RESEARCH PAPER

Formulation Development and Characterization of Anthralin Proniosomal Gel for Topical Treatment of Psoriasis

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ABSTRACT

Psoriasis is a chronic inflammatory skin disorder characterized by excessive keratinocyte proliferation and immune dysregulation, requiring effective localized therapy with minimal systemic exposure. Anthralin remains a potent antipsoriatic agent, but its therapeutic utility is hindered by instability, irritation, oxidation, and poor patient compliance. The present study aimed to develop a novel anthralin-loaded proniosomal gel to enhance drug stability, improve skin targeting, and provide controlled topical delivery. Proniosomal gel was prepared by the coacervation phase separation method using non-ionic surfactants (tween 80 and span 60), cholesterol, and lecithin, followed by incorporation into a Carbopol gel base. The formulations were comprehensively evaluated for physicochemical properties, vesicle characteristics, in-vitro release, ex-vivo skin permeation, cytocompatibility, hemocompatibility, and in-vivo anti-psoriatic efficacy. The optimized formulation (ANPG7) showed high drug entrapment (86.58%), appropriate viscosity, skin-compatible pH, and excellent spreadability, indicating suitability for topical application. Vesicle size (~239 nm), low polydispersity index, and negative zeta potential confirmed formation of a stable and uniform vesicular system. Controlled drug release was observed over 24 hours, while ex-vivo permeation studies demonstrated minimal transdermal permeation with significant drug retention in the epidermis and dermis, supporting targeted skin delivery. Safety assessment revealed negligible hemolysis and good cytocompatibility toward normal fibroblasts L929, with enhanced cytotoxicity toward hyperproliferative keratinocytes HaCaT. In the imiquimod-induced psoriasis mouse model, the proniosomal gel significantly reduced PASI score, minimized dermal irritation, and restored normal skin and spleen histology. Overall, the developed anthralin proniosomal gel offers a stable, safe, and effective vesicular carrier that improves drug localization and therapeutic efficacy highlighting its potential as a promising topical therapy for psoriasis.

Keywords: Anthralin, Proniosomal Gel, Topical Delivery, Psoriasis, Vesicular Drug Delivery, Skin Permeation, Controlled Release

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INTRODUCTION

Psoriasis is a chronic immune-mediated inflammatory skin disease marked by excessive keratinocyte proliferation and abnormal immune activity, resulting in erythematous, scaly plaques that affect about 2–3% of the global population and markedly reduce quality of life[1]. Conventional topical therapies such as corticosteroids, vitamin D analogues, and keratolytics mainly provide symptomatic relief and may cause adverse effects like skin atrophy, irritation, and tachyphylaxis with prolonged use[2, 3]. Anthralin (dithranol) is a well-established antipsoriatic agent that suppresses keratinocyte proliferation, normalizes epidermal differentiation, and reduces inflammatory cell activity[4]. However, its clinical use is limited by poor solubility, instability, susceptibility to oxidation, irritation, and staining of skin and clothing, prompting the need for improved delivery systems[5].

Proniosomal gels have emerged as promising carriers for topical drug delivery[6-8]. These dry formulations convert into niosomes upon hydration and consist of non-ionic surfactants, cholesterol, and phospholipids[9]. They enhance drug stability, provide controlled release, improve skin permeation, and reduce irritation while offering better spreadability and

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residence time on the skin[10]. Incorporating anthralin into a proniosomal gel protects it from degradation, promotes controlled epidermal delivery, enhances penetration through stratum corneum lipid fluidization, and minimizes irritation and staining[11]. Thus, anthralin-loaded proniosomal gels represent a promising strategy for safer and more effective psoriasis management.

MATERIALS AND METHODS

Anthralin was obtained as a gift sample from a certified pharmaceutical supplier. Cholesterol, soya lecithin, and non-ionic surfactants (Span 40, Span 60, Span 80, Tween 20, Tween 60, and Tween 80) were procured from analytical-grade sources. Carbopol 934, glycerin, triethanolamine, methyl paraben, ethanol, methanol, Imiquimod Cream, Salicylic Acid Gel, and phosphate buffer saline (PBS, pH 7.4) were purchased from Aryan Scientifics (Nagpur, India). All chemicals and solvents used were of analytical or pharmacopeial grade.

Preparation of ANPG

Anthralin proniosomal gel (ANPG) was formulated using the coacervation phase separation method. Anthralin was first dissolved in methanol (10 mg/5 mL). Cholesterol, soya lecithin, and a 1:1 mixture of Tween 80 and Span 60 were then incorporated and heated at 60–65°C with stirring (40 rpm) for 5–10 minutes until fully dissolved. Subsequently, preheated phosphate buffer (60–65°C) was added slowly under continuous stirring to obtain a clear or translucent proniosomal gel[12].

Evaluation of Proniosomal Gel

Physical observation of proniosomal gel

The proniosomal gels were visually inspected to assess color, clarity, consistency, and uniformity. Variations in surfactant and membrane stabilizer composition resulted in different appearances, including brown transparent liquid, white semisolid mass, and cream-colored liquid dispersion[7].

Entrapment efficiency

Entrapment efficiency was determined by dispersing 1 g of proniosomal gel in deionized water and gently heating it to form niosomes. The dispersion was centrifuged at 18,000 rpm for 40 minutes at 25°C (Remi CPR-24). The supernatant was collected, and the amount of unentrapped drug was quantified using a UV spectrophotometer[8]. Entrapment efficiency (EE%) was calculated using the following equation:

where t is the total drug concentration and f is the concentration of free drug in the supernatant.

Drug content

For drug content determination, 2 g of each proniosomal gel (ANPG and AEPG) was placed in a volumetric flask with 100 mL of methanol and sonicated or shaken to extract the drug completely. Appropriate dilutions were prepared, and absorbance was measured using UV spectrophotometry at 248 nm for Anthralin and 220 nm for Aloe emodin against a suitable blank. Drug content was calculated from the respective calibration curves[8].

Viscosity

In order to do this experiment, 10 gm of the gel was placed in a beaker and the T-shaped spindle of the Fungilab viscometer was submerged in the gel. The spindle was then rotated at different speeds to find the mean viscosity[13].

pH measurement

The pH of the formulations was determined using a calibrated pH meter. The instrument was standardized with buffer solutions at pH 4.0 and 7.0 before use. One gram of gel was dispersed in 20 mL of distilled water, and the pH of the resulting dispersion was recorded[14].

Spreadability

Spreadability was assessed by placing 0.5 g of gel within a pre-marked 1 cm circle on a glass slide. A second slide was placed over it, and a 500 g weight was applied for 15 seconds. The spreading area was measured to determine spreadability and ease of application[15].

Rate of spontaneity

About 20 mg of proniosomal gel was evenly coated on the inner wall of a clean glass container. Two milliliters of saline were gently added along the wall without disturbing the film, and the system was left undisturbed for 20 minutes to allow hydration and vesicle formation. The formed niosomes were then counted using a Neubauer chamber to assess the spontaneity of vesicle formation[16].

In-vitro drug release study

In-vitro drug release was evaluated using Franz diffusion cells with donor and receptor compartments. The receptor chamber contained 20 mL phosphate buffer (pH 7.4), and a dialysis membrane pre-soaked for 24 h was mounted between the compartments. The system was maintained at 37 ± 1°C with continuous stirring at 100 rpm. One gram of proniosomal gel was placed in the donor compartment. Samples were withdrawn hourly for 24 h, replaced with fresh buffer to maintain sink conditions, and analyzed by UV spectrophotometry to calculate cumulative drug release[17].

Measurement of zeta potential

Zeta potential of the proniosomal gel formulations was measured using a Litesizer 500 Zeta Potential Analyzer (Balpande College of Pharmacy, Nagpur). Samples were analyzed in triplicate at 25°C with a detection angle of 173°, and the mean values were recorded to evaluate vesicle surface charge and stability[18].

Determination of vesicle size

Vesicle size and distribution were measured using the Litesizer 500 by photon correlation spectroscopy. A 633 nm He–Ne laser was used to monitor light scattering caused by Brownian

motion, enabling determination of mean particle size and polydispersity index (PDI). Measurements were performed in triplicate at 25°C with a 173° detection angle, and vesicle sizes ranged from 10–1000 nm[12].

Vesicular shape and surface morphology

Scanning electron microscopy (SEM) was used to examine the surface morphology of niosomes, including empty vesicles. A drop of the niosomal dispersion was placed on a glass stub, air-dried, and sputter-coated with gold–palladium (Au/Pd) using a vacuum evaporator (Edwards). Samples were then observed under a JSM-5510 scanning electron microscope[11, 19].

Ex-vivo skin permeation study

Ex-vivo permeation of the optimized proniosomal gels was studied using rat abdominal skin with approval from the Animal Ethics Committee of Trans-Genica Services Pvt. Ltd., Jalgaon, Maharashtra. Rats were euthanized with an overdose of sodium thiopental, abdominal hair was removed, and full-thickness skin was excised. After removing adhering fat, the skin was checked for defects and equilibrated in phosphate-buffered saline (PBS) for 10 minutes. The skin was mounted on a Franz diffusion cell with the stratum corneum facing the donor compartment. One gram of proniosomal gel was applied to the donor chamber, and the receptor compartment was filled with PBS (pH 7.4) maintained at 37 ± 1 °C with continuous stirring. Samples were collected at hourly intervals and replaced with fresh buffer to maintain sink conditions. Drug permeation was analyzed using UV spectrophotometry[11, 20, 21].

Study of drug retention

After completion of the permeation study, skin samples (~1 cm^2) were collected in triplicate and sectioned into stratum corneum, epidermis, and dermis using a cryotome (LEICA CM 1100). The sections were mounted on cork discs with tissue-freezing medium and sliced into thin layers. Each layer was soaked in methanol overnight to extract the drug, followed by centrifugation. The supernatant was analyzed spectrophotometrically to quantify drug retention in each layer, and the concentration (µg/cm^2) was plotted to compare retention profiles[21].

In-vitro hemolysis studies

In-vitro hemolysis was assessed to determine hemocompatibility of the proniosomal formulations. Fresh human blood collected in acid citrate dextrose was mixed (1 mL) with 100 µL of formulations at concentrations of 0.1–1 mg/mL and incubated at 37°C on an orbital shaker (50 rpm) for 2 hours. The samples were then centrifuged at 4500 rpm for 10 minutes to separate plasma[11].

An aliquot of 100 µL plasma was diluted with 1 mL of 0.01% Na_2CO_3, and optical density was recorded at 380, 415, and 450 nm using a microplate reader. Plasma hemoglobin concentration was calculated using the following equation :

The results were compared with those of a positive control (Triton X) and a negative control (normal saline). All measurements were performed in triplicate.

MTT Assay

Cytotoxicity of anthralin and aloe-emodin proniosomal gels was assessed in L929 mouse fibroblast and HaCaT keratinocyte cell lines using plain proniosomal gel as control. Cells were cultured in DMEM at 37 °C with 5% CO_2, trypsinized, and seeded in 96-well plates (~1×10^4 cells/well). After reaching ~90% confluence, cells were treated with serial dilutions (0.1–100 µg/mL) of free Anthralin, free Aloe emodin, ANPG, and plain gel for 24 h. The medium was then replaced with MTT solution and incubated for 4 h to allow formazan formation. Crystals were dissolved in solubilization buffer, and absorbance was recorded at 570 nm using an ELISA reader. Cell viability was calculated relative to untreated cells[12].

Animal Studies

Animals

Nulliparous Swiss albino mice and New Zealand white rabbits were maintained under standard laboratory conditions (12-h light/dark cycle, 25 ± 2 °C, 50 ± 5% RH) with free access to pellet diet and water. The study was approved by the Institutional Animal Ethics Committee of Trans-Genica Services Pvt. Ltd., Jalgaon, India (Approval No.: TRS/PT/025/000).

IMQ-induced psoriasis in animals

The anti-psoriatic effect of APG3 was evaluated using an imiquimod-induced psoriasis model in nulliparous Swiss albino mice (n = 6). The dorsal area of each mouse was shaved prior to the experiment, and animals were divided into five groups: normal control, psoriatic control, plain proniosomal gel (PPG), anthralin proniosomal gel (ANPG), and a salicylic acid–treated standard group. Treatments with ANPG and PPG were started on day 1 and continued until the end of the study till day 15. Disease severity was monitored using PASI scoring (0–4 scale). At the end of the study, animals were sacrificed, and samples were collected for biochemical, pro-inflammatory cytokine, and histopathological analyses[22].

Primary dermal skin irritation study

Skin irritation was assessed in New Zealand white rabbits divided into five groups. Dorsal hair was removed using depilatory cream. The left side of the shaved skin was treated with ANPG and 0.8% v/v formalin as an irritant control, while the right side served as untreated control. Erythema and edema were evaluated at 30 minutes, 1 hour, and 4 hours post-application[11, 23].

Histology

At the end of the study, all animals were euthanized, and dorsal skin samples were excised for histological examination. Tissues were fixed in 10% neutral buffered formalin, dehydrated through graded ethanol, embedded in paraffin, and sectioned (~5 µm) using a rotary microtome. Sections were stained with hematoxylin and eosin and examined under a light microscope[11].

Statistical Analysis

Data were analyzed using one-way and two-way ANOVA in GraphPad Prism 6.0 (USA). Results are presented as mean ± SEM from two independent experiments, with statistical significance set at $p < 0.001$.

RESULTS AND DISCUSSION

Characterization of proniosomal gel

Table 1. Characterization of Proniosomal gel

Formulation Batch	Observation of proniosomal gel	EE (%)	Viscosity (cps)	pH	Spreadability with 500gm weight (Mm)	Rate of spontaneity
ANPG1	Light-brownish gel	76.10±0.37	6837±3.81	7.0±0.57	41±0.93	10±1.52
ANPG2	Light-brownish gel	64.33±0.70	7671±5.08	6.7±0.42	35±0.88	08±0.94
ANPG3	Light-brownish gel	72.71±0.48	7294±4.64	6.9±0.71	40 ±1.17	07±1.78
ANPG4	Creamy whitish gel	63.18±0.90	6962±2.67	5.7±1.10	39 ±1.33	07±2.03
ANPG5	Light-brownish gel	70.09±0.46	8467±2.98	5.3±0.85	43±0.98	10±0.97
ANPG6	Light-brownish gel	69.32±0.81	6009±3.47	6.2±0.64	39±0.55	09±1.43
ANPG7	Creamy whitish gel	86.58±0.69	8457±2.73	7.1±0.19	45±0.83	12±1.69
ANPG8	Creamy gel	67.91±0.42	7637±5.99	5.9±1.03	34±1.24	10±1.13
ANPG9	Creamy gel	71.37±1.04	7971±3.87	6.3±0.97	35±0.78	09±2.05

Proniosomal gels were visually inspected to verify these specifications. According to the findings, the proniosomal gels had a white to light brown colour and a white, semi-solid, cream-colored liquid look.

Entrapment efficiency

Drug entrapment efficiency is a crucial part in the preparation of the optimized manufactured formulations. The amount of medication that diffuses at the application site increases with the amount of medication trapped in the vesicles. The ANPG's drug entrapment efficiency values ranged from 63.18±0.90 to 86.58±0.69, indicating adequate to high entrapment efficiency.

Viscosity

With the help of Fungilab viscometer viscosities of the formulated proniosomal gels was measured using a T-shaped spindle. All of the formulations had optimal consistency when their viscosities were measured; the maximum viscosities among the ANPG batches, respectively, were 8467±2.98 cps for ANPG5.

pH measurement

The most important prerequisite for both a successful topical and transdermal formulation is skin compatibility. It was observed that all of the formulations pH values fell between 5.3±0.85 and 7.1±0.19 for the batches of ANPG showing that they are skin-compatible. The pH determination findings are shown in Table 5.23.

Spreadability

The diameter after spreading of the gel for the stipulated time was noted and it was shown in Table ranges from 34±1.24 to 45±0.83 mm for ANPG.

Rate of spontaneity

The rate of spontaneity, defined as the number of niosomes formed after 15 min of proniosomal gel hydration, ranged from 7 ± 1.78 to 12 ± 1.69 for ANPG indicating efficient and rapid niosome formation.

In-vitro drug release studies

In-vitro diffusion was performed using a Franz diffusion cell with a dialysis membrane pre-soaked in phosphate buffer (pH 7.4) for 24 h. The receptor compartment contained 20 mL phosphate buffer, maintained at 37 ± 1 °C and stirred at 100 rpm. One gram of proniosomal gel was placed in the donor chamber, and sink conditions were maintained by hourly replacement with fresh buffer for 24 h. Samples were analyzed using HPLC.

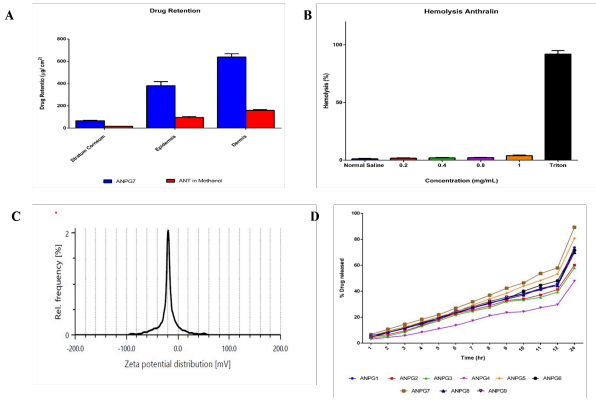


Figure 1 Evaluation of Proniosomal Gel A. Drug Retention B. Hemolysis C. Zeta Potential D. % Drug Release

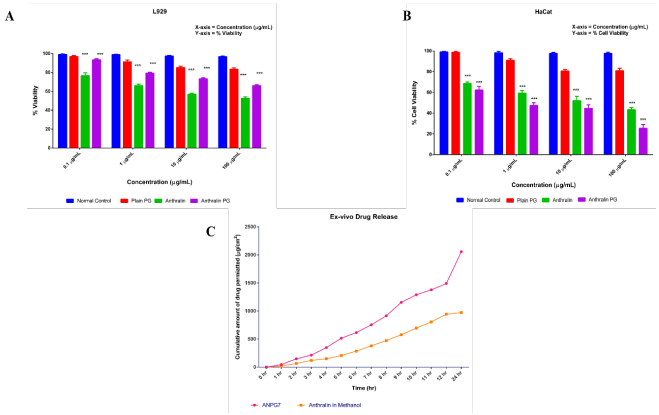


Figure 2: MTT Assay and Ex vivo Drug Release

Vesicle size and zeta potential

The optimized formulation ANPG7 was characterized for vesicle size and zeta potential. Dynamic light scattering showed an average vesicle size of 239.4 nm with a polydispersity index of 0.167, indicating a uniform size distribution. The zeta potential was −19.8 mV, suggesting adequate stability of the Niosomal system.

Ex-vivo skin permeation studies

Ex-vivo permeation of the optimized proniosomal gel was evaluated using rat abdominal skin (CPCSEA approval no. 1277/PO/RcBt/S/09/CPCSEA/TRS/ PT/023/000). Full-thickness skin was excised, defatted, equilibrated in PBS, and mounted on a Franz diffusion cell with the stratum corneum facing the donor compartment. One gram of proniosomal gel was applied, and sink conditions were maintained for 24 h with hourly PBS replacement. Samples were analyzed by HPLC. Minimal drug levels in the receptor medium indicated low transdermal permeation, while significant drug deposition in the stratum corneum and viable epidermis/dermis confirmed enhanced skin retention of Anthralin and Aloe emodin from ANPG7 and AEPG7.

Drug retention study

For permeation analysis, three 1 cm² skin samples were cryosectioned (LEICA CM1100) into stratum corneum, epidermis, and dermis. The sections were extracted overnight in methanol (ANPG7), followed by centrifugation. Drug content in the supernatant was quantified spectrophotometrically and plotted as drug concentration (µg/cm²) across the different skin layers.

Haemotoxicity study

Ex vivo skin retention studies showed higher drug accumulation in proniosomal gels in the vascularized skin layer, suggesting potential systemic exposure. Therefore, hemocompatibility was evaluated. In-vitro hemolysis results confirmed that ANPG7 was safe, with hemolysis below 5% after encapsulation, meeting the ISO/TR 7406 safety limit for biomaterials and indicating no risk of hemolysis or coagulation.

Cytotoxicity study on L929 and HaCaT cell lines

The MTT assay evaluated cytocompatibility of free Anthralin, free Aloe emodin, plain proniosomal gel, ANPG7 (0.1–100 µg/mL) on L929 and HaCaT cell lines. Plain proniosomal gel and free Anthralin showed minimal toxicity toward normal L929 cells, while drug encapsulation in proniosomal gels further improved cell viability. In contrast, higher cytotoxicity was observed in rapidly proliferating HaCaT cells, which increased after encapsulation, indicating enhanced selective activity of the proniosomal formulations.

Effect of ANPG7 on body weight and Spleen weight in IMQ induced psoriasis in mice

Topical ANPG7 treatment in IMQ-induced psoriatic mice produced a significant increase in body weight and Spleen weight compared with the psoriatic control group. Variations in body weight and Spleen weight were also observed in the normal saline group.

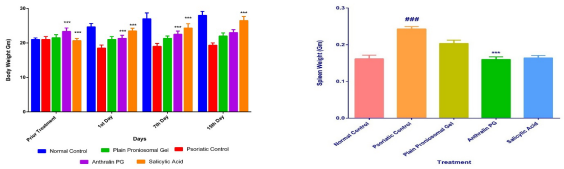
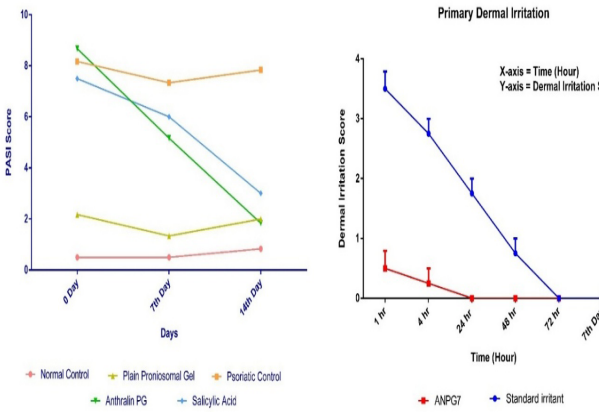


Figure 3: Effect of Anthralin on Body Weight and Spleen Weight

Effect of ANPG7 on PASI score in IMQ induced psoriasis in mice

The PASI score significantly increases ($p < 0.0001$) in IMQ -induced psoriatic animals. Following therapy with Anthralin proniosomal gel, PASI score was significantly decreased in ANPG7 treated group in comparison to psoriatic mice. The groups that received ordinary saline had a null PASI score.



Effect of ANPG7 on primary dermal irritation in rabbit

From day 1 to day 7, a skin irritation score was assessed in each of the animal groups. We observed that the psoriasis control group had a significantly greater skin irritation score. However, from day 1 to day 7, the animals treated with ANPG7 exhibited a significant decrease in their skin irritation score.

Histopathology

Psoriatic control mice exhibited severe epidermal abnormalities, including edema and inflammatory cell infiltration, while ANPG7 treatment restored near-normal skin structure with reduced inflammation. In spleen histology, normal mice showed clear red pulp, white pulp, marginal zone, and hematopoietic tissue, whereas these features were disrupted in the disease control group. ANPG7 markedly improved splenic architecture, re-establishing clear regional differentiation. (A: Normal control; B: Psoriatic control; C: Plain proniosomal gel; D: ANPG7; E: Salicylic acid)

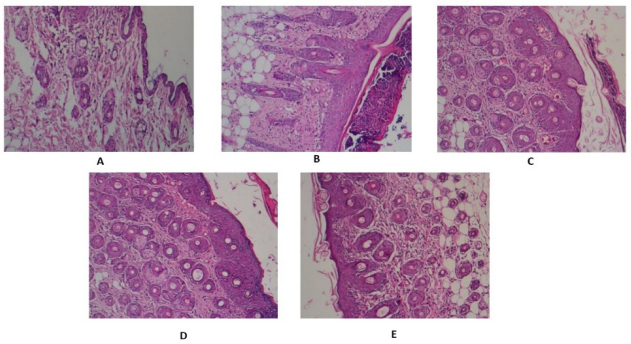


Figure 5: Histopathology of Skin treated with ANPG7

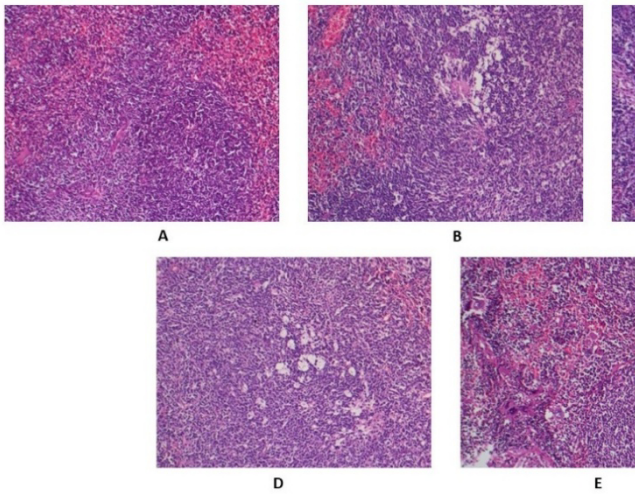


Figure 6 Histology of Spleen treated with ANPG7

The study developed an anthralin-loaded proniosomal gel (ANPG) as an improved topical system for psoriasis treatment[11]. Anthralin's clinical limitations—instability, irritation, and staining—were addressed through proniosomal encapsulation, which enhanced stability, skin targeting, and sustained drug release[24]. The formulations showed appropriate pH, viscosity, spreadability, and appearance for topical use, with high drug entrapment, particularly in ANPG7 (86.58%), indicating efficient incorporation within stable vesicular bilayers[25, 26]. The optimized system exhibited a uniform nanosized vesicle population (~239 nm) with low polydispersity and a negative zeta potential, suggesting good physical stability and reduced aggregation[27, 28]. Rapid niosome formation upon hydration confirmed the practicality of proniosomes for consistent topical delivery[6].

Drug diffusion studies demonstrated prolonged release, while ex-vivo permeation results showed limited systemic passage

but strong drug deposition within skin layers, supporting localized therapy and reduced adverse effects[29]. Safety assessments indicated excellent hemocompatibility and minimal toxicity to normal fibroblasts, alongside higher activity against proliferating keratinocytes, reflecting therapeutic selectivity[30]. In vivo testing in an imiquimod-induced psoriasis model revealed marked improvement in PASI score, organ weight normalization, reduced irritation, and restoration of skin and spleen histology[31]. In Conclusion, ANPG7 demonstrated favorable physicochemical properties, controlled release, strong skin retention, safety, and significant anti-psoriatic efficacy, supporting its promise as a patient-friendly topical therapy with potential for further clinical evaluation.

Conflict of interest statement

The authors have no conflict of interest.

References

(1) Orzan, O. A.; Tutunaru, C. V.; Ianoși, S. L. Understanding the Intricate Pathophysiology of Psoriasis and Related Skin Disorders. *Int J Mol Sci* **2025**, *26* (2). DOI: 10.3390/ijms26020749 From NLM.

(2) Aravinda Kumar, B. Dermatological pharmacology. In *Introduction to Basics of Pharmacology and Toxicology: Volume 2: Essentials of Systemic Pharmacology: From Principles to Practice*, Springer, 2021; pp 1129-1148.

(3) Ali Muhammad, H. H.; Elsayed, M. M.; Elghareeb, M. I. Brief Overview About Topical Treatment Of Psoriasis And Seborrehic Dermatitis. *Journal of Pharmaceutical Negative Results* **2022**, *13*.

(4) Elkordy, A. A.; Hill, D.; Attia, M.; Chaw, C. S. Liposomes and Their Therapeutic Applications in Enhancing Psoriasis and Breast Cancer Treatments. *Nanomaterials (Basel)* **2024**, *14* (21). DOI: 10.3390/nano14211760 From NLM.

(5) Stefanov, S. R.; Andonova, V. Y. Lipid Nanoparticulate Drug Delivery Systems: Recent Advances in the Treatment of Skin Disorders. *Pharmaceuticals (Basel)* **2021**, *14* (11). DOI: 10.3390/ph14111083 From NLM.

(6) Khatoon, M.; Shah, K. U.; Din, F. U.; Shah, S. U.; Rehman, A. U.; Dilawar, N.; Khan, A. N. Proniosomes derived niosomes: recent advancements in drug delivery and targeting. *Drug delivery* **2017**, *24* (2), 56-69.

(7) Govindarajan, S.; Swamivelmanickam, M.; Nair, S.; Sivagnanam, S. A Comprehensive Study on Provesicular Drug Delivery System: Proniosomal Gel. *Indian Journal of Pharmaceutical Sciences* **2022**, *84* (1).

(8) Baig, R. P.; Wais, M. Formulation and development of proniosomal gel for topical delivery of Amphotericin B. *Int J Pharm Pharm Sci* **2022**, *14*, 37-49.

(9) Bautista-Solano, A. A.; Dávila-Ortiz, G.; Perea-Flores, M. d. J.; Martínez-Ayala, A. L. A comprehensive review of niosomes: composition, structure, formation, characterization, and applications in bioactive molecule delivery systems. *Molecules* **2025**, *30* (17), 3467.

(10) R. Khan, N.; S. Harun, M.; Nawaz, A.; Harjoh, N.; W. Wong, T. Nanocarriers and their actions to improve skin permeability and transdermal drug delivery. *Current Pharmaceutical Design* **2015**, *21* (20), 2848-2866.

(11) Fathalla, D.; Youssef, E. M.; Soliman, G. M. Liposomal and ethosomal gels for the topical delivery of anthralin: preparation, comparative evaluation and clinical assessment in psoriatic patients. *Pharmaceutics* **2020**, *12* (5), 446.

(12) Darson, J.; Thirunellai Seshadri, R.; Katariya, K.; Mohan, M.; Srinivas Kamath, M.; Etyala, M. A.; Chandrasekaran, G. Design development and optimisation of multifunctional Doxorubicin-loaded Indocynanine Green proniosomal gel derived niosomes for tumour management. *Scientific Reports* **2023**, *13* (1), 1697.

(13) Shah, H.; Nair, A. B.; Shah, J.; Bharadia, P.; Al-Dhubiab, B. E. Proniosomal gel for transdermal delivery of lornoxicam: Optimization using factorial design and in vivo evaluation in rats. *DARU Journal of Pharmaceutical Sciences* **2019**, *27* (1), 59-70.

(14) Gandhi, K.; Maganti, R. S.; Kaur, H.; Vinod, K.; Verma, P. Formulation and evaluation of sol-gel drug delivery system for Intracanal pH sensitive controlled delivery of chlorhexidine. *Journal of clinical and diagnostic research: JCDR* **2017**, *11* (4), ZC68.

(15) Shehata, T. M.; Ibrahim, M. M.; Elsewedy, H. S. Curcumin niosomes prepared from proniosomal gels: In vitro skin permeability, kinetic and in vivo studies. *Polymers* **2021**, *13* (5), 791.

(16) Ugochukwu, A. E.; Nnedimkpa, O. J.; Rita, N. O. Preparation and characterization of Tolterodine tartrate proniosomes. *Universal Journal of Pharmaceutical Research* **2017**.

(17) Abdelbary, G. A.; Amin, M. M.; Zakaria, M. Y. Ocular ketoconazole-loaded proniosomal gels: formulation, ex vivo corneal permeation and in vivo studies. *Drug delivery* **2017**, *24* (1), 309-319.

(18) Fathalla, D.; Youssef, E. M. K.; Soliman, G. M. Liposomal and Ethosomal Gels for the Topical Delivery of Anthralin: Preparation, Comparative Evaluation and Clinical Assessment in Psoriatic Patients. *Pharmaceutics* **2020**, *12* (5). DOI: 10.3390/pharmaceutics12050446 From NLM.

(19) Fareed, N. Y.; Kassab, H. J. Effect of formulation variables on the properties of a new vesicular system of an anthraquinone derivative. *Journal of Advanced Pharmacy Education & Research| Oct–Dec* **2023**, *13* (4).

(20) Lather, V.; Sharma, D.; Pandita, D. Proniosomal gel-mediated transdermal delivery of bromocriptine: in vitro and

ex vivo evaluation. *Journal of Experimental Nanoscience* **2016**, *11* (13), 1044-1057.
(21) Farooqui, N. A.; Kar, M.; Singh, R. P.; Jain, S. Development of Proniosomal Gel: in-vitro, ex-vivo and in-vivo Characterization. *Indian Journal of Pharmaceutical Education and Research* **2017**, *51* (4), 758-764.
(22) Gilani, S. J.; Moglad, E.; Afzal, M.; Rafeeq, M.; Habib, A. H.; Alzarea, S. I.; Sayyed, N.; Kazmi, I. Exploring the Aloenin-Loaded Nanogel's Therapeutic Potential for IMQ-Induced Psoriasis-Like Skin Conditions: In-vitro and In-vivo Assessment. *The Journal of Pharmacology and Experimental Therapeutics* **2025**, 103647.
(23) Sakarkar, S.; Jagdale, S.; Dargude, S.; Chabukswar, A.; Urooj, S.; Bilal, A.; Mengash, H. A. Optimization of Anthralin Microemulgel Targeted Delivery for Psoriasis and Acne. *Molecules* **2025**, *30* (12), 2629.
(24) Kumar, P.; Savita, K. K.; Dubey, A.; Gaur, S. S. Unlocking Dithranol's Potential: Advanced Drug Delivery Systems for Improved Pharmacokinetics. *International Journal of Drug Delivery Technology* **2024**, *14* (2), 1174-1180.
(25) Abdallah, M. H.; Shahien, M. M.; El-Horany, H. E.-S.; Ahmed, E. H. Modified Phospholipid Vesicular Gel for Transdermal Drug Delivery: The Influence of Glycerin and/or Ethanol on Their Lipid Bilayer Fluidity and Penetration Characteristics. *Gels* **2025**, *11* (5), 358.
(26) Witika, B. A.; Mweetwa, L. L.; Tshiamo, K. O.; Edler, K.; Matafwali, S. K.; Ntemi, P. V.; Chikukwa, M. T.; Makoni, P. A. Vesicular drug delivery for the treatment of topical disorders: Current and future perspectives. *Journal of Pharmacy and Pharmacology* **2021**, *73* (11), 1427-1441.
(27) Midekessa, G.; Godakumara, K.; Ord, J.; Viil, J.; Lattekivi, F.; Dissanayake, K.; Kopanchuk, S.; Rinken, A.; Andronowska, A.; Bhattacharjee, S. Zeta potential of extracellular vesicles: toward understanding the attributes that determine colloidal stability. *ACS omega* **2020**, *5* (27), 16701-16710.
(28) Imam, S. S.; Alshehri, S.; Altamimi, M. A.; Hussain, A.; Alyahya, K. H.; Mahdi, W. A.; Qamar, W. Formulation and evaluation of luteolin-loaded nanovesicles: In vitro physicochemical characterization and viability assessment. *ACS omega* **2021**, *7* (1), 1048-1056.
(29) Steyn, J. D.; Haasbroek-Pheiffer, A.; Pheiffer, W.; Weyers, M.; van Niekerk, S. E.; Hamman, J. H.; van Staden, D. Evaluation of Drug Permeation Enhancement by Using In Vitro and Ex Vivo Models. *Pharmaceuticals* **2025**, *18* (2), 195.
(30) Zhu, Y.; Zhou, Y.; Ma, X.; Duan, Z.; Xu, H.; Li, Y.; Kong, Y.; Yang, L.; Xin, X. Topical therapy in psoriasis: clinical benefits, advances in novel drug delivery strategies, and gene therapy regimen. *Pharmaceutics* **2025**, *17* (3), 283.
(31) Jabeen, M.; Boisgard, A.-S.; Danoy, A.; El Kholti, N.; Salvi, J.-P.; Boulieu, R.; Fromy, B.; Verrier, B.; Lamrayah, M. Advanced characterization of imiquimod-induced psoriasis-like mouse model. *Pharmaceutics* **2020**, *12* (9), 789.