release per unit surface area versus the square root of time plot, further supports the sustained release behaviour. The flux for DG6 was determined to be 6.7 ± 2.2 $\mu g \cdot cm^{-2} \cdot min^{-1}$, which was significantly lower than that of DG8 (11.2 ± 3.6 $\mu g \cdot cm^{-2} \cdot min^{-1}$), confirming the slower and more controlled diffusion of DES from the niosomal formulation. This release pattern not only ensures maintenance of therapeutic drug concentrations over an extended period but also minimizes dosing frequency—factors that are critical for improving adherence to topical treatments and optimizing clinical outcomes [26].

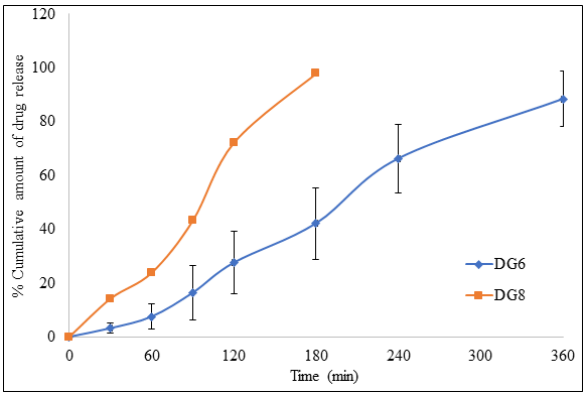

Fig 5. In vitro drug release of DG6 and DG8

3.4.3. Ex vivo skin deposition of DES from gels

Ex vivo skin permeation study was performed using excised pig's ear skin to assess the distribution of the DES across different skin strata and into the receptor phase. The comparative analysis of DG6 and DG8, revealed formulation-dependent differences in drug localization. As shown in Fig. 6, DG6 exhibited significantly greater accumulation of DES within the epidermal and dermal layers (192.3 ± 55.1 µg) whereas DG8 demonstrated a significantly lower skin retention of 140.9 ± 51.7 µg. In contrast, the amount of DES permeated into the receptor fluid over the study duration was minimal for both formulations, with DG6 showing 2.1 ± 1.1 µg and DG8 1.1 ± 0.3 µg.

This enhanced transdermal permeation, accompanied by enhanced intradermal retention, suggests that DG6 acts as an efficient carrier system for localized delivery. These findings highlight the potential of niosomal gel formulations to enhance topical drug delivery by promoting dermal retention while minimizing systemic exposure. The increased retention of DES in the skin may contribute to improved local therapeutic efficacy, making DG6 a promising candidate for the management of dermatological conditions requiring sustained drug presence in the target tissue. This is particularly desirable in the treatment of localized dermatological conditions such as psoriasis, where high local concentrations and minimal systemic exposure are essential for efficacy and safety [27].

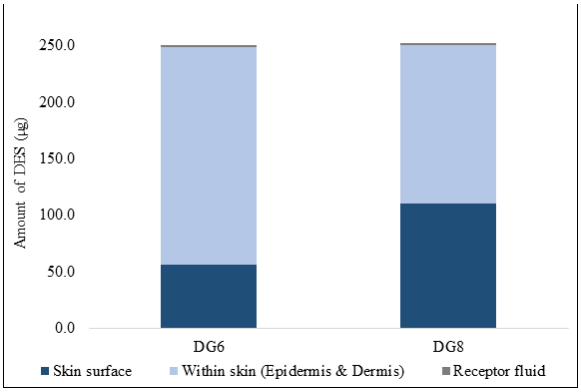

Fig 6. Ex vivo skin deposition study of DES from DG6 and DG8

3.4.4. Stability studies of DES niosomal gel

The stability studies showed that there was no major changes were observed in DG6 gel compared to the initial time point. All the parameters, visual observation, pH viscosity and drug content were found to be in acceptable ranges whithout major changes compared to the initial time point. Thus, indicating that DG6 was stable at accelerated and real time conditions for 6 month duration of the study. The observations and results of the stability studies are available in table 3.

Table 3. Stability studies of DG6

Stability condition		Visual observation	pH	Viscosity (Pa.s)	Drug content (%)
Initial		Uniform gel	7.41 (±0.07)	1867.23 (±161.9)	97.3% (±0.1)
40°C±2°C / 75%±5%RH (accelerated)	1M	Uniform gel	7.38 (±0.04)	1589.3 (±126.2)	98.60% (±0.6)
	3M	Uniform gel	7.52 (±0.09)	1634.0 (±148.5)	97.80% (±0.1)
	6M	Uniform gel	7.44 (±0.11)	1569.5 (±133.8)	98.20% (±0.3)
25°C±2°C / 60%±5%RH (Real time)	1M	Uniform gel	7.46 (±0.03)	1784.7 (±157.1)	97.90% (±0.2)
	3M	Uniform gel	7.51 (±0.07)	1806.8 (±130.7)	98.80% (±0.8)
	6M	Uniform gel	7.35 (±0.02)	1699.9 (±142.3)	97.20% (±0.1)

Values reported as mean (±SD), n=3

3.4.5. Comparative In vivo assessment of DES gels

Morphological changes were photographed on treatment days 1, 3 and 7. It was observed that the morphological changes were evident in IMQ treated group with highest erythema, scaling and thickness scores compared to the NC group, indicating the induction of psoriasis like inflammatory response in the IMQ group. The morphological observations of the treated skin demonstrated considerable reduction in inflammation and morphological improvements in the DG6 treated group compared to the DG8 group. The skin showed smoother texture, decreased scaling, and less inflammation in DG6 compared to the DG8 indicating improved recovery from the IMQ treatment effects. The images of morphological changes is provided in Fig. 7(a) for all the four groups. PASI scoring was done by investigator where no inflammation or absence of inflammation shall be noted as 0, mild inflammation to be noted as 1, moderate inflammation to be noted as 2, severe to be noted with 3 and very severe to be noted with 4 rating [28]. Scoring was done for erythema, thickness and scaling parameters. PASI score showed significant changes. Erythema, scaling, and psoriasis-like inflammation were evident in the IMQ group with highest total PASI score of 12.0 (±1.2) by the end of day 8, compared to NC group which showed total PASI score of 0 throughout the study duration. However, the groups that received DES treatment had a lower in PASI scores suggesting an improvement in the symptoms of psoriasis. DG6 had the best improvement with a total PASI score of 3.8 (±1.0) by the end of the study, indicating better therapeutic potential in reducing inflammation and scaling than the DG8 having total PASI score of 6.4 (±1.1). Thus, the niosomal formulation improved topical drug delivery and localized therapy which may lead to improved therapeutic effects. The graphs were plotted for the PASI score for erythema, thickness, scaliness and total PASI score (which is sum of erythema, thickness and scaliness score) as depicted in Fig. 7b-e.

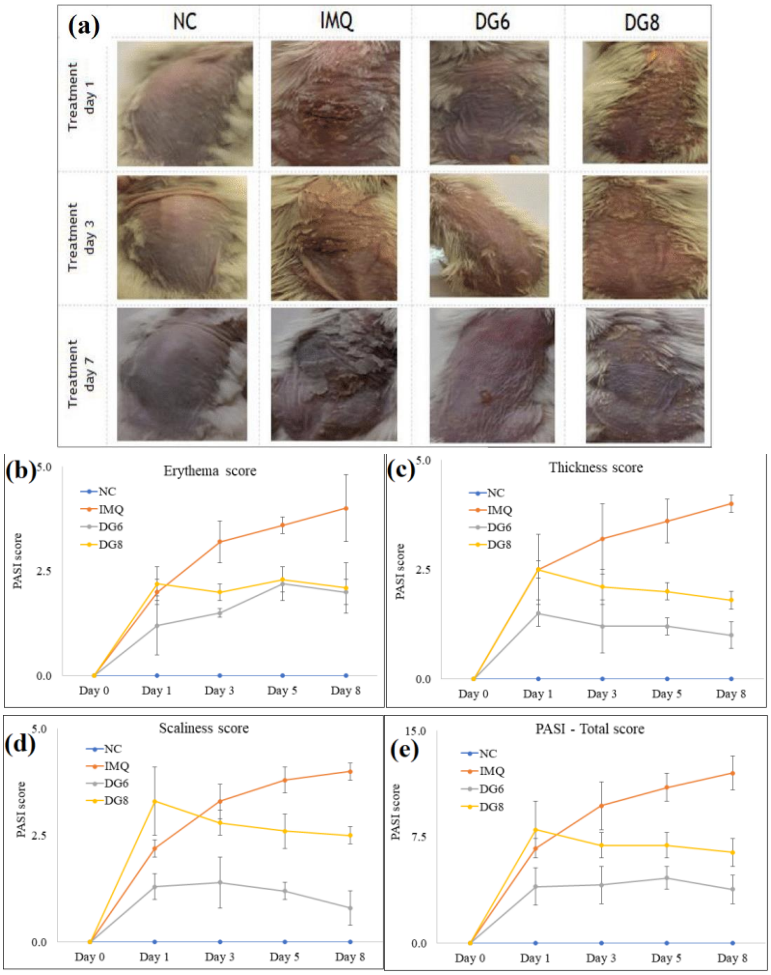

Fig 7. In vivo studies of DG6 and DG8 in Swiss albino mice. (a) Morphological observations. (b) Erythema PASI score. (c) Thickness PASI score. (d) Scaliness PASI score. (e) Total PASI score

The induction of psoriasis-like inflammation using IMQ led to a noticeable reduction in the moisture content of the stratum corneum, as evidenced by the dry, scaly appearance of the skin compared to the NC, which did not receive any treatment [29]. The NC group had a moisture content of 41.7 (±5.1) at the start of the study and was maintained throughout the study period. Whereas, IMQ group had a moisture content of 39.2 (±9.1) at the start of the study but reduced drastically to 5.3 (±3.9) by the end of the study on day 8, indicating dryness of the skin, a marked manifestation of psoriasis. Treatment with DES had a marked improvement in the moisture content of the skin. DG6 was observed to be better in restoring skin hydration from 22.4 (±5.7) on day 1 to 38.2 (±6.8) on day 8 than DG8 which showed hydration levels of 17.0 (±5.4) on day 1 to 22.4 (±6.9) on day 8 after the treatment. A significant difference between moisture content of DG6 and DG8 was noted at the end of study period. A graph was plotted with days on X –axis and moisture content on y axis, as depicted in Fig. 8a. Similarly, TEWL was measured using Vapometer. IMQ group showed high TEWL of 48.7 g/m^2h (±5.3), indicating compromised skin barrier and loss of moisture from the skin, a typical observation in the psoriatic skin types compared to the NC group which showed normal levels of TEWL between 17.9 and 19.8 g/m^2h during the study period [22]. It was observed that DES treated groups showed improvement in moisture retention from after administering the treatments with DG6 showing 24.7 g/m^2h (±5.1) and DG8 showing 32.6 g/m^2h (±4.8), showing a significant difference. A graph was plotted with days on X –axis and TEWL on y axis as shown in Fig. 8b.

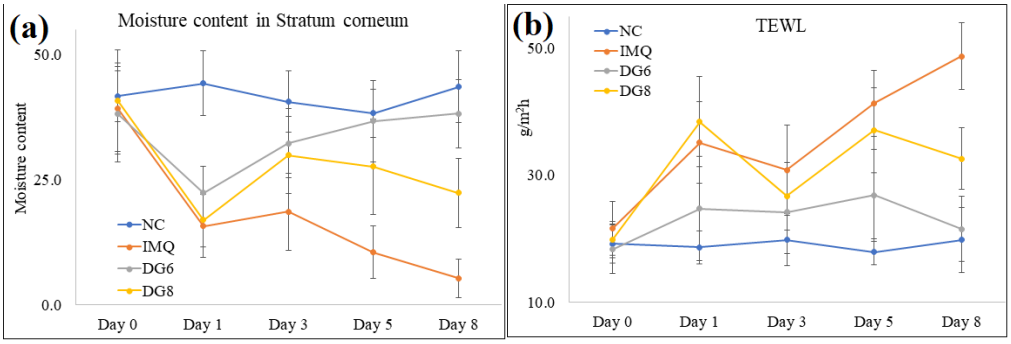

Fig 8. In vivo studies of DG6 and DG8 in Swiss albino mice. (a) Graph depicting moisture content in stratum corneum during the study period. (b) Graph depicting transepidermal water loss during the study period

At the end of the study the animals were euthanized to collect the spleen samples and skin samples from the administration site. The samples were wiped clean to remove any excess tissue, debris or blood. The skin samples were stored in formalin solution for further histology studies. The spleen samples were measured for their weight and morphological observations. IMQ-induced psoriasis-like inflammation resulted in an enlarged spleen as evidenced in the inflammatory responses [30]. Thus, IMQ group has a highest spleen index of 9.4 ± 0.5 compared to baseline, NC group (5.0 ± 0.2). DES treated groups showed improvement in spleen index. DG6 showed significant reduction in spleen index (3.6±1.2) than DG8 (7.4±0.7), which showed that the inflammation-induced splenomegaly was reversed with better improvement in DG6 proving the improved efficacy of the niosomal formulation in terms of anti-inflammatory properties. The morphology of spleens is presented in the Fig. 9a and graphical depiction of spleen index in Fig. 9b.

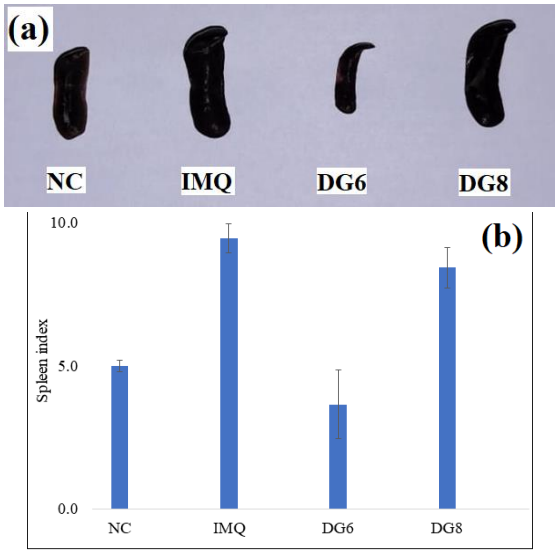

Fig 9. In vivo studies of DG6 and DG8 in Swiss albino mice. a) Morphological observations of spleen. (b) Graph depicting spleen index

The skin samples were stained using hematoxylin and eosin (H&E) dye to visualize and identify any pathological changes in the skin structure [22]. The NC skin samples were analyzed under the microscope and found the skin was normal without any indications of inflammation. On the other hand, IMQ group treated with Imiquimod Cream 5% showed severe deformities in the skin layers with marked parakeratosis, epidermal hyperplasia, notable infiltration of inflammatory cells and rete ridges. These observations confirm the successful induction of psoriasis [28]. In the skin samples of DG6 and DG8, the manifestations induced by IMQ were considerably reduced indicating regaining of the skin structure due to the treatment with DES. It could be further observed that the DG6 showed lesser number of rete ridges and keratosis than DG8 indicating improvement in the treatment regimen with the use of niosomal formulation. The histological manifestations were presented in the Fig. 10a-d. These results suggest that the niosomal formulation significantly enhanced the drug's penetration and efficacy in reversing psoriasis-induced changes offering superior therapeutic benefits compared to conventional gel formulation. The enhanced performance of the niosomal gel can be attributed to its superior ability to penetrate the skin barrier, localizing within the skin and sustained release of DES which would have allowed for quicker healing in the animal model.

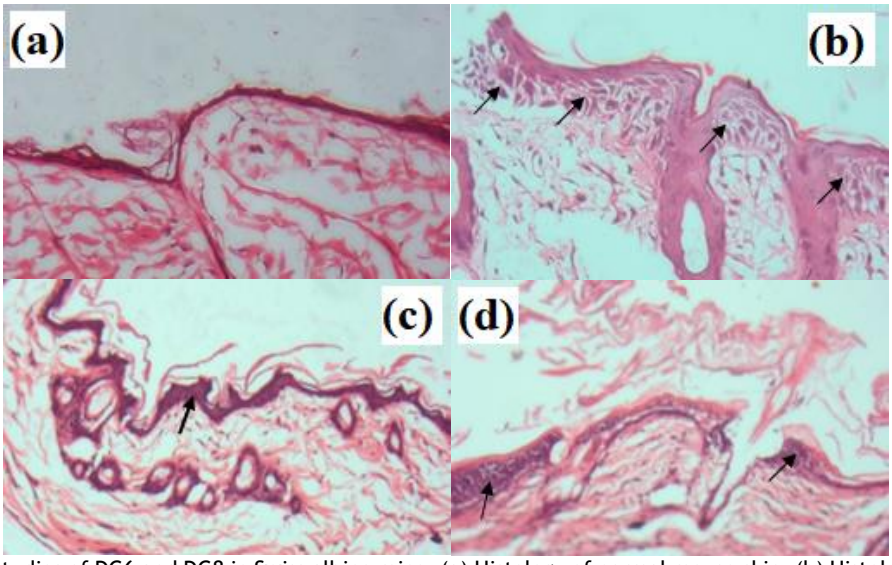

Fig 10. In vivo studies of DG6 and DG8 in Swiss albino mice. (a) Histology of normal mouse skin, (b) Histology of IMQ treated skin, (c) Histology of DG6 treated skin, (d) Histology of DG8 treated skin

4. Conclusion

This study successfully demonstrated the formulation and evaluation of a Desonide-loaded niosomal gel (DG6) with superior physicochemical characteristics, sustained drug release and enhanced dermal retention compared to a conventional Desonide gel (DG8). The niosomal formulation exhibited significant improvements in skin deposition, morphological recovery, PASI score reduction, and histopathological restoration in an imiquimod-induced psoriasis model. Additionally, DG6 showed favorable rheological properties and barrier restoration, indicating its potential for improved patient compliance and therapeutic outcomes.

These findings underscore the efficacy of niosomal drug delivery systems in the localized treatment of inflammatory skin conditions such as psoriasis. The sustained release, enhanced permeation, and minimized systemic absorption offered by DG6 make it a promising alternative to traditional topical therapies. This approach may serve as a valuable platform for the delivery of other anti-inflammatory agents used in the management of chronic skin diseases such as psoriasis, eczema, and dermatitis. Further clinical translation could establish this formulation as a safer and more effective option for long-term psoriasis management.

Author contributions: Megha Shyam Matlapudi: Conceptualization, Methodology, Resources, Formal analysis, Investigation, Data curation, Visualization, Writing – original draft. Anka Rao Areti: Methodology, Project administration, Supervision, Writing – review and editing. Yukti Jaiswal: Resources, Formal analysis, Investigation. Veeresh Bantal: Resources, Formal analysis, Investigation, Project administration, Writing – review and editing.

Funding: This research received no external funding

Acknowledgements: The authors would like to express their gratitude to Orbicular Pharmaceutical Technologies Pvt. Ltd., KL College of Pharmacy, G. Pulla Reddy College of Pharmacy and to Dr. Raghavender Medishetti for their invaluable support throughout this research work.

Conflict of interests: The authors declare that there are no competing interests.

References

[1] Wang, K.; Zhao, Y.; Cao, X. Global burden and future trends in psoriasis epidemiology: insights from the global burden of disease study 2019 and predictions to 2030. *Arch. Dermatol. Res.* **2024**,316(4),114. https://doi.org/10.1007/s00403-024-02846-z

[2] Rapalli, V.K.; Singhvi, G.; Dubey, S.K.; Gupta, G.; Chellappan, D.K.; Dua, K. Emerging landscape in psoriasis management: From topical application to targeting biomolecules. *Biomed. Pharmacother.* **2018**,106,707-713. https://doi.org/10.1016/j.biopha.2018.06.136

[3] Lowes, M.A.; Suárez-Fariñas, M.; Krueger, J.G. Immunology of psoriasis. *Annu. Rev. Immunol.* **2014**,32,227-255. https://doi.org/10.1146/annurev-immunol-032713-120225

[4] Patient information leaflet of Desonide cream & Lotion (Desowen) available at https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a7e5f030-b849-4805-94e6-f45631eaa37f

[5] Ma, Q.; Zhang, J.; Lu, B.; Linm H.; Sarkar, R.; Wu, T.; Li, X. Nanoemulgel for Improved Topical Delivery of Desonide: Formulation Design and Characterization. *AAPS PharmSciTech.* **2021**,22,163. https://doi.org/10.1208/s12249-021-02035-5

[6] Uva, L.; Miguel, D.; Pinheiro, C.; Antunes, J.; Cruz, D.; Ferreira, J.; Filipe, P. Mechanisms of action of topical corticosteroids in psoriasis. *Int. J.*

Endocrinol. **2012**,2012(1), 561018. https://doi.org/10.1155/2012/561018

[7] Sharma, K; Sapra, B; Kant, S; Bedi, N. Formulation and Evaluation of Desonide Loaded Microemulsion Based Gel for Management of Atopic Dermatitis. *J. Nanomed*. **2021**,4(1),1035.

[8] Zhang, J.; Yao, Y.; Liu, H.; Ma, Q.; Huang, L.; Chen, Y.; Lin, H. Desonide Nanoemulsion Gel for Transdermal Absorption Drug Delivery: Pharmacodynamic and Safety Evaluation. *Curr. Drug Deliv.* **2023**,20(10),1525-1532. https://doi.org/10.2174/15672018196662208191101 28

[9] Seenivasan, K.; Priyadharshini, R.; Barish; Mahalakshmi, S. Formulation and evaluation of desonide ethosomal gel. *Int. J. Res. Pharm and Pharm Sci*. **2024**,9(3),49-53.

[10] Antonow, M.B.; Lorenzoni, R.; Barbosa, G.M.; Ourique, A.F.; Gomes, P.; Raffin, R.P. Development and Physicochemical Characterization of Desonide-Loaded Nanocapsule Suspensions. *Adv. Mater. Sci. Eng*. **2016**,2016,7395896. http://dx.doi.org/10.1155/2016/7395896

[11] Rosa, P.; Friedrich, M.L.; dos Santos, J.; Pegoraro, N.S.; Camponogara, C.; Oliveira, S.M.; Adams, A.I.H.; de Bona da Silva, C. Development of a nanotechnological hydrogel containing desonide nanocapsules in association with acai oil: design and in vivo evaluation. *Pharm. Dev. Technol*. **2022**,27(6),654–664. https://doi.org/10.1080/10837450.2022.2103147

[12] Todke, P.; Shah, V.H. Psoriasis: implication to disease and therapeutic strategies, with an emphasis on drug delivery approaches. *Int. J. Dermatol*. **2018**,57(11),1387–1402. https://doi.org/10.1111/ijd.14047

[13] Cerqueira-Coutinho, C.; Dos Santos, E.P.; Mansur, C.R. Niosomes as Nano-Delivery Systems in the Pharmaceutical Field. *Crit. Rev. Ther. Drug Carrier Syst*. **2016**,33(2),195–212. https://doi.org/10.1615/CritRevTherDrugCarrierSyst.2016016167

[14] Zaid Alkilani, A.; Hamed, R.; Abdo, H.; Swellmeen, L.; Basheer, H.A.; Wahdan, W.; Abu Kwiak A.D. Formulation and Evaluation of Azithromycin-Loaded Niosomal Gel: Optimization, In Vitro Studies, Rheological Characterization, and Cytotoxicity Study. *ACS Omega*. **2022**,7(44),39782-39793.https://doi.org/10.1021/acsomega.2c03762

[15] Patel, K.K.; Kumar, P.; Thakkar, H.P. Formulation of Niosomal Gel for Enhanced Transdermal Lopinavir Delivery and Its Comparative Evaluation with Ethosomal Gel. *AAPS PharmSciTech*. **2012**,13,1502–1510. https://doi.org/10.1208/s12249-012-9871-7

[16] Matlapudi, M.S.; Areti, A.R. Formulation and Evaluation of Desonide Loaded Niosomes Prepared by Film Hydration Technique Using Box-Behnken Design. in Current Trends in Drug Discovery, Development and Delivery (CTD4-2022), ed. M. Murahari, B. N. Nalluri, and G. Chakravarthi, *Royal Society of Chemistry*. **2023**,358,351-360. https://doi.org/10.1039/9781837671090-00351

[17] Pandey, S.S.; Shah, K.M.; Maulvi, F.A.; Desai, D.T.; Gupta, A.; Joshi, S.V.; Shah, D.O. Topical delivery of cyclosporine loaded tailored niosomal nanocarriers for improved skin penetration and deposition in psoriasis: Optimization, ex vivo and animal studies. *J. Drug Deliv. Sci. Technol*. **2021**,63,102441.https://doi.org/10.1016/j.jddst.2021.102441

[18] Soni, S.; Baghel. K.; Soni. M.L.; Kashaw. S.K.; Soni, V. Size-dependent effects of niosomes on the penetration of methotrexate in skin layers. *Futur. J. Pharm. Sci*. **2024**,10(48),1-18. http://doi.org/10.1186/s43094-024-00624-2

[19] Qiu, F.; Xi, L.; Chen, S.;l Zhao, Y.; Wang, Z.; Zheng, Y. Celastrol Niosome Hydrogel Has Anti-Inflammatory Effect on Skin Keratinocytes and Circulation without Systemic Drug Exposure in Psoriasis Mice. *Int. J. Nanomedicine*. **2021**,16,6171-6182. https://doi.org/10.2147/IJN.S323208

[20] El-Say, K.M.; Abd-Allah, F.I.; Lila, A.E.; Hassan Ael-,S.; Kassem, A.E. Diacerein niosomal gel for topical delivery: development, in vitro and in vivo assessment. *J. Liposome Res*. **2016**,26(1),57-68. https://doi.org/10.3109/08982104.2015.1029495

[21] Matlapudi, M.S.; Areti, A.R.; Jaiswal, Y.; Bantal, V.; Medishetti, R. Enhancing topical drug delivery of Apremilast through niosomal gel formulation: Ex vivo skin permeation and in vivo evaluation for psoriasis. *Thai J. Pharm. Sci*. **2025**,49(1),3. https://doi.org/10.56808/3027-7922.2978

[22] Sathe, P.; Saka, R.; Kommineni, N.; Raza, K.; Khan, W. Dithranol-loaded nanostructured lipid carrier-based gel ameliorate psoriasis in imiquimod-induced mice psoriatic plaque model. *Drug Dev. Ind. Pharm*. **2019**,45(5),826–838. https://doi.org/10.1080/03639045.2019.1576722

[23] Obeid, M.A.; Khadra, I.; Aljabali, A.A.A.; Amawi, H.; Ferro, V.A. Characterisation of niosome nanoparticles prepared by microfluidic mixing for drug delivery. *Int. J. Pharm. X*. **2022**,4,100137. https://doi.org/10.1016/j.ijpx.2022.100137

[24] Gouda, R.; Baishya, H.; Qing, Z. Application of Mathematical Models in Drug Release Kinetics of Carbidopa and Levodopa ER Tablets. *J. Develop. Drugs*. **2017**,6(2),1-8. https://doi.org/10.4172/2329-6631.1000171

[25] Mahdavi Moghddam, S.R.; Ahad, A; Aqil, M; Imam, S.S.; Sultana, Y. Formulation and optimization of niosomes for topical diacerein delivery using 3-factor, 3-level Box-Behnken design for the management of psoriasis. *Mater. Sci. Eng. C*. **2016**,69,789–797. https://doi.org/10.1016/j.msec.2016.07.043

[26] Bhardwaj, P.; Tripathi, P.; Pandey, S.; Gupta, R.; Patil, P.R. Cyclosporine and Pentoxifylline laden tailored niosomes for the effective management of

psoriasis: In-vitro optimization, Ex-vivo and animal study. *Int. J. Pharm.* **2022**,626,122143. https://doi.org/10.1016/j.ijpharm.2022.122143

[27] Fadaei, M.S.; Fadaei, M.R.; Kheirieh, A.E.; Rahmanian-Devin, P.; Dabbaghi, M.M.; Nazari Tavallaei, K.; Shafaghi, A.; Hatami, H.; Baradaran Rahimi, V.; Nokhodchi, A.; Askari, V.R. Niosome as a promising tool for increasing the effectiveness of anti-inflammatory compounds. *EXCLI J.* **2024**,23,212-263. https://doi.org/10.17179/excli2023-6868

[28] Neu, S.D.; Strzepa, A.; Martin, D.; Sorci-Thomas, M.G.; Pritchard, K.A.Jr; Dittel, B.N. Myeloperoxidase Inhibition Ameliorates Plaque Psoriasis in Mice. *Antioxidants.* **2021**,10(9),1338. https://doi.org/10.3390/antiox10091338

[29] Guo, J.W.; Cheng, Y.P.; Liu, C.Y.; Thong, H.Y.; Huang, C.J.; Lo, Y.; Wu, C.Y.; Jee, S.H. Salvianolic Acid B in Microemulsion Formulation Provided Sufficient Hydration for Dry Skin and Ameliorated the Severity of Imiquimod-Induced Psoriasis-Like Dermatitis in Mice. *Pharmaceutics.* **2020**, 12(5), 457. https://doi.org/10.3390/pharmaceutics12050457

[30] Xu, Y.; Shi, Y.; Huang, J.; Gu, H.; Li, C.; Zhang, L.; Liu, G.; Zhou, W.; Du, Z. The Essential Oil Derived from Perilla frutescens (L.) Britt. Attenuates Imiquimod-Induced Psoriasis-like Skin Lesions in BALB/c Mice. *Molecules.* **2022**,27(9),2996. https://doi.org/10.3390/molecules27092996