Drug Design, Development and Therapy

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REVIEW

Therapeutic Potential of Curcumin and Novel Formulations in Psoriasis Treatment: Evidence and Future Prospects

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Abstract: Psoriasis is a chronic inflammatory skin disease characterized by thickened, erythematous, and scaly plaques that significantly impact patients' quality of life. Although various treatments are available, they often cause adverse effects, prompting the exploration of alternative therapies. Curcumin, a bioactive compound in *Curcuma longa* Linn. (turmeric), has demonstrated potential benefits in managing psoriasis. This article aims to comprehensively evaluate the anti-psoriatic activity, efficacy, and safety profiles of curcumin and its novel formulations, as well as to discuss future directions for enhancing their use as an alternative treatment for psoriasis. Curcumin exerts its anti-psoriatic effects through multi-targeted actions, including inhibiting cell proliferation, inducing apoptosis, suppressing pro-inflammatory cytokines, and enhancing skin barrier proteins, thereby alleviating psoriasis lesions. However, both oral and topical curcumin formulations face challenges, such as low bioavailability and limited skin penetration, underscoring the need for novel formulations to improve therapeutic outcomes. Clinical findings suggest that oral curcumin may provide greater efficacy and better tolerance as an adjunctive therapy for moderate to severe psoriasis, while topical formulations may help reduce severity and improve well-being in mild to moderate cases. Overall, curcumin and its novel formulations show promise as therapeutic agents for psoriasis treatment. However, further research, particularly large-scale clinical trials, is essential to evaluate long-term efficacy and safety comprehensively.

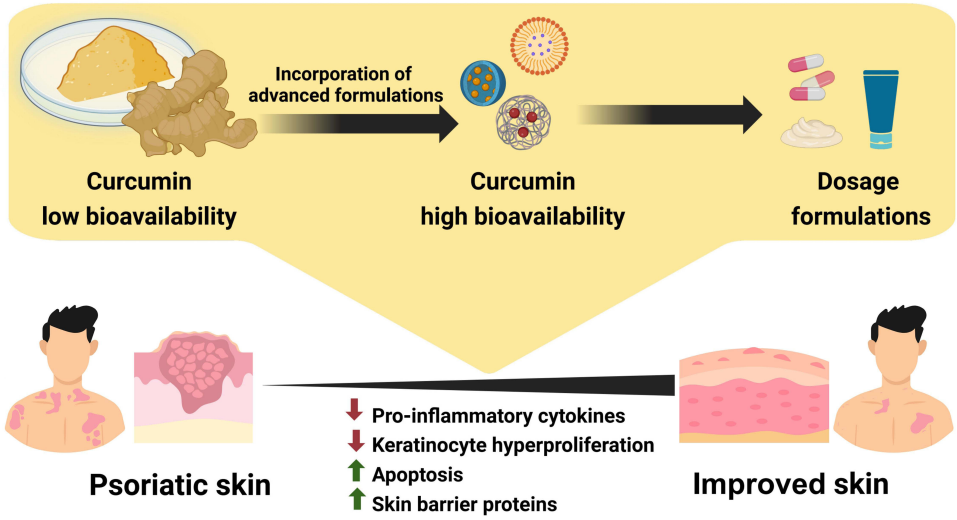
Keywords: curcumin, curcuma, psoriasis, herbal medicine, formulation

Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that affects approximately 2–3% of the global population.[1] It has been recognized by the World Health Organization as a serious non-communicable disease.[2] Psoriasis is classified into several types: plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, and erythrodermic psoriasis.[3] Plaque psoriasis, or psoriasis vulgaris, is the most prevalent form, characterized by circumscribed, thickened, scaly, and itchy plaques commonly found on the elbows, knees, scalp, and lower back, though it can appear on any skin surface.[4] Additionally, psoriasis is frequently associated with comorbidities such as psoriatic arthritis, metabolic syndrome, cardiovascular disease, and psychosocial disability, all of which significantly reduce patients' quality of life and well-being.[5] Moreover, several psoriasis patients still face challenges, including variable treatment responses, limited healthcare access, and social stigma.[4]

Received: 3 February 2025
Accepted: 28 May 2025
Published: 25 June 2025

Graphical Abstract



The pathogenesis of psoriasis is primarily driven by immune cell dysregulation, particularly involving T cells and dendritic cells, alongside keratinocyte hyperproliferation. This process unfolds in two main stages: the initial activation stage and the psoriasis stage. In the initial stage, keratinocytes are activated by various factors, including genetic predisposition and environmental triggers such as infections, medications, and trauma.[6] These stimuli activate immune responses, leading to the recruitment and activation of dendritic cells.[7] Activated dendritic cells then release pro-inflammatory cytokines like interferon-γ (IFN-γ), tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and IL-1β, which drive an inflammatory cascade.[8] This cascade promotes activation and migration of T helper cell (Th) 1 (Th1) and Th17 cells, resulting in the release of additional psoriasis-related pro-inflammatory cytokines, including IL-17, IL-22, IL-23, TNF-α, and IFN-γ. These cytokines activate keratinocytes, setting off further events that culminate in hyperproliferation and abnormal differentiation, which are hallmark features of the psoriasis stage.[9] This cytokine-mediated feedback loop further exacerbates the disease by sustaining chronic inflammation, ultimately resulting in thickened, scaly plaques and erythema observed in psoriatic lesions.[10]

Treatment for psoriasis includes various therapeutic approaches aimed at reducing inflammation, alleviating skin lesions, and improving patients' quality of life.[11] The choice of treatment depends on the location and severity of the disease.[9] For mild to moderate psoriasis, topical treatments such as corticosteroids, vitamin D3 analogs, and calcineurin inhibitors are commonly used.[12] In cases of insufficient response, phototherapy approaches, including ultraviolet B (UVB) and psoralen plus ultraviolet A (PUVA) therapies, may be considered adjunctive treatments.[13,14] For moderate to severe psoriasis, management typically includes systemic agents such as methotrexate, cyclosporine, and acitretin, as well as biologics like adalimumab (a TNF-α inhibitor), ustekinumab (an IL-12,23 inhibitor), secukinumab (an IL-17 inhibitor), and guselkumab (an IL-23 inhibitor).[2,12–16] However, patients receiving systemic agents should be closely monitored for adverse effects and potential drug-drug interactions, which can limit long-term use.[17] Consequently, exploring alternative treatments for psoriasis is imperative, with a focus on ensuring both safety and efficacy.

Recently, herbal medicine has gained significant interest as an alternative treatment for psoriasis due to its potential to offer a lower risk of adverse effects compared to synthetic medications, while still providing effective therapeutic outcomes.[17] Several herbs such as *Capsicum annuum, Aloe vera, Nigella sativa*, and *Matricaria recutita* have been traditionally used in the management of psoriasis.[18] Among these options, curcumin, the principal bioactive compound in *Curcuma longa* Linn. (turmeric), stands out as the most extensively evidenced compound for psoriasis management due to its well-documented antioxidant, anti-inflammatory, immunomodulatory, anti-

proliferative, and anti-angiogenic activities.[19–25] Furthermore, curcumin demonstrates superior versatility in pharmaceutical development, with a wide range of formulations such as oral, topical, and advanced delivery systems enhancing its therapeutic potential compared to other herbal treatments.[25] Notably, curcumin constitutes approximately 76.9% of the total curcuminoid content, while demethoxycurcumin and bisdemethoxycurcumin make up around 17.6% and 5.5%, respectively.[26] Ongoing research endeavors aim to elucidate the mechanisms of action of curcumin in its anti-psoriatic effects, evaluate its safety and efficacy for psoriasis treatment, and address limitations in its practical application by developing novel formulations. This review article aims to comprehensively evaluate the anti-psoriatic activity, efficacy, and safety profiles of curcumin and its novel formulations in psoriasis treatment, based on non-clinical and clinical trial data. It explores future directions to enhance their potential as an alternative treatment for psoriasis.

Therapeutic Potential of Curcumin in Psoriasis Treatment and Its Potential Mechanism of Action

Curcumin exhibits anti-psoriatic effects through various mechanisms, including inhibiting cell proliferation, inducing apoptosis, suppressing pro-inflammatory cytokine levels, and enhancing the expression of skin barrier proteins.[27–31] Table 1 summarizes the anti-psoriatic effects of curcumin in non-clinical studies, while Figure 1 illustrates its potential mechanisms based on currently available evidence.

In vitro Studies

In vitro studies typically evaluate the anti-psoriatic activity of curcumin using skin cell lines, such as immortalized human keratinocytes (HaCaT), induced by immune-stimulating agents like TNF-α, IL-22, and imiquimod (IMQ), which mimic psoriatic conditions. One study demonstrated that curcumin, at a concentration of 7.37 μg/mL, inhibited cell proliferation by suppressing cell cycle proteins, specifically cyclin D1 and cyclin E.[30] It also induced apoptosis by increasing the expression of TNF-related apoptosis-inducing ligand (TRAIL) and reducing anti-apoptotic proteins, including inhibitor of apoptosis (IAP) 1, IAP2, and B-cell lymphoma extra-large (Bcl-XL), in TNF-α induced HaCaT cells.[27] These effects help manage psoriasis signs and symptoms by reducing hyperproliferation and eliminating dysfunctional keratinocytes, thereby minimizing the formation of thickened, itchy, scaly plaques characteristic of the disease.

Curcumin is well known for its anti-inflammatory properties. Several studies have shown that curcumin, at concentrations ranging from 5 to 100 μM, effectively reduces the expression of pro-inflammatory cytokines, including IL-6, IL-17, IL-22, IFN-γ, and TNF-α, which play roles in the pathogenesis and progression of psoriasis.[27–29] The anti-inflammatory activity of curcumin could be attributed to its modulation of multiple intracellular signaling pathways, such as Nuclear Factor-Kappa B (NF-κB), Mitogen-Activated Protein Kinase (MAPK), and Janus Kinase (JAK)-Signal Transducer and Activator of Transcription (STAT) pathways.[27,29] These pathways are central to driving skin inflammation, hyperproliferation, and keratinocyte differentiation in psoriasis.[6] Additionally, curcumin was reported to regulate inflammatory cytokines and inhibit T-cell proliferation by blocking the potassium channel subtype Kv1.3.[32] In addition, curcumin enhances the levels of skin barrier proteins, including involucrin and filaggrin, suggesting that it may improve the protective function of psoriatic skin and reduce transepidermal water loss.[28]

Ex vivo Studies

Findings from ex vivo studies align with in vitro results, showing that curcumin (≥ 5 μM) significantly reduces levels of pro-inflammatory cytokines, including IL-17 and IFN-γ, in peripheral blood mononuclear cells from both psoriasis patients and healthy controls.[33] Additionally, curcumin was shown to suppress phosphorylase kinase (PhK) activity, an enzyme involved in the persistence of psoriatic plaques, indicating that curcumin may help mitigate both acute and chronic phases of psoriasis.[34] In addition to ex vivo studies, combining curcumin with other treatments has shown potential in reducing pro-inflammatory cytokines[33,40] and inhibiting cell proliferation in psoriatic keratinocytes compared to normal cells.[41]

https://doi.org/10.2147/DDDT.S520555

Table 1 Anti-Psoriatic Effects of Curcumin: Findings from Non-Clinical Studies

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
1. In vitro studies						
Solution	• CUR (7.37 μg/mL)	TNF-α-induced HaCaT cells	24 hours	1. Anti-apoptotic protein levels 2. Expression of TRAIL receptors 3. Inflammatory protein levels 4. Pro-inflammatory cytokines	1. ↓ Expression of IAP1, IAP2, Bcl-XL 2. ↑ Expression of TRAIL-R1/R2 3. ↓ Expression of NF-κB-p65 4. ↓ IL-6, IL-8 levels	[27]
Solution	• CUR (25, 50 μM) • CAL (100 μM)	IMQ-induced HaCaT cells	24 hours	1. Cell proliferation 2. Apoptosis 3. Pro-inflammatory cytokines 4. Pro-inflammatory cytokine mRNA 5. Skin barrier proteins	1. ↓ DNA yield by 1.4-fold and 1.6-fold, respectively at 25 μM and 50 μM 2. ↓ Cell number and round-shaped dead or apoptotic cells 3. ↓ IL-17, TNF-α, IFN-γ, and IL-6 levels by 72.1 ± 2.8%, 77.4 ± 2.2%, 55.1 ± 2.2%, and 65.5 ± 1.6%, respectively at 50 μM 4. ↓ IL-17, TNF-α, IL-6 and IFN-γ mRNA expressions 5. ↑ Involucrin and filaggrin content by 47.5 ± 3.1% and 53.9 ± 1.7%, respectively, at 50 μM	[28]
Solution	• CUR (7.37 μg/mL)	IL-22 induced HaCaT cells	24 hours	1. Cell proliferation 2. Cell cycle (protein) 3. Cell cycle (mRNA)	1. ↓ Cell proliferation 2. ↓ Expression of p-STAT3 3. ↓ Expression of cyclin D1, cyclin E	[30]
Solution	• CUR (10, 100 μM)	HEK293 cells	16 hours	1. Cell proliferation 2. Pro-inflammatory protein levels 3. Kv1.3 channel expression	1. ↓ T cells proliferation by more than 50% at 100 μM 2. ↓ IL-22, IFN-γ, IL-2, IL-8, TNF-α by 36%, 24%, 50%, 69%, 49% and 29%, respectively at 10 μM 3. ↓ TNF-α, IL-2, IFN-γ by 100% at 100 μM 4. ↓ Kv1.3 currents by 45% at 10 μM	[32]
Solution	• CUR (5 μM) • CUR-MPA conjugated (5 μM) • MPA (5 μM)	TNF-α-induced HaCaT cells	24 hours	1. Cell proliferation 2. Pro-inflammatory cytokines 3. MAPK protein levels	1 ↓ Cell proliferation at 5 μM BF CUR 2 ↓ IL-6, IL-8, IL-1β levels by 16%, 28%, 31%, respectively at 5 μM BF CUR 3 ↓ p-p38/p38 ratio, p-ERK/ERK ratio, p-JNK/JNK ratio	[31]
2. Ex-vivo studies						
Solution	• CUR (1–500 μg/mL)	PBMCs in healthy volunteers and patients with psoriasis and psoriatic arthritis (Induced by PMA/Io)	48 hours	1. IFN-γ, IL-17A production by T cells 2. IFN-γ production by CD4+, CD8+ T cells, NK and NKT cells 3. IL-17 production by CD4+ T cells (Th17) 4. Percentage of p-STAT3+CD4+ T cells 5. MFI of p-STAT3+CD4+ T cells	1. ↓ IFN-γ, IL-17A at ≥ 5 μg/mL CUR 2. ↓ IFN-γ production by CD4+, CD8+ T cells, and NK and NKT cells at 10 μg/mL CUR 3. ↓ IL-17 production by CD4+ T cells (Th17) 4. ↑ Percentage of p-STAT3+CD4+ T cells (5, 10 μg/mL CUR) 5. ↑ MFI of p-STAT3+CD4+ T cells (5, 10 μg/mL CUR)	[33]
Solution	• CUR + Anti-TNFα biologics • CUR + Anti-IL17 biologics • CUR + DMARDs	PBMCs in patients with psoriasis and psoriatic arthritis (Induced by PMA/Io)	48 hours	1. IFN-γ production by CD4+, CD8+ T cells, NK and NKT cells	1. ↓ IFN-γ production by CD4+, CD8+ T cells, NK, and NKT cells	

Gel	• CUR (1%) • CAL ointment (0.005%)	Skin biopsy in healthy volunteers and patients with plaque psoriasis	4 weeks	1. Phosphorylase kinase (PhK) activity 2. Percentage of TRR+ keratinocytes 3. Percentage of parakeratosis 4. Number of epidermal CD8+ T cells 5. Percentage of Ki-67 per rete ridge	1. ↓ PhK activity (207.2 ± 97.6 units/mg protein) 2. ↓ Percentage of TRR+ keratinocytes (4.3 ± 2.2%) 3. ↓ Percentage of parakeratosis (1.4 ± 2.4%) 4. ↓ Number of epidermal CD8+ T cells (0.6 ± 0.8%) 5. ↓ Percentage of Ki-67 expression (3.7 ± 2.1%)	[34]
3. In vivo studies						
3.1 Oral treatment						
N/A	• CUR (50 and 100 mg/kg)	IMQ-induced BALB/c mice	6 days	1. PASI score 2. Pro-inflammatory cytokines (proteins and mRNA) 3. Expression levels of STAT3 and its downstream signaling molecules	1. ↓ PASI score 2. ↓ IL-6, TNF-α protein, and mRNA levels 3. ↓ Expression levels of p-STAT3, Cyclin D1, Bcl-2, Pim1	[35]
N/A	• CUR (40 mg/kg) • Cs A (40 mmol/kg)	Keratin 14-VEGF transgenic mice with a psoriatic	20 days	1. Psoriasis signs 2. Pro-inflammatory cytokines	1. ↓ Ear redness, ear thickness, ear weight, and lymph node weight 2. ↓ IL-17, IL-22, IFN-γ, IL-2, IL-8, TNF-α levels	[32]
N/A	• CUR (200 mg/kg) + Ustekinumab (4.7 mg/kg) • Ustekinumab (4.7 mg/kg)	IMQ-induced albino rats	15 days	1. PASI score 2. Epidermis thickness 3. Pro-inflammatory cytokine levels in serum and skin homogenate 4. Number of PCNA-positive cells 5. Antioxidant enzyme levels	1. ↓ PASI score[#] 2. ↓ Epidermis thickness[#] 3. ↓ TNF-α, IL-17A levels in serum, ↓ percentage of TNF-α immunoexpression in skin homogenate[#] 4. ↓ Number of PCNA-positive cells[#] 5. ↑ GPx, SOD, CAT levels[#]	[36]
Solution	• CUR (100 mg/kg/d) • MTX (1 mg/kg/d)	IMQ-induced BALB/c mice	6 days	1. PASI score 2. Epidermis thickness 3. Pro-inflammatory cytokines 4. Anti-inflammatory cytokine 5. Percentage of PCNA intensity	1. ↓ PASI score 2. ↓ Epidermis thickness 3. ↓ IL-6, IL-17A, IL-22, IL-23, TNF-α, TGF-β1 levels 4. ↑ IL-10 levels 5. ↓ Percentage of PCNA intensity	[37]
3.2 Topical treatment						
Cream	• CUR (0.5, 1.0, 2.0 g/kg) • HMS cream (0.5 mg/kg)	IMQ-induced Kun-Ming mice	14 days	1. PASI score	1. ↓ PASI score (6.5 ± 3.0, 5.7 ± 2.0 with 1.0, 2.0 g/kg CUR, respectively, on Day 7) 2. ↓ PASI score (4.8 ± 2.1, 4.2 ± 1.5 with 1.0, 2.0 g/kg CUR, respectively, on Day 14)	[38]
		Propranolol-induced guinea pig	14 days	1. CK expression 2. PCNA expression 3. TRL expression	1. ↓ CK16[#] (129.0 ± 21.0, 144.9 ± 16.1 with 1.0, 2.0 g/kg CUR, respectively), and ↓ CK17 (129.0 ± 21.7 at 2.0 g/kg CUR) 2. ↓ PCNA (135.6 ± 17.1, 136.7 ± 11.6 with 1.0, 2.0 g/kg CUR, respectively) 3. ↓ TRL-2 (142.0 ± 16.1, 131.8 ± 15.7, 123.0 ± 7.5 at 0.5, 1.0[#], 2.0[#] g/kg CUR, respectively), and ↓ TRL-4 (140.0 ± 16.4, 134.7 ± 11.5, 120.0 ± 12.9 at 0.5, 1.0[#], 2.0[#] g/kg CUR, respectively)	

(*Continued*)

https://doi.org/10.2147/DDDT.S520555

Table 1 (Continued).

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
Gel	• CUR gel (1%) • CP cream (0.02%)	IMQ-induced BALB/c mice	10 days	1. PASI score 2. Ear thickness 3. Pro-inflammatory cytokines mRNA 4. Number of TCR γδ positive cells 5. CCR6 expression in skin	1. ↓ PASI score 2. ↓ Ear thickness 3. ↓ IL-17A, IL-17F, IL-22, IL-1β, TNF-α mRNA levels 4. ↑ Number of TCR γδ positive cells 5. ↓ CCR6 expression	[39]

Notes: The results of the treatment groups were compared with those of the model group (Inducer). The symbol "#" denotes a comparison with a similar formulation that does not contain curcumin.

Abbreviations: Bcl-2, B-cell lymphoma-2; Bcl-XL, B-cell lymphoma-extra-large; BF, Bioavailable fraction; CAL, Calcipotriol; CAT, Catalase; CCR6, C-C chemokine receptor 6; CD4+, Cluster of differentiation 4; CD8+, Cluster of differentiation 8; CK16, Cytokeratin 16; CK17, Cytokeratin 17; CP, Clobetasol propionate; Cs A, Cyclosporin A; CUR, Curcumin; DMARDs, Disease-modifying anti-rheumatic drugs; ERK, Extracellular signal-regulated kinase; g/kg, Grams per kilogram; HaCaT, Human immortalized keratinocytes; HEK, Human embryonic kidney; HMS, Halometasone; IAP1, Inhibitor of apoptosis protein 1; IAP2, Inhibitor of apoptosis protein 2; IFN-γ, Interferon-gamma; IL-10, Interleukin-10; IL-17, Interleukin-17; IL-17A, Interleukin-17A; IL-17F, Interleukin-17F; IL-1β, Interleukin-1 beta; IL-2, Interleukin-2; IL-22, Interleukin-22; IL-23, Interleukin-23; IL-6, Interleukin-6; IL-8, Interleukin-8; IMQ, Imiquimod; JNK, Jun N-terminal kinase; Ki67, Antigen kiel 67; Kv1.3, Voltage-gated potassium channel KV1.3; MAPK, Mitogen-Activated Protein Kinase; MFI, Mean fluorescence intensity; mg/kg, Milligrams per kilogram; mg/kg/d, Milligrams per kilogram per day; mmol/kg, Millimoles per kilogram; MPA, Mycophenolic acid; mRNA, Messenger ribonucleic acid; MTX, Methotrexate; NF-κB-p65, Nuclear factor-kappa B subunit p65; NK, Natural killer cells; NKT, Natural killer T cells; p-ERK, Phosphorylated extracellular signal-regulated kinase; p-JNK, Phosphorylated-c-Jun N-terminal kinase; p-p38, Phosphorylated p38 mitogen-activated protein kinase; p-STAT3, Phosphorylated signal transducer and activator of transcription 3; p-STAT3+CD4+, Phosphorylated signal transducer and activator of transcription 3 in cluster of differentiation 4; p38 MAPK, p38 mitogen-activated protein kinase; PASI, Psoriasis area severity index; PBMCs, Peripheral blood mononuclear cells; PCNA, Proliferating cell nuclear antigen; PhK, Phosphorylase kinase; Pim-1, Proviral integration site for moloney murine leukemia virus 1; PMA/Io, Phorbol 12-myristate 13-acetate/Ionomycin; SOD, Superoxide dismutase; STAT3, Signal transducer and activator of transcription 3; TCR γδ, T-cell receptor gamma-delta; TGF-β1, Transforming growth factor-beta 1; Th17, T-helper 17; TNF-α, Tumor necrosis factor-alpha; TRAIL, Tumor necrosis factor-related apoptosis-inducing ligand; TRAIL-R1/R2, Tumor necrosis factor-related apoptosis-inducing ligand receptor 1 and receptor 2; TRL-2, Toll-like receptor-2; TRL-4, Toll-like receptor 4; TRR+, Transferrin receptor; VEGF, Vascular endothelial growth factor; μg/mL, Micrograms per milliliter; μM, Micromolar.

https://doi.org/10.2147/DDDT.S520555

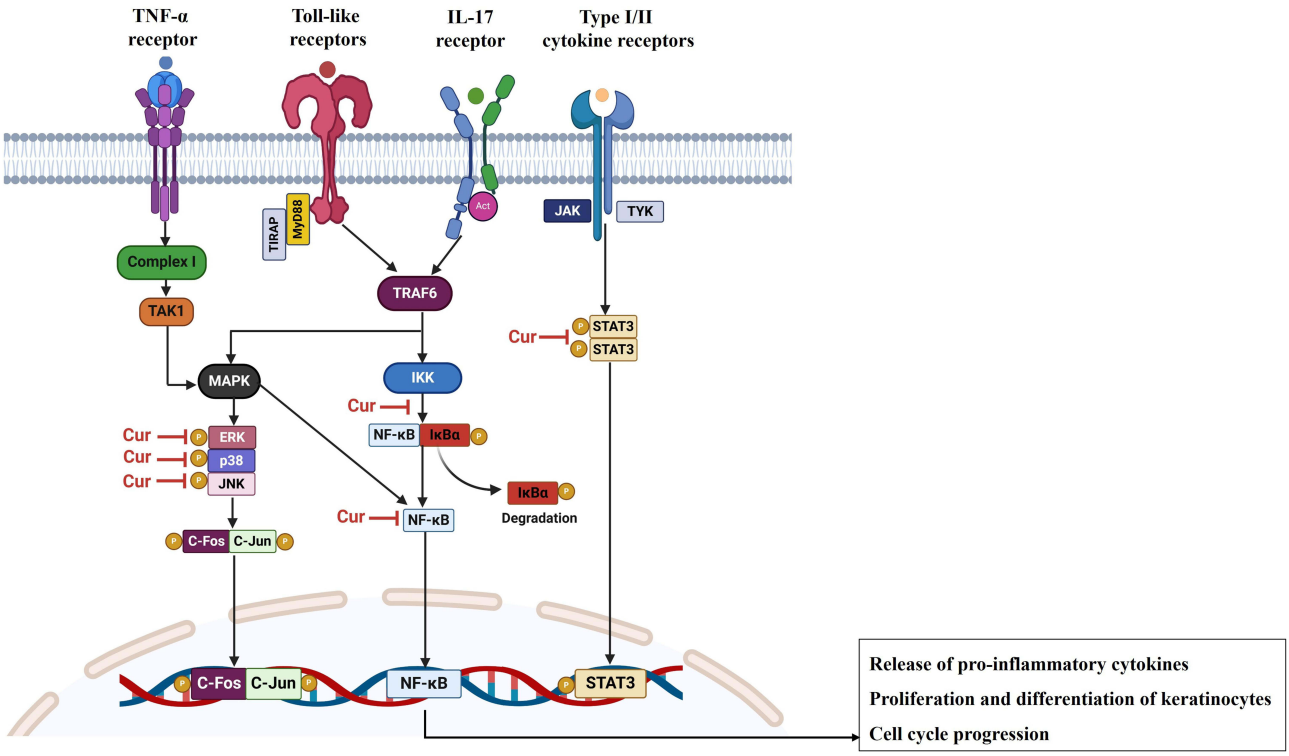


Figure 1 The mechanisms underlying curcumin's anti-psoriatic effects are supported by scientific evidence.
Abbreviations: Act, Act 1 adaptor protein; Cur, Curcumin; c-Fos, Fos proto-oncogene; c-Jun, Jun proto-oncogene; ERK, Extracellular signal-regulated kinase; IKK, Inhibitor of kappa B kinase; IκBα, Inhibitor of kappa B alpha; IL-17, Interleukin 17; JNK, c-Jun N-terminal kinase; MAPK, Mitogen-activated protein kinase; MyD88, Myeloid differentiation primary response gene 88; NF-κB, Nuclear factor kappa-light-chain-enhancer of activated B cells; p, phosphorylated; p38, p38 MAPK; STAT3, Signal transducer and activator of transcription 3; TAK1, TGF-beta-activated Kinase1; TNF-α, Tumor necrosis factor-alpha; TRAF6, TNF-α receptor-associated factor 6; TIRAP, TIR-domain-containing adaptor protein; TYK, Tyrosine kinase.

In vivo Studies

Animal studies suggest that curcumin not only modifies underlying molecular mechanisms but also alleviates signs of psoriasis. Previous studies have demonstrated that oral curcumin (40–200 mg/kg) can significantly reduce the Psoriasis Area and Severity Index (PASI) score, a standard measure for assessing psoriasis severity and therapeutic response, as evidenced by reductions in erythema, scaling, and skin thickness in IMQ-induced mice compared to the control group.[32,36,37] Additionally, curcumin significantly decreased the expression of pro-inflammatory cytokines, such as IL-17, IL-22, IL-8, IFN-γ, and TNF-α, while increasing levels of antioxidant enzymes, including glutathione peroxidase (GPx), catalase (CAT), and superoxide dismutase (SOD), in psoriatic lesions.[32,36] These findings highlight curcumin's potential as a multi-target therapeutic agent for psoriasis, offering both anti-inflammatory and antioxidant effects. Moreover, adjunctive use of curcumin with another therapeutic agent, such as ustekinumab and ibrutinib, has demonstrated superiority in reducing PASI scores, oxidative stress, and levels of psoriasis-associated cytokines compared to monotherapy, suggesting a potential synergistic effect.[36,42,43] Whether used as an adjunct to conventional therapy or as a standalone intervention, curcumin may contribute to potentially improved clinical outcomes.

Challenges in the Low Bioavailability of Curcumin and Approaches to Enhance It

Curcumin is well-known for its low systemic bioavailability due to its poor solubility, low intrinsic activity, poor absorption, high metabolic rate, and rapid elimination from the body.[44,45] Thus, the doses of curcumin used in animal studies cannot be directly compared to those in vitro due to factors such as solubility and the pharmacokinetic profile of curcumin. When administered orally to Sprague-Dawley rats at a dose of 1 g/kg, a negligible amount of curcumin is detected in blood plasma, indicating poor absorption from the gut.[46] Once absorbed, curcumin undergoes rapid

https://doi.org/10.2147/DDDT.S520555

metabolism via conjugation processes like sulfation and glucuronidation in the liver, its major metabolism.[47] Consequently, curcumin is largely excreted in feces, with an elimination half-life of approximately 1.45 h in rats.[48] Additionally, curcumin is chemically unstable, particularly in the alkaline environment of the intestines.[49] Due to its low bioavailability, curcumin in food cannot be utilized for therapeutic purposes, despite turmeric's widespread use as a dietary ingredient across various cultures. Furthermore, since turmeric contains curcumin at relatively low concentrations, approximately 3.14% by weight, its therapeutic potential may be limited.[50] These challenges have been identified as significant barriers to the practical application of oral curcumin in psoriasis treatment, particularly in vivo and clinical trials, where its low bioavailability limits therapeutic efficacy.

Transdermal drug delivery is a promising strategy for enhancing the therapeutic potential of curcumin in psoriasis treatment. By bypassing the gastrointestinal tract and hepatic first-pass metabolism, this approach delivers the drug directly to the target site, potentially improving its effect.[51] Studies have shown that topical curcumin formulations (0.5 to 4 g/kg/d) alleviate psoriatic signs, as evidenced by reduced PASI scores and lowered inflammatory cytokine levels in psoriasis mouse models after 6–14 days of treatment.[35,38,39] Furthermore, topical curcumin significantly decreases the expression of proliferating cell nuclear antigen (PCNA) and immune factors such as cytokeratin 16 (CK16), cytokeratin 17 (CK17), Toll-like receptor 2 (TLR-2), and TLR-4,[38] all of which are associated with epidermal cell hyperproliferation and abnormal differentiation.[35] Additionally, it inhibits C-C chemokine receptor 6 (CCR6), a marker for IL-17A-producing cells in psoriatic skin.[39] These findings confirm that curcumin can effectively alleviate psoriasis signs in animal models through topical administration. However, the efficacy of transdermal delivery depends on the drug's physicochemical properties.[52] The hydrophobic nature, low solubility, instability, and large molecular size of curcumin present significant challenges to its effective delivery through the skin, limiting its potential as a topical agent.[53] Consequently, numerous efforts have been made to enhance the bioavailability of curcumin, primarily through, at least, two strategies: (1) inhibition of metabolic pathways via co-administration with adjuvants such as piperine, and (2) improvement of physicochemical properties through advanced delivery systems, structural modifications, and prodrug development,[47,54] thereby enhancing curcumin's bioavailability and therapeutic effect.

Novel Curcumin Formulations to Enhance Anti-Psoriatic Effects

To address the challenges of poor bioavailability and limited skin penetration, novel curcumin formulations, such as liposomes, polymeric nanoparticles, hydrogels, and nanostructured lipid carriers, have been developed to improve their anti-psoriatic effects.[55] The anti-psoriatic effects of these formulations are detailed in Table 2.

In vitro and ex vivo Studies of Novel Curcumin Formulations

Most in vitro and ex vivo studies demonstrated that these novel formulations significantly enhance the anti-psoriatic effects of curcumin compared to conventional formulations.[56,57,59,60] For example, ionic liquid liposomes significantly improved curcumin's ability to inhibit cell proliferation and reduce pro-inflammatory cytokine levels, including IL-1β, IL-17, IL-22, IFN-γ, and TNF-α, in psoriatic-like HaCaT cells compared to a curcumin solution at the same concentration.[56] Another study found that ethosomes could enhance the free radical-scavenging effects of curcumin combined with glycyrrhetinic acid.[58] In addition to ex vivo findings, curcumin-loaded niosomal gel significantly reduced gene expression levels of pro-inflammatory cytokines, including IL-17, IL-22, IL-23, and TNF-α, as well as inflammatory antimicrobial peptides such as S100A7, S100A12, and Ki67, in skin biopsies from psoriasis patients compared to the placebo group.[40] The enhanced anti-psoriatic effects of these formulations can be attributed to increased cellular uptake through multifaceted mechanisms, including endocytosis, phagocytosis, and pinocytosis, rather than the simple diffusion observed with conventional small molecules.[76] However, this enhancement not only enhances curcumin's bioactivity but also amplifies its cytotoxic potential, posing a dual-faceted challenge. Additionally, encapsulating curcumin within these systems provides protection from degradation and enables sustained release, resulting in higher drug concentrations at target sites.[77]

Although these formulations enhance the bioactivity of curcumin, they may present limitations, such as challenges with drug loading capacity, potential drug leakage, and release profiles, which could impact their stability and overall effectiveness. Therefore, it is essential to ensure that the concentration of curcumin released from the carrier is sufficient to exert the desired anti-psoriatic effects and that the formulation has good long-term stability to maintain consistent therapeutic effects.

Table 2 Anti-Psoriatic Effects of Novel Curcumin Formulations: Findings from Non-Clinical Studies

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
1. In vitro studies						
Ionic liquid liposome	• CUR-Bet-IL (6.25–200 μg/mL) • CUR-Bet-IL-Lipo (6.25–200 μg/mL)	TNF-α-induced HaCaT cells	24 hours	1. Cell proliferation	1. ↓ Cell proliferation (Cur-Bet-IL-Lipo was better than that of Cur-Bet-IL)	[56]
		IMQ-induced HaCaT cells		1. Pro-inflammatory cytokines 2. Collagen-I levels	1. ↓ TNF-α, IL-1β, IL-17A, IL-22, IL-17F levels (Cur-Bet-IL-Lipo was better than that of Cur-Bet-IL) 2. ↑ Collagen-I (CUR-Bet-IL-Lipo)	
Peptide-modified liposomes	• CUR-DMSO (Eqv CUR 2.5, 5, 10, 20, 40 μg/mL) • CUR-Lipo (Eqv CUR 2.5, 5, 10, 20, 40 μg/mL) • CUR-Peptide-Lipo (Eqv CUR 2.5, 5, 10, 20, 40 μg/mL) • CP ointment (0.05% w/w)	HaCaT cells	24 hours	1. Cell proliferation	1. ↓ Cell proliferation across all concentrations 2. ↓ Cell proliferation (CUR-peptide-Lipo was better than CUR-Lipo at ≥ 10 μg/mL)	[57]
Peptide-modified liposomes	• CUR-Peptide-Lipo (Eqv CUR 2.5, 5, 10, 20, 40 μg/mL)	TNF-α-induced HaCaT cells	24 hours	1. Cell proliferation	1. ↓ Cell proliferation across all concentrations	
Ethosome	• CUR-GA in EtOH (Eqv CUR 6 μM) • CUR-ES (Eqv CUR 6 μM) • CUR-GA-TPGS-ES (Eqv CUR 6 μM) • DXM (10 μM)	IL-6-induced HaCaT cells	24 hours	1. Cell proliferation 2. Inflammatory protein levels 3. Intracellular ROS levels	1. ↓ Cell proliferation (CUR-GA-TPGS-ES was better than CUR-ES) 2. ↓ p-IκBα, p-p65, p-STAT3 levels (CUR-GA-TPGS-ES showed the most potent effect) 3. ↓ Intracellular ROS levels (CUR-GA-TPGS-ES showed the most potent effect)	[58]
Nanoemulgel	• CUR-TQ-*RS* solution (5, 10, 25, 50 μM) • CUR-TQ-*RS* nanoemulgel (5, 10, 25, 50 μM)	A431 cells	24 hours	1. Cell proliferation	1. ↓ Cell proliferation (36.4 ± 2.1% and 20.4 ± 2.0% at 50 μM of solution and nanoemulgel, respectively)	[59]

(*Continued*)

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Table 2 (Continued).

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
Chitosan/ Alginate NPs	• CUR-DMSO with/without blue LED (Eqv CUR 0.05, 0.1 μg/mL) • CUR-CS/Alg NPs with/without blue LED (Eqv CUR 0.05, 0.1 μg/mL)	TNF-α-induced HaCaT cells	24 hours	1. Cell proliferation	1.1 ↓ Cell proliferation (0.05 μg/mL of CUR-DMSO with blue LED, 0.1 μg/mL of CUR-DMSO with/without LED blue light) 1.2 ↓ Cell proliferation (0.05, 0.1 μg/mL with CUR-CS/Alg NPs with/without LED blue light)	[60]
2. Ex-vivo studies						
Niosome gel	• CUR (5, 10, 15 μM) • CUR-NIO gel (Eqv CUR 5, 10, 15 μm)	PBMCs in healthy volunteers and patients with psoriasis	4 days	1. Pro-inflammatory gene expression	1. ↔ IL-17 gene expression in PBMCs from the patient and healthy donor groups	[40]
		Skin biopsy in patients with psoriasis	4 weeks	1. Pro-inflammatory mRNA expressions 2. Inflammatory antimicrobial peptides mRNA expressions	1. ↓ IL-17, IL-22, IL-23, TNF-α mRNA expressions[#] 2. ↓ S100A7, S100A12, Ki67 mRNA expressions[#]	
NPs loaded in collagen patch	• Coll-CS-CUR (Eqv CUR 0.1%) • Coll-Cross-CS-CUR (Eqv. CUR 0.1%) • Coll-Cross-Hep-CS-CUR (Eqv. CUR 0.1%)	Isolation of human keratinocytes from skin biopsies of patients with psoriasis vulgaris	24 hours	1. Cell proliferation	1. ↓ Cell proliferation	[41]
3. In vivo studies						
Topical treatment						
Liposphere gel	• 10 mg CUR-TAC liposphere gel (Eqv CUR 0.025% w/w) • Betamethasone ointment (0.1% w/w)	IMQ-induced BALB/c mice	6 days	1. PASI score 2. Ear thickness 3. Spleen weight: body weight ratio 4. Pro-inflammatory cytokine levels	1. ↓ PASI score 2. ↓ Ear thickness 3. ↓ Spleen weight to body weight ratio 4. ↓ TNF-α by 1.6-fold*, ↓ IL-17 by 2.1-fold, ↓ IL-22 by 4.0-fold	[61]
Nanoemulgel	• CUR-IMQ-NEG (0.5% w/w)	BALB/C mice	10 days	1. Psoriasis sign (redness, scaling, thickness)	1. Disappearance of psoriasis sign	[62]

Nanohydrogel	• CALIX/CUR hydrogel (1.8 mg)	IMQ-induced BALB/C mice	7 days	1. Histological score 2. Pro-inflammatory cytokine expression 3. iNOS level 4. Number of mast cell infiltrations 5. Skin barrier protein expressions	1. ↓ Histological score 2. ↓ TNF-α, IL-1β expressions 3. ↓ iNOS level 4. ↓ Number of mast cell infiltrations 5. ↑ Percentage of ZO-1, occludin	[63]
LPHNPs	• CUR-LPHNPs (0.1% w/v) • BMV cream (0.1% w/w)	IMQ-induced Wistar albino rats	5 days	1. Psoriasis signs (erythema, swelling, scaling, thickening)	1. ↓ Psoriasis signs*	[64]
Nanoemulgel	• CUR gel (0.5% w/w) • CUR-NEG (0.5% w/w) • BMV gel (0.1% w/w)	IMQ-induced BALB/C mice	10 days	1. Psoriasis signs (redness, scaling, thickness)	1. ↓ Severity scores of psoriasis[¶] (CUR-NEG)	[65]
Bio-polysaccharide gel	• CUR-LBG gel (Eqv CUR 2.087% w/w) • CUR-LBG gel-CAGE-IL (Eqv CUR 2.087% w/w)	IMQ-induced BALB/c mice	20 days	1. PASI score (erythema, desquamation) 2. Ear epidermis thickness	1. ↓ Erythema and desquamation score [#] 2. ↓ Ear epidermis thickness (CUR-LBG gel-CAGE-IL)	[66]
Ethosome	• CUR-GA in EtOH • CUR-ES • CUR-GA-TPGS-ES • DXM ointment (5 mg/kg)	• Healthy SD rats • BALB/c mice • Nude mice	7 days	1. PASI score 2. Pro-inflammatory cytokine levels in serum and skin homogenate 3. Antioxidant enzyme levels in serum and skin homogenate	1. ↓ PASI scores (CUR-GA-TPGS-ES showed the most potent effect*[¶]) 2.1 Serum: ↓ IL-17 (All ES group), ↓ IL-23, ↑ GR-α 2.2 Skin homogenate: ↓ IL-17, ↓ IL-23 (All ES group), ↑ GR-α (CUR-GA-TPGS-ES) 3.1 Serum: ↑ SOD (All ES group), ↑ CAT (CUR-GA-TPGS-ES) 3.2 Skin homogenate: ↑ CAT (All ES group), ↑ SOD	[58]
Solid cluster	• CUR (0.42 mg/d) • CUR-GA-silica gel (Eqv CUR 0.42 mg/d)	IMQ-induced C57BL/6 mice	7 days	1. PASI score 2. Pro-inflammatory cytokines	1. ↓ PASI score (CUR, CUR-GA-silica gel[¶]) 2. ↓ IL-17A (CUR-GA-silica gel[¶])	[67]
Mesoporous silica gel	• CUR (0.42 mg) • CUR-μmS (0.08 g) • CUR-μmS-Low GA (0.10 g) • CUR-μmS-High GA (0.11 g)	IMQ-induced C57BL/6 mice	7 days	1. PASI score 2. Pro-inflammatory cytokines	1. ↓ PASI score (μmS group[¶]) 2. ↓ IL-17A in the dermis (CUR-μmS-High GA[¶]), IL-23 in the epidermis (CUR-μmS, CUR-μmS-High GA[¶])	[68]

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Table 2 (Continued).

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
Invasomal gel	• CUR gel (Eqv CUR 1% w/v) • CUR-IVS gel (Eqv CUR 1% w/v)	IMQ-induced BALB/c mice	20 days	1. PASI score (redness, scaling, thickness)	1. ↓ Redness, scaling, and skin thickness[¶]	[69]
NPs gel	• CUR gel (Eqv CUR 500 μg) • CUR-NPs gel (Eqv CUR 500 μg) • Clobetasol cream	IMQ-induced BALB/c mice	8 days	1. PASI score 2. Skin thickness 3. Number of TNF-α staining-positive cells 4. Number of IL-6 staining-positive cells 5. Number of NF-κB staining-positive cells	1. ↓ PASI score (from 4 to 2 with CUR gel, and from 4 to 1 with CUR-NPs gel[¶] on Day 5) 2. ↓ Skin thickness 3. ↓ Number of TNF-α staining-positive cells 4. ↓ Number of IL-6 staining-positive cells 5. ↓ Number of NF-κB staining-positive cells	[70]
Nanoemulgel	• CUR gel (Eqv CUR 100 mg) • CUR emulgel (Eqv CUR 100 mg)	IMQ-induced Albino rats	15 days	1. PASI score	1. ↓ PASI score (from 8.5 to 3.3 with emulgel on Day 15[¶])	[71]
Water responsive gel	• CUR (30 μM) • CUR-WRG (30 μM)	IMQ-induced BALB/c mice	7 days	1. Ear thickness 2. PASI score 3. Pro-inflammatory cytokines 4. Relative CD4+ and CD8+ area 5. Relative Ki67 and CK10 expression 6. Oxidative stress markers 7. Antioxidant enzyme levels 8. Spleen/body weight ratio 9. Angiogenesis markers	1. ↓ Ear thickness (CUR, CUR-WRG[¶]) 2. ↓ PASI score (CUR, CUR-WRG[¶]) 3. ↓ IL-17, IL-22 in skin tissues and serum (CUR, CUR-WRG[¶]) 4. ↓ Relative CD4+ and CD8+ area (CUR, CUR-WRG[¶]) 5. ↓ Relative Ki67 and CK10 expression (CUR, CUR-WRG[¶]) 6. ↓ MDA in skin tissues and serum (CUR, CUR-WRG[¶]) 7. ↑ SOD in skin tissues (CUR, CUR-WRG) and in serum (CUR, CUR-WRG[¶]) 8. ↓ Spleen/body weight ratio (CUR, CUR-WRG[¶]) 9. ↓ Relative vessel length, relative VEGF expression, relative PECAM expression (CUR, CUR-WRG[¶])	[72]

https://doi.org/10.2147/DDDT.S520555

Liposome	• CUR-DMSO • CUR-Lipo • CUR-Peptide-Lipo • CP ointment (0.05% w/w)	IMQ-induced BALB/c mice	10 days	1. PASI score 2. Pro-inflammatory cytokines mRNA levels	1. ↓ PASI score (CUR-DMSO, CUR-Lipo, CUR-Peptide-Lipo[¶*]) 2. ↓ IL-17A, IL-17F, IL-22, TNF-α, IL-1β (CUR-DMSO, CUR-Lipo, CUR-Peptide-Lipo[¶*])	[57]
Nanosponge gel	• CUR-CFN-NS gel • Marketed CUR gel	IMQ-induced BALB/c mice	Daily	1. PASI score (erythema, scaling)	1. ↓ PASI score (from 4 to 0 with CUR-CFN-NS gel on Day 7)	[73]
Liposomal gel	• CUR gel (Eqv CUR 20 mg/kg) • CUR-Lipo gel (Eqv CUR 20 mg/kg) • CUR-IBR (Eqv CUR 20 mg/kg) • CUR-IBR-Lipo gel (Eqv CUR 20 mg/kg) • BMP ointment (0.1% w/w)	IMQ-induced BALB/c mice	6 days	1. PASI score 2. Pro-inflammatory cytokine levels 3. Ear epidermis thickness 4. Spleen weight to body weight ratio	1. ↓ PASI score 2. ↓ IL-22, TNF-α, IL-17, IL-23, IL-6, IL-2 (Lipo group[¶]) 3. ↓ Ear thickness (Lipo group*) 4. ↓ Spleen weight to body weight ratio (Lipo group)	[43]
Nanostructured lipid carrier gel	• CUR gel (Eqv CUR 20 mg/kg) • CUR-NLC (Eqv CUR 20 mg/kg) • CUR-IBR gel (Eqv CUR 20 mg/kg) • CUR-IBR-NLC (Eqv CUR 20 mg/kg)	IMQ-induced BALB/c mice	6 days	1. PASI score 2. Pro-inflammatory cytokines 3. Ear thickness 4. Spleen weight to body weight ratio	1. ↓ PASI score 2. ↓ IL-22, TNF-α, IL-17, IL-2, IL-6, IL-23 (NLC group) 3. ↓ Ear thickness 4. ↓ Spleen weight to body weight ratio	[42]
LPHNPs	• CUR-MS-LPHNPs • BMV cream	IMQ-induced Wistar rats	7 days	1. PASI score	1. ↓ PASI score (from 12 to 0 with CUR-MS-LPHNPs* and from 12 to 5 with BMV cream on Day 5)	[74]
Mesoporous silica	• CUR-GA-μmS (Eqv CUR 0.42 mg) • CUR-Apt-GA-μmS (Eqv CUR 0.42 mg)	IMQ-induced C57BL/6 mice	7 days	1. Pro-inflammatory cytokine levels	1. ↓ IL-17A levels	[75]

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https://doi.org/10.2147/DDDT.S520555

Table 2 (Continued).

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcome Assessments	Results	References
Nanoemulgel	• CUR-TQ-*RS* gel (0.67 μg/mL) • CUR-TQ-*RS* nanoemulgel (0.67 μg/mL) • BMD (0.05% w/w)	IMQ-induced BALB/c mice	7 days	1. PASI score	1. ↓ PASI score (from 3.0 to 1.6 with CUR-TQ-*RS* gel and from 3.0 to 0.3 with CUR-TQ-*RS* nanoemulgel[¶])	[59]

Notes: The results of the treatment groups were compared with those of the model group (Inducer), except where *indicates a comparison with the positive control group, [#]indicates a comparison with a similar formulation that does not contain curcumin, and [¶]indicates a comparison with the conventional formulation.

Abbreviations: BMD, Betamethasone dipropionate; BMP, Betamethasone propionate; BMV, Betamethasone valerate; CALIX/CUR, Micellar choline-calix[4]arene amphiphile and curcumin; CAT, Catalase; CD4+, Cluster of differentiation 4; CD8+, Cluster of differentiation 8; CK10, Cytokeratin 10; Coll-Cross-CS-CUR, Collagen patch cross-linked with EDC/NHS-curcumin-loaded chitosan nanoparticles; Coll-Cross-Hep-CS-CUR, Collagen patch cross-linked with EDC/NHS/heparin-curcumin-loaded chitosan nanoparticles; Coll-CS-CUR, Collagen patches loaded with curcumin-loaded chitosan nanoparticles; CP, Clobetasol propionate; CUR, Curcumin; CUR-Apt-GA-μmS, Co-delivering curcumin and aptamer conjugated glycyrrhizic acid in mesoporous silica in μmS; CUR-Bet-IL, Curcumin-betaine-ionic liquid; CUR-Bet-IL-Lipo, Curcumin-betaine-ionic liquid-loaded liposome; CUR-CFN-NS, Curcumin and caffeine-loaded nanosponge; CUR-CS/Alg NPs, Curcumin-loaded chitosan/alginate nanoparticles; CUR-DMSO, Curcumin in dimethyl sulfoxide; CUR-ES, Curcumin-loaded ethosome; CUR-GA, Combination of curcumin and glycyrrhetinic acid; CUR-GA-silica gel, Curcumin and glycyrrhetinic acid-loaded silica gel; CUR-GA-TPGS-ES, Curcumin-loaded glycyrrhetinic acid-D-α-tocopherol acid polyethylene glycol succinate-modified multifunctional ethosomes; CUR-GA-μmS, Curcumin and glycyrrhetinic acid-loaded mesoporous silica in μmS; CUR-IBR, Combination of curcumin and ibrutinib; CUR-IBR-Lipo gel, Curcumin and ibrutinib co-loaded liposomal gel; CUR-IBR-NLC, Curcumin and ibrutinib co-loaded nanostructured lipid carrier gel; CUR-IMQ-NEG, Combination of curcumin nanoemulgel and imiquimod nanoemulgel; CUR-IVS gel, Curcumin-loaded invasomal gel; CUR-LBG, Combination of curcumin and locust bean gum; CUR-LBG gel-CAGE-IL, Combination of curcumin and locust bean gum gel-choline and geranic acid ionic liquid; CUR-Lipo, Curcumin-loaded liposome; CUR-LPHNPs, Curcumin-loaded lipid-polymer hybrid nanoparticles; CUR-MS-LPHNPs, Curcumin-co-loaded methoxsalen lipid-polymer hybrid nanoparticles; CUR-NEG, Curcumin-loaded nanoemulgel; CUR-NIO, Curcumin-loaded niosome; CUR-NLC, Curcumin-loaded nanostructured lipid carrier gel; CUR-Peptide-Lipo, Peptide-modified curcumin-loaded liposome; CUR-TAC liposphere gel, Curcumin and tacrolimus co-loaded liposphere gel; CUR-TQ-RS, Combination of curcumin, thymoquinone and resveratrol; CUR-WRG, Curcumin-loaded water responsive gel; CUR-μmS, Curcumin-loaded mesoporous silica in μmS; CUR-μmS-High GA, Curcumin-loaded mesoporous silica in μmS with high GA proportion; CUR-μmS-Low GA, Curcumin-loaded mesoporous silica in μmS with low GA proportion; DXM, Dexamethasone; Eqv, Equivalent; ES, Ethosome; EtOH, Ethanol; g, Grams; GA, Glycyrrhizic acid; GR-α, Glucocorticoid receptor-alpha; HaCaT, Human immortalized keratinocytes; IL-17, Interleukin-17; IL-17A, Interleukin-17A; IL-17F, Interleukin-17F; IL-1β, Interleukin-1 beta; IL-2, Interleukin-2; IL-22, Interleukin-22; IL-23, Interleukin-23; IL-6, Interleukin-6; IMQ, Imiquimod; iNOS, Inducible nitric oxide synthase; Ki67, Antigen kiel 67; LED, Light emitting diodes; Lipo, Liposome; LPHNPs, Lipid-polymer hybrid nanoparticle; MDA, Malondialdehyde; mg, Milligrams; mg/d, Milligrams per day; mg/kg, Milligrams per kilogram; mM, Millimolar; mRNA, Messenger ribonucleic acid; NF-κB, Nuclear factor-kappa B; NLC, Nanostructured lipid carrier gel; NPs, Nanoparticles; p-IκBα, Phosphorylated-inhibitor of kappa B alpha; p-p65, phosphorylated form of p65; p-STAT3, Phosphorylated signal transducer and activator of transcription 3; PASI, Psoriasis area severity index; PBMCs, Peripheral blood mononuclear cells; PECAM, Platelet endothelial cell adhesion molecule; ROS, Reactive oxygen species; S100A12, Calgranulin c; S100A7, Psoriasin; SOD, Superoxide dismutase; TNF-α, Tumor necrosis factor-alpha; VEGF, Vascular endothelial growth factor; w/v, Weight per volume; w/w, Weight per weight; ZO-1, Zonula occludens-1; μg, Micrograms; μg/mL, Micrograms per milliliter; μM, Micromolar; μmS, micro size.

Table 3 Efficacy of Curcumin in Psoriasis Treatment: Findings from Clinical Studies

Dosage Form	Treatment Group & Dose (n)	Control Group (n)	Study Design	Population	Treatment Duration	Outcome Assessments	Results	References
1. Oral treatment								
1.1 Conventional formulations								
Capsule	Curcuminoid (Curcumin C3 Complex®) 4.5 g/d (n=12)	N/A	Phase 2, prospective, single-arm, open-label	Patients with moderate-to-severe psoriasis vulgaris	12 weeks	Primary outcome 1. PGA score Secondary outcome 1. PASI score 2. QOL: Skindex-29 score	1. Response rate based on achieving at least a PGA score of "good" (50–74% improvement): 16.7% (ITT), 25.0% (PP) 2. Responders achieved a PASI 75 at week 12: 16.7% (ITT), 25.0% (PP) 3. Skindex-29 change (median, IQR): 0.4 (−5.5, 5.0) for PP, 0.0 (−2.6, 5.0) for ITT	[81]
Tablet	CUR 2 g/d; tablet + MPA 0.1%; ointment (n=31)	PLA + MPA 0.1%; ointment (n=32)	Phase 3, RCT, parallel, double-blind	Patients with mild-to-moderate psoriasis vulgaris(PASI < 10)	12 weeks and a 4-week follow-up period	Primary outcome 1. PASI score Secondary outcome 2. PASI50, PASI75, PASI90, PASI100 3. Serum inflammatory cytokine levels	1. ↓ Median PASI scores[#] [25th–75th percentile]: from 5.6 [4.2–7.3] at baseline to 1.3 [0.6–1.7] at week 12 and 1.4 [1.2–1.8] at week 16 ($p < 0.05$) 2. High PASI response rate: 92% (PASI50), 48% (PASI75), 20% (PASI90), 12% (PASI100) at week 12; and 88% (PASI50), 44% (PASI75), 8% (PASI90), 4% (PASI100) at week 16 3. ↓ IL-22 levels[#]: from 35.2 ± 9.5 pg/mL at baseline to 21.1 ± 7.5 pg/mL at week 12 ($p < 0.001$)	[82]
1.2 Novel formulations								
Capsule	CUR 3 g/d (NPs size); capsule + Acitretin 0.4 mg/kg/d (n=15)	PLA + Acitretin 0.4 mg/kg/d (n=15)	Phase 3, RCT, parallel, double-blind	Patients with moderate-to-severe psoriasis (PASI ≥ 10)	12 weeks and a 4-week follow-up period	1. PASI score	1. ↓ Median PASI scores[#]: from 16.4 at baseline to 3.4 at week 12, and 3.6 at week 16 ($p < 0.0001$)	[83]

(*Continued*)

https://doi.org/10.2147/DDDT.S520555

Table 3 (Continued).

Dosage Form	Treatment Group & Dose (n)	Control Group (n)	Study Design	Population	Treatment Duration	Outcome Assessments	Results	References
2. Topical treatment								
2.1 Novel formulations								
Niosomal gel	0.1% w/w CUR-NIO gel (n=5)	PLA (n=5)	Phase 2, RCT, parallel, double-blind	Patients with mild-to-moderate psoriasis vulgaris (PASI scores < 30)	4 weeks	1. Clinical manifestations of psoriasis	1. ↓ Redness, scaling, itching, skin dryness, and inflammatory surrounding lesions[#]	[40]
Microemulgel	0.5% TUR microemulgel (containing 30 μg/mL of CUR) (n=17)	PLA (n=17)	Phase 2, RCT, prospective, parallel, double-blind	Patients with mild-to-moderate plaque psoriasis	9 weeks	1. PASI score 2. QOL: DLQI	1. ↓ PASI scores[#]: ↓ mean redness scores (from 1.3 at baseline to 0.2 at week 9), ↓ mean thickness score (from 1.1 to 0.3 at week 9), ↓ mean scaling score (from 1.5 to 0.1 at week 9), ↓ mean lesion area ($p < 0.05$) 2. Improvement in DLQI ($p < 0.05$)	[84]

Notes: [#]Indicates a comparison with a similar formulation that does not contain curcumin.

Abbreviations: CUR, Curcumin; CUR-NIO, Curcumin-loaded niosome; DLQI, Dermatology life quality index; g/d, Grams per day; IL-22, Interleukin-22; IQR, Interquartile range; ITT, Intention-to-treat; mg/kg/d, Milligrams per kilogram per day; MPA, Mycophenolic acid; n, Number of participants; NIO, niosomal gel; NPs, Nanoparticles; PASI, Psoriasis area and severity index; pg/mL, Picograms per milliliter; PGA, Physician global assessment; PLA, Placebo; PP, Per protocol; QOL, Quality of life; RCT, Randomized controlled trials; TUR, Turmeric; w/w, Weight per weight; μg/mL, Micrograms per milliliter.

https://doi.org/10.2147/DDDT.S520555

In vivo Studies of Novel Curcumin Formulations

The stratum corneum, the outermost layer of the skin, presents a significant barrier to transdermal drug delivery.[78] Effective transdermal delivery requires drug molecules to have a low molecular weight (less than 500 Daltons) and balanced solubility in both water and oil.[79] However, due to its poor solubility and hydrophobic nature, curcumin struggles to penetrate deeper skin layers, remaining primarily within the stratum corneum.[47]

Studies on novel topical formulations have shown significant effects in alleviating psoriasis signs, reducing pro-inflammatory cytokines, increasing antioxidant enzymes, and enhancing skin barrier protein levels in psoriasis-induced mice compared to conventional formulations.[67,68,70,72] Some novel curcumin formulations, specifically lipid-polymer hybrid nanoparticles, exhibited superior efficacy in improving psoriasis signs compared to 0.1% betamethasone valerate, a commonly used positive control.[61,64,66,74] This enhanced anti-psoriatic effect may be attributed to the ability of these novel formulations to improve skin penetration and retention, ensuring more effective delivery of curcumin to the target site within the skin.

Novel formulations such as nanostructured lipid carriers, mesoporous silica gel, nanoemulgel, liposome, ethosomes, and invasome gel have shown promise in enhancing the transdermal delivery of curcumin.[42,43,58,62,65,67–69,71,73,75] These formulations increase cumulative curcumin permeation, permeation rate, permeation coefficient, and the amount of curcumin deposited within the skin, outperforming curcumin solution in modified Franz diffusion cell assays. Improved skin penetration may result from the small particle size, which increases surface area and solubility, as well as the proper particle charge.[80] Additionally, some formulations provide a lipid matrix that integrates effectively with the stratum corneum. Consequently, increased transdermal delivery of curcumin has led to enhanced anti-psoriatic effects in animal studies.

However, the permeability and retention of these formulations in psoriatic skin remain unclear, as most studies use healthy mouse models that may not accurately represent the characteristics of psoriasis skin, such as a weakened barrier, thickened stratum corneum, and scaling plaques. Another potential concern is that novel topical formulations may have unintended systemic effects. Studies have shown that these formulations can reduce the spleen-to-body weight ratio, alter serum inflammatory cytokine levels, and increase serum antioxidant enzyme levels,[42,43,58,61,72] suggesting potential penetration into deeper skin layers and entry into the bloodstream, which may affect other organs. Since the local and systemic effects of these novel curcumin formulations have not been fully evaluated, further research is needed for a comprehensive assessment.

Clinical Efficacy of Curcumin Administration in the Treatment of Psoriasis in Humans

Oral Administration

To date, rigorous clinical trials evaluating curcumin's efficacy for psoriasis treatment remain limited. The diverse clinical presentations and complex pathophysiology of psoriasis pose significant challenges in establishing standardized treatment protocols and outcome assessment. Table 3 summarizes the efficacy of oral curcumin in psoriasis-related outcomes in humans. Although oral curcumin has demonstrated the ability to alleviate psoriasis signs in animal models, clinical evidence supporting its use as a monotherapy is sparse. It is primarily used as an adjunct therapy for managing psoriasis.

A prospective Phase II, open-label clinical trial by Kurd et al (2008) investigated the efficacy of 4.5 g/day of curcuminoid (Curcumin C3 complex®) capsules in 12 patients with moderate to severe psoriasis.[81] The study reported a low overall response rate for achieving at least a "good" Physician Global Assessment (PGA) score (50–74% improvement), with rates of 16.7% in the intention-to-treat analysis and 25% in the per-protocol analysis. This outcome is likely attributed to poor bioavailability, suggesting that oral curcumin alone may not provide sufficient efficacy in managing psoriasis.

Most clinical studies have evaluated oral curcumin in combination therapies, underscoring the need for dose adjustments when used alongside other treatments. For instance, one study in patients with mild to moderate psoriasis demonstrated that a 12-week regimen combining 2 g/day of oral curcumin with 0.1% mycophenolic acid ointment significantly reduced median PASI values from 5.6 to 1.3, and decreased serum IL-22 levels from 35.2 ± 9.5 pg/mL to 21.1 ± 7.5 pg/mL, compared to monotherapy with mycophenolic acid.[82] Additionally, the efficacy of novel oral formulations has been

documented in recent studies. In one example, 3 g/d of curcumin nanoparticles were administered orally to patients with moderate-to-severe psoriasis (PASI ≥ 10) alongside acitretin treatment.[83] After 12 weeks, the combination therapy resulted in superior efficacy in reducing psoriasis severity, as evidenced by a greater reduction in median PASI scores from 16.4 to 3.4, compared to acitretin monotherapy, which reduced PASI scores from 14.8 to 6.8. These findings suggest that curcumin, when used as an adjunctive therapy, may offer a more effective and better-tolerated approach for managing psoriasis than high-dose monotherapy.

Topical Administration

Topical curcumin is commonly used to manage signs and symptoms in patients with mild to moderate psoriasis, although clinical studies evaluating its efficacy remain limited. Table 3 summarizes the efficacy of topical curcumin formulations in clinical studies. Curcumin in niosome gel and microemulgel demonstrated significant efficacy in alleviating psoriasis signs, such as redness and scaling, in patients with mild-to-moderate plaque psoriasis.[40,84] These treatments resulted in an overall improvement in disease severity and enhanced patient well-being. Novel curcumin formulations thus represent promising alternative therapeutic options for managing psoriasis.

Despite promising findings, several practical challenges may hinder the broader clinical application of curcumin-based formulations. Most existing studies are limited by small sample sizes and short treatment durations. Additionally, there is a lack of clinical research directly comparing novel curcumin delivery systems with conventional formulations, particularly regarding long-term efficacy, scalability, and cost-effectiveness. From an industrial standpoint, large-scale production of advanced delivery systems, such as liposomes, solid lipid nanoparticles, and nanostructured lipid carriers, require specialized equipment and stringent quality control, substantially increasing manufacturing costs.[85] Furthermore, storage stability remains a concern; for instance, liposomal formulations are susceptible to leakage or aggregation over time, potentially compromising their therapeutic efficacy.[86] Patient acceptance is another barrier, especially for topical curcumin preparations, which may cause visible yellow-orange staining and reduce adherence when used on cosmetically sensitive areas.[87] Economic considerations are also crucial in determining the clinical viability of curcumin; however, direct pharmacoeconomic evaluations of curcumin in psoriasis therapy have not yet been conducted. However, the cost of curcumin-based interventions can vary considerably depending on formulation type, the use of bioavailability-enhancing technologies, route of administration, and treatment duration, all of which should be systematically assessed in future research.

To address these challenges, well-justified and methodologically rigorous future research is warranted. Table 4 presents an overview of ongoing clinical trials investigating the efficacy of curcumin primarily in topical formulations for the psoriasis treatment. Furthermore, future efforts should prioritize large-scale, long-term clinical trials, optimization of formulations, and the development of cost-effective manufacturing strategies. A focus on patient-centered design, along with comprehensive assessments of cost-effectiveness and long-term economic sustainability, will be critical in fully realizing the therapeutic potential and practical applicability of curcumin in psoriasis management.

Safety Profiles of Curcumin and Its Novel Formulations

Ensuring safety is a critical aspect of using curcumin for psoriasis treatment. Table 5 summarizes the safety profiles of curcumin and its novel formulations.

In vitro and ex vivo Studies

With the intention of using curcumin to treat psoriasis, numerous studies have evaluated its cytotoxicity in skin cell lines, specifically the immortalized human keratinocyte cell line (HaCaT) and human skin fibroblasts (HSF), to identify safe dosage levels for further investigation of curcumin's biological activity. Varma et al (2017) reported that curcumin exhibited a half-maximal inhibitory concentration (IC_{50}) at a concentration of 219.42 μM on HaCaT cells.[28] Curcumin was tested for cytotoxicity in Caco-2 cells to simulate oral administration as an intestinal epithelial barrier model. Curcumin had no cytotoxic effect in Caco-2 cells at concentrations below 5 μM but caused significant cytotoxicity at 10 μM.[31] Additionally, curcumin's cytotoxicity was significantly enhanced when combined with other therapeutic agents, such as ibrutinib.[43] This

Table 4 Ongoing Clinical Trials on Curcumin for Psoriasis Treatment

Study Title	Registry Number	Population	Intervention	Treatment Duration	Outcome Assessments	Country	Status
Oral treatment							
Efficiency of curcuminoids as an adjuvant treatment in plaque-type psoriasis	TCTR20180419003	Plaque psoriasis	Standard treatments with curcuminoids supplementation	16 weeks	1. PASI score 2. C-reactive protein level 3. Liver and renal function tests	Thailand	Not yet recruiting
Topical treatment							
Efficacy and safety of cream containing sericin and turmeric in psoriasis patients	NCT06482398	Mild psoriasis	Turmeric extract and sericin extract cream	8 weeks	1. PASI score 2. PGA sore 3. Body surface area of the lesion 4. QOL: DLQI 5. Itching score 6. Adverse reaction	Thailand	Not yet recruiting
Turmeric-based therapy in the treatment of psoriasis: A clinical trial	NCT04071106	Mild to moderate psoriasis	Turmeric extract in ointment Turmeric extract in olive oil	12 weeks	1. PASI score 2. Pathology 3. NF-κB expression 4. Psoriasis severity	Egypt	Unknown
Effectiveness of cannabis and turmeric cream for the treatment of dermatitis and psoriasis	TCTR20240902001	Psoriasis or eczema	Herbal cream containing *Cannabis sativa* and *Curcuma longa*	4 weeks	1. PASI and EASI score 2. QOL: DLQI	Thailand	Completed

Note: Italicized alphabets denote species names.

Abbreviations: DLQI, Dermatology life quality index; EASI, Eczema area and severity index; QOL, quality of life; NF-κB, Nuclear factor-kappa B; PASI, Psoriasis area and severity index; PGA, Physician global assessment.

https://doi.org/10.2147/DDDT.S520555

Table 5 Safety Profiles of Curcumin: Evidence from Non-Clinical and Clinical Studies

Dosage Form	Treatment Group (Dose)	Population	Treatment Duration	Outcomes	Results	References
1. In vitro studies						
Solution	• CUR (15.625–1000 μM)	HaCaT cells	24 hours	Cytotoxicity (IC_{50} values)	IC_{50} of 219.42 μM	[28]
Solution	• CUR (0.1–10 μM) • CUR-MPA conjugated (0.1–10 μM)	Caco-2 cells	24 hours	Cell viability	No significant cytotoxic effect (≤ 5 μM)	[31]
Ionic liquid-liposome	• CUR-Bet-IL (6.25–200 ug/mL) • CUR-Bet-IL-Lipo (6.25–200 ug/mL)	HSF cells	24 hours	Cell viability	Low cytotoxic effect	[56]
Water responsive gel	• CUR-WRG (0–50 mg/mL)	HaCaT cells	12 hours	Cell viability	Low cytotoxic effect	[72]
Nanostructured lipid carrier gel	• CUR gel (20 mg/kg) • CUR-NLC (20 mg/kg)	HaCaT cells	24 hours	Cytotoxicity (IC_{50} values)	CUR-NLC gel exhibited greater toxicity than CUR-gel	[42]
Liposomal gel	• CUR-gel (20 mg/kg) • CUR-Lipo gel (20 mg/kg) • CUR-IBR (Eqv CUR 20 mg/kg) • CUR-IBR-Lipo gel (Eqv CUR 20 mg/kg)	HaCaT cells	24 hours	Cytotoxicity (IC_{50} values)	CUR-Lipo gel exhibited greater toxicity than CUR-gel CUR-IBR-Lipo gel showed the highest cytotoxic effect among the formulations	[43]
2. Ex vivo studies						
Niosomal gel	• CUR-NIO (5, 10, 15 μM)	PBMCs in healthy volunteers	4 days	Cytotoxicity	Low cytotoxic effect across all concentrations	[40]
3. In vivo studies						
3.1 Oral treatment						
N/A	• CUR (40 mg/kg)	Keratin 14-VEGF transgenic mice	20 days	Histological evaluation	No adverse effect on the kidneys of the mice	[32]
3.2 Topical treatment						
Liposomal gel	• CUR-gel (20 mg/kg) • CUR-Lipo gel (20 mg/kg) • CUR-IBR (Eqv CUR 20 mg/kg) • CUR-IBR-Lipo gel (Eqv CUR 20 mg/kg)	BALB/c mice	6 days	Cutaneous toxicity	No visible signs of erythema or swelling	[43]
Water responsive gel	• CUR (30 μM) • CUR-WRG (Eqv CUR 30 μM)	BALB/c mice	3 days	Body weight	Similar weight change as normal group	[72]
Nanosponge gel	• CUR-CFN-NS gel • Marketed CUR	BALB/c mice	72 hours	Acute skin irritation	No signs of edema or erythema	[73]
Nanoemulgel	• CUR-TQ-*RS* nanoemulgel (Eqv CUR 3 mg/mL)	Albino rats	-	Primary Irritation Index (PII)	No signs of irritation (PII score = 1.4, indicating its non-irritating nature)	[59]
Liposphere gel	• CUR-TAC liposphere gel (Eqv CUR 25μg) • CUR-TAC solution (Eqv CUR 25 μg)	BALB/c mice	6 days	Skin compliance study	No obvious change in histopathological features and inflammatory signs was observed.	[61]

4. Clinical studies						
4.1 Oral treatment						
Capsule	• Curcuminoid (C3 Complex®) capsules 4.5 g/d (n=12)	Patients with moderate-to-severe psoriasis vulgaris	12 weeks	1. AEs	Possibly related AEs: Mild gastrointestinal upset or heat intolerance/hot flashes (n=10)	[81]
Tablet	• CUR 2 g/d; tablet + MPA 0.1%; ointment (n=31)	Patients with mild-to-moderate psoriasis vulgaris (PASI < 10)	12 weeks	AEs	Diarrhea (n=1) in the active group, which was attributed to viral gastroenteritis rather than CUR	[82]
Capsule	• CUR 3 g/d (nanoparticles filled in hard gelatine capsules) + Acitretin 0.4 mg/kg/d (n=15) • PLA + Acitretin 0.4 mg/kg/d (n=15)	Patients with moderate-to-severe psoriasis (PASI ≥ 10)	12 weeks	1. AEs 2. Serum biochemical lab	1. Nausea and vomiting (Active: n=1), mild cheilitis (Active: n=6; PLA: n=8), peeling of palms and soles (Active: n=1; PLA: n=1) 2. Significant increase in total cholesterol in the PLA group	[83]
4.2 Topical treatment						
Niosomal gel	• 0.1% w/w CUR-NIO gel (n=5) • PLA (n=5)	Patients with mild-to-moderate psoriasis vulgaris (PASI scores < 30)	4 weeks	AEs	No AEs	[40]
Microemulgel	• 0.5% TUR microemulgel [containing 30 μg/mL of CUR] (n=17) • PLA (n=17)	Patients with mild-to-moderate plaque psoriasis	9 weeks	AEs	Burning (6%), dryness (6%), and irritation (3%) in the active group	[84]

Notes: The results of the treatment groups were compared with those of the untreated group or vehicle group.

Abbreviations: AEs, Adverse events; Caco-2, Colorectal adenocarcinoma; CUR, Curcumin; CUR-Bet-IL, Curcumin-betaine-ionic liquid; CUR-Bet-IL-Lipo, Curcumin-betaine-ionic liquid-loaded liposome; CUR-CFN-NS, Curcumin and caffeine-loaded nanosponge; CUR-IBR, Combination of curcumin and ibrutinib; CUR-IBR-Lipo gel, Curcumin and ibrutinib co-loaded liposomal gel; CUR-Lipo, Curcumin-loaded liposome; CUR-MPA, Curcumin and mycophenolic acid; CUR-NIO, Curcumin-loaded niosome; CUR-NLC, Curcumin-loaded nanostructured lipid carrier gel; CUR-TAC liposphere gel, Curcumin and tacrolimus co-loaded liposphere gel; CUR-TQ-RS, Combination of curcumin, thymoquinone and Resveratrol; CUR-WRG, Curcumin-loaded water responsive gel; Eqv, Equivalent; g/d, Grams per day; HaCaT, Human immortalized keratinocytes; HSF, Human skin fibroblast; IC_{50}, Half maximal inhibitory concentration; mg/kg, Milligrams per kilogram; mg/kg/d, Milligrams per kilogram per day; n, Number of participants; PASI, Psoriasis area severity index; PBMCs, Peripheral blood mononuclear cells; PLA, Placebo; TUR, Turmeric; VEGF, Vascular endothelial growth factor; w/w, Weight per weight; μg, Micrograms; μg/mL, Micrograms per milliliter; μM, Micromolar.

https://doi.org/10.2147/DDDT.S520555

might result from a synergistic effect, as indicated by a combination index value of 0.476, amplifying curcumin's cytotoxic potential.

Studies on novel curcumin formulations, such as ionic liquid-loaded liposomes and water-responsive gel, exhibit no significant cytotoxicity in both HaCaT and HSF cells.[56,72] However, it is noteworthy that the novel formulations significantly increased the cytotoxicity of curcumin, as evidenced by a decrease in the IC_{50} value, which dropped from 6.90 ± 0.36 μM for the curcumin solution to 3.86 ± 0.67 μM for the curcumin-loaded liposomal gel when tested on HaCaT cells.[43] Additionally, this result was consistent with observations from curcumin-loaded nanostructured lipid carriers.[42] This enhancement could be attributed to increased cellular uptake, resulting in elevated concentrations of curcumin within cells and, consequently, enhanced cytotoxic effects. Therefore, optimizing the dosage and formulation of curcumin is essential to achieve a balance between its therapeutic effects and safety profile.

The ex vivo study examining curcumin and curcumin niosome formulations on peripheral blood mononuclear cells (PBMCs) from healthy volunteers showed consistently low cytotoxicity across all tested concentrations (5, 10, and 15 μM).[40] Overall, these findings affirm the safety of curcumin and its formulations in non-clinical studies, underscoring the need for further investigation in animal studies.

In vivo Studies

Oral Administration

Oral curcumin has demonstrated safety in both acute and sub-chronic toxicity animal studies, with minimal adverse effects observed. In an acute toxicity study, Swiss albino mice and Wistar albino rats were administered a 5000 mg/kg dose of curcumin over 14 days.[88] No mortality, toxic effects, or significant differences in body weight were observed. In a subchronic toxicity study, Wistar rats were fed curcumin (≥ 90% purity) at doses of 0, 130–140, 250–290, and 850–960 mg/kg body weight per day for males, and 0, 160, 310–320, and 1000–1100 mg/kg body weight/day for females over 21 weeks for the parental generation and 24 weeks for the F1 generation.[89] There were no treatment-related toxicological effects in the parental animals, and no gross or microscopic changes were observed in any organs. Reproductive parameters were unaffected, and the only effect on the offspring was a slight reduction in pre-weaning body weight gain in F2 pups at the highest dose level. Consequently, this study established the No Observed Adverse Effect Level (NOAEL) for curcumin's reproductive toxicity to be 847–1076 mg/kg body weight/day, equivalent to an estimated human dose of 8.2–10.4 g/day for a 60 kg individual. Additionally, mutagenicity has not been observed in rodent models treated with curcumin.[90] In terms of chronic toxicity, a six-month study was conducted using curcumin-loaded nanocomplexes in rats and mice, with equivalent curcumin doses ranging from 50–450 mg/kg/day in hamsters and 25–225 mg/kg/day in mice.[91] The study found that high-dose treatment significantly increased the organ-to-body weight ratios of the stomach and intestine in mice, and the lung and heart in hamsters. In mice, elevated levels of glucose, total protein, liver enzymes, and globulin were observed, while hamsters exhibited increased liver enzyme levels and decreased cholesterol levels. Importantly, these abnormalities were reversed within 28 days after treatment cessation. These findings highlight the importance of cautious administration of high doses of curcumin for long-term use.

In psoriasis mouse models, oral curcumin has also demonstrated safety. Kang et al (2016) evaluated renal histology in keratin 14-VEGF transgenic mice treated with either oral curcumin (40 mg/kg) or cyclosporine (40 mg/kg), a potent immunosuppressant approved by the United States Food and Drug Administration (FDA) for psoriasis treatment, over a 20-day period.[32] This study found no significant histopathological changes in the kidneys of curcumin-treated mice compared to those treated with cyclosporine, which is known to cause significant nephrotoxicity.[92,93] However, the study's short duration did not allow for the assessment of potential systemic adverse effects that could result from oral curcumin administration over a longer period.

Topical Administration

The safety of curcumin incorporated into nanocarriers, such as liposomes, water-responsive gel, nanosponge, nanoemulsion, and liposphere, in topical formulations has been documented, with no evidence of skin irritation or histological changes observed in animal models.[43,59,61,73] These findings underscore the potential of curcumin for safe topical application, representing a critical preliminary step prior to human clinical evaluation. However, these investigations

have certain limitations. Firstly, the protocols of these animal studies have not always followed standardized guidelines for skin toxicity assessments, such as those outlined by the Organization for Economic Co-operation and Development (OECD), which may affect the reliability and reproducibility of the findings. Secondly, the treatment durations were relatively short, and thirdly, comprehensive safety assessments addressing potential systemic adverse effects were lacking. Therefore, further comprehensive safety studies adhering to standardized guidelines are essential to thoroughly evaluate the safety profiles of these novel formulations.

Clinical Studies

Oral Administration

The safety of oral curcumin in healthy volunteers has been well-established in clinical studies. In a study of 59 healthy young individuals, a daily dose of 200 mg of curcumin for 8 weeks caused no adverse effects, with blood counts and metabolic panels remaining within normal ranges.[94] Similarly, Lao et al (2006) evaluated curcumin's safety in 24 healthy volunteers with doses ranging from 0.5 to 12 g of C3 Complex™ capsules, equivalent to curcumin doses of 0.38 to 9 g.[95] Over 72 hours of monitoring, seven participants experienced mild adverse effects, such as diarrhea, headache, rash, and yellowish stool. These effects were not dose-dependent, highlighting curcumin's safety at high doses. Additionally, a prospective Phase I study by Cheng et al (2001) assessed the safety of curcumin in 25 patients who received curcumin (99.3% purity) for three months.[96] The initial dose of 0.5 g/day gradually escalated to 1, 2, 4, 8, and finally 12 g/day. However, the highest dose of 12 g/day was not well-tolerated due to the large volume of the tablets, leading to a dose reduction and discontinuation at 8 g/day. No adverse effects were observed at doses up to 8 g/day. Based on the findings, it could be implied that the safety of oral curcumin administration was assessed at doses up to 8 g/day over a period of up to three months. Regarding the long-term safety of curcumin, a study randomized thirty-six individuals with mild-to-moderate Alzheimer's disease to receive either a placebo, 2 g/day, or 4 g/day of oral curcumin for 48 weeks.[97] The incidence of adverse events did not differ significantly between the curcumin and placebo groups. Reported adverse events included endocrine-related complaints, diarrhea, and joint pain. It can be inferred that oral curcumin, at doses up to 4 g/day, may be safe for use over a 48-week period.

Oral curcumin has been shown to be safe in psoriasis patients, with no significant systemic adverse events observed. The findings from Kurd's study demonstrated that curcumin was safe for patients with moderate-to-severe psoriasis vulgaris who received 4.5 g/day of C3 Complex™ capsules (approximately equivalent to 3.4 g/d of curcumin) for 10 weeks, with only mild adverse events observed in a single-arm, open-label study.[81] In a study by Antiga et al (2015), among 31 patients treated with oral curcumin (2 g/day) and mycophenolic acid ointment (0.1%) over 12 weeks, one patient experienced diarrhea, while the placebo group noted one case of papular eruption and two cases of nausea.[82] Additionally, a 12-week study evaluating an oral formulation combining curcumin nanoparticles (3 g/day) and acitretin (0.4 mg/kg/day) reported mild adverse effects, such as cheilitis, and peeling of the palms and soles.[83] However, the study suggested that these adverse effects may be more related to acitretin rather than curcumin. Concerning the safety of adjunctive therapy, caution is warranted when curcumin is administered in combination with other therapeutic agents, particularly immunosuppressants. Due to the immunomodulatory effects of curcumin, such combinations may enhance the immunosuppressive effects, thereby increasing the risk of infections.[98,99] Furthermore, curcumin may potentially affect other therapeutic agents by modulating the cytochrome P450 enzyme system or transporters involved in drug clearance.[100] Such interactions may alter the pharmacokinetics of co-administered drugs, thereby contributing to therapeutic challenges and increasing the risk of adverse events.

Overall, oral curcumin is generally considered safe for psoriasis treatment, with mild and manageable adverse effects. Nevertheless, the limited sample sizes and short durations (10–12 weeks) of these studies may not adequately capture the long-term safety profile of curcumin, particularly concerning potential systemic adverse effects.

Topical Administration

To date, novel curcumin-based topical formulations have been shown to be safe and well-tolerated for psoriasis treatment with no significant adverse effects, including allergic reactions, skin irritation, or photosensitivity. A 0.1% curcumin-loaded niosome gel, applied over a 4-week period, was well-tolerated in mild-to-moderate psoriasis patients, with no

adverse events observed.[40] Another study demonstrated that mild-to-moderate plaque psoriasis patients who applied turmeric microemulgel (containing 30 μg/mL curcumin) for nine weeks experienced mild adverse effects: 6% reported a burning sensation, 6% reported dryness, and 3% reported irritation.[84] However, the study suggested that these adverse events were more likely due to other ingredients in the formulation rather than curcumin itself. Although these topical formulations are reported to be safe in previous studies, the lack of standardized assessments for skin irritation or sensitization poses challenges in drawing definitive conclusions about their safety. Future studies should incorporate standardized safety assessments and include participants with varied skin sensitivities to account for a broader spectrum of potential skin reactions to curcumin-based topical treatments. Given the chronic nature of psoriasis and the likelihood of prolonged administration, rigorous long-term safety studies are essential to thoroughly evaluate the risk-benefit profile of these formulations.

Conclusion

Curcumin exerts an anti-psoriatic effect through multi-targeted actions, including inhibiting cell proliferation, inducing apoptosis, suppressing pro-inflammatory cytokines, exhibiting antioxidant effects, and enhancing skin barrier protein expression. Through these mechanisms of action, curcumin significantly improves psoriasis lesions, such as reducing thickened and scaly plaques. Additionally, its multi-targeted actions may offer a more comprehensive approach to managing psoriasis, especially when used in conjunction with other treatment modalities, potentially reducing the risk of adverse effects associated with high-dose monotherapies. Despite its therapeutic potential, both oral and topical curcumin formulations face challenges related to low bioavailability and limited skin penetration, emphasizing the need for advanced formulations. Novel topical curcumin formulations, such as liposome, nanosponge, nanoemulsion, and liposphere, have been developed to enhance its anti-psoriatic effects by improving skin penetration, protecting it from degradation, and facilitating sustained release. Moreover, curcumin has demonstrated a favorable safety profile in both clinical and non-clinical studies. However, current clinical evidence remains limited, with small sample sizes, short durations, and a lack of comprehensive assessments, thereby warranting further investigation. Overall, curcumin and its novel formulations may be promising candidates for psoriasis treatment; however, further studies, particularly large-scale clinical trials, are needed to fully assess their efficacy and safety.

Data Sharing Statement

This review manuscript does not contain original data or unpublished research. All referenced data supporting the results discussed in this manuscript are derived from publicly available sources.

Acknowledgments

This research was partially supported by Chiang Mai University. We acknowledge that the figures presented in this publication were created using BioRender (BioRender.com).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, acquisition of data, and interpretation, or in all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research project was supported by Fundamental Fund 2025, Chiang Mai University, and Thailand Science Research and Innovation (TSRI) (Granted number FRB680102/0162).

Disclosure

The authors declare no conflicts of interest in this work.

References

1. Boehncke WH, Schön MP. Psoriasis. *Lancet*. 2015;386(9997):983–994. doi:10.1016/s0140-6736(14)61909-7
2. World Health Organization. Global report on psoriasis. Noncommunicable diseases, rehabilitation and disability (NCD). 2016. Available from: https://www.who.int/publications/i/item/9789241565189. Accessed June 10, 2025.
3. Sarac G, Koca TT, Baglan T. A brief summary of clinical types of psoriasis. *North Clin Istanb*. 2016;3(1):79–82. doi:10.14744/nci.2016.16023
4. Greaves MW, Weinstein GD. Treatment of psoriasis. *N Engl J Med*. 1995;332(9):581–588. doi:10.1056/nejm199503023320907
5. Augustin M, Radtke MA. Quality of life in psoriasis patients. *Expert Rev Pharmacoecon Outcomes Res*. 2014;14(4):559–568. doi:10.1586/14737167.2014.914437
6. Zhou X, Chen Y, Cui L, Shi Y, Guo C. Advances in the pathogenesis of psoriasis: from keratinocyte perspective. *Cell Death Dis*. 2022;13(1):81. doi:10.1038/s41419-022-04523-3
7. Soares CLR, Wilairatana P, Silva LR, et al. Biochemical aspects of the inflammatory process: a narrative review. *Biomed Pharmacother*. 2023;168:115764. doi:10.1016/j.biopha.2023.115764
8. Nussbaum L, Chen YL, Ogg GS. Role of regulatory T cells in psoriasis pathogenesis and treatment. *Br J Dermatol*. 2021;184(1):14–24. doi:10.1111/bjd.19380
9. Bovenschen HJ, Seyger MM, Van de Kerkhof PC. Plaque psoriasis vs. atopic dermatitis and lichen planus: a comparison for lesional T-cell subsets, epidermal proliferation and differentiation. *Br J Dermatol*. 2005;153(1):72–78. doi:10.1111/j.1365-2133.2005.06538.x
10. Wu M, Dai C, Zeng F. Cellular mechanisms of psoriasis pathogenesis: a systemic review. *Clin Cosmet Invest Dermatol*. 2023;16:2503–2515. doi:10.2147/ccid.S420850
11. Nicolescu AC, Ionescu MA, Constantin MM, et al. Psoriasis management challenges regarding difficult-to-treat areas: therapeutic decision and effectiveness. *Life*. 2022;12(12):2050. doi:10.3390/life12122050
12. Oranje AP, Marcoux D, Svensson A, et al. Topical calcipotriol in childhood psoriasis. *J Am Acad Dermatol*. 1997;36(2 Pt 1):203–208. doi:10.1016/s0190-9622(97)70281-0
13. Zhu B, Jing M, Yu Q, Ge X, Yuan F, Shi L. Treatments in psoriasis: from standard pharmacotherapy to nanotechnology therapy. *Postepy Dermatol Alergol*. 2022;39(3):460–471. doi:10.5114/ada.2021.108445
14. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol*. 2021;84(2):432–470. doi:10.1016/j.jaad.2020.07.087
15. Lee HJ, Kim M. Challenges and future trends in the treatment of psoriasis. *Int J Mol Sci*. 2023;24(17). doi:10.3390/ijms241713313
16. Mansouri B, Patel M, Menter A. Biological therapies for psoriasis. *Expert Opin Biol Ther*. 2013;13(12):1715–1730. doi:10.1517/14712598.2013.853739
17. Peters BP, Weissman FG, Gill MA. Pathophysiology and treatment of psoriasis. *Am J Health Syst Pharm*. 2000;57(7):645–59;quiz660–1. doi:10.1093/ajhp/57.7.645
18. Singh KK, Tripathy S. Natural treatment alternative for psoriasis: a review on herbal resources. *J Appl Pharm Sci*. 2014;4:114–121. doi:10.7324/JAPS.2014.41120
19. Abd El-Hack ME, El-Saadony MT, Swelum AA, et al. Curcumin, the active substance of turmeric: its effects on health and ways to improve its bioavailability. *J Sci Food Agric*. 2021;101(14):5747–5762. doi:10.1002/jsfa.11372
20. Barbalho SM, de Sousa Gonzaga HF, de Souza GA, de Alvares Goulart R, de Sousa Gonzaga ML, de Alvarez Rezende B. Dermatological effects of Curcuma species: a systematic review. *Clin Exp Dermatol*. 2021;46(5):825–833. doi:10.1111/ced.14584
21. Nardo V, Gianfaldoni S, Tchernev G, et al. Use of Curcumin in psoriasis. *Open Access Maced J Med Sci*. 2018;6:218–220. doi:10.3889/oamjms.2018.055
22. Nguyen TA, Friedman AJ. Curcumin: a novel treatment for skin-related disorders. *J Drugs Dermatol*. 2013;12(10):1131–1137.
23. Thangapazham RL, Sharma A, Maheshwari RK. Beneficial role of curcumin in skin diseases. *Adv Exp Med Biol*. 2007;595:343–357. doi:10.1007/978-0-387-46401-5_15
24. Vollono L, Falconi M, Gaziano R, et al. Potential of curcumin in skin disorders. *Nutrients*. 2019;11(9):2169. doi:10.3390/nu11092169
25. Prasad S, Tyagi AK, Aggarwal BB, et al. Recent developments in delivery, bioavailability, absorption and metabolism of curcumin: the golden pigment from golden spice. *Cancer Res Treat*. 2014;46(1):2–18. doi:10.4143/crt.2014.46.1.2
26. Purkait MK, Haldar D, Duarah P. Applications of herb-derived bioactive phytochemicals. In: *Advances in Extraction and Applications of Bioactive Phytochemicals*. New York: Academic Press; 2023:167–195.
27. Sun J, Han J, Zhao Y, Zhu Q, Hu J. Curcumin induces apoptosis in tumor necrosis factor-alpha-treated HaCaT cells. *Int Immunopharmacol*. 2012;13(2):170–174. doi:10.1016/j.intimp.2012.03.025
28. Varma SR, Sivaprakasam TO, Mishra A, et al. Imiquimod-induced psoriasis-like inflammation in differentiated Human keratinocytes: its evaluation using curcumin. *Eur J Pharmacol*. 2017;813:33–41. doi:10.1016/j.ejphar.2017.07.040
29. Zhang J, Ma Y, Li W. Curcumin reduces inflammation in mice with the psoriasis model by inhibiting NLRP3 inflammatory bodies. *Cell Mol Biol*. 2022;67(6):48–54. doi:10.14715/cmb/2021.67.6.7
30. Zhao Y, Sun J, Dou W, Hu JH. Curcumin inhibits proliferation of interleukin-22-treated HaCaT cells. *Int J Clin Exp Med*. 2015;8(6):9580–9584.
31. Yuyun Y, Ratnatilaka Na Bhuket P, Supasena W, et al. A novel curcumin-mycophenolic acid conjugate inhibited hyperproliferation of tumor necrosis factor-alpha-induced human keratinocyte cells. *Pharmaceutics*. 2021;13(7):956. doi:10.3390/pharmaceutics13070956
32. Kang D, Li B, Luo L, et al. Curcumin shows excellent therapeutic effect on psoriasis in mouse model. *Biochimie*. 2016;123:73–80. doi:10.1016/j.biochi.2016.01.013
33. Skyvalidas D, Mavropoulos A, Tsiogkas S, et al. Curcumin mediates attenuation of pro-inflammatory interferon γ and interleukin 17 cytokine responses in psoriatic disease, strengthening its role as a dietary immunosuppressant. *Nutr Res*. 2020;75:95–108. doi:10.1016/j.nutres.2020.01.005
34. Heng MC, Song MK, Harker J, Heng MK. Drug-induced suppression of phosphorylase kinase activity correlates with resolution of psoriasis as assessed by clinical, histological and immunohistochemical parameters. *Br J Dermatol*. 2000;143(5):937–949. doi:10.1046/j.1365-2133.2000.03767.x

35. Cai Z, Zeng Y, Liu Z, Zhu R, Wang W. Curcumin alleviates epidermal psoriasis-like dermatitis and IL-6/STAT3 pathway of mice. *Clin Cosmet Invest Dermatol*. 2023;16():2399–2408. doi:10.2147/CCID.S423922
36. Mousa AM, Alhumaydhi FA, Abdellatif AAH, et al. Curcumin and ustekinumab cotherapy alleviates induced psoriasis in rats through their antioxidant, anti-inflammatory, and antiproliferative effects. *Cutan Ocul Toxicol*. 2022;41(1):33–42. doi:10.1080/15569527.2021.2003377
37. Cai Z, Wang W, Zhang Y, Zeng Y. Curcumin alleviates imiquimod-induced psoriasis-like inflammation and regulates gut microbiota of mice. *Immun Inflamm Dis*. 2023;11(8):e967. doi:10.1002/iid3.967
38. Li JQ, Zhang SH, Tong RS, He D, Zhong ZD, She SY. Curcuma's extraction attenuates propranolol-induced psoriasis like in mice by inhibition of keratin, proliferating cell nuclear antigen and toll-like receptor expression. *Pak J Pharm Sci*. 2020;33(3):1033–1048.
39. Sun J, Zhao Y, Hu J. Curcumin inhibits imiquimod-induced psoriasis-like inflammation by inhibiting IL-1beta and IL-6 production in mice. *PLoS One*. 2013;8(6):e67078. doi:10.1371/journal.pone.0067078
40. Kolahdooz H, Khori V, Erfani-Moghadam V, Livani F, Mohammadi S, Memarian A. Niosomal curcumin suppresses IL17/IL23 immunopathogenic axis in skin lesions of psoriatic patients: a pilot randomized controlled trial. *Life*. 2023;13(5):1076. doi:10.3390/life13051076
41. Terzopoulou Z, Michopoulou A, Palamidi A, Koliakou E, Bikiaris D. Preparation and evaluation of collagen-based patches as curcumin carriers. *Polymers*. 2020;12(10):2393. doi:10.3390/polym12102393
42. Jain H, Devabattula G, Bhat A, et al. Topical delivery of Bruton's tyrosine kinase inhibitor and curcumin-loaded nanostructured lipid carrier gel: repurposing strategy for the psoriasis management. *Pharm Dev Technol*. 2022;27(9):975–988. doi:10.1080/10837450.2022.2142610
43. Jain H, Geetanjali D, Dalvi H, Bhat A, Godugu C, Srivastava S. Liposome mediated topical delivery of Ibrutinib and Curcumin as a synergistic approach to combat imiquimod induced psoriasis. *J Drug Deliv Sci Technol*. 2022;68:103103. doi:10.1016/j.jddst.2022.103103
44. Yang K-Y, Lin L-C, Tseng T-Y, Wang S-C, Tsai T-H. Oral bioavailability of curcumin in rat and the herbal analysis from Curcuma longa by LC–MS/MS. *J Chromatogr B*. 2007;853(1):183–189. doi:10.1016/j.jchromb.2007.03.010
45. Aggarwal BB, Kumar A, Bharti AC. Anticancer potential of curcumin: preclinical and clinical studies. *Anticancer Res*. 2003;23(1a):363–398.
46. Maiti K, Mukherjee K, Gantait A, Saha BP, Mukherjee PK. Curcumin-phospholipid complex: preparation, therapeutic evaluation and pharmacokinetic study in rats. *Int J Pharm*. 2007;330(1–2):155–163. doi:10.1016/j.ijpharm.2006.09.025
47. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. *Mol Pharm*. 2007;4(6):807–818. doi:10.1021/mp700113r
48. Wahlström B, Blennow G. A study on the fate of curcumin in the rat. *Acta Pharmacol Toxicol*. 1978;43(2):86–92. doi:10.1111/j.1600-0773.1978.tb02240.x
49. Wang Y-J, Pan M-H, Cheng A-L, et al. Stability of curcumin in buffer solutions and characterization of its degradation products. *J Pharm Biomed Anal*. 1997;15(12):1867–1876. doi:10.1016/S0731-7085(96)02024-9
50. Tayyem RF, Heath DD, Al-Delaimy WK, et al. Curcumin content of turmeric and curry powders. *Nutr Cancer*. 2006;55(2):126–131. doi:10.1207/s15327914nc5502_2
51. Jhawat V, Saini V, Kamboj S, Maggon N. Transdermal drug delivery systems: approaches and advancements in drug absorption through skin. *Int J Pharm Sci Rev Res*. 2013;20(1):47–56.
52. Brown MB, Martin GP, Jones SA, Akomeah FK. Dermal and transdermal drug delivery systems: current and future prospects. *Drug Deliv*. 2006;13(3):175–187. doi:10.1080/10717540500455975
53. Waghule T, Gorantla S, Rapalli VK, et al. Emerging trends in topical delivery of curcumin through lipid nanocarriers: effectiveness in skin disorders. *AAPS Pharm Sci Tech*. 2020;21(7):284. doi:10.1208/s12249-020-01831-9
54. Ratnatilaka Na Bhuket P, El-Magboub A, Haworth IS, et al. Enhancement of curcumin bioavailability via the prodrug approach: challenges and prospects. *Eur J Drug Metab Pharmacokinet*. 2017;42(3):341–353. doi:10.1007/s13318-016-0377-7
55. Stielow M, Witczyńska A, Kubryń N, Fijałkowski Ł, Nowaczyk J, Nowaczyk A. The bioavailability of drugs—the current state of knowledge. *Molecules*. 2023;28(24):8038.
56. Lu B, Zhang J, Zhang J. Enhancing transdermal delivery of curcumin-based ionic liquid liposomes for application in psoriasis. *ACS Appl Bio Mater*. 2023;6(12):5864–5873. doi:10.1021/acsabm.3c01026
57. Yu F, Zhang Y, Yang C, Li F, Qiu B, Ding W. Enhanced transdermal efficiency of curcumin-loaded peptide-modified liposomes for highly effective antipsoriatic therapy. *J Mater Chem B*. 2021;9(24):4846–4856. doi:10.1039/d1tb00557j
58. Guo T, Lu J, Fan Y, et al. TPGS assists the percutaneous administration of curcumin and glycyrrhetinic acid coloaded functionalized ethosomes for the synergistic treatment of psoriasis. *Int J Pharm*. 2021;604:120762. doi:10.1016/j.ijpharm.2021.120762
59. Khatoon K, Ali A, Ahmad FJ, et al. Novel nanoemulsion gel containing triple natural bio-actives combination of curcumin, thymoquinone, and resveratrol improves psoriasis therapy: in vitro and in vivo studies. *Drug Delivery Trans Res*. 2021;11(3):1245–1260. doi:10.1007/s13346-020-00852-y
60. Gomez C, Muangnoi C, Sorasitthiyanukarn FN, Wongpiyabovorn J, Rojsitthisak P, Rojsitthisak P. Synergistic effects of photo-irradiation and curcumin-chitosan/alginate nanoparticles on tumor necrosis factor-alpha-induced psoriasis-like proliferation of keratinocytes. *Molecules*. 2019;24(7). doi:10.3390/molecules24071388
61. Jain A, Doppalapudi S, Domb AJ, Khan W. Tacrolimus and curcumin co-loaded liposphere gel: synergistic combination towards management of psoriasis. *J Control Release*. 2016;243:132–145. doi:10.1016/j.jconrel.2016.10.004
62. Algahtani MS, Ahmad MZ, Nourein IH, Ahmad J. Co-delivery of imiquimod and curcumin by nanoemugel for improved topical delivery and reduced psoriasis-like skin lesions. *Biomolecules*. 2020;10(7):968. doi:10.3390/biom10070968
63. Filippone A, Consoli GML, Granata G, et al. Topical delivery of curcumin by choline-calix[4]arene-based nanohydrogel improves its therapeutic effect on a psoriasis mouse model. *Int J Mol Sci*. 2020;21(14):5053. doi:10.3390/ijms21145053
64. Jaiswal P, Das S, Das M. Boosting the skin delivery of curcumin through stearic acid-ethyl cellulose blend hybrid nanocarriers-based approach for mitigating psoriasis. *Int J Appl Pharm*. 2021;13:150–164. doi:10.22159/ijap.2021v13i3.40668
65. Algahtani MS, Ahmad MZ, Ahmad J. Nanoemulsion loaded polymeric hydrogel for topical delivery of curcumin in psoriasis. *J Drug Deliv Sci Technol*. 2020;59:101847. doi:10.1016/j.jddst.2020.101847
66. Boscariol R, Caetano ÉA, Grotto D, et al. Transdermal permeation assays of curcumin aided by CAGE-IL: in vivo control of psoriasis. *Pharmaceutics*. 2022;14(4):779. doi:10.3390/pharmaceutics14040779

67. Jin N, Lin J, Yang C, et al. Enhanced penetration and anti-psoriatic efficacy of curcumin by improved smartPearls technology with the addition of glycyrrhizic acid. *Int J Pharm*. 2020;578:119101. doi:10.1016/j.ijpharm.2020.119101
68. Jin N, He J, Wu C, et al. Glycyrrhizic acid assists anti-psoriatic efficacy of a self-deformable curcumin loaded transdermal gel. *Pharm Dev Technol*. 2022;27(3):282–289. doi:10.1080/10837450.2022.2039943
69. Kumar B, Sahoo PK. Augmented transdermal delivery of curcumin for the effective management of plaque psoriasis - design, formulation, characterisation, and in vivo studies. *AAPS Pharm Sci Tech*. 2023;24(5):134. doi:10.1208/s12249-023-02595-8
70. Mao K-L, Fan Z-L, Yuan J-D, et al. Skin-penetrating polymeric nanoparticles incorporated in silk fibroin hydrogel for topical delivery of curcumin to improve its therapeutic effect on psoriasis mouse model. *Colloids Surf B Biointerfaces*. 2017;160:704–714. doi:10.1016/j.colsurfb.2017.10.029
71. Reena K, Mittal S, Faizan M, et al. Enhancement of curcumin's anti-psoriatic efficacy via formulation into tea tree oil-based emulgel. *Gels*. 2023;9(12):973. doi:10.3390/gels9120973
72. Yao Q, Zhai Y, He Z, et al. Water-responsive gel extends drug retention and facilitates skin penetration for curcumin topical delivery against psoriasis. *Asian J Pharm Sci*. 2023;18(2):100782. doi:10.1016/j.ajps.2023.100782
73. Iriventi P, Gupta NV, Osmani RAM, Balamuralidhara V. Design & development of nanosponge loaded topical gel of curcumin and caffeine mixture for augmented treatment of psoriasis. *DARU J Pharm Sci*. 2020;28(2):489–506. doi:10.1007/s40199-020-00352-x
74. Jamatia T, Das S, Das MK. Topical delivery of methoxsalen co-loaded curcumin using hybrid nanocarrier-based polymeric hydrogel for synergistic therapy in the treatment of psoriasis. *J Pharm Innov*. 2023;18(4):2305–2324. doi:10.1007/s12247-023-09794-7
75. Jin N, Chen R, Li Y, Zhang Z, Zhang B, Chen J. Transcutaneous amorphous preparation co-delivering curcumin and modified aptamer as a synergistic approach for the amelioration of psoriasis-like skin inflammation. *Eur J Pharm Sci*. 2023;180:106314. doi:10.1016/j.ejps.2022.106314
76. Shahzad R, Bilal S, Khan A, Shehzad A, Al-Suhaimi EA. Chapter two - Emerging concept on cellular uptake mechanism of nanoparticles. In: Tombuloglu H, Tombuloglu G, Al-Suhaimi E, Baykal A, Hakeem KR, editors. *Molecular Impacts of Nanoparticles on Plants and Algae*. New York: Academic Press; 2024:31–40.
77. N'Guessan-Gnaman K, Tuo-Kouassi N, Dally I, et al. Encapsulation methods and releasing mechanisms of encapsulated active drug. *J Drug Delivery Ther*. 2024;14(1):155–168. doi:10.22270/jddt.v14i1.6356
78. Gaikwad SS, Zanje AL, Somwanshi JD. Advancements in transdermal drug delivery: a comprehensive review of physical penetration enhancement techniques. *Int J Pharm*. 2024;652:123856. doi:10.1016/j.ijpharm.2024.123856
79. Souto EB, Fangueiro JF, Fernandes AR, et al. Physicochemical and biopharmaceutical aspects influencing skin permeation and role of SLN and NLC for skin drug delivery. *Heliyon*. 2022;8(2):e08938. doi:10.1016/j.heliyon.2022.e08938
80. Yu Y-Q, Yang X, Wu X-F, Fan Y-B. Enhancing permeation of drug molecules across the skin via delivery in nanocarriers: novel strategies for effective transdermal applications. *Front Bioeng Biotechnol*. 2021;9. doi:10.3389/fbioe.2021.646554
81. Kurd SK, Smith N, VanVoorhees A, et al. Oral curcumin in the treatment of moderate to severe psoriasis vulgaris: a prospective clinical trial. *J Am Acad Dermatol*. 2008;58(4):625–631. doi:10.1016/j.jaad.2007.12.035
82. Antiga E, Bonciolini V, Volpi W, Del Bianco E, Caproni M. Oral curcumin (Meriva) is effective as an adjuvant treatment and is able to reduce IL-22 serum levels in patients with psoriasis vulgaris. *Biomed Res Int*. 2015;2015:283634. doi:10.1155/2015/283634
83. Bilia AR, Bergonzi MC, Isacchi B, Antiga E, Caproni M. Curcumin nanoparticles potentiate therapeutic effectiveness of acitrein in moderate-to-severe psoriasis patients and control serum cholesterol levels. *J Pharm Pharmacol*. 2018;70(7):919–928. doi:10.1111/jphp.12910
84. Sarafian G, Afshar M, Mansouri P, Asgarpanah J, Raoufinejad K, Rajabi M. Topical turmeric microemulgel in the management of plaque psoriasis; A clinical evaluation. *Iran J Pharm Res*. 2015;14(3):865–876.
85. Crommelin DJ, Florence AT. Towards more effective advanced drug delivery systems. *Int J Pharm*. 2013;454(1):496–511. doi:10.1016/j.ijpharm.2013.02.020
86. Agrawal SS, Baliga V, Londhe VY, et al. Liposomal formulations: a recent update. *Pharmaceutics*. 2024;17(1):36. doi:10.3390/pharmaceutics17010036
87. Vaughn AR, Haas KN, Burney W, et al. Potential role of curcumin against biofilm-producing organisms on the skin: a review. *Phytother Res*. 2017;31(12):1807–1816. doi:10.1002/ptr.5912
88. Aggarwal ML, Chacko KM, Kuruvilla BT. Systematic and comprehensive investigation of the toxicity of curcuminoid-essential oil complex: a bioavailable turmeric formulation. *Mol Med Rep*. 2016;13(1):592–604. doi:10.3892/mmr.2015.4579
89. Ganiger S, Malleshappa HN, Krishnappa H, Rajashekhar G, Ramakrishna Rao V, Sullivan F. A two generation reproductive toxicity study with curcumin, turmeric yellow, in Wistar rats. *Food Chem Toxicol*. 2007;45(1):64–69. doi:10.1016/j.fct.2006.07.016
90. Vijayalaxmi B. Genetic effects of turmeric and curcumin in mice and rats. *Mutation Res*. 1980;79(2):125–132. doi:10.1016/0165-1218(80)90080-4
91. Jantawong C, Priprem A, Intuyod K, et al. Curcumin-loaded nanocomplexes: acute and chronic toxicity studies in mice and hamsters. *Toxicol Rep*. 2021;8:1346–1357. doi:10.1016/j.toxrep.2021.06.021
92. Warren RB, Griffiths CE. Systemic therapies for psoriasis: methotrexate, retinoids, and cyclosporine. *Clin Dermatol*. 2008;26(5):438–447. doi:10.1016/j.clindermatol.2007.11.006
93. Griffiths CE, Dubertret L, Ellis CN, et al. Ciclosporin in psoriasis clinical practice: an international consensus statement. *Br J Dermatol*. 2004;150(s67):11–23. doi:10.1111/j.0366-077X.2004.05949.x
94. Oliver JM, Stoner L, Rowlands DS, et al. Novel form of curcumin improves endothelial function in young, healthy individuals: a double-blind placebo controlled study. *J Nutr Metab*. 2016;2016:1089653. doi:10.1155/2016/1089653
95. Lao CD, Raffin MT, Normolle D, et al. Dose escalation of a curcuminoid formulation. *BMC Complement Altern Med*. 2006;6(1):10. doi:10.1186/1472-6882-6-10
96. Cheng AL, Hsu CH, Lin JK, et al. Phase I clinical trial of curcumin, a chemopreventive agent, in patients with high-risk or pre-malignant lesions. *Anticancer Res*. 2001;21(4b):2895–2900.
97. Ringman JM, Frautschy SA, Teng E, et al. Oral curcumin for Alzheimer's disease: tolerability and efficacy in a 24-week randomized, double blind, placebo-controlled study. *Alzheimers Res Ther*. 2012;4(5):43. doi:10.1186/alzrt146

98. Chueh SC, Lai MK, Liu IS, et al. Curcumin enhances the immunosuppressive activity of cyclosporine in rat cardiac allografts and in mixed lymphocyte reactions. *Transplant Proc*. 2003;35(4):1603–1605. doi:10.1016/s0041-1345(03)00377-4
99. Allegra A, Mirabile G, Ettari R, Pioggia G, Gangemi S. The impact of curcumin on immune response: an immunomodulatory strategy to treat sepsis. *Int J Mol Sci*. 2022;23(23):14710. doi:10.3390/ijms232314710
100. Bahramsoltani R, Rahimi R, Farzaei MH, et al. Pharmacokinetic interactions of curcuminoids with conventional drugs: a review. *J Ethnopharmacol*. 2017;209:1–12. doi:10.1016/j.jep.2017.07.022