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Original Article

Evaluation of a *Semecarpus anacardium*-Based Liposomal System for Psoriasis Treatment

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ABSTRACT

Background: Psoriasis is a chronic immune-mediated inflammatory skin disorder characterized by epidermal hyperproliferation, abnormal keratinocyte differentiation, and inflammatory cell infiltration. Conventional therapies are often associated with adverse effects and limited long-term efficacy, necessitating the development of safer and more effective therapeutic approaches. The present study aimed to develop and evaluate *Semecarpus anacardium*-loaded liposomes for anti-psoriatic activity using an *in vivo* model. **Objectives:** To assess the safety, therapeutic efficacy, and histopathological improvements following topical treatment with the developed formulation. **Materials and Methods:** *Semecarpus anacardium*-loaded liposomes were prepared using the thin-film hydration method with phospholipids and cholesterol. Acute dermal toxicity was evaluated according to OECD guideline 402. Psoriasis was induced in Swiss albino mice using Complete Freund's Adjuvant (CFA) and formaldehyde. Disease severity was assessed using the Psoriasis Severity Index (PSI), while histopathological examination and orthokeratosis studies were performed to evaluate therapeutic efficacy. Results: The formulation was found to be safe at a dose of 2000 mg/kg, with no signs of erythema, irritation, behavioral abnormalities, or mortality. The induction model successfully produced psoriasis-like lesions characterized by erythema, scaling, epidermal hyperplasia, keratinocyte hyperproliferation, Munro's microabscess formation, and capillary loop dilation. Treatment with *Semecarpus anacardium*-loaded liposomes significantly reduced psoriatic symptoms and improved histopathological parameters. The treated group showed reduced epidermal thickness (79.84±1.40 µm), improved orthokeratosis (45.42±0.94%), and decreased inflammatory infiltration. **Conclusion:** The findings indicate that *Semecarpus anacardium*-loaded liposomes possess significant anti-psoriatic activity and may represent a promising topical therapeutic strategy for psoriasis management. Further mechanistic and clinical investigations are warranted to confirm their long-term therapeutic potential.

Keywords: Anti-psoriatic activity, Histopathology, Liposomes, Psoriasis, Psoriasis Severity Index, *Semecarpus anacardium*.

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INTRODUCTION

Psoriasis is a chronic, immune-mediated inflammatory skin disorder with a strong genetic predisposition, characterized by erythematous, scaly, and thickened plaques. It affects approximately 2-3% of the global population and significantly impacts patients' quality of life (Azfar and Gelfand, 2002). The condition arises due to dysregulation of the immune system, which accelerates the epidermal turnover cycle, leading to excessive proliferation and abnormal differentiation of keratinocytes (Azfar and Gelfand, 2002). Histopathologically, psoriasis is marked by pronounced keratinocyte hyperproliferation, infiltration of immune cells such as T lymphocytes and neutrophils, and vascular alterations including dilation and neovascularization. Earlier considered primarily a disorder of epidermal proliferation, psoriasis is now recognized as a complex immune-mediated disease involving multiple cytokines and signaling pathways (Fry, 1988).

The pathogenesis of psoriasis involves abnormal keratinocyte differentiation, enhanced angiogenesis, and activation of T helper (Th1 and Th17) cells, which contribute to sustained inflammation (Pelle *et al.*, 2005). These immune responses are associated with increased production of pro-inflammatory cytokines and reactive oxygen species, resulting in oxidative stress and lipid peroxidation in psoriatic lesions (Yildirim *et al.*, 2003). Such oxidative imbalance plays a crucial role in disease progression, suggesting that therapeutic strategies targeting both inflammation and oxidative stress may provide improved clinical outcomes (Young *et al.*, 2008).

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In recent years, medicinal plants have gained considerable attention as potential therapeutic agents for psoriasis due to their multi-targeted pharmacological actions and relatively safer profiles. Several plant species, including Radix paeoniae alba, *Rubia cordifolia, Coptis chinensis, Alpinia galanga, Annona squamosa*, and *Curcuma longa*, have demonstrated significant anti-psoriatic activity through anti-inflammatory, antioxidant, and antiproliferative mechanisms (Koo and Arain, 1998; Koo and Desai, 2003; Lin *et al*., 2010; Prepare *et al*., 1995; Tan *et al*., 2011; Tse *et al*., 2006; Zhou *et al*., 2012). These findings highlight the growing interest in phytoconstituents as alternative or complementary therapies for chronic inflammatory skin disorders.

Building upon this evidence, various Indian medicinal plants such as *Phyllanthus simplex, Crotalaria juncea, Leucas aspera*, and *Vitex glabrata* have been traditionally used for the management of psoriasis and other inflammatory skin conditions. Ethnopharmacological reports indicate that *P. simplex* is employed for treating inflammatory disorders (Unander *et al*., 1990), while *C. juncea* seeds are used for chronic skin diseases and psoriasis (Sharma *et al*., 2001). Such traditional claims support the need for scientific validation of plant-based therapies.

Among medicinal plants, *Semecarpus anacardium* has emerged as a promising candidate due to its well-documented anti-inflammatory, antioxidant, and immunomodulatory properties. The plant is rich in bioactive compounds such as flavonoids and phenolic constituents, which are known to modulate inflammatory pathways and reduce oxidative stress. However, despite its therapeutic potential, the clinical application of plant-derived compounds is often limited by poor solubility, low bioavailability, and inadequate skin penetration.

To overcome these limitations, advanced drug delivery systems such as liposomes have been extensively explored. Liposomes are phospholipid-based vesicular carriers that enhance drug solubility, improve skin permeation, and provide controlled and targeted drug release. Their biocompatibility and ability to encapsulate both hydrophilic and lipophilic compounds make them particularly suitable for topical delivery in dermatological disorders, including psoriasis. Liposomal formulations have been shown to improve therapeutic efficacy while minimizing systemic toxicity.

Despite the reported pharmacological potential of *Semecarpus anacardium*, there is limited research on its incorporation into nanocarrier-based delivery systems for psoriasis treatment. Furthermore, comprehensive studies integrating molecular docking, *in vitro* evaluation, and *in vivo* validation remain scarce. Therefore, the present study aims to develop and optimize *Semecarpus anacardium*-loaded liposomes and evaluate their anti-psoriatic activity using an *in vivo* experimental model. The study also integrates *in silico* and *in vitro* approaches to elucidate the possible mechanism of action and to support its therapeutic potential in the management of psoriasis.

MATERIALS AND METHODS

All chemicals and reagents used in the study were of analytical grade. Phospholipids and cholesterol used for liposome preparation were procured from standard commercial suppliers. Complete Freund's Adjuvant (CFA) and formaldehyde were used for induction of psoriasis. Retino-A cream (0.05%) was used as a standard drug. All solutions were prepared using distilled water.

Plant material

Semecarpus anacardium was selected for the present investigation based on its reported pharmacological properties. The plant material was collected and authenticated, and the extract was prepared for further formulation studies.

Preparation of *Semecarpus anacardium*-loaded liposomes

Liposomal formulation of *Semecarpus anacardium* was prepared using a thin-film hydration method. Briefly, phospholipids and cholesterol were dissolved in an organic solvent mixture and subjected to rotary evaporation to form a thin lipid film. The dried film was hydrated with an aqueous phase containing the plant extract, followed by sonication to obtain uniform vesicles. The prepared liposomes were stored under refrigerated conditions until further use.

Animals

Healthy Swiss albino mice (25-30 g) of either sex were used for the study. Animals were housed under standard laboratory conditions with a 12 hr light/dark cycle at 25±2°C and relative humidity of 44-56%. They were provided with standard pellet diet and water *ad libitum*. All experimental procedures were conducted in accordance with CPCSEA guidelines and approved by the Institutional Animal Ethics Committee

Acute dermal toxicity study

Acute dermal toxicity of *Semecarpus anacardium*-loaded liposomes was evaluated in accordance with OECD guideline 402. Swiss albino mice were divided into three groups, each comprising six animals. 24 hr prior to treatment, the dorsal surface of the animals (approximately 10% of total body surface area) was carefully shaved using a depilatory method.

A single dose of 2000 mg/kg body weight of the liposomal formulation was applied topically to the shaved area. Following application, the animals were observed continuously for the initial hours and subsequently monitored daily for a period of 14 days for signs of toxicity. Observations included changes in skin condition such as redness and erythema, as well as alterations in fur, behavioral patterns, sleep activity, and mortality.

Induction of psoriasis

Psoriasis was induced using a modified *in vivo* model based on the combined application of Complete Freund's Adjuvant (CFA) and formaldehyde. This model utilizes the immunostimulatory and inflammatory properties of CFA, while formaldehyde acts as a phlogistic agent to potentiate the inflammatory response. A stable mixture of CFA and formaldehyde (1:10) was prepared. The dorsal region of mice (approximately 2 × 2 cm) was shaved using a depilatory cream. A volume of 0.1 mL of the prepared mixture was applied topically to the shaved area on days 1, 2, and 3. Animals were then observed daily for a period of 7 days for the development of psoriatic lesions.

The severity of psoriasis was evaluated using a scoring system based on the Psoriasis Severity Index (PSI). Redness, erythema, and scaling were scored independently on a scale of 0-4 (0=none, 1=slight, 2=moderate, 3=marked, and 4=very marked). The cumulative score (0-12) was considered as the PSI. At the end of the experimental period, animals were anesthetized, and skin samples were collected and fixed in 10% formalin. Longitudinal sections (~5 µm thickness) were prepared using microtomy and stained with hematoxylin and eosin (H&E) for histopathological examination.

Experimental design

After successful induction of psoriasis, animals were randomly divided into three groups (n=6):

- Group I: Disease control (untreated).
- Group II: Standard (Retino-A cream, 0.05%).
- Group III: *Semecarpus anacardium*-loaded liposomes.

Treatment was administered topically once daily for a period of three weeks.

Anti-psoriatic activity of test formulations

Following induction of psoriasis, animals were treated according to the experimental design. Treatments were administered topically once daily for three weeks. The severity of psoriatic lesions was evaluated weekly using the Psoriasis Severity Index (PSI). Redness, erythema, and scaling were scored independently on a scale of 0-4, and the cumulative score was recorded as the PSI (0-12). At the end of the study, animals were anesthetized, and skin samples were collected, fixed in 10% formalin, and processed for histopathological evaluation using hematoxylin and eosin staining.

Histopathological examination

At the end of the experimental period, animals were sacrificed under anesthesia, and skin samples were collected and fixed in 10% formalin. Tissue sections of approximately 5 µm thickness were prepared using microtomy and stained with hematoxylin and eosin (H&E). The stained sections were examined microscopically for histopathological changes, including epidermal thickness, keratinocyte hyperproliferation, presence of Munro's microabscess, elongation of rete ridges, and capillary loop dilation.

Determination of orthokeratosis

The degree of orthokeratosis was calculated using the following formula:

$$\text{Orthokeratosis (\%)} = \frac{\text{Length of granular layer}}{\text{Total epidermal length}} \times 100$$

Statistical analysis

All data were expressed as Mean±SEM. Statistical analysis was performed using one-way Analysis of Variance (ANOVA) followed by Tukey-Kramer multiple comparison test using GraphPad software. A value of $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSIONS

Acute dermal toxicity study

The acute dermal toxicity study demonstrated that the *Semecarpus anacardium*-loaded liposomal formulation was safe for topical application. No signs of toxicity such as erythema, irritation, behavioral changes, or mortality were observed in any of the animals during the 14-day observation period. The absence of adverse effects indicated that the formulation was non-toxic at a dose of 2000 mg/kg and suitable for further *in vivo* evaluation.

Induction of psoriasis

Topical application of the CFA and formaldehyde mixture successfully induced psoriatic lesions in mice. A progressive increase in redness, erythema, and scaling was observed from day 1 to day 7, resulting in a gradual increase in the Psoriasis Severity Index (PSI) (Table 1 and Figure 1). Histopathological examination of diseased skin confirmed characteristic psoriatic features, including increased epidermal thickness, keratinocyte hyperproliferation, presence of Munro's microabscess, elongation of rete ridges, and capillary loop dilation. These observations indicated successful establishment of the psoriasis model.

Histopathological evaluation

Histopathological examination of skin sections revealed distinct differences among the experimental groups. The control group exhibited characteristic features of psoriasis, including marked epidermal thickening (128.34±1.20 µm), hyperproliferation of keratinocytes, presence of Munro's microabscess, elongation of rete ridges, and capillary loop dilation, confirming successful disease induction. In contrast, the standard-treated group (Retino-A) showed significant restoration of normal skin architecture, with a marked reduction in epidermal thickness

(54.78±1.73 µm), reduced inflammatory infiltration, and absence of pathological features such as Munro's microabscess.

The group treated with *Semecarpus anacardium*-loaded liposomes demonstrated a considerable improvement in histological parameters, with a significant reduction in epidermal thickness (79.84±1.40 µm), decreased keratinocyte proliferation, reduced inflammatory cell infiltration, and partial restoration of the granular layer (Figure 2). These findings indicate that the liposomal formulation effectively alleviated psoriatic changes and promoted normalization of skin tissue.

Determination of orthokeratosis

Quantitative evaluation showed that the control group exhibited low orthokeratosis and increased epidermal thickness, indicating impaired keratinization. The standard-treated group showed significant improvement, with higher orthokeratosis and reduced epidermal thickness (Table 2). The liposome-treated group demonstrated moderate improvement, with increased orthokeratosis and reduced epidermal thickness compared to the control group. These results indicate restoration of normal keratinization and reduction of hyperproliferative activity.

DISCUSSION

The present study demonstrated the successful development and evaluation of *Semecarpus anacardium*-loaded liposomes as a potential topical anti-psoriatic formulation. The acute dermal toxicity study confirmed the safety of the formulation, as no signs of erythema, irritation, behavioral abnormalities, or mortality were observed during the 14-day observation period. According to OECD guideline 402, the absence of toxic manifestations at a limit dose of 2000 mg/kg indicates a favorable safety profile for topical application. Similar findings have been reported for appropriately processed *Semecarpus anacardium* preparations, which exhibited minimal toxicity and no significant adverse effects in experimental animals (David *et al.*, 2026; Sundaram *et al.*, 2018). The observed safety may be attributed to the liposomal carrier system, which enhances biocompatibility and provides controlled release of bioactive constituents, thereby minimizing direct skin irritation.

The CFA- and formaldehyde-induced psoriasis model successfully reproduced the clinical and histopathological features of psoriasis, as evidenced by progressive increases in redness, erythema, scaling, and Psoriasis Severity Index (PSI) scores. Histological examination further confirmed disease induction through

Table 1: Development of psoriasis (PSI during induction phase).

Day	Redness	Erythema	Scales	PSI
1	1.03±0.02	-	-	1.03±0.05
2	1.41±0.05	0.43±0.06	-	1.84±0.01
3	1.75±0.08	1.01±0.05	-	2.77±0.08
4	2.17±0.06	1.68±0.02	0.81±0.06	4.68±0.26
5	2.61±0.07	2.22±0.04	1.77±0.05	6.60±0.84
6	2.94±0.06	2.59±0.06	2.34±0.04	7.87±0.64
7	3.25±0.01	2.87±0.09	2.79±0.05	8.91±0.29

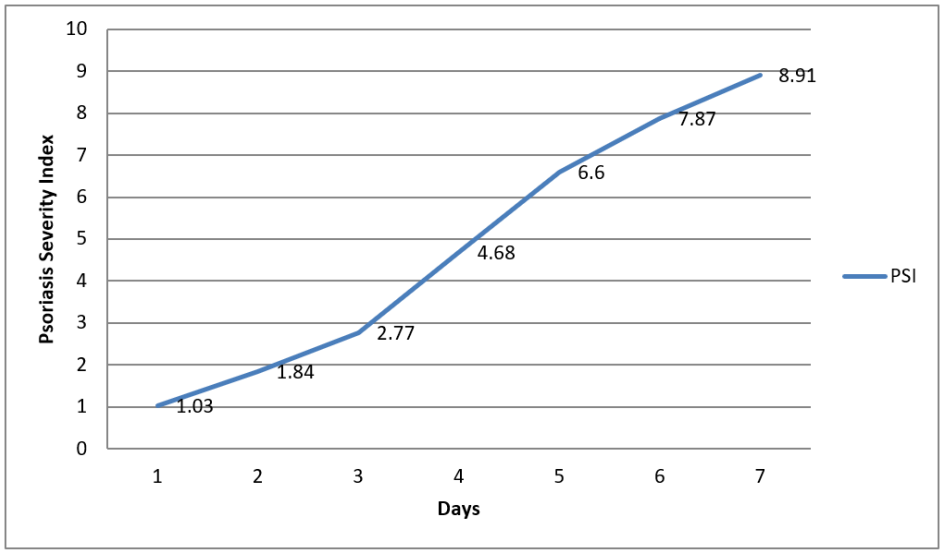


Figure 1: Progression of Psoriasis Severity Index (PSI) during induction phase in CFA- and formaldehyde-treated mice.

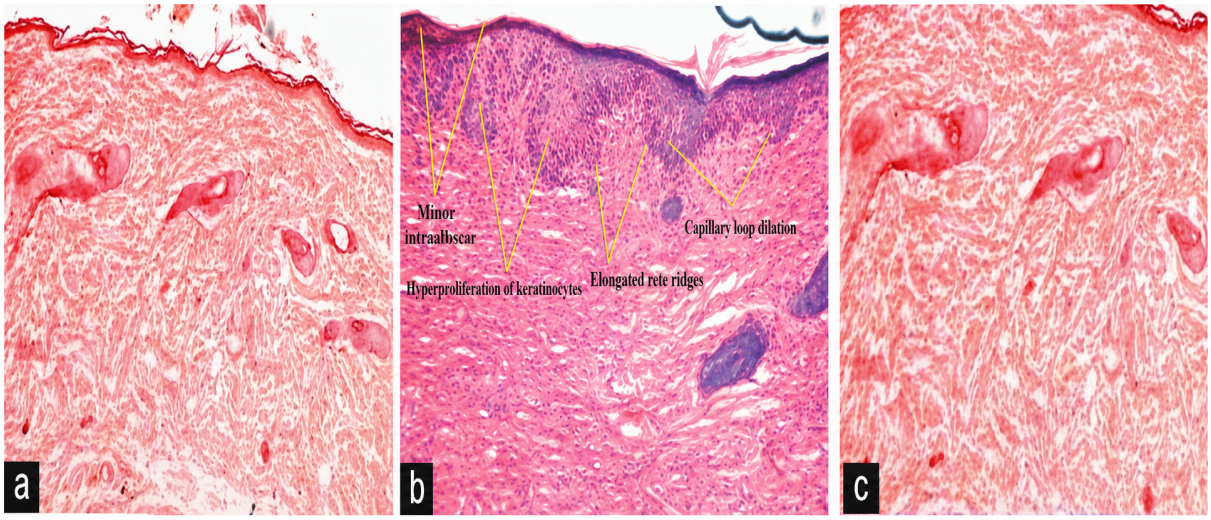


Figure 2: Histopathological evaluation of mouse skin sections (H&E, ×40) showing a-normal, b-psoriatic, and c-liposome-treated groups.

Table 2: Anti-psoriatic activity parameters.

Group	Orthokeratosis (%)	Drug activity (%)	Epidermal thickness (µm)
Control	18.33±0.88	-	128.34±1.20
Standard	68.33±0.88	60.97%	54.78±1.73
Liposomes	45.42±0.94	28.04%	79.84±1.40

epidermal hyperplasia, keratinocyte hyperproliferation, Munro's microabscess formation, elongation of rete ridges, and capillary loop dilation. These findings are in agreement with previous reports demonstrating that experimentally induced psoriasis models closely mimic the pathological features of human psoriasis (Srivastava *et al.*, 2016; Ez-zahir *et al.*, 2022). The effectiveness of the induction model can be attributed to the synergistic action of CFA and formaldehyde. CFA stimulates immune responses through recruitment and activation of inflammatory cells, while formaldehyde acts as a potent phlogistic agent that promotes the release of inflammatory mediators, thereby amplifying local inflammation and epidermal hyperproliferation (Broderson, 1989; Wanstrup and Christensen, 1965; Saito *et al.*, 2011).

Treatment with *Semecarpus anacardium*-loaded liposomes resulted in a marked improvement in both clinical and histopathological parameters. Histological evaluation revealed a significant reduction in epidermal thickness, decreased keratinocyte proliferation, reduced inflammatory cell infiltration, and partial restoration of the granular layer compared with the untreated control group. These findings indicate effective suppression of the hyperproliferative and inflammatory processes that characterize psoriasis. Similar reductions in epidermal thickness and inflammatory changes have been reported following treatment with anti-psoriatic herbal formulations, suggesting that attenuation of keratinocyte hyperproliferation and inflammatory responses represents a key mechanism of therapeutic action (Ez-zahir *et al.*, 2022). Furthermore, the characteristic histopathological features observed in the present study are recognized diagnostic hallmarks of psoriasis, supporting both the validity of the experimental model and the therapeutic response achieved following treatment (Fernandez-Figueras and Puig, 2025; Kim *et al.*, 2015; Noronha-Neta *et al.*, 2019).

The orthokeratosis study further supported the anti-psoriatic efficacy of the liposomal formulation. The increase in orthokeratosis and concomitant reduction in epidermal thickness observed in the treated group indicate restoration of normal keratinization and suppression of excessive epidermal proliferation. Improvement in these parameters is commonly associated with effective anti-psoriatic therapies that promote normal keratinocyte differentiation and epidermal homeostasis (Gudjonsson and Elder, 2007; Nickoloff *et al.*, 2007). Although the standard treatment exhibited superior activity, the liposomal formulation produced substantial improvement compared with the untreated control group, highlighting its therapeutic potential.

The overall anti-psoriatic activity observed in the present study may be attributed to the anti-inflammatory, antioxidant, and immunomodulatory properties of *Semecarpus anacardium*. Encapsulation of the extract within liposomes likely enhanced dermal penetration, improved stability of bioactive compounds, and facilitated sustained release at the target site, thereby improving therapeutic efficacy. Collectively, the findings suggest that *Semecarpus anacardium*-loaded liposomes effectively alleviate psoriasis-like lesions by reducing inflammation, suppressing keratinocyte hyperproliferation, restoring normal keratinization, and improving skin architecture.

CONCLUSION

The present study successfully demonstrated the anti-psoriatic potential of *Semecarpus anacardium*-loaded liposomes using a CFA- and formaldehyde-induced *in vivo* psoriasis model. The developed liposomal formulation exhibited a favorable safety profile, with no signs of dermal toxicity or behavioral abnormalities observed during the acute dermal toxicity study. The induced psoriasis model effectively reproduced the characteristic clinical and histopathological features of psoriasis, validating its suitability for evaluating anti-psoriatic therapies.

Treatment with *Semecarpus anacardium*-loaded liposomes resulted in a significant reduction in psoriasis severity, as evidenced by decreased redness, erythema, scaling, epidermal thickness, and inflammatory infiltration, along with improvement in orthokeratosis and restoration of normal skin architecture. Histopathological findings further confirmed suppression of keratinocyte hyperproliferation and normalization of epidermal structure following treatment. The observed therapeutic effects may be attributed to the anti-inflammatory, antioxidant, and immunomodulatory properties of *Semecarpus anacardium*, together with the enhanced dermal delivery and biocompatibility offered by the liposomal carrier system.

Altogether, the findings of the present investigation suggest that *Semecarpus anacardium*-loaded liposomes represent a promising topical therapeutic approach for the management of psoriasis. However, further studies involving detailed molecular mechanisms, cytokine profiling, pharmacokinetic evaluation, and clinical investigations are required to establish its long-term efficacy and translational potential.

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ABBREVIATIONS

CFA: Complete Freund's Adjuvant; **PSI:** Psoriasis Severity Index; **OECD:** Organisation for Economic Co-operation and Development; **H&E:** Hematoxylin and Eosin; **SEM:** Standard Error of the Mean; **µm:** Micrometer; **mg/kg:** Milligram per kilogram body weight; **PASI:** Psoriasis Area and Severity Index; **IL:** Interleukin; **TNF-α:** Tumor Necrosis Factor-alpha; **ROS:** Reactive Oxygen Species; **Th1:** T-helper 1 Cells; **Th17:** T-helper 17 Cells; **Retino-A:** Tretinoin (Reference Standard Drug).

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Subhranshu Panda: Conceived and designed the study, supervised the research work, contributed to data interpretation, and critically reviewed the manuscript. **Mahesh Uttamrao:** Shinde carried out the experimental work, including formulation development, *in vivo* studies, data collection, statistical analysis, and preparation of the initial manuscript draft. **Aamer Iqbal Quazi:** Contributed to the experimental design, pharmacological evaluation, validation of results, and critical revision of the manuscript. **Naziya M.A. Rehman:** Contributed to literature review, data analysis, interpretation of findings, manuscript writing, editing, formatting, and reference management. All authors have read, reviewed, and approved the final version of the manuscript and agree to be accountable for the accuracy and integrity of the work.

SUMMARY

This study successfully formulated *Semecarpus anacardium*-loaded liposomes utilizing a thin-film hydration method. In a CFA/formaldehyde-induced *in vivo* model, the topical application of these liposomes significantly reduced psoriasis severity, normalized epidermal thickness, and improved orthokeratosis without demonstrating dermal toxicity. The findings suggest this liposomal system is a highly promising and safe nanoscale strategy for the topical management of psoriasis.

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