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Research Article

IMPACT OF CARBOPOL-LOADED CURCUMIN NANOEMULSION ON PSORIASIS: INVESTIGATING TREATMENT EFFICACY AND HISTOPATHOLOGICAL CHANGES IN AN ANIMAL MODEL

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ABSTRACT

Objectives: This study sought to evaluate the medicinal and therapeutic advantages of a locally used herbal preparation for psoriasis management. It specifically assessed the efficacy of curcumin-based nanoemulsions and nanoemulgels in a rat model of psoriasis produced by complete Freund's adjuvant and formaldehyde. The formulations were tested against the conventional corticosteroid treatment, triamcinolone acetonide.

Methods: Thirty albino Wistar rats were placed into five groups: Control, placebo, standard, F1 (CURNE 5%), and F2 (CURNE 10%). The psoriasis area and severity index were used to determine the severity of erythema, scaling, and skin thickness. To compare the treatment effects, histopathological investigation was performed, followed by statistical analysis using one-way analysis of variance.

Results: The study found substantial disparities in treatment efficacy. The 10% F2 formulation (Carbopol-loaded curcumin nanoemulsion) significantly improved skin health ($p<0.0001$). When used as an ointment, both the 5% F1 and 10% F2 formulations had positive outcomes, but they did not outperform the usual corticosteroid therapy. Histopathological study revealed that the F2 10% formulation resulted in normal epidermal thickness, decreased mitotic activity, and a less nucleated stratum corneum.

Conclusion: Curcumin-based nanoemulsions, particularly the 10% F2 formulation, show promise in dermatological treatment for psoriasis control. The findings underline the need of continuing to enhance drug delivery technologies, particularly nanoemulsions, to improve psoriasis therapy choices.

Keywords: Psoriasis area and severity index score, Psoriasis, Histopathological study, Nanoemulsion, Nanoemulgel, Curcumin, Complete Freund's adjuvant and formaldehyde.

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INTRODUCTION

The immune system defends humans against microbial infections; bacteria emerge intolerant immune systems [1]. Autoimmunity, or an aberrant response, is produced by both genetic predisposition and environmental circumstances. The most prevalent autoimmune illnesses include rheumatoid arthritis, myasthenia gravis, Crohn's disease, sarcoidosis, psoriasis, scleroderma, and systemic lupus erythematosus [2]. These disorders generate psychological and physiological stress due to their early onset, continuous therapeutic requirements, and chronic nature. Researchers must comprehend the underlying processes and devise effective treatment and preventive techniques [3,4]. Psoriasis is an inflammatory, non-communicable skin disorder. It is distinguished by recurring bouts of inflammation, erythematous, hard, flaky skin blisters, and abundant keratin deposits [5-7]. Psoriasis, which appears as patches on the skin, is caused by the accumulation of skin debris on the skin's surface [8,9]. According to the International Federation of Psoriasis Association [10], psoriasis affects about 2–3% of the world's population. Psoriatic arthritis can occur from the long-term impact of an inflammatory psoriatic disease, which affects 10–30% of patients [11]. Psoriatic arthritis causes permanent joint degradation as a result of persistent inflammation, followed by joint cartilage loss [12,13]. According to the American Academy of Dermatology [14], some of the different types of psoriasis include inverse psoriasis, eruptive psoriasis, pustular and erythrodermic (also known as exfoliative psoriasis), and pustular and erythrodermic (also known as psoriasis vulgaris). Plaque psoriasis, which causes painful red skin lesions with brittle silver scales, is a well-known condition that affects around 80% of psoriasis patients. These lesions can be seen in a variety of bodily regions, including the oral cavity and sexual organs [15]. The National Psoriasis Foundation categorizes psoriasis as mild, moderate, or severe based on how much of the body is affected: no more than 3% of the entire body, 3–10% of the overall body, and more than 10% of the body parts, respectively [15,16].

Psoriasis pathogenesis involves not only keratinocytes but also the immune system. Other lymphocytes, such as CD4+ and CD8+T cells, have been associated with inflammation and the development of psoriasis; these lymphocytes have been found in the epidermal and peripheral blood of psoriatic patients. As a result, CD4+T helper cells in mice developed psoriatic lesions, in contrast to CD8+ lymphocytes. Elevated levels of Th1 cytokines (cytokine-interferon-gamma [c-IFN-γ], tumor necrosis factor-α [TNF-α], and interleukin-12 [IL-12]) and Th2 cytokines (IL-4, IL-5, and IL-10) can activate psoriatic lesions. Hence, the report verified whether the sickness is a Th1-type disease [17]. The source of CD4+ lymphocytes has been identified as the source of IL-17A cells. These IL-17A cytokine cells, namely six members (IL-17A to IL-1F), are primarily involved in the defense mechanism against extracellular pathogen infection. As a result, prior studies have shown that IL-17 is critical for neutrophil recruitment and maintenance, as well as avoiding fungal and Gram-negative bacterial infections [18-20]. Pro-inflammatory cytokines IL-6 and IL-8, produced from IL-17A, have been linked to the worsening of psoriasis. IL-17A and IL-17F expressions were enhanced in conjunction with psoriasis

and dermatitis. The imiquimod model research on mice demonstrated this link [21]. Pro-inflammatory cytokines such as IL-17A, IFN-γ, and IL-23p19 have been associated with the development of psoriasis [22,23]. IL-22 is a cytokine that causes epidermal hyperplasia by boosting keratinocyte proliferation, as previously demonstrated [24]. T cells, B cells, activated monocytes, dendritic cells (DC), and macrophages all generate IL-23, which is a continuous chain made up of IL-12p and IL-23p [25,26]. IL-23 regulates the Th17 population by stimulating its increase. The role of IL-23 in Th17 was demonstrated utilizing animal models of Th17-related inflammation, autoimmune encephalomyelitis, and collagen-induced arthritis. A lack of IL-23 receptors composed of IL-23p19 and IL-12p40 (IL-12/23p40) significantly reduced such conditions [27,28]. In psoriatic skin lesions, IL-23p and IL-12p40 are overexpressed, causing Th17 cells to generate IL-23. Monocytes and DC produce TNF-α, IL-23p19, and IL-20R2, which induce hyperkeratosis and acanthosis in mice [29-31]. DCs are the primary source of IL-23. DCs carry antigens and regulate the maturation of naïve T cells into mature lymphocytes. DC cells initiate the body's T-cell responses. TNF and inducible nitric oxide synthase produce DC, leading to elevated levels of TNF-α in psoriatic lesions [32]. TNF-α has a crucial role in keratinocyte growth, survival, proliferation, and anti-apoptotic properties. Furthermore, it causes keratinocytes to generate IL-8, resulting in the formation of microabscesses, whereas TNF-a promotes neutrophil recruitment in psoriasis [15,33,34]. TNF-a stimulates Th17 to create pro-inflammatory cytokines through the NF-jB pathway in psoriatic lesions, and when the NF-jB pathway is suppressed, CD4+T cells stop producing IL-17A, whereas psoriatic lesions have increased TNF-a activity, and TNF medications reduce inflammation [35,36].

Corticosteroids are commonly used to treat psoriasis by reducing inflammation and immunological responses. Long-term use, however, may result in undesirable consequences such as skin thinning and an increased risk of infection. Topical Vitamin D analogs, when paired with other therapies, can reduce symptoms without causing significant systemic consequences. Tazarotene can successfully treat plaque psoriasis. However, it may cause skin irritation [37-40]. Herbal remedies made from natural plants are useful for treating illnesses such as psoriasis. Fish oil and Vitamin E supplements, as well as dietary and lifestyle changes, may help to relieve psoriasis symptoms [41]. Researchers discovered that curcumin (CUR) had high effectiveness and a wide range of applications for treating psoriasis. Its usage is also critical for improving the psoriasis phenotype and lowering the inflammatory milieu, and evidence shows that CUR, either alone or in combination with other standard medications, can effectively cure psoriasis [42].

The current literature highlights various treatments for psoriasis, with an emphasis on the use of curcumin due to its anti-inflammatory and antioxidant properties. Several studies have explored the potential of curcumin in different delivery systems, including nanoemulsions, to improve its bioavailability and therapeutic efficacy [42,43]. Nanoemulsions have been shown to enhance the skin penetration of curcumin, improving its topical effectiveness for conditions such as psoriasis [44,45]. In addition, carbopol has been widely used as a stabilizing agent in drug delivery systems, but its potential to enhance the performance of curcumin-loaded nanoemulsions for psoriasis treatment remains underexplored. While individual studies have examined the benefits of curcumin, nanoemulsions, and carbopol, there is limited research on the synergistic effects of a carbopol-loaded curcumin nanoemulsion for treating psoriasis. This gap in the literature underscores the need for novel formulations that can improve curcumin's therapeutic outcomes. Our study aims to address this gap by investigating the impact of carbopol-loaded curcumin nanoemulsion on psoriasis, offering a unique approach to enhance curcumin's efficacy through improved stability, controlled release, and targeted delivery. This novel formulation is expected to provide enhanced therapeutic effects compared to traditional curcumin-based treatments, making it a promising candidate for more effective psoriasis management. In this work, we explored curcumin-containing nanoemulsions to establish their therapeutic efficacy on psoriasis using an animal model and detected morphological changes in the skin layers with and without the administration of the created nanoemulsion.

METHODS

For this investigation, 30 healthy albino Wistar rats were maintained in separate polyproline cages. Animals were kept in typical laboratory settings. The complete Freund's adjuvant CFA) and formaldehyde model were used to generate psoriasis. The concept is based on CFA's potential to activate the immune system and create inflammation, as well as the use of formaldehyde as a phlogistic agent to augment CFA's inflammatory properties [46]. A highly stable combination of CFA and formaldehyde (1:10) has been developed. Hairs on the dorsal part of each rat were removed using depilatory lotion. On days 1–3, each test animal (n=10) received 0.1 ml of the produced mixture administered topically to the shaved region.

Fig. 1 depicts two distinct variations of the produced test formulation for treating psoriatic skin in animals induced using the CFA and formaldehyde models. There are two types of curcumin nanoemulsion formulations: 5% (F1) and 10% (F2). Two measures were used to assess the treatment efficacy of the produced formulations: The psoriatic area severity index (PASI) and histological investigation of isolated skin.

Drug administration pattern

Five groups of animals have been formed, each consisting of six rats for this study.

- Group 1 (Normal control): Is untreated normal control
- Group 2 (Induced control): Six animals were treated with distilled water as a placebo for 21 days
- Group 3 (Standard test group): Six psoriasis-induced animals received local care using triamcinolone acetonide cream 0.1% for 21 days
- Group 4 (Test group): Six psoriasis-induced animals received local care using F1 for 21 days
- Group 5 (Test group): Six psoriasis-induced animals received local care using F2 for 21 days.

The animals were evaluated daily for psoriatic lesions for 21 days. An objective grading system was developed based on the Clinical Psoriasis and Severity Index. Redness, erythema, and scales were scored separately on a scale of 0–4, with none at all, faint at one, moderate at two, marked at three, and highly marked at four. The cumulative score, which is the sum of redness, erythema, and scaling, was used to calculate the population stability index (0–4) scale [47].

Skin isolation and processing

On the 20th day, ketamine was administered intramuscularly at a dosage of 40 mg/kg. Fig. 1 shows how psoriatic skin was taken using an 8 mm biopsy punch and kept in buffered formaldehyde for histological examination. The isolated skin was placed in buffet formalin for 24 h. Following that, 12 h of washing under running water were completed. This washed lung tissue has been placed in a tissue processor. The treated tissues were inserted in a "L"-shaped module filled with paraffin

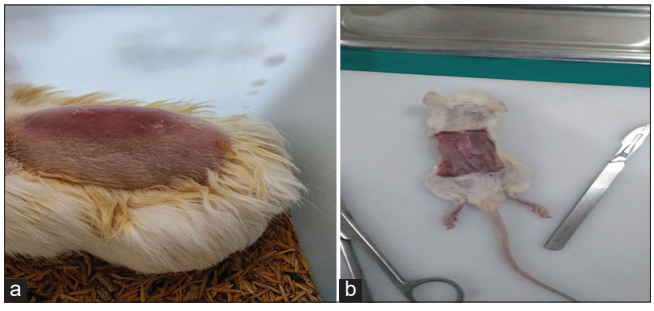

Fig. 1: (a and b) Experimental animal psoriatic skin and skin isolation

wax, which was then cast. These tissue blocks were securely connected to a metal holder. Staining was then used for microscopic investigation [47].

Statistical analysis

The statistical analyses performed for the psoriasis area severity index (PASI) scores on the 21st day of drug administration involved a one-way analysis of variance (ANOVA) followed by Dunnett's multiple comparisons test. We calculated p-values (<0.0001) to assess statistical significance and confidence intervals (95% CI) for the mean differences between groups.

RESULTS

PASI

The scores include the average of erythema, scaling, and skin thickness on the 21st day of drug administration. The PASI scores on the 21st day of drug administration were as follows: Group 1 had a mean PASI score of 0.17±0.167, Group 2 had 3.00±0.258, Group 3 had 0.33±0.211, Group 4 had 1.67±0.494, and Group 5 had 0.67±0.333. These results indicate varying degrees of psoriasis severity across the groups, with Group 2 showing the highest severity and Group 1 the least, as shown in Table 1 and Fig. 2.

The PASI scores on the 21st day of drug administration were analyzed using one-way ANOVA and Dunnett's multiple comparisons test. Significant differences were observed between Group 2 and the other groups. Group 2 showed a mean difference of 2.833 (95% CI: 1.674 to 3.993) compared to Group 1, with a highly significant p-value (<0.0001). Similarly, significant differences were found between Group 2 and Group 3 (mean difference 2.667, p<0.0001), Group 4 (mean difference 1.333, p=0.0208), and Group 5 (mean difference 2.333, p<0.0001), indicating a higher severity in Group 2, as shown in Table 2.

Histopathological screening in psoriasis

The architectural skin design remains unchanged for Group 1 skin characteristics. Group 2 had a thick epidermis, nucleated stratum corneum, and mitotic figures. Group 3 had normal epidermal thickness, fewer nucleated stratum corneum cells, and fewer mitotic signals. In addition to normal epidermal thickness, Group 5 showed less nucleated stratum corneum and split cells. Fig. 3 shows that Group 4 had a reasonably high number of nucleated stratum corneum cells, a moderate epidermal thickness, and fewer mitotic signals than Group 2, as shown in Fig. 3.

DISCUSSION

PASI score

The clinical examination of psoriasis using the PASI provides a comprehensive approach to understanding how the illness affects individuals [42,46]. By methodically analyzing erythema, scaling, and thickness, the PASI gives a detailed rating of the severity of these symptoms [47]. Each parameter score, which ranges from 0 to 4, indicates what type of symptoms are present, from none to extremely obvious. This allows doctors to prescribe the best medicines and scientists to select formulations with the most exact composition. This standardized technique improves clinician-patient communication and empowers patients by giving them a better grasp of how their disease progresses over time. Such comprehensive assessments can lead to breakthroughs in psoriasis care, eventually enhancing patient outcomes and quality of life [48]. Throughout the trial, the PASI was calculated for each group, as shown in Table 1 and Fig. 2. Although one animal in Group 1 acquired a PASI score, possibly due to its own skin toxicity, Group 1 served as the normal control. Group 2, which got distilled water treatment as the induced control group, served as a baseline for comparison with Groups 1, 3, 4, and 5. The PASI score for Group 1 was 0.17±0.167, as shown in the MEAN SEM table, with a significant difference (p<0.0001). This study implies that illness induction resulted in a significant morphological difference between Groups 1 and 2. When Groups 2 and 3 were compared, the traditional ointment showed considerable therapeutic effectiveness (p<0.0001).

Table 1: Mean SEM of PASI score in psoriatic animals

Mean±SEM				
Group 1	**Group 2**	**Group 3**	**Group 4**	**Group 5**
0.17±0.167	3.00±0.258	0.33±0.211	1.67±0.494	0.67±0.333

Data presented as mean±SEM for PASI score; n=6 for each group. SEM: Standard error of the mean, PASI: Psoriatic area severity index

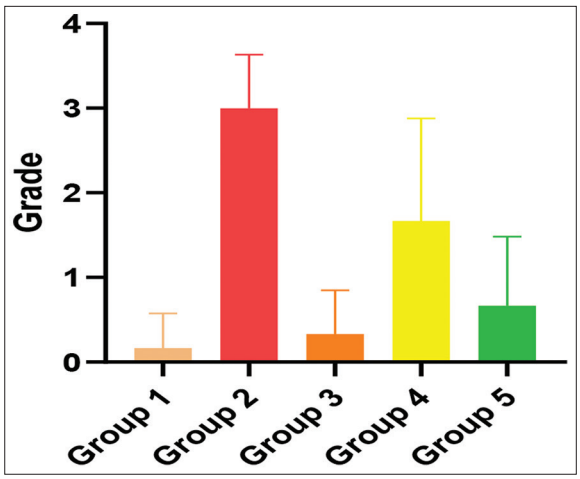

Fig. 2: Graphical representation of psoriatic area severity index score

Despite being less effective than the usual ointment, an interesting but not highly significant discovery (p=0.0208) demonstrated that the 5% nanoemulsion had therapeutic benefits on Groups 2 and 4. A substantial difference (p<0.0001) was detected between Groups 2 and 5, indicating that the 10% nanoemulsion was effective as a medication. Despite being slightly less powerful than normal cream, both the 5% and 10% curcumin nanoemulsions, as well as the carbopol-loaded curcumin nanoemulsion, provide therapeutic advantages. Furthermore, the 10% carbopol-loaded curcumin nanoemulsion exhibited a much larger therapeutic impact than the 5% curcumin nanoemulsion, as shown in Table 2.

Histopathology

The study employs CURNE 5% (F1) and CURNE 10% (F2) in a rat model of psoriasis by externally producing a psoriasis-like condition using CFA and formaldehyde (1:10 ratio). The PASI score (0-–4) represents the average of erythema, scaling, and skin thickness on the 21st day. Mean SEM was calculated using Anova, and their findings from the comparative analysis of nanoemulsion treatments highlight the notable therapeutic potential of the 10% F2 formulation, which demonstrates a statistically significant effect on skin health (p < 0.0001). While both the 5% F1 and 10% F2 show promising results, they do not outperform the conventional cream (triamcinolone). However, in terms of nanoemulsion alternatives, the 10% F2 formulation variation exceeds the 5% F1 formulation, showing its better therapeutic properties. This data synthesis demonstrates that while nanoemulsions represent a new approach to skincare therapy, particularly at higher concentrations, conventional creams continue to set a standard for their effectiveness in practical application [41]. The histological results of the investigation on mitosis and epidermal thickness demonstrate a clear relationship between these variables in each group. Group 1 (normal control) has no architectural differences, but Group 2 (induced control) has greater mitotic activity, thickness, and nucleated stratum corneum, indicating that it is self-healing. In Group 3 (standard medication), the stratum corneum was less nucleated and had decreased mitotic activity, but the epidermis was standard thickness. According to this study, the epidermis is less active and more stable. The stratum corneum level was slightly elevated, the epidermis was of ordinary

Table 2: One-way ANOVA analysis of PASI score within groups

Dunnett's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Significant	Summary	Adjusted p-value
Group 2 versus Group 1	2.833	1.674–3.993	Yes	****	<0.0001
Group 2 versus Group 3	2.667	1.507–3.826	Yes	****	<0.0001
Group 2 versus Group 4	1.333	0.1739–2.493	Yes	*	0.0208
Group 2 versus Group 5	2.333	1.174–3.493	Yes	****	<0.0001

Data presented as mean±SEM; n=6 for each group. PASI scores were analyzed using one-way ANOVA and Dunnett's multiple comparisons test. ANOVA: Analysis of variance, PASI: Psoriatic area severity index

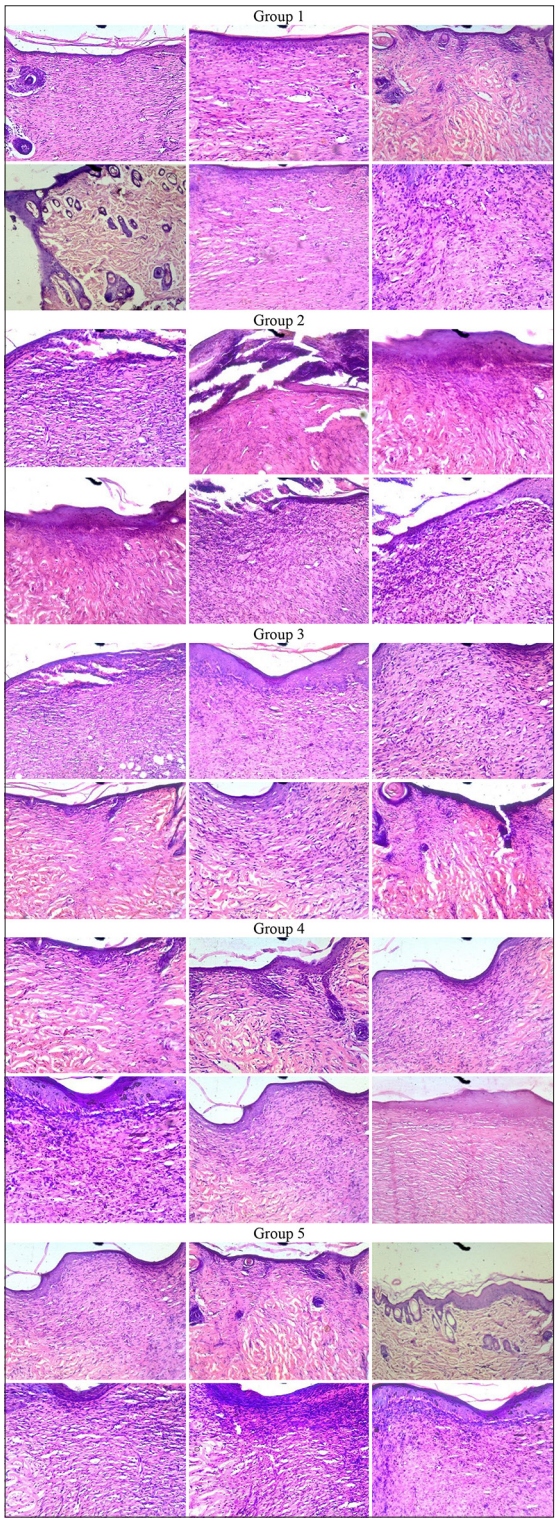

Fig. 3: Histopathological screening (Group 1–5)

thickness, and there were fewer mitoses in Group 4 CURNE 5% (F1) skin. Group 5 has normal epidermal thickness, less nucleated stratum corneum, and fewer mitoses. This phase was a transitory stage that might reflect different levels of cellular turnover. Overall, our findings highlight the delicate balance between epidermal structure and cellular development. They also show how differences in these factors affect the skin's state and reaction to external stimuli. As a result, skin functions as a semi-permeable barrier, separating molecules based on their size and physicochemical properties [46]. Psoriasis is a disorder characterized by inflammation and swelling of the epidermis, which breaks this barrier, as demonstrated by this CFA and formaldehyde-induced psoriasis rat model. These alterations may improve the body's ability to absorb anti-psoriatic medications, whether taken orally or applied to the skin in the form of nanoparticles. This nano vectorization approach, which lowers the medication concentration, can lessen adverse effects and enhance patient compliance [46,47]. These strategies have previously been developed and tested in an animal model of psoriasis induced by CFA and formaldehyde. Given the numerous advantages this strategy offers, its widespread appeal cannot be overlooked. Nonetheless, a comprehensive *in vivo* model is still necessary to close the information gap concerning human psoriasis. Hence, the criteria discussed in this article can aid in a more comprehensive assessment of psoriatic characteristics utilizing a rat model. This might lead to more accurate pre-clinical evaluations of numerous medicinal items.

CONCLUSION

In this study, we investigated the potential of curcumin-based nanoemulsions, particularly the 10% F2 formulation, as a treatment for psoriasis induced by CFA and formaldehyde. The results indicate that the 10% F2 nanoemulsion shows promise in enhancing treatment efficacy, surpassing the 5% F1 formulation. However, while the F1 formulation demonstrated comparable effectiveness to the standard corticosteroid triamcinolone acetonide cream 0.1%, its impact was not superior. Histopathological analysis highlighted the ability of both F1 and F2 formulations to optimize drug delivery, modulate cell turnover, mitotic activity, and improve epidermal thickness. These findings underscore the potential of nanoemulsions to enhance psoriasis treatments by increasing patient compliance and therapeutic outcomes. However, further research with advanced *in vivo* models is essential to bridge the gap between pre-clinical findings and clinical application, ultimately facilitating the development of more effective treatments for psoriasis. This study contributes to the growing body of knowledge on curcumin-based therapies in dermatology.

ETHICAL CLARENCE

Form B was submitted to the Institutional Animal Ethical Committee of the Drug Innovation Centers at Bilwal Medchem and Research Laboratory Private Limited in Reengus, Rajasthan. The Institutional Ethical Committee BMRL/DIC/CCSEA/IAEC/2025/I/1 authorized the experimental procedure and the CCSEA Registration No. is 2304/PO/Rc/S/2024/CCSEA.

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COMPETING INTEREST

None.

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AUTHORS CONTRIBUTION

Deepa Lashkari: Conceptualization, Methodology, Writing – Original draft preparation, Data curation, visualization, and investigation. Tejpal Yadav: Investigation, Review editing. Shiv Kumar Garg: Validation of data and proofreading of manuscript. Vikram Kumar: Supervised in designing the study, Conceptualization, Writing – Reviewing and Editing.

DECLARATION OF INTEREST

The authors claim to have no competing financial interests.

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