

Formulation Development and Characterization of Aloe emodin Proniosomal Gel for Topical Treatment of Psoriasis

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ABSTRACT

Psoriasis is a chronic immune-mediated inflammatory skin disorder characterized by excessive keratinocyte proliferation and immune dysregulation, requiring effective localized therapy with minimal systemic exposure. Although Aloe emodin shows promising antipsoriatic potential, its clinical utility is limited by poor stability, oxidation sensitivity, skin irritation, and reduced patient compliance. This study aimed to develop a novel Aloe emodin-loaded proniosomal gel to improve stability, enhance targeted skin delivery, and achieve controlled topical release. The proniosomal gel formulation was prepared by the coacervation phase separation method using non-ionic surfactants (Tween 80 and Span 60), cholesterol, and lecithin, and incorporated into a Carbopol gel base. Comprehensive evaluation included physicochemical characterization, vesicle analysis, in vitro drug release, ex vivo permeation, cytocompatibility, hemocompatibility, and in vivo antipsoriatic assessment. The optimized formulation (AEPG7) demonstrated high drug entrapment efficiency (83.93%), appropriate viscosity, skin-compatible pH, and good spreadability. Vesicle size (~540 nm), low polydispersity index, and negative zeta potential confirmed a stable and uniform vesicular system. Sustained drug release was observed for 24 hours. Ex vivo studies revealed minimal systemic permeation with enhanced drug retention in epidermal and dermal layers, supporting localized therapy. Safety studies showed negligible hemolysis and good compatibility with normal L929 fibroblasts, along with increased cytotoxicity toward hyperproliferative HaCaT keratinocytes. In the imiquimod-induced psoriasis model, AEPG7 significantly reduced PASI scores, decreased dermal inflammation, and restored normal skin and spleen histology. Overall, the developed proniosomal gel represents a stable, safe, and effective topical delivery system with strong potential for psoriasis management.

Keywords: Aloe emodin, 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 disorder characterized by excessive keratinocyte proliferation and dysregulated immune responses, leading to the formation of erythematous, scaly plaques¹. It affects nearly 2–3% of the global population and significantly impairs patients' quality of life². Conventional topical treatments, including corticosteroids, vitamin D analogues, and keratolytic agents, primarily offer symptomatic relief but are often associated with adverse effects such as skin atrophy, irritation, and tachyphylaxis during long-term use³⁻⁵.

Aloe emodin is a naturally occurring anthraquinone derivative predominantly isolated from species of *Aloe*, *Rheum*, and *Cassia*^{6,7}. It has gained considerable attention in dermatological research due to its potent anti-inflammatory, antiproliferative, antioxidant, and

immunomodulatory properties⁸. In the context of psoriasis, Aloe emodin exhibits significant therapeutic potential by targeting key pathological mechanisms underlying the disease^{8,9}.

Proniosomal gels have gained attention as effective carriers for topical drug delivery^{10,11}. These proniosomal gel formulations transform into niosomal vesicles upon hydration and are composed of non-ionic surfactants, cholesterol, and phospholipids¹². They enhance drug stability, enable controlled and sustained release, improve skin permeation, and reduce irritation while offering superior spreadability and prolonged skin residence time^{13,14}. Encapsulation of Aloe emodin within a proniosomal gel protects it from degradation, facilitates controlled epidermal targeting, enhances permeation through stratum corneum lipid fluidization, and minimizes irritation and staining issues¹⁵. Therefore, Aloe emodin-loaded

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proniosomal gels present a promising approach for safer, more effective topical management of psoriasis.

MATERIALS AND METHODS

Aloe emodin 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 AEPG

Aloe emodin proniosomal gel (AEPG) was formulated using the coacervation phase separation method. Aloe emodin 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 gel¹⁶.

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 dispersion¹⁶⁻¹⁸.

Entrapment efficiency

Entrapment efficiency was determined by dispersing 1 g of proniosomal gel in deionized water and gently heating it to form niosomes¹⁶. 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 untrapped drug was quantified using a UV spectrophotometer⁸. Entrapment efficiency (EE%) was calculated using the following equation:

$$\text{Entrapment efficiency (\%)} = \frac{(t - f)}{t} \times 100$$

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 (AEPG 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 Aloe emodin and 220 nm for Aloe emodin against a suitable blank. Drug content was calculated from the respective calibration curves^{16, 19}.

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 viscosity¹⁶.

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 recorded¹⁶.

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 application¹⁶.

Rate of spontaneity

Approximately 20 mg of proniosomal gel was uniformly spread on the inner wall of a clean glass container. Two milliliters of saline were carefully added along the wall without disturbing the film, and the system was left undisturbed for 20 minutes to allow hydration and vesicle formation. The resulting niosomes were counted using a Neubauer chamber to evaluate the spontaneity of vesicle formation¹⁸.

In-vitro drug release study

In vitro drug release was assessed using Franz diffusion cells consisting of 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 placed between the compartments. The system was maintained at 37 ± 1 °C with continuous stirring at 100 rpm. One gram of proniosomal gel was applied to the donor compartment. Samples were withdrawn hourly for 24 h, replaced with fresh buffer to maintain sink conditions, and analyzed by UV spectrophotometry to determine cumulative drug release¹⁸.

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). Measurements were performed in triplicate at 25 °C with a 173° detection angle, and mean values were recorded to assess vesicle surface charge and physical stability²⁰.

Determination of vesicle size

Vesicle size and distribution were determined using a Litesizer 500 by photon correlation spectroscopy. A 633 nm He–Ne laser detected light scattering resulting from Brownian motion to measure mean particle size and polydispersity index (PDI). Analyses were performed in triplicate at 25 °C with a 173° detection angle, and vesicle sizes were observed within the range of 10–1000 nm²¹.

Vesicular shape and surface morphology

Scanning electron microscopy (SEM) was employed to evaluate the surface morphology of niosomes, including empty vesicles. A drop of niosomal dispersion was placed on a glass stub, air-dried, and sputter-coated with gold–palladium (Au/Pd) using a vacuum evaporator (Edwards). The samples were then examined under a JSM-5510 scanning electron microscope²¹.

Ex-vivo skin permeation study

Ex vivo permeation of the optimized proniosomal gel was conducted 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, and full-thickness abdominal skin was excised after hair removal and defatting. The skin was inspected, equilibrated in PBS for 10 minutes, and mounted on a Franz diffusion cell with the stratum corneum facing the donor compartment. One gram of gel was applied, and the receptor chamber containing PBS (pH 7.4) was maintained at 37 ± 1 °C with continuous stirring. Samples were withdrawn hourly and replaced with fresh buffer to maintain sink conditions. Drug permeation was quantified using UV spectrophotometry²².

Study of drug retention

After completion of the permeation study, skin samples (~1 cm²) were collected in triplicate and sectioned into stratum corneum, epidermis, and dermis using a cryotome (LEICA CM 1100). Sections were mounted on cork discs with tissue-freezing medium and sliced into thin layers. Each layer was extracted overnight in methanol, followed by centrifugation. The supernatant was analyzed spectrophotometrically to determine drug retention, and concentrations (µg/cm²) were plotted to compare retention across skin layers^{23, 24}.

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^{22, 25}.

An aliquot of 100 µL plasma was diluted with 1 mL of 0.01% Na₂CO₃, and optical density was recorded at 380, 415, and 450 nm using a microplate reader. Plasma hemoglobin concentration was calculated using the following equation :

$$\text{Plasma hemoglobin} = \{(2 \times A_{415}) - (A_{380} + A_{450})\} - 76.25$$

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 Aloe emodin and Aloe emodin proniosomal gel (AEPG) was evaluated 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% CO₂, trypsinized, and seeded in 96-well plates (~1 × 10⁴ cells/well). After reaching ~90% confluence, cells were treated with serial concentrations (0.1–100 µg/mL) of free

Aloe emodin, AEPG, and plain gel for 24 h. The medium was then replaced with MTT solution and incubated for 4 h to allow formazan formation. The crystals were dissolved in solubilization buffer, and absorbance was measured at 570 nm using an ELISA reader. Cell viability was calculated relative to untreated control cells²⁶.

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 activity of AEPG was evaluated in an imiquimod-induced psoriasis model using nulliparous Swiss albino mice (n = 6). The dorsal skin was shaved, and animals were divided into five groups: normal control, psoriatic control, plain proniosomal gel (PPG), AEPG, and a salicylic acid-treated standard group. Topical treatments were given from day 1 to day 15. Disease progression was assessed using PASI scoring (0–4 scale). At study completion, animals were sacrificed, and samples were collected for biochemical, pro-inflammatory cytokine, and histopathological evaluations²⁷.

Primary dermal skin irritation study

Skin irritation was evaluated in New Zealand white rabbits divided into five groups. Dorsal hair was removed using a depilatory cream. The left shaved area was treated with AEPG and 0.8% v/v formalin (irritant control), while the right side remained untreated as control. Erythema and edema were assessed at 30 minutes, 1 hour, and 4 hours after application²⁸.

Histology

At the end of the study, animals were euthanized and dorsal skin samples were collected for histological evaluation. Tissues were fixed in 10% neutral buffered formalin, dehydrated in graded ethanol, embedded in paraffin, and sectioned (~5 µm) using a rotary microtome. The sections were stained with hematoxylin and eosin and examined under a light microscope²⁹.

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
AEPG 1	Light-brownish gel	71.73±1.06	6735±6.56	6.9±0.97	39±0.57	07±0.43
AEPG 2	Light-brownish gel	60.12±0.49	7337±4.87	6.4±0.60	41±0.23	08±1.03

AEPG 3	Light-brownish gel	63.34±0.65	7690±3.43	6.6±0.81	42 ±0.90	09±2.12
AEPG 4	Creamy whitish gel	52.08±0.61	6718±5.43	5.9±1.25	39 ±0.94	06±1.16
AEPG 5	Creamy whitish gel	75.81±1.14	8173±2.65	5.8±0.19	46±0.73	11±1.74
AEPG6	Light-brownish gel	68.17±1.74	6925±5.98	6.3±0.55	37±0.96	07±1.08
AEPG7	Creamy whitish gel	83.93±1.51	8393±2.87	6.9±0.43	42±1.21	10±1.87
AEPG8	Creamy gel	74.18±0.73	6641±3.72	5.5±1.13	39±1.09	08±0.76
AEPG9	Creamy gel	76.03±0.79	7824±5.44	5.9±1.05	40±1.77	08±1.69

Proniosomal gels were visually examined for appearance and uniformity. The formulations exhibited a white to light brown color with a smooth, semi-solid, cream-like consistency.

Entrapment efficiency

Drug entrapment efficiency is a critical parameter in optimizing formulation performance, as higher vesicular entrapment enhances drug availability at the application site. The entrapment efficiency of AEPG formulations ranged from $52.08 \pm 0.61\%$ to $83.93 \pm 1.51\%$, indicating moderate to high drug incorporation.

Viscosity

The viscosity of the formulated proniosomal gels was measured using a Fungilab viscometer with a T-shaped spindle. All formulations exhibited suitable consistency, with the highest viscosity observed for AEPG7 (8393 ± 2.87 cps).

pH measurement

Skin compatibility is a key requirement for effective topical and transdermal formulations. The pH of all AEPG batches was found to be in the range of 5.5 ± 1.13 to 6.9 ± 0.97 ,

indicating suitability and compatibility with skin. The pH determination findings are shown in Table 1.

Spreadability

The diameter of the gel after spreading for the specified time was measured and recorded. The spreadability values ranged from 39 ± 0.57 to 46 ± 0.73 mm for AEPG formulations.

Rate of spontaneity

The spontaneity rate, measured as the number of niosomes formed within 15 minutes of proniosomal gel hydration, ranged from 7 ± 0.43 to 11 ± 1.74 for AEPG, indicating rapid and efficient niosome formation.

In-vitro drug release studies

In vitro diffusion was carried out using a Franz diffusion cell fitted with a dialysis membrane pre-soaked in phosphate buffer (pH 7.4) for 24 h. The receptor compartment contained 20 mL of phosphate buffer, maintained at 37 ± 1 °C and stirred at 100 rpm. One gram of proniosomal gel was applied to the donor chamber, and sink conditions were ensured by hourly replacement with fresh buffer over 24 h. Collected samples were analyzed by UV Spectroscopy.

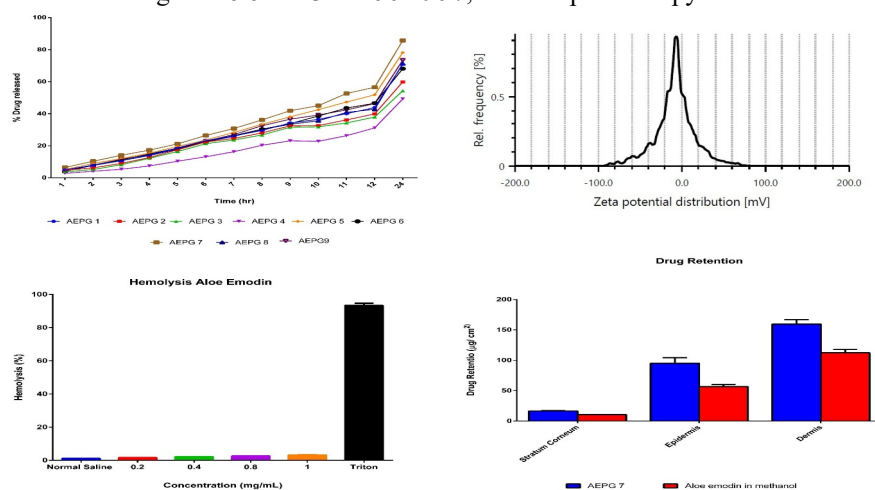


Figure 1 Evaluation of Proniosomal Gel A. % Drug Release B. Zeta Potential C. Hemolysis D. Drug Retention

Vesicle size and zeta potential

The optimized formulation, AEPG7, was characterized for vesicle size and zeta potential. Dynamic light scattering revealed an average vesicle size of 539.8 nm with a polydispersity index of 0.291, indicating a uniform and narrow size distribution. The zeta potential was -8.5 mV, suggesting sufficient electrostatic stability of the niosomal system.

Ex-vivo skin permeation studies

Ex vivo permeation of the optimized proniosomal gel was performed 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 gel was applied, and sink conditions were maintained for 24 h with hourly PBS replacement. Samples were analyzed by UV Spectroscopy. Minimal drug levels in the receptor medium indicated low transdermal permeation, whereas significant drug deposition in the stratum corneum and viable epidermis/dermis confirmed enhanced skin retention of Aloe emodin from AEPG7.

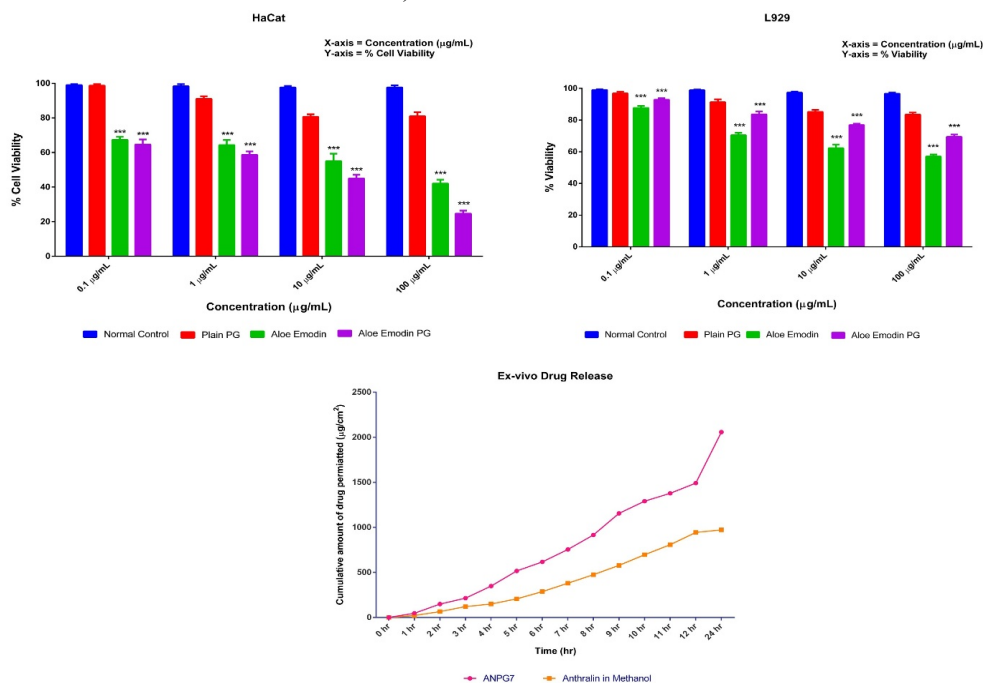


Figure 2: MTT Assay and Ex vivo Drug Release

Drug retention study

For permeation analysis, three 1 cm² skin samples were cryosectioned (LEICA CM1100) into stratum corneum, epidermis, and dermis. Each layer was extracted overnight in methanol (AEPG7) and centrifuged. The drug content in the supernatant was measured spectrophotometrically and expressed as drug concentration (µg/cm²) across the respective skin layers. The results presented retention higher concentration of Aloe emodin in epidermis and dermis.

Haemotoxicity study

Ex vivo skin retention studies demonstrated greater drug accumulation from the proniosomal gel within the vascularized skin layer, indicating possible systemic exposure; therefore, hemocompatibility was assessed. In vitro hemolysis testing showed that AEPG7 was safe, with hemolysis below 5% after encapsulation, complying with the ISO/TR 7406 safety threshold for biomaterials and confirming no risk of hemolysis or coagulation.

Cytotoxicity study on L929 and HaCaT cell lines

The MTT assay assessed the cytocompatibility of free Aloe emodin, plain proniosomal gel, and AEPG7 (0.1–100 µg/mL) on L929 and HaCaT cell lines. Plain gel and free Aloe emodin showed minimal toxicity toward normal L929 cells, while encapsulation further enhanced cell viability. In contrast, greater cytotoxicity was observed in proliferating HaCaT cells, which increased after encapsulation, indicating improved selective activity of the proniosomal formulation.

Effect of AEPG7 on body weight and Spleen weight in IMQ induced psoriasis in mice

Topical treatment with AEPG7 in IMQ-induced psoriatic mice resulted in a significant improvement in body weight and normalization of spleen weight compared with the psoriatic control group. The normal saline group also showed variations in body and spleen weights during the study period.

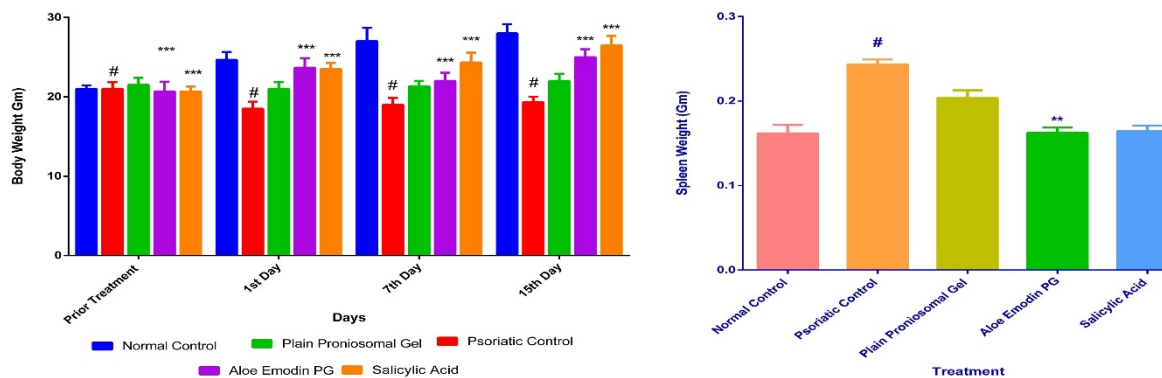


Figure 3: Effect of Aloe emodin on Body Weight and Spleen Weight

Effect of AEPG7 on PASI score in IMQ induced psoriasis in mice

The PASI score increased significantly ($p < 0.0001$) in IMQ-induced psoriatic animals. Treatment with Aloe

emodin proniosomal gel (AEPG7) markedly reduced the PASI score compared to the psoriatic control group, while the normal saline group maintained a zero PASI score throughout the study.

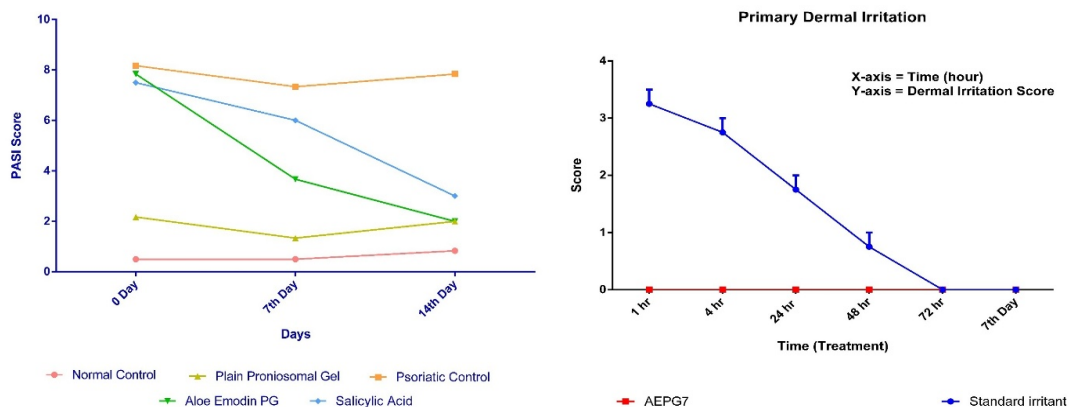


Figure 1 Effect of AEPG7 on PASI score in IMQ induced psoriasis in mice

Effect of AEPG7 on primary dermal irritation in rabbit

Skin irritation was evaluated from day 1 to day 7 in all groups. The psoriasis control group showed significantly higher irritation scores, whereas AEPG7-treated animals demonstrated a marked reduction in skin irritation over the study period.

Histopathology

Psoriatic control mice showed marked epidermal damage with edema and inflammatory infiltration, whereas AEPG7 treatment restored near-normal skin architecture and reduced inflammation. In spleen histology, normal mice displayed well-defined red pulp, white pulp, marginal zone, and hematopoietic tissue, which were disrupted in the disease control group. Treatment with AEPG7 significantly improved splenic structure and regional differentiation. (A: Normal control; B: Psoriatic control; C: Plain proniosomal gel; D: AEPG7; E: Salicylic acid)

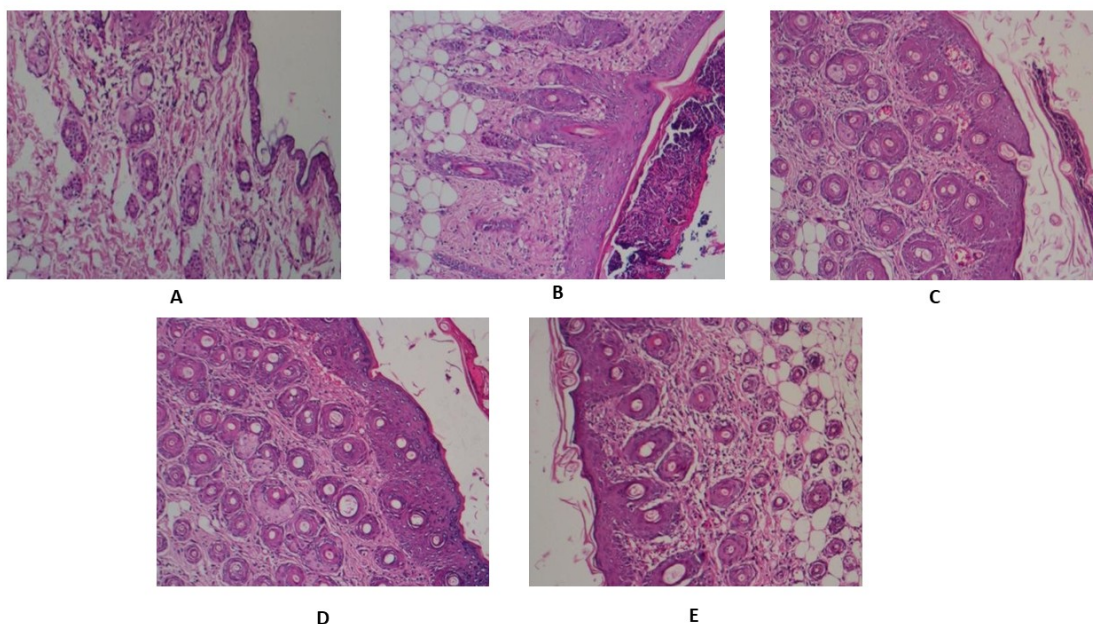


Figure 5: Histopathology of Skin treated with AEPG7

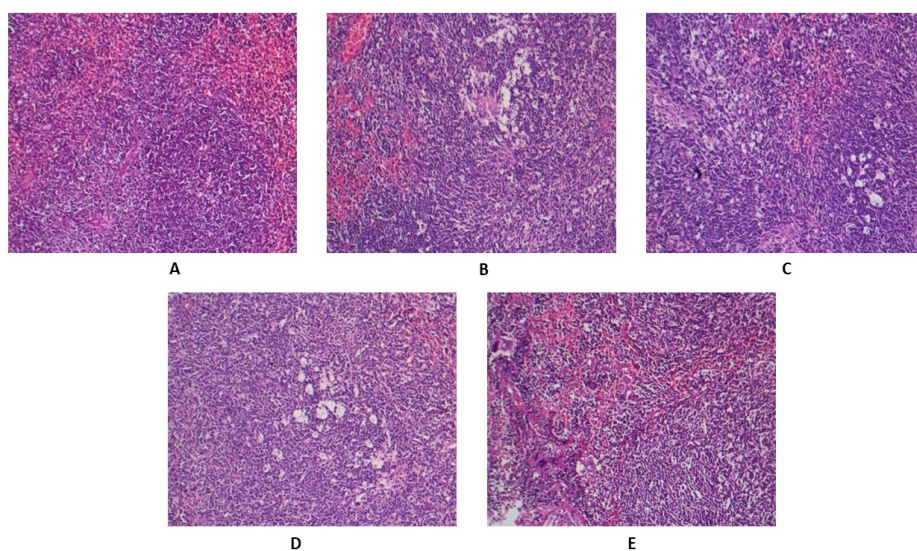


Figure 6 Histology of Spleen treated with AEPG7

The study developed an Aloe emodin-loaded proniosomal gel (AEPG) as an enhanced topical delivery system for psoriasis management³⁰. The clinical drawbacks of Aloe emodin—such as instability, irritation, and staining—were overcome through proniosomal encapsulation, which improved drug stability, targeted skin delivery, and provided sustained release⁸. The prepared formulations exhibited suitable pH, viscosity, spreadability, and appearance for topical application, along with high drug entrapment efficiency, particularly in AEPG7 (83.93%), indicating effective incorporation within stable vesicular bilayers³¹. The optimized formulation displayed uniformly distributed nanosized vesicles (~540 nm) with a low polydispersity index and a negative zeta potential, suggesting good physical stability and minimal

aggregation³². Immediate niosome formation upon hydration confirmed the practicality and consistency of the proniosomal system for topical delivery^{25, 33}. In vitro diffusion studies revealed prolonged drug release, while ex vivo permeation studies demonstrated limited systemic permeation with significant skin deposition, supporting localized therapy and minimized side effects^{34, 35}.

Safety evaluation showed excellent hemocompatibility and low cytotoxicity toward normal fibroblasts, along with enhanced activity against hyperproliferative keratinocytes, indicating therapeutic selectivity³⁶. In vivo evaluation using an imiquimod-induced psoriasis model demonstrated significant improvement in PASI scores, normalization of organ weights, reduced skin irritation, and restoration of normal skin and spleen histology³⁷. In conclusion, AEPG7

exhibited desirable physicochemical characteristics, controlled release behavior, strong skin retention, safety, and pronounced anti-psoriatic efficacy, highlighting its potential as a patient-friendly topical formulation suitable for further clinical investigation.

Conflict of interest statement

The authors have no conflict of interest.

REFERENCE

- (1) Orzan, O. A.; Tutunaru, C. V.; Ianoși, S. L. Understanding the intricate pathophysiology of psoriasis and related skin disorders. *International Journal of Molecular Sciences* **2025**, *26* (2), 749.
- (2) Ponikowska, M.; Vellone, E.; Czapla, M.; Uchmanowicz, I. Challenges Psoriasis and Its Impact on Quality of Life: Challenges in Treatment and Management. *Psoriasis (Auckl)* **2025**, *15*, 175-183. DOI: 10.2147/ptt.S519420 From NLM.
- (3) Caputo, V.; Strafella, C.; Cosio, T.; Lanna, C.; Campione, E.; Novelli, G.; Giardina, E.; Cascella, R. Pharmacogenomics: An Update on Biologics and Small-Molecule Drugs in the Treatment of Psoriasis. *Genes (Basel)* **2021**, *12* (9). DOI: 10.3390/genes12091398 From NLM.
- (4) Abuarij, M.; Alyahawi, A.; Alkaf, A. The current trends of psoriasis treatment in dermatological practice. *Universal Journal of Pharmaceutical Research* **2024**.
- (5) Bakshi, H.; Nagpal, M.; Singh, M.; Dhingra, G. A.; Aggarwal, G. Treatment of psoriasis: a comprehensive review of entire therapies. *Current drug safety* **2020**, *15* (2), 82-104.
- (6) Malmir, M.; Serrano, R.; Silva, O. Anthraquinones as potential antimicrobial agents-A review. *Antimicrobial Research: Novel Bioknowledge and Educational Programs; Mendez-Vilas, A., Ed* **2017**, 55-61.
- (7) Merino, J. J.; Durán, A. G.; Chinchilla, N.; Macías, F. A. Biological activities of hydroxyanthracene derivatives (HADs) from Aloe species and their potential uses. *Phytochemistry Reviews* **2025**, *24* (3), 2387-2415.
- (8) Luo, H.; Ji, X.; Zhang, M.; Ren, Y.; Tan, R.; Jiang, H.; Wu, X. Aloe-emodin: progress in pharmacological activity, safety, and pharmaceutical formulation applications. *Mini Reviews in Medicinal Chemistry* **2024**, *24* (19), 1784-1798.
- (9) Xie, J.; Zhang, J.; Chen, X. Aloe-emodin: from pharmacological mechanisms to clinical applications and future perspectives. *Frontiers in Pharmacology* **2025**, *16*, 1741679.
- (10) 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).
- (11) Rehman, K.; Zulfakar, M. H. Recent advances in gel technologies for topical and transdermal drug delivery. *Drug development and industrial pharmacy* **2014**, *40* (4), 433-440.
- (12) Patel, P.; Parashar, A. K.; Kaurav, M.; Yadav, K.; Singh, D.; Gupta, G.; Kurmi, B. D. Niosome: a vesicular drug delivery tool. In *Nanoparticles and nanocarriers based pharmaceutical preparations*, Bentham Science Publishers, 2022; pp 333-364.
- (13) Liga, S.; Paul, C.; Moacă, E.-A.; Péter, F. Niosomes: Composition, formulation techniques, and recent progress as delivery systems in cancer therapy. *Pharmaceutics* **2024**, *16* (2), 223.
- (14) Alburyhi, M. M.; El-Shaibany, A.; Al-Wajih, A. M.; Alqadhi, A. A.; Almlhani, A. Advancements in Nano-Formulation Systems for Enhancing the Delivery of Herbal Ingredients. *European Journal of Pharmaceutical and Medical Research* **2025**, *12* (1), 212-231.
- (15) Abuelella, K. E.; Salem, A. Y. Advanced nanocarrier-based strategies for enhancing herbal actives in cosmetic and cosmeceutical applications. *Nanotechnology and Applied Sciences Journal* **2025**, *1* (2), 23-43.
- (16) Baig, R. P.; Wais, M. Formulation and development of proniosomal gel for topical delivery of Amphotericin B. *Int J Pharm Pharm Sci* **2022**, *14* (1), 37-49.
- (17) Gudigennavar, A. S.; Hiremath, J.; Desai, A. R.; Halakatti, P. K.; Vijapur, L.; Shidramshettar, S.; Bhattad, S.; Tegginamani, K. S. Development and evaluation of fenoprofen calcium loaded proniosomal gel for topical anti-inflammatory activity. *Asian Journal of Biology* **2025**, *21* (2), 35-58.
- (18) Barot, M.; Prajapati, A. P.; Vadgama, N.; Narkhede, S. B.; Luhar, S. Formulation Development and Evaluation of Proniosomal Gel containing Crisaborole. *Research Journal of Pharmacy and Technology* **2025**, *18* (5), 2261-2268.
- (19) Sakdiset, P.; See, G. L.; Sawatdee, S.; Yoon, A. S. Preparation and characterization of lidocaine HCl-loaded proniosome gels with skin penetration enhancers. *Journal of Drug Delivery Science and Technology* **2023**, *86*, 104639.
- (20) Mohamed, L. K.; Abdelmottaleb, M.; Geneidi, A. S. Formulation and Characterization of Proniosomal Gels loaded with Levofloxacin for dermal drug Delivery. *Archives of Pharmaceutical Sciences Ain Shams University* **2021**, *5* (2), 288-303.
- (21) Nimbawar, M.; Upadhye, K.; Dixit, G. Fabrication and evaluation of ritonavir proniosomal transdermal gel as a vesicular drug delivery system. *Pharmacophore* **2016**, *7* (2-2016), 82-95.
- (22) 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.
- (23) Gupta, A.; Prajapati, S. K.; Balamurugan, M.; Singh, M.; Bhatia, D. Design and development of a proniosomal transdermal drug delivery system for captopril. **2007**.
- (24) 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.
- (25) 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.

- (26) Chou, T.-H.; Liang, C.-H. The molecular effects of aloe-emodin (AE)/liposome-AE on human nonmelanoma skin cancer cells and skin permeation. *Chemical research in toxicology* **2009**, *22* (12), 2017-2028.
- (27) Badanthadka, M.; DSOUZA, L. Imiquimod-induced psoriasis mice model: a promising tool for psoriasis research? *Research Journal of Pharmacy and Technology* **2020**, *13* (7), 3508-3515.
- (28) Abu Bakar, N.; Othman, H.; Rajab, N.; Budin, S.; Shamsuddin, A.; Mohamed Nor, N. Primary skin irritation and dermal sensitization assay: In vivo evaluation of the essential oil from *Piper sarmentosum* Roxb. *Pharmacognosy Magazine* **2019**, *15* (64).
- (29) Mihiu, C.; Neag, M. A.; Bocşan, I. C.; Melincovici, C. S.; Vesa, Ş. C.; Ionescu, C.; Baican, A. L.; Lisencu, L.-A.; Buzoianu, A.-D. Novel concepts in psoriasis: histopathology and markers related to modern treatment approaches. *Romanian Journal of Morphology and Embryology* **2022**, *62* (4), 897.
- (30) Pandey, A.; Srivastava, N.; Dubey, R. C.; Dhaneshwar, S.; Shukla, A. K. Anti-psoriatic evaluation of aloe emodin-loaded topical hydrogel in an imiquimod-induced human plaque-type psoriasis in BALB/c mice. *Journal of Applied Pharmaceutical Science* **2024**, *14* (9), 279-291.
- (31) Wong, C. N.; Lee, S.-K.; Lim, Y. M.; Yang, S.-B.; Chew, Y.-L.; Chua, A.-L.; Liew, K. B. Recent advances in vitamin E TPGS-based organic nanocarriers for enhancing the oral bioavailability of active compounds: a systematic review. *Pharmaceutics* **2025**, *17* (4), 485.
- (32) 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.
- (33) Nemr, A. A.; El-Mahrouk, G. M.; Badie, H. A. Development and evaluation of proniosomes to enhance the transdermal delivery of cilostazole and to ensure the safety of its application. *Drug development and industrial pharmacy* **2021**, *47* (3), 403-415.
- (34) 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. *Pharmaceutics* **2025**, *18* (2), 195.
- (35) Ahmed, O. A.; Badr-Eldin, S. M. Development of an optimized avanafil-loaded invasomal transdermal film: Ex vivo skin permeation and in vivo evaluation. *International journal of pharmaceutics* **2019**, *570*, 118657.
- (36) Zhao, T.; Zhen, W.; Chen, X.; Zhang, J. Nanocosmeceuticals for Dermatological and Aesthetic Applications: Bridging Material Innovation with Clinical and Regulatory Translation. *ACS Nano Medicine* **2025**.
- (37) Jabeen, M.; Boisgard, A.-S.; Danoy, A.; El Kholti, N.; Salvi, J.-P.; Bouliou, R.; Fromy, B.; Verrier, B.; Lamrayah, M. Advanced characterization of imiquimod-induced psoriasis-like mouse model. *Pharmaceutics* **2020**, *12* (9), 789