Bratislava Medical Journal (2026) 127:1440–1451
https://doi.org/10.1007/s44411-026-00516-2

RESEARCH

Topical *Dracunculus vulgaris* Schott Extract Attenuates Imiquimod-Induced Psoriasis in BALB/c Mice via Clinical and Histopathological Modulation

Ayse Nur Hazar-Yavuz[1] · Busra Cetin[1] · Humeysa Kiyak-Kirmaci[2] · Gül Sinemcan Karataş[3] · Turgut Taskin[4] · İsmail Senkardes[5] · Cansu Arslan[1] · Hatice Kubra Elcioglu[1,6] · Levent Kabasakal[1]

Received: 26 November 2025 / Revised: 23 January 2026 / Accepted: 25 January 2026 / Published online: 26 February 2026
© The Author(s) 2026

Abstract

Background Psoriasis is a chronic, immune-mediated dermatological disorder marked by abnormal keratinocyte proliferation, persistent inflammation, and dysregulation of immune pathways, often accompanied by systemic comorbidities. Despite available treatments, many patients experience side effects or relapse. Recent interest has turned to plant-based therapies with anti-inflammatory potential.

Objective This study aimed to investigate the therapeutic potential of *Dracunculus vulgaris* Schott extract on imiquimod (IMQ)-induced psoriasis in BALB/c mice.

Methods BALB/c mice were divided into four groups: Control, IMQ-induced psoriasis, IMQ + *D. vulgaris*, and IMQ + betamethasone. IMQ cream (5%) was applied topically for 6 days to induce psoriatic lesions. *D. vulgaris* extract and betamethasone were administered topically once daily. The extent and severity of lesions were evaluated through a modified version of the Psoriasis Area and Severity Index (PASI) scoring system. Skin thickness, spleen weight, histological changes (via hematoxylin and eosin staining), and interleukin (IL)-17 cytokine levels (via ELISA) were also analysed.

Results *D. vulgaris* significantly reduced PASI scores, skin thickening, and splenomegaly, with effects comparable to betamethasone. Histological examination confirmed substantial improvement in epidermal architecture and a reduction in inflammatory infiltration. Although IMQ-induced IL-17 elevation was not statistically significant—possibly due to strain-specific immune responses—treatment groups showed mild normalization of IL-17 levels.

Conclusion Treatment with *D. vulgaris* extract produced significant improvements in clinical presentation and histopathological features, indicating its promise as a topical, plant-based therapeutic option for psoriasis.

Keywords Psoriasis · *Dracunculus vulgaris* · Imiquimod · PASI · IL-17 · Histopathology

Abbreviations

ARRIVE	Animal Research: Reporting of In Vivo Experiments
COX	Cyclooxygenase
DEHAMER	Experimental Animals Research and Implementation Centre
E	Erythema
ELISA	Enzyme-linked immunosorbent assay
H&E	Hematoxylin and eosin

✉ Ayse Nur Hazar-Yavuz
ayse.hazar@marmara.edu.tr

[1] Department of Pharmacology, Faculty of Pharmacy, Marmara University, 34854 Istanbul, Türkiye

[2] Department of Pharmacology, Hamidiye Faculty of Pharmacy, Health Sciences University, 34668 Istanbul, Türkiye

[3] Stem Cell and Gene Therapies Research and Applied Center, Faculty of Medicine, Kocaeli University, 41001 Kocaeli, Türkiye

[4] Department of Pharmacognosy, Faculty of Pharmacy, Marmara University, 34854 Istanbul, Türkiye

[5] Department of Pharmaceutical Botany, Faculty of Pharmacy, Marmara University, 34854 Istanbul, Türkiye

[6] Marmara Pharmacy Drug and Innovative Product Development Unit, Faculty of Pharmacy, Marmara University, 34854 Istanbul, Türkiye

I	Induration
IL	Interleukin
IMQ	Imiquimod
PASI	Psoriasis Area and Severity Index
S	Scaling
SEM	Standard error of the mean
TLR	Toll-like receptor

1 Introduction

Psoriasis is a chronic, immune-driven skin disease affecting roughly 2–3% of the world's population, often impairing quality of life due to its recurrent course and possible association with psoriatic arthritis [21, 23]. Although primarily a dermatological condition, emerging evidence links psoriasis to cardiovascular disease and metabolic syndrome [10, 18]. Its etiology remains not fully understood, however, psoriasis is widely recognized as a T cell–mediated autoimmune condition involving complex immunological pathways and oxidative stress [7, 26].

From a histopathological perspective, psoriatic skin exhibits features including excessive keratinocyte proliferation, impaired differentiation, increased dermal vascularization, and dense infiltration of immune cells such as T lymphocytes, macrophages, dendritic cells, and neutrophils [10, 35]. Among these, plasmacytoid dendritic cells are particularly crucial as they produce large amounts of interferon-α in response to self-DNA bound to antimicrobial peptides, triggering the expansion of pathogenic T cells [18].

Imiquimod (IMQ), a ligand for Toll-like receptor (TLR)-7 and TLR-8, is commonly used to induce murine models of psoriasis-like inflammation and has become one of the most reliable preclinical models. Its topical administration upregulates the expression of interleukin (IL)-17A, IL-17F, and IL-23—key cytokines in psoriatic plaque formation [19, 20, 35]. Mice lacking components of the IL-17 or IL-23 pathways fail to develop psoriasis in the IMQ model [26]. In recent years, this model has been widely employed to evaluate the efficacy of emerging therapeutic strategies, including small molecules, experimental immunomodulators, and plant-derived compounds, underscoring its continued relevance in preclinical psoriasis research [1, 4].

Given the limitations of current treatments, interest in phytotherapeutic alternatives has increased. One such candidate is *Dracunculus vulgaris* Schott (Araceae family), a plant native to Türkiye and traditionally used for various skin conditions including eczema, vitiligo, and psoriasis [8]. The tubers and leaves of this species contain biologically active compounds such as flavonoids, tannins, coumarins, and phenylpropanoids, many of which exhibit potent anti-inflammatory and antioxidant properties [5, 6, 12]. These compounds have been shown to suppress IL-17 production and cyclooxygenase (COX)-2 expression, thereby suggesting a potential mechanism for therapeutic benefit in IL-17–driven diseases such as psoriasis. Despite traditional uses, scientific data validating the efficacy of *D. vulgaris* in dermatological conditions are scarce. In this context, the present study was designed to explore both the protective and therapeutic potential of topically administered *D. vulgaris* extract in a murine model of psoriasis induced by IMQ. Evaluations include macroscopic scoring using the Psoriasis Area and Severity Index (PASI), histological assessment using hematoxylin and eosin (H&E) staining to evaluate epidermal changes, and enzyme-linked immunosorbent assay (ELISA) for quantification of IL-17 levels in skin and spleen tissues.

2 Materials and Methods

2.1 Materials

Imiquimod 5% cream (Aldara®, MEDA) was used to induce psoriasis model in mice. Betamethasone dipropionate 0.1% cream (Betnovate®, GlaxoSmithKline) served as the positive control. A cold cream base (Havilland® oil-free cream, Evrensel Kozmetik A.S., Türkiye) was used as a vehicle. ELISA kit was sourced from Bioassay Technology Laboratory (Shanghai, China).

2.2 Animals

Twenty-four BALB/c mice (male and female, aged 2–3 months, weighing 25–30 g) were procured from the Marmara University Experimental Animals Research and Implementation Centre (DEHAMER, Istanbul, Türkiye). Experimental protocols received approval from the Marmara University Animal Ethics Committee (approval number 104.2021mar, dated 14 December 2021) and were performed in compliance with the Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines and the European Directive 2010/63/EU on the protection of animals used for scientific purposes. Animals were maintained under controlled environmental conditions (12-h light/dark cycle, temperature 22 ± 2 °C, relative humidity 50–60%) with unrestricted access to standard chow and water. All mice underwent a one-week acclimatization period before the start of the study.

2.3 Preparation of Plant Extract

D. vulgaris was taxonomically identified by Asst. Prof. Dr. Ismail Senkardes (Department of Pharmaceutical Botany, Faculty of Pharmacy, Marmara University, Türkiye), and a voucher specimen has been deposited in the Herbarium

under the accession number MARE-22299-a. The air-dried tubers were powdered and subjected to cold maceration in methanol. After filtration, the solvent was evaporated under reduced pressure at ≤ 50 °C using a rotary evaporator. The extract was stored at + 4 °C until use. Although the extract was not fully standardized to individual active compounds, it was prepared under controlled conditions using a consistent extraction protocol to ensure batch reproducibility.

2.4 Experimental Design

Mice were randomly divided into four groups (n = 6 per group):

Control group: 80 mg of cold cream (non-medicated base cream) was applied once daily.

IMQ group: Received 80 mg of 5% IMQ cream (equivalent to 4 mg IMQ) topically, once daily, to induce psoriasis [35]. To ensure consistency with treatment groups, a similar volume of cold cream (vehicle) was also applied after each IMQ dose.

IMQ + *D. vulgaris* group: Received IMQ as above, followed by 10 mg of *D. vulgaris* extract cream (in cold cream base) applied topically, once daily. Topical dosing of *D. vulgaris* (10 mg extract in 80 mg cold cream per application; ≈12.5% w/w) was chosen based on previous reports using crude botanical extracts or fractions in IMQ-induced psoriasis models [19, 20, 27].

IMQ + Betamethasone dipropionate group (positive control): Received IMQ as above, followed by 5 mg of betamethasone dipropionate cream topically, once daily [25].

All mice were monitored daily for skin changes and sacrificed on day 7. The application of a vehicle base to all groups ensured standardization of cream-related mechanical effects, which is recommended to control for nonspecific topical responses in experimental dermatology models [13, 14, 35].

2.5 Induction of Psoriasis

Psoriasis was induced following the protocol of van der Fits et al. [35]. The dorsal skin (~2 × 3 cm) was shaved and depilated. IMQ was administered topically to induce psoriasis for 6 days. Treatment creams were applied 30 min after each IMQ application in relevant groups.

2.6 Assessment of Skin Inflammation and Thickness

Clinical severity was evaluated using a modified Psoriasis Area and Severity Index (PASI) [24] adapted for murine models, based on semi-quantitative scoring of erythema, scaling, and skin thickness from 0 to 4 as previously described in IMQ-induced psoriasis studies in mice. Given the localized dorsal application area, the scoring focused on lesion severity parameters rather than whole-body surface area. To minimize observer-related subjectivity, PASI scoring was performed in a blinded manner by two independent observers who were unaware of the treatment groups. The final PASI score for each animal was calculated as the mean of the scores assigned by both observers. For erythema, scores were defined as follows: 0 = none, 1 = light red, 2 = red, 3 = dark red, and 4 = very dark red. Induration was graded as 0 = none, 1 = mild but detectable elevation, possibly with irregular borders, 2 = moderate elevation, 3 = marked elevation with well-defined borders, and 4 = very marked elevation with sharply demarcated borders. Scaling was scored as 0 = none, 1 = mild scaling covering part of the lesion, 2 = moderate to coarse scaling covering a large portion of the lesion, 3 = coarse, thick scaling covering most of the lesion, and 4 = very thick, coarse scales covering the entire lesion. The extent of body surface area involvement was graded as follows: < 10% = 1, 10–29% = 2, 30–49% = 3, 50–69% = 4, 70–89% = 5, and 90–100% = 6. The final PASI score was calculated using the formula (PASI = E + I + S) and recorded every 24 h throughout the study. This scoring approach is consistent with previously validated preclinical studies applying modified PASI systems to quantify disease severity in IMQ-induced murine psoriasis models [16], 30]. Skin thickness was additionally measured using a digital calliper (Hilka Tools, England) prior to each application [33, 35, 36].

2.7 Spleen Weight Measurement

At the end of the experimental period, all animals were euthanized under anaesthesia. The spleens were carefully excised and immediately weighed using a precision analytical balance. Spleen weights were recorded for each animal and used as an indicator of systemic immune activation, particularly in relation to the IL-17 in psoriasis pathogenesis [15, 32].

2.8 Histopathological Analysis

At the end of the experimental period, skin samples were excised from the IMQ-treated dorsal skin areas. Tissue specimens were fixed in 10% neutral-buffered formalin for at least 48 h at room temperature. After fixation, samples were dehydrated through graded ethanol solutions (70%, 90%, 96%, and 100%), cleared in xylene, and embedded in paraffin. Paraffin blocks were sectioned at a thickness of 5 µm using a rotary microtome.

Sections were stained with H&E for general histological evaluation. All sections were examined using a light microscope (LEICA DM 1000, Germany). For each animal, five non-overlapping, randomly selected fields from representative sections were evaluated at × 100 and × 200 magnifications. Histopathological assessment

was performed according to hallmark features of IMQ-induced psoriasis-like dermatitis, including epidermal hyperproliferation, abnormal keratinocyte differentiation, inflammatory cell infiltration, and dermal vascular alterations (Table 1). Total histopathological score is minimum 0, maximum 24. Higher scores indicate increased severity of psoriasis-like histopathological alterations. Histopathological scoring parameters were selected based on previously established criteria for IMQ-induced psoriasis-like dermatitis, including epidermal hyperplasia, parakeratosis, hyperkeratosis, Munro microabscess formation, dermal inflammatory infiltration, and vascular alterations [9, 13, 14, 34].

2.9 Cytokine Measurement

IL-17 levels were measured in both skin and spleen tissues using an ELISA, in accordance with the manufacturer's instructions [28].

2.10 Statistical Analysis

All results are presented as the mean ± standard error of the mean (SEM). Statistical evaluations were carried out using GraphPad Prism version 9.0 (GraphPad Software Inc., San Diego, CA, USA). Differences between groups were assessed using one-way or two-way analysis of variance (ANOVA), followed by Tukey's multiple-comparison post hoc test. A p-value < 0.05 was considered indicative of statistical significance.

3 Results

3.1 Clinical Assessment of Psoriatic Lesions

Topical administration of 5% IMQ for 6 consecutive days on the dorsal skin of BALB/c mice successfully induced psoriasis-like skin inflammation characterized by progressive erythema, induration, and scaling. PASI, which integrates scores for erythema, induration, and scaling (each rated 0–4), was used for semi-quantitative clinical evaluation. The IMQ-only group showed a significant increase in PASI scores from day 2 onward, peaking on days 5–7 ($p < 0.001$ *vs*. control), confirming robust model induction.

In contrast, mice treated with *D. vulgaris* extract and betamethasone displayed a marked reduction in all clinical parameters, especially from day 3; erythema and scaling scores were significantly decreased by day 6–7, suggesting an anti-inflammatory and keratinocyte-modulating effect. *D. vulgaris* treatment resulted in the most pronounced clinical improvement, with PASI scores approaching control levels by day 6 ($p < 0.001$ *vs*. IMQ group). The daily progression of PASI scores is presented in Fig. 1, while representative macroscopic skin appearances are shown in Table 2.

3.2 Skin Thickness Measurements

In parallel with clinical severity, dorsal skin thickness significantly increased in the IMQ group due to acanthosis and dermal oedema ($p < 0.001$ *vs*. control). Treatment with *D. vulgaris* significantly attenuated this increase ($p < 0.001$), almost as effective as betamethasone ($p < 0.001$), which nearly normalized skin thickness by day 6. Figure 2

Table 1 Histopathological scoring system for IMQ-induced psoriasis

Category	Parameter	Score 0	Score 1	Score 2	Score 3
Epidermal changes	Acanthosis (epidermal hyperplasia)	Normal epidermal thickness	Mild hyperplasia	Moderate hyperplasia	Severe hyperplasia with elongated rete ridges
	Hyperkeratosis	Absent	Mild	Moderate	Severe
	Parakeratosis	Absent	Focal	Multifocal	Diffuse
	Granular layer alteration	Normal	Slightly Focal reduced	Markedly reduced	Absent
Inflammatory changes	Neutrophil accumulation	Absent	Rare	Moderate	Abundant
	Dermal inflammatory cell infiltration	Absent	Mild	Moderate	Severe
Dermal and vascular changes	Dermal papilla elongation	Absent	Mild	Moderate	Severe
	Vascular dilatation/angiogenesis	Normal	Mild capillary dilatation	Moderate increase in vascular density	Marked dilatation and prominent angiogenesis

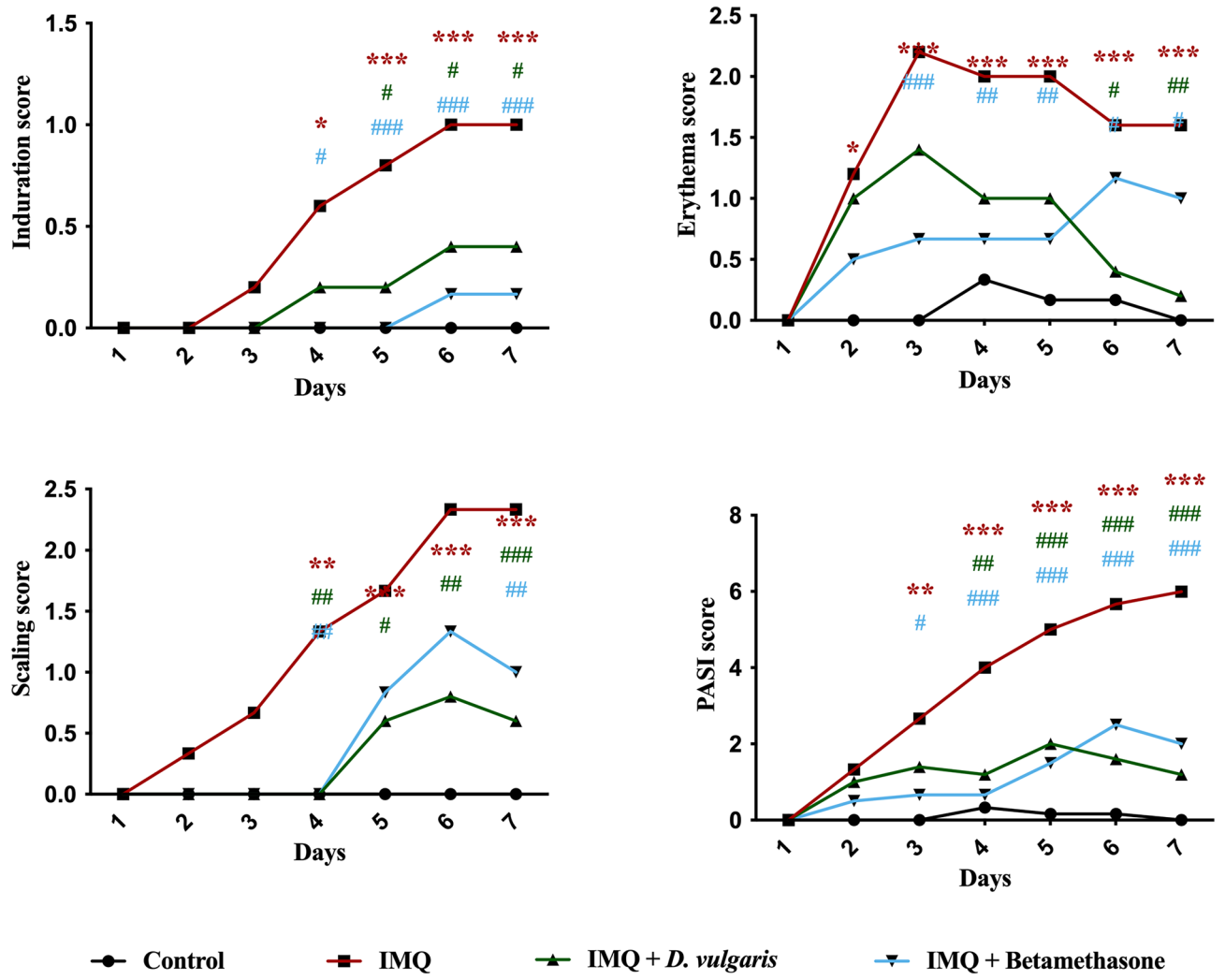


Fig. 1 Effects of *Dracunculus vulgaris* on psoriasis skin lesions. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; IMQ + Betamethasone: Psoriasis + Betamethasone group; PASI: Psoriasis Area and Severity Index. Data are presented as mean. Statistical analysis was performed using two-way ANOVA followed by Tukey's post hoc test. ** $p < 0.01$, and *** $p < 0.001$ *vs*. Control group. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$, and $^{\#\#\#}p < 0.001$ *versus* IMQ group

illustrates the group-wise comparison of skin thickness values, supporting the macroscopic findings.

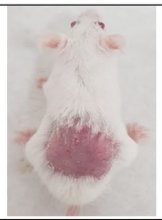
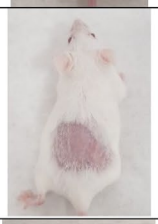
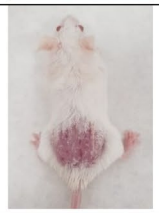
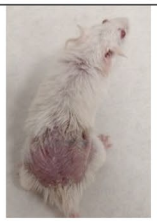
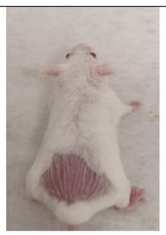
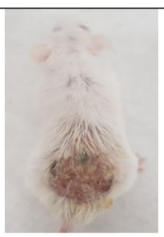
3.3 Spleen Weight as a Systemic Inflammation Indicator

IMQ application also led to a significant increase in spleen weight (splenomegaly), reflecting systemic immune activation, particularly via IL-17–mediated pathways. Mean spleen weight in the IMQ group was significantly higher than in controls ($p < 0.001$). Treatment with *D. vulgaris* extract moderately reduced spleen weight ($p < 0.01$ *vs*. IMQ), while the reduction was more substantial and statistically significant in the betamethasone group ($p < 0.001$ *vs*. IMQ), indicating stronger suppression of systemic inflammation (Fig. 3). In addition, the spleen photographs of different groups are shown in Table 3.

3.4 Histopathological Analysis

Histological examination of H&E-stained skin sections from the control group revealed a normal epidermal architecture, intact granular layer, and absence of inflammatory cell infiltration. In the IMQ-treated group, histological examination revealed severe disruption of the epidermal architecture. The epithelial layer exhibited a completely irregular and disorganized structure, with marked loss of normal stratification. These alterations were accompanied by pronounced epidermal thickening, diffuse hyperkeratosis, parakeratosis, elongated rete ridges, and prominent spongiosis. Dermal

Table 2 Macroscopic observation of the effects of *Dracunculus vulgaris* on psoriasis skin lesions

Days/ Groups	Control	IMQ	IMQ + *D. vulgaris*	IMQ + Betamethasone
1				
2				
3				
4				
5				
6				
7				

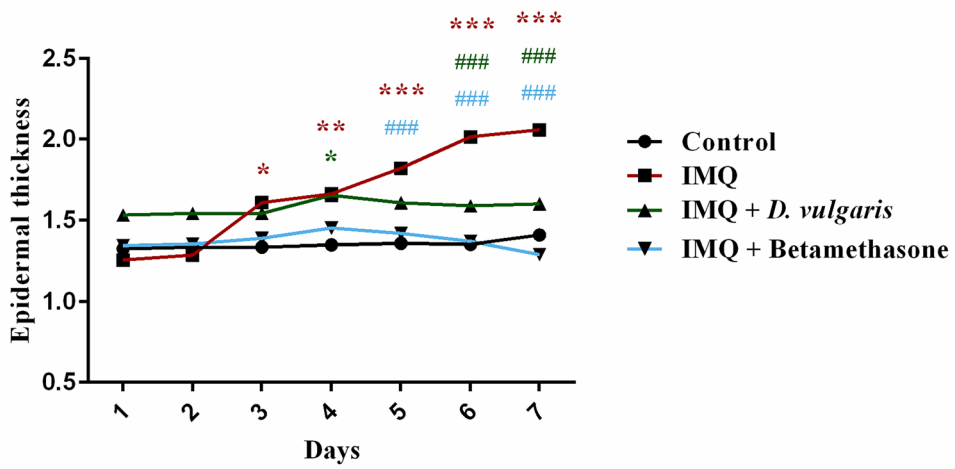


Fig. 2 Effects of *Dracunculus vulgaris* on psoriasis skin lesions. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; IMQ + Betamethasone: Psoriasis + Betamethasone group. Data are presented as mean ± SEM. Statistical analysis was performed using two-way ANOVA followed by Tukey's post hoc test. * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$ *vs*. Control group. ### $p < 0.001$ *versus* IMQ group

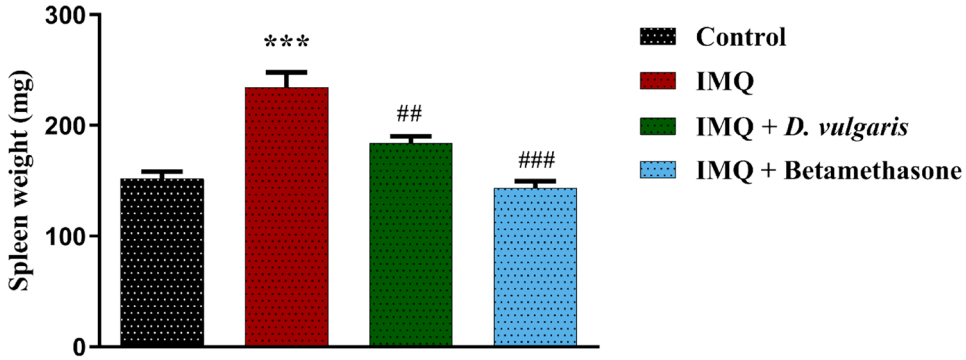


Fig. 3 Effect of *Dracunculus vulgaris* on spleen weights of IMQ-induced mice. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; IMQ + Betamethasone: Psoriasis + Betamethasone group. Data are presented as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test. *** $p < 0.001$ *vs*. Control group. ## $p < 0.01$ and ### $p < 0.001$ *versus* IMQ group

Table 3 Photographs of mouse spleens on the last day of the experiment

Groups	Spleen Photograph
Control	
IMQ	
IMQ + *D. vulgaris*	
IMQ + Betamethasone	

IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; IMQ + Betamethasone: Psoriasis + Betamethasone group

alterations in the IMQ group included elongation of dermal papillae, dilated and congested capillaries, and dense inflammatory cell infiltration, confirming the successful induction of psoriasis-like dermatitis.

In contrast, skin sections from the *D. vulgaris*–treated group demonstrated a partial restoration of normal epidermal architecture. Epidermal hyperplasia was notably reduced, with attenuated acanthosis, improved stratification, and a marked decrease in dermal inflammatory cell infiltration compared to the IMQ group. Similar but less pronounced histological improvements were observed in the betamethasone-treated group (Fig. 4).

Semi-quantitative histopathological scoring revealed a significant increase in total psoriasis scores in the IMQ group compared with the control group ($p < 0.001$). Both treatment groups showed a statistically significant reduction in histopathological scores relative to the IMQ group ($p < 0.001$ *vs.* IMQ) (Fig. 5).

In summary, the histopathological data demonstrated severe psoriasiform changes in the IMQ group, a moderate

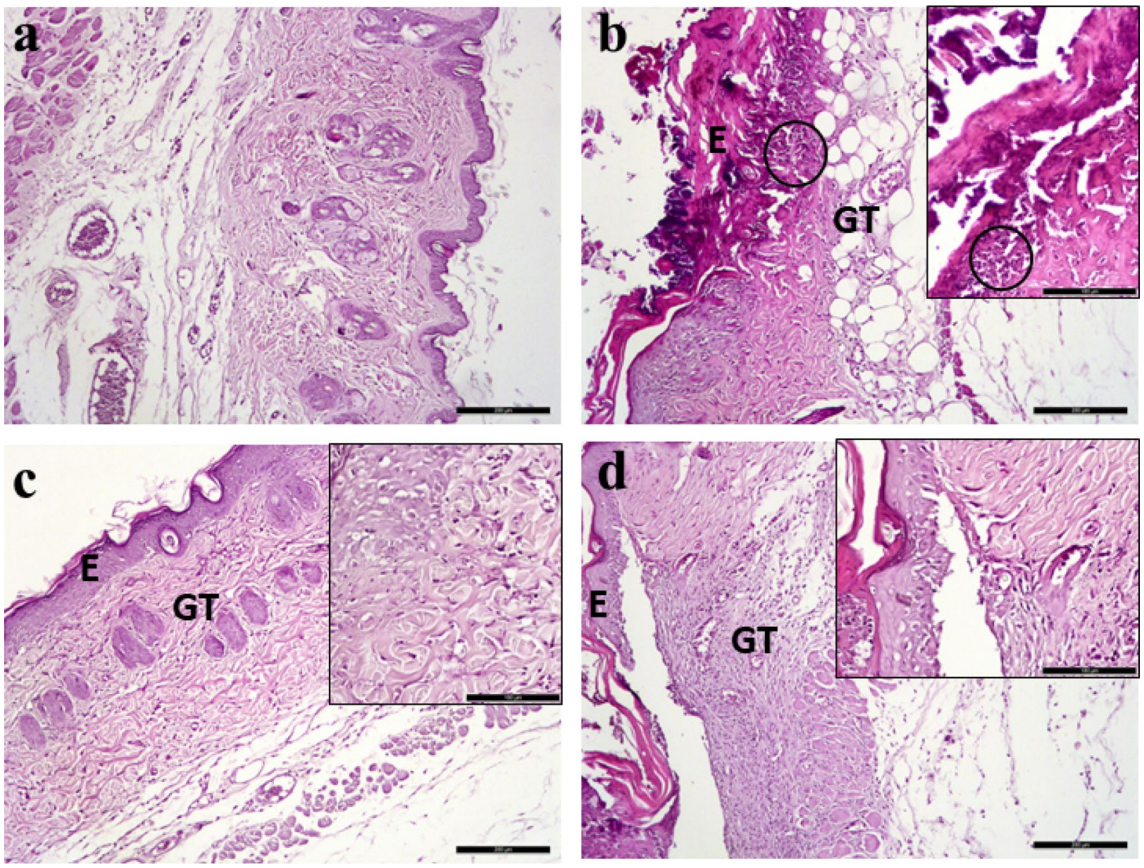


Fig. 4 Photomicrographs of H&E-stained skin from control (**a**), IMQ (**b**), IMQ + *D. vulgaris* (**c**), and IMQ + Betamethasone (**d**). The circles indicate neutrophil infiltration. E: epithelium, GT: granulation tissue. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; and IMQ + Betamethasone: Psoriasis + Betamethasone group. Inserts show better epidermal and dermal organization between groups. Scale bars: 200 µm; Scale bars of inserts: 100 µm

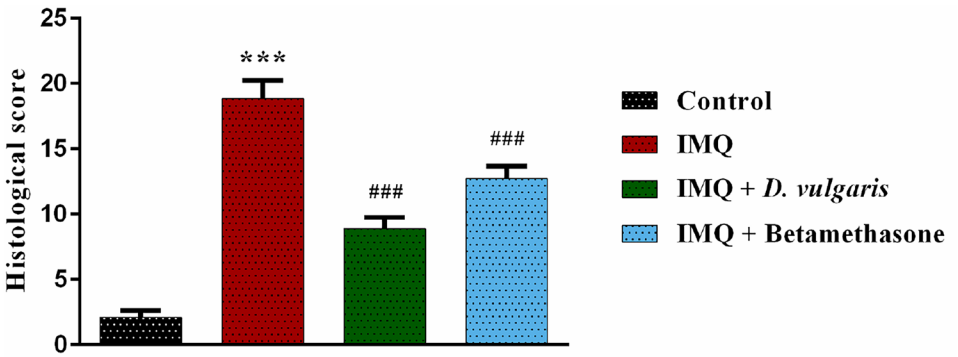


Fig. 5 Quantitative analysis of semi-histopathological scores. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; and IMQ + Betamethasone: Psoriasis + Betamethasone group. Data are presented as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test. *** $p < 0.001$ *versus* Control group, ### $p < 0.01$ *versus* IMQ group

reduction in histological severity in the betamethasone-treated group, and a more marked reduction in histopathological scores in the *D. vulgaris* –treated group.

3.5 IL-17 Cytokine Levels in Skin and Spleen Tissues

To assess the impact of treatments on T helper 17 (Th17)-mediated inflammation, IL-17 levels were measured in spleen and epidermal tissue homogenates using ELISA (Fig. 6). Topical application of 5% IMQ did not significantly elevate IL-17 levels in either tissue compared to the control group. In spleen samples, IL-17 concentrations were even slightly reduced in the IMQ group, whereas betamethasone and *D. vulgaris*-treated groups exhibited moderately higher levels, although differences were not statistically significant. In epidermal tissues, IL-17 levels remained comparable

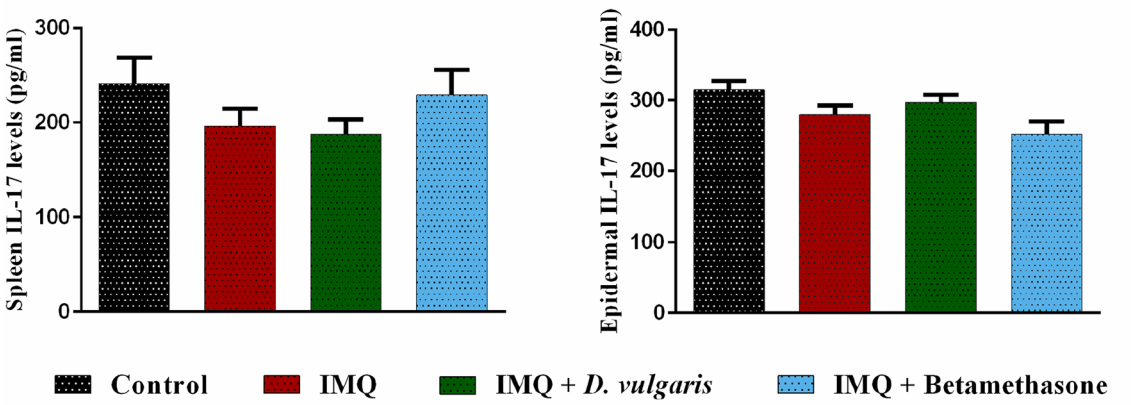


Fig. 6 IL-17 levels in spleen (left) and epidermal (right) tissue homogenates measured by ELISA. IMQ: Psoriasis group; IMQ + *D. vulgaris*: Psoriasis + *D. vulgaris* group; IMQ + Betamethasone: Psoriasis + Betamethasone group. Data are presented as mean ± SEM. Statistical analysis was performed using one-way ANOVA followed by Tukey's post hoc test

across all groups, with a slight decrease observed in the betamethasone group.

4 Discussion

This study suggests that *D. vulgaris* extract provides evidence for therapeutic effects in an IMQ-induced murine model of psoriasis. Evaluation across several outcome measures—including clinical, histological, and biochemical parameters—demonstrated parallel improvements in disease severity, supporting the possibility that *D. vulgaris* may influence psoriasis through diverse biological effects.

Topical IMQ successfully induced psoriatic inflammation, as evidenced by sharp increases in PASI components: erythema, induration, and scaling. From day 2 onwards, IMQ-treated mice displayed progressive lesion severity, peaking at days 5–7. In contrast, topical application of *D. vulgaris* extract markedly reduced all PASI parameters. These improvements were statistically significant and became evident as early as day 3, with PASI scores approaching baseline by day 6. Across several evaluated parameters, topical *D. vulgaris* treatment produced improvements that were within a similar quantitative range to those observed with betamethasone, without indicating statistical superiority. Similar phenotype-oriented improvements have been widely reported in IMQ-induced psoriasis models treated with experimental small molecules and herbal derivatives, even in the absence of uniform cytokine modulation, supporting the relevance of phenotypic and histopathological endpoints in preclinical screening [2, 3]. These results align with the known anti-inflammatory [12] and antioxidant [5, 6] properties of *D. vulgaris*, documented in previous phytopharmacological studies.

Macroscopic photographs of the dorsal skin further support these findings. While IMQ-treated mice exhibited widespread erythema, scaling, and thick plaques, those treated with *D. vulgaris* showed visibly attenuated lesions, with clearer skin and reduced desquamation by the end of the treatment period. The improved gross morphology, in combination with objective PASI scoring, strengthens the evidence for the topical efficacy of *D. vulgaris*.

The measurement of skin thickness—a surrogate for keratinocyte hyperproliferation and dermal inflammation—also confirmed therapeutic effects. IMQ significantly increased dorsal skin thickness, likely due to acanthosis and oedema, consistent with previous models [35]. Treatment with *D. vulgaris* significantly reduced this thickening, nearly normalizing epidermal measurements. The reduction was comparable to that seen with betamethasone, reinforcing the potential of the extract as an anti-psoriatic agent.

To evaluate systemic inflammation, spleen weights were analysed. IMQ-induced splenomegaly is a well-known indicator of systemic immune activation [32]. In our study, spleen weights were significantly elevated in the IMQ group. Treatment with *D. vulgaris* led to a noticeable reduction, suggesting that its effects may not be limited to the epidermis but may also modulate systemic immune responses. Visual examination of spleen size corroborated these findings, with gross photographs showing smaller spleens in the treatment groups compared to IMQ-only animals.

The histopathological findings strongly support the clinical observations and provide structural evidence for the anti-psoriatic activity of *D. vulgaris*. IMQ application induced classical psoriasiform alterations, including marked epidermal hyperplasia, parakeratosis, elongation of rete ridges, spongiosis, and dense dermal inflammatory infiltration, confirming successful model induction infiltration [35]. Topical treatment with *D. vulgaris* substantially

ameliorated these pathological features, as demonstrated by reduced acanthosis, improved epidermal stratification, and attenuated dermal inflammation. Although both *D. vulgaris* and betamethasone significantly improved histological parameters compared to the IMQ group, differences between the two treatment groups should be interpreted cautiously and are best viewed as quantitative trends rather than definitive evidence of superior efficacy. These findings suggest that the extract exerts a meaningful modulatory effect on both epidermal hyperproliferation and dermal inflammation, which are hallmarks of psoriatic pathology, and reinforce the therapeutic relevance of the observed macroscopic and clinical improvements. Notably, recent studies emphasize that histopathological normalization in IMQ-induced models often correlates more consistently with clinical severity scores than with single-cytokine readouts, highlighting the translational value of tissue-level endpoints [17].

Regarding cytokine analysis, IL-17 levels in skin and spleen homogenates did not significantly increase in the IMQ group compared to controls. In fact, IL-17 levels were slightly decreased, which initially appeared counterintuitive given its well-established role in psoriasis pathogenesis [11, 22, 35]. However, this result may be attributed to the immunological profile of the BALB/c mouse strain used in this study. BALB/c mice have been shown to exhibit a more Th2-prone response and may not replicate the same IL-17–dominant cytokine environment seen in C57BL/6 mice [33]. Accordingly, the absence of robust IL-17 elevation should be interpreted as a limitation of the model rather than evidence against disease induction. Consistent with recent literature, this finding further supports the notion that IMQ-induced psoriasiform inflammation—particularly in BALB/c mice—may proceed through heterogeneous or partially overlapping inflammatory pathways. Beyond IL-17–centered pathways, recent exploratory studies using the IMQ-induced psoriasis model have highlighted the involvement of additional inflammatory and cellular mechanisms, including dysregulation of keratinocyte proliferation, oxidative stress responses, and modulation of innate immune signalling cascades. For instance, recent studies have demonstrated that therapeutic agents targeting epidermal differentiation, NF-κB signalling, and cytokine–keratinocyte crosstalk can significantly ameliorate psoriasiform pathology in IMQ-treated mice, even in the absence of robust IL-17 modulation [29, 31]. These findings support the interpretation that phenotypic and histopathological improvements may arise through multifactorial mechanisms rather than a single dominant cytokine axis.

While the present study demonstrated consistent clinical, histopathological, and systemic improvements following topical administration of *D. vulgaris* extract in an IMQ-induced mouse model, several limitations should be considered when interpreting the findings. The relatively small sample size (n = 6 per group) may limit statistical power and generalizability. In addition, the use of a single animal strain (BALB/c) and one experimental psoriasis model (IMQ) may not fully capture the complexity and heterogeneity of psoriasis pathophysiology. Importantly, the present work was designed as an exploratory, phenotype-oriented study, and mechanistic investigations were therefore limited. As also highlighted in recent IMQ-based preclinical studies, robust phenotypic and histopathological improvements may precede or occur independently of clearly defined cytokine signatures, particularly in strain-dependent contexts [3, 17]. Molecular analyses were confined primarily to IL-17 measurement, which did not show significant modulation in this dataset. As such, the observed therapeutic effects of *D. vulgaris* should not be interpreted as evidence of a defined cytokine-specific mechanism, but rather as an indication of broader anti-inflammatory or tissue-modulating activity. Comprehensive molecular and cellular analyses, including expanded cytokine profiling, gene expression studies, and characterization of immune cell populations and keratinocyte activation markers, would provide deeper mechanistic insight in future studies. In line with recent exploratory studies in the IMQ model, future investigations into *D. vulgaris* may benefit from assessing its effects on broader inflammatory signalling networks, epidermal differentiation markers, oxidative stress pathways, and immune–epidermal interactions, which have been shown to critically influence disease severity and therapeutic response in preclinical psoriasis research [29, 31]. Finally, although the extract exhibited clear biological activity, further phytochemical characterization and standardization of its active constituents will be important to enhance reproducibility and support translational development.

5 Conclusion

In this study, *D. vulgaris* extract showed significant therapeutic potential in reducing clinical symptoms, histopathological damage, and spleen enlargement in an IMQ-induced psoriasis model. The extract's efficacy was comparable to that of betamethasone, particularly in improving skin thickness, erythema, and scaling. Histological improvements further supported the anti-inflammatory and regenerative effects of the treatment. Although IL-17 levels did not differ significantly, this may be attributed to strain-specific immune responses in BALB/c mice. These findings highlight *D. vulgaris* as a promising candidate for future research in plant-based topical psoriasis therapies.

Acknowledgements This study was supported by The Scientific and Technological Research Council of Türkiye (TÜBİTAK) under Grant number 1919B012110748.

Author Contributions Ayse Nur Hazar-Yavuz: Investigation, Data curation, Visualization, Writing – original draft. Busra Cetin: Methodology, Validation, Data curation. Humeysa Kiyak-Kirmaci: Methodology, Validation, Data curation. Gül Sinemcan Karataş: Investigation, Formal analysis. Turgut Taskin: Investigation, Formal analysis. İsmail Senkardes: Investigation, Data curation. Cansu Arslan: Methodology. Hatice Kubra Elcioglu: Resources, Supervision. Levent Kabasakal: Resources, Supervision, Writing – review & editing.

Funding Open access funding provided by the Scientific and Technological Research Council of Türkiye (TÜBİTAK).

Data Availability The authors do not have permission to share data.

Declarations

Conflict of interest The authors declare no competing interests.

Open Access This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

References

1. Abbas AH, Abbood MS, Ridha-Salman H, Fakhri SA, Abbas ZH, Al-Athari AJH. Suppressive effect of topical moxifloxacin on imiquimod-induced model of psoriasis in mice. Naunyn Schmiedebergs Arch Pharmacol. 2025;398(12):17089–108. https://doi.org/10.1007/s00210-025-04317-2.
2. Abbas AH, Hassan ZM, Albarki MA, Zigam QA, Ridha-Salman H, Abbas HAM, et al. Mitigative effects of a topically-applied combination of cimifugin and vinpocetine on a murine psoriasis-like model. Pharmakeftiki. 2025;37:20–4. https://doi.org/10.60988/p.v37i2S.134.
3. Ali BF, Abu-Raghif AR, Ridha-Salman H. Protective effect of cinnarizine on imiquimod-induced mouse model of psoriasis. J Res Pharm. 2025;29(4):1783–91. https://doi.org/10.12991/jrespharm.1734970.
4. Ali BF, Abu-Raghif AR, Ridha-Salman H, Al-Athari AJH. Vildagliptin topical ointment: an effective treatment for imiquimod-induced psoriasis in mice. J Mol Histol. 2025;56(3):143. https://doi.org/10.1007/s10735-025-10416-4.
5. Aslantürk ÖS, Aşkın Çelik T. Potential antioxidant activity and anticancer effect of extracts from *Dracunculus vulgaris* Schott. tubers on MCF-7 breast cancer cells. Int J Res Pharm Biomed Sci. 2013;4(2):394–404.
6. Aydın Ç, Özay C, Düşen O, Mammadov R, Orhan F. Total phenolics, antioxidant, antibacterial and cytotoxic activity studies of ethanolic extracts Arisarum vulgare O. Targ. Tozz. and *Dracunculus vulgaris* Schott. Int J Second Metab. 2017;4(2):114–22. https://doi.org/10.21448/ijsm.307944.
7. Baliwag J, Barnes DH, Johnston A. Cytokines in psoriasis. Cytokine. 2015;73(2):342–50. https://doi.org/10.1016/j.cyto.2014.12.014.
8. Erarslan ZB, Ecevit-Genç G, Kültür Ş. Medicinal plants traditionally used to treat skin diseases in turkey–eczema, psoriasis, vitiligo. J Fac Pharm Ankara Univ. 2020;44(1):137–66. https://doi.org/10.33483/jfpau.586114.
9. Flutter B, Nestle FO. TLRs to cytokines: mechanistic insights from the imiquimod mouse model of psoriasis. Eur J Immunol. 2013;43(12):3138–46. https://doi.org/10.1002/eji.201343801.
10. Furue M, Furue K, Tsuji G, Nakahara T. Interleukin-17A and keratinocytes in psoriasis. Int J Mol Sci. 2020;21(4):1275. https://doi.org/10.3390/ijms21041275.
11. Gaffen SL, Jain R, Garg AV, Cua DJ. The IL-23-IL-17 immune axis: from mechanisms to therapeutic testing. Nat Rev Immunol. 2014;14(9):585–600. https://doi.org/10.1038/nri3707.
12. Gürağaç FT, Ilhan M, Küpeli Akkol E. The struggle with rheumatism through *Dracunculus vulgaris* Schott: in the light of ethnobotanical information. J Orthop Trauma Surg Relat Res. 2018;13:25.
13. Hawkes JE, Chan TC, Krueger JG. Psoriasis pathogenesis and the development of novel targeted immune therapies. J Allergy Clin Immunol. 2017;140(3):645–53. https://doi.org/10.1016/j.jaci.2017.07.004.
14. Hawkes JE, Gudjonsson JE, Ward NL. The snowballing literature on imiquimod-induced skin inflammation in mice: a critical appraisal. J Invest Dermatol. 2017;137(3):546–9. https://doi.org/10.1016/j.jid.2016.10.024.
15. Horváth S, Komlódi R, Perkecz A, Pintér E, Gyulai R, Kemény Á. Methodological refinement of Aldara-induced psoriasiform dermatitis model in mice. Sci Rep. 2019;9(1):3685. https://doi.org/10.1038/s41598-019-39903-x.
16. Khafaji AWM, Al-Zubaidy AAK, Farhood IG, Ridha-Salman H. Ameliorative effects of topical ramelteon on imiquimod-induced psoriasiform inflammation in mice. Naunyn Schmiedebergs Arch Pharmacol. 2024;397(8):6231–48. https://doi.org/10.1007/s00210-024-03017-7.
17. Khorsheed SM, Abu-Raghif AR, Ridha-Salman H. Alleviative effects of combined topical melatonin and rutin on imiquimod-induced psoriasis mouse model. Pharmacia (Warsz). 2024;71:1–13. https://doi.org/10.3897/pharmacia.71.e128832.
18. Lande R, Gregorio J, Facchinetti V, Chatterjee B, Wang YH, Homey B, et al. Plasmacytoid dendritic cells sense self-DNA coupled with antimicrobial peptide. Nature. 2007;449(7162):564–9. https://doi.org/10.1038/nature06116.
19. Li Q, Liu W, Gao S, Sun J, Zhang L, Shen X. Application of imiquimod-induced murine psoriasis model in evaluating interleukin-17A antagonist. BMC Immunol. 2021;22:11. https://doi.org/10.1186/s12865-021-00401-3.
20. Li Y, Zong J, Ye W, Fu Y, Gu X, Pan W, et al. *Pithecellobium clypearia*: amelioration effect on ımiquimod-ınduced psoriasis in mice based on a tissue metabonomic analysis. Front Pharmacol. 2021;12:748772. https://doi.org/10.3389/fphar.2021.748772.
21. Lima EdeA, Lima MdeA. Reviewing concepts in the immunopathogenesis of psoriasis. An Bras Dermatol. 2011;86(6):1151–8. https://doi.org/10.1590/s0365-05962011000600014.
22. Lowes MA, Suárez-Fariñas M, Krueger JG. Immunology of psoriasis. Annu Rev Immunol. 2014;32:227–55. https://doi.org/10.1146/annurev-immunol-032713-120225.
23. Luo DQ, Wu HH, Zhao YK, Liu JH, Wang F. Original research: different imiquimod creams resulting in differential effects for imiquimod-induced psoriatic mouse models. Exp Biol Med (Maywood). 2016;241(16):1733–8. https://doi.org/10.1177/1535370216647183.
24. Marks R, Barton SP, Shuttleworth D, Finlay AY. Assessment of disease progress in psoriasis. Arch Dermatol. 1989;125(2):235–40. https://doi.org/10.1001/archderm.1989.01670140087017.
25. Mori H, Arita K, Yamaguchi T, Hirai M, Kurebayashi Y. Effects of topical application of betamethasone on imiquimod-induced

psoriasis-like skin inflammation in mice. Kobe J Med Sci. 2016;62(4):79–88.
26. Moos S, Mohebiany AN, Waisman A, Kurschus FC. Imiquimod-induced psoriasis in mice depends on the IL-17 signaling of keratinocytes. J Invest Dermatol. 2019;139(5):1110–7. https://doi.org/10.1016/j.jid.2019.01.006.
27. Parmar KM, Itankar PR, Joshi A, Prasad SK. Anti-psoriatic potential of *Solanum xanthocarpum* stem in imiquimod-induced psoriatic mice model. J Ethnopharmacol. 2017;198:158–66. https://doi.org/10.1016/j.jep.2016.12.046.
28. Polat EB, Hazar-Yavuz AN, Guler E, Ozcan GS, Taskin T, Duruksu G, et al. Sublingual administration of *Teucrium polium*-loaded nanofibers with ultra-fast release in the treatment of diabetes mellitus: *in vitro* and *in vivo* evaluation. J Pharm Sci. 2024;113(4):1068–87. https://doi.org/10.1016/j.xphs.2023.12.013.
29. Ridha-Salman H, Al-Zubaidy AA, Abbas AH, Hassan DM, Malik SA. The alleviative effects of canagliflozin on imiquimod-induced mouse model of psoriasis-like inflammation. Naunyn Schmiedebergs Arch Pharmacol. 2025;398(3):2695–715. https://doi.org/10.1007/s00210-024-03406-y.
30. Ridha-Salman H, Al-Zubaidy AA, Abbas AH, Zigam QA. The ameliorative effects of topical gemifloxacin alone or in combination with clobetasol propionate on imiquimod-induced model of psoriasis in mice. Naunyn Schmiedebergs Arch Pharmacol. 2024;397(1):599–616. https://doi.org/10.1007/s00210-023-02629-9.
31. Ridha-Salman H, Shihab EM, Hasan HK, Abbas AH, Khorsheed SM, Ayad Fakhri S. Mitigative effects of topical norfloxacin on an imiquimod-induced murine model of psoriasis. ACS Pharmacol Transl Sci. 2024;7(9):2739–54. https://doi.org/10.1021/acsptsci.4c00152.
32. Shinno-Hashimoto H, Eguchi A, Sakamoto A, Wan X, Hashimoto Y, Fujita Y, et al. Effects of splenectomy on skin inflammation and psoriasis-like phenotype of imiquimod-treated mice. Sci Rep. 2022;12(1):14738. https://doi.org/10.1038/s41598-022-18900-7.
33. Swindell WR, Michaels KA, Sutter AJ, Diaconu D, Fritz Y, Xing X, et al. Imiquimod has strain-dependent effects in mice and does not uniquely model human psoriasis. Genome Med. 2017;9(1):24. https://doi.org/10.1186/s13073-017-0415-3.
34. Tran PTT, Le LT, Le TTV, Van TT, Vu NB. Effects of ımiquimod application durations on psoriasis-like lesions and cytokine expression in mice. Biomed Res Ther. 2024;11(5):6387–401. https://doi.org/10.15419/bmrat.v11i5.885.
35. van der Fits L, Mourits S, Voerman JSA, Kant M, Boon L, Laman JD, et al. Imiquimod-induced psoriasis-like skin inflammation in mice is mediated via the IL-23/IL-17 axis. J Immunol. 2009;182(9):5836–45. https://doi.org/10.4049/jimmunol.0802999.
36. Wu DH, Zhang MM, Li N, Li X, Cai QW, Yu WL, et al. PSORI-CM02 alleviates IMQ-induced mouse dermatitis via differentially regulating pro- and anti-inflammatory cytokines targeting of Th2 specific transcript factor GATA3. Biomed Pharmacother. 2019;110:265–74. https://doi.org/10.1016/j.biopha.2018.11.092.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.