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# MOLECULAR EVALUATION OF AN ALOE VERA–CURCUMA LONGA NANO GEL IN EXPERIMENTAL PSORIASIS THROUGH INFLAMMATORY CYTOKINE GENE EXPRESSION AND HISTOPATHOLOGICAL ANALYSIS

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**Abstract**
Background: Psoriasis is a chronic immune-mediated inflammatory skin disorder characterized by excessive keratinocyte proliferation and dysregulated inflammatory cytokine signaling. The present study aimed to develop and evaluate an Aloe vera–Curcuma longa nano gel and investigate its anti-psoriatic efficacy through pharmaceutical characterization, pharmacological assessment, and inflammatory cytokine gene expression analysis.
Methods: The nano gel was prepared using curcumin-loaded nanoparticles incorporated into an Aloe vera-based gel matrix and characterized for physicochemical properties, particle size, zeta potential, drug content, and in vitro drug release. Anti-psoriatic activity was evaluated in an imiquimod-induced psoriasis model. Disease severity was assessed using the Psoriasis Area and Severity Index (PASI), histopathological examination, oxidative stress biomarkers, immunohistochemistry, and quantitative real-time PCR analysis of IL-17A, IL-23, TNF-α, IL-6, NF-κB, and STAT3 gene expression.
Results: The optimized nano gel exhibited favorable physicochemical characteristics, sustained drug release, and excellent stability. Treatment significantly reduced PASI scores, restored normal skin histology, improved antioxidant enzyme activities, and markedly suppressed inflammatory cytokine gene expression compared with the psoriatic control group ($P < 0.001$). Immunohistochemical analysis further confirmed reduced NF-κB activation and keratinocyte proliferation.
Conclusion: The Aloe vera–Curcuma longa nano gel demonstrated significant anti-psoriatic efficacy through modulation of inflammatory and oxidative stress pathways, highlighting its potential as a promising herbal nanotherapeutic strategy for psoriasis management.

**Keywords:** Aloe vera; Curcuma longa; Nano gel; Psoriasis; Inflammatory cytokine gene expression.

## 1. Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by recurrent episodes of erythematous, well-demarcated, scaly plaques resulting from excessive keratinocyte proliferation, abnormal epidermal differentiation, angiogenesis, and persistent immune activation. The disease affects nearly 2–3% of the global population and represents a substantial public health burden because of its chronic relapsing nature, associated comorbidities, and significant impairment of patients' physical, psychological, and social well-being. Beyond cutaneous manifestations, psoriasis is now recognized as a systemic inflammatory disease associated with psoriatic arthritis, cardiovascular disorders, metabolic syndrome, obesity, diabetes mellitus, and depression, emphasizing the need for safe and effective long-term therapeutic strategies [1,2].
The molecular pathogenesis of psoriasis is highly complex and involves intricate interactions among genetic susceptibility, environmental triggers, innate immunity, adaptive immune responses, and epidermal keratinocytes.

Genome-wide association studies have identified numerous psoriasis susceptibility loci, including HLA-C06:02*, IL23R, IL12B, TNFAIP3, TRAF3IP2,* and CARD14, highlighting the genetic basis of disease susceptibility. Environmental factors such as infections, trauma, stress, obesity, and certain medications initiate immune activation in genetically predisposed individuals, leading to activation of dendritic cells and differentiation of naïve T lymphocytes into T helper (Th)1 and Th17 subsets. Activated immune cells subsequently release pro-inflammatory cytokines including tumor necrosis factor-alpha (TNF-α), interleukin (IL)-17A, IL-17F, IL-22, IL-23, IL-1β, and IL-6, thereby establishing a self-perpetuating inflammatory cascade responsible for epidermal hyperplasia and chronic skin inflammation [3–5].

Among these inflammatory mediators, the IL-23/IL-17 signaling axis has emerged as the principal molecular pathway driving psoriasis progression. IL-23 promotes differentiation, proliferation, and maintenance of Th17 lymphocytes, which subsequently produce IL-17A, IL-17F, and IL-22. These cytokines stimulate keratinocytes to secrete chemokines, antimicrobial peptides, and additional inflammatory mediators, thereby amplifying leukocyte recruitment and sustaining chronic inflammation. Furthermore, activation of intracellular signaling pathways such as nuclear factor-kappa B (NF-κB), signal transducer and activator of transcription-3 (STAT3), mitogen-activated protein kinase (MAPK), and Janus kinase/signal transducer and activator of transcription (JAK/STAT) contributes significantly to keratinocyte proliferation, inhibition of apoptosis, and dysregulated epidermal differentiation. Consequently, molecular evaluation of these inflammatory cytokines and signaling pathways has become increasingly important for understanding disease mechanisms and evaluating emerging therapeutic interventions [4–7].

Current management of psoriasis includes topical corticosteroids, vitamin D analogues, calcineurin inhibitors, retinoids, systemic immunosuppressive agents, phototherapy, phosphodiesterase-4 inhibitors, and biologic therapies targeting TNF-α, IL-17, and IL-23. Although these therapies have substantially improved disease management, prolonged treatment is frequently associated with adverse effects including cutaneous atrophy, irritation, hepatotoxicity, nephrotoxicity, immunosuppression, increased susceptibility to infections, treatment resistance, frequent relapse following discontinuation, and considerable economic burden. Moreover, biologic therapies require prolonged administration and remain inaccessible to many patients because of their high cost. These limitations have stimulated intensive research into naturally derived therapeutic agents possessing multiple pharmacological targets with improved safety profiles [8,9].

Medicinal plants have received considerable scientific attention because they contain structurally diverse phytochemicals capable of modulating multiple inflammatory pathways simultaneously. Among these, Aloe vera (Aloe barbadensis Miller) has been extensively investigated for its anti-inflammatory, antioxidant, antimicrobial, wound-healing, moisturizing, and immunomodulatory properties. The therapeutic efficacy of Aloe vera is attributed to a diverse range of bioactive constituents including acemannan, anthraquinones, flavonoids, chromones, polysaccharides, vitamins, amino acids, enzymes, sterols, and phenolic compounds. These phytoconstituents suppress inflammatory mediator production, reduce oxidative stress, accelerate collagen synthesis, promote fibroblast proliferation, and improve epidermal barrier function. Experimental and clinical studies have demonstrated that topical Aloe vera preparations reduce erythema, scaling, epidermal inflammation, and disease severity in patients with mild-to-moderate psoriasis, supporting its potential as an effective phytotherapeutic agent [2,10].

Similarly, Curcuma longa L. (turmeric) has emerged as one of the most extensively investigated medicinal plants owing to its broad spectrum of pharmacological activities. Curcumin, the principal polyphenolic constituent of turmeric, exhibits potent antioxidant, anti-inflammatory, antiproliferative, antimicrobial, and immunomodulatory properties. At the molecular level, curcumin inhibits activation of NF-κB, STAT3, MAPK, cyclooxygenase-2 (COX-2), inducible nitric oxide synthase (iNOS), and activator protein-1 (AP-1), thereby reducing transcription of pro-inflammatory cytokines including TNF-α, IL-1β, IL-6, IL-17A, IL-22, and IL-23. Experimental studies using imiquimod-induced psoriasis models have further demonstrated that topical curcumin significantly suppresses IL-17A/IL-23-mediated inflammatory responses, reduces epidermal hyperplasia, normalizes keratinocyte proliferation, and improves histopathological alterations. These molecular mechanisms highlight curcumin as a promising candidate for psoriasis therapy [6,11].

Despite their remarkable therapeutic potential, topical delivery of Aloe vera phytoconstituents and curcumin remains challenging because of limited skin penetration, poor aqueous solubility, chemical instability, rapid degradation, and inadequate bioavailability. Curcumin, in particular, exhibits extremely low aqueous solubility and poor permeability across the stratum corneum, restricting its therapeutic concentration within psoriatic lesions. Consequently, conventional topical formulations often fail to achieve sustained drug release and optimal clinical efficacy [12].

Nanotechnology-based drug delivery systems have emerged as an effective strategy to overcome these pharmaceutical limitations. Nanoformulations improve solubility, protect bioactive molecules from degradation, enhance epidermal and dermal penetration, prolong residence time at the target site, and enable controlled drug release while minimizing systemic exposure. Among the various nanocarrier systems, nanogels have attracted considerable interest because they combine the advantages of nanoparticles with the favorable physicochemical

properties of hydrogels. Nanogels consist of three-dimensional cross-linked polymeric networks capable of encapsulating both hydrophilic and hydrophobic compounds while maintaining excellent biocompatibility, high water content, biodegradability, and prolonged adhesion to the skin surface. Recent studies have demonstrated that phytochemical-loaded nanogels significantly improve dermal drug retention, decrease inflammatory cytokine expression, reduce epidermal thickness, and enhance anti-psoriatic efficacy compared with conventional topical formulations [1,5,13].

The combination of Aloe vera and Curcuma longa within a nanogel platform offers a rational multifunctional therapeutic strategy for psoriasis. Aloe vera contributes moisturizing, wound-healing, antioxidant, and immunomodulatory activities that improve skin barrier restoration, whereas curcumin directly suppresses inflammatory signaling pathways responsible for keratinocyte hyperproliferation and cytokine overexpression. Encapsulation of these phytoconstituents within a nanogel system is expected to improve topical bioavailability, facilitate deeper skin penetration, sustain localized drug release, and maximize therapeutic efficacy while minimizing adverse effects. Furthermore, integrating molecular biomarkers with conventional pharmacological evaluation provides a comprehensive understanding of the therapeutic mechanisms underlying herbal nanomedicine [1,6,13].

Therefore, the present study was designed to develop and characterize an Aloe vera–Curcuma longa nanogel and investigate its anti-psoriatic efficacy using an experimental psoriasis model. In addition to phytochemical characterization and pharmaceutical evaluation, the study aimed to elucidate the molecular mechanisms underlying its therapeutic effects through quantitative analysis of inflammatory cytokine gene expression, including IL-17A, IL-23, TNF-α, IL-6, and NF-κB, together with histopathological assessment of psoriatic lesions. This integrated molecular and pharmacological approach is expected to provide scientific evidence supporting the development of a novel phytopharmaceutical nanogel for the effective management of psoriasis and to further establish herbal nanomedicine as a promising strategy for targeted treatment of chronic inflammatory skin diseases.

## 2. Materials and Methods

### 2.1 Plant Materials

Fresh mature leaves of Aloe vera (Aloe barbadensis Miller) were collected from a medicinal plant garden and authenticated by a qualified taxonomist. Fresh rhizomes of Curcuma longa L. were procured from a certified herbal supplier and authenticated at the Department of Pharmacognosy. Voucher specimens were deposited in the departmental herbarium for future reference. Plant materials were thoroughly washed with distilled water, shade-dried at room temperature (25 ± 2°C), pulverized using a mechanical grinder, and stored in airtight containers until extraction [14].

### 2.2 Preparation of Plant Extracts

Powdered Aloe vera leaves and Curcuma longa rhizomes were separately extracted using 70% ethanol by Soxhlet extraction for 8 h. The extracts were concentrated under reduced pressure using a rotary vacuum evaporator maintained below 45°C and subsequently freeze-dried to obtain dry extracts. Percentage yield was calculated, and dried extracts were preserved in airtight amber-colored containers at 4°C until further analysis [15].

### 2.3 Preliminary Phytochemical Screening

Both extracts were subjected to qualitative phytochemical screening to identify the presence of alkaloids, flavonoids, phenolic compounds, tannins, glycosides, terpenoids, saponins, steroids, carbohydrates, proteins, amino acids, and anthraquinones using standard phytochemical procedures. The presence or absence of each phytochemical constituent was recorded based on characteristic color changes or precipitate formation [16].

### 2.4 Quantification of Total Phenolic and Total Flavonoid Contents

The total phenolic content (TPC) was estimated using the Folin–Ciocalteu method and expressed as milligrams of gallic acid equivalents (GAE)/g extract. Total flavonoid content (TFC) was determined by the aluminum chloride colorimetric assay and expressed as milligrams of quercetin equivalents (QE)/g extract. All analyses were performed in triplicate [17].

### 2.5 Preparation of Aloe vera–Curcuma longa Nano Gel

Curcumin-loaded nanoparticles were prepared using the ionic gelation technique employing chitosan and sodium tripolyphosphate as polymeric carriers. The optimized nanoparticles were dispersed into a Carbopol 940 gel base containing glycerol, propylene glycol, triethanolamine, methylparaben, propylparaben, and freshly prepared Aloe vera extract under continuous stirring until a homogeneous nanogel was obtained. The formulation was allowed to equilibrate for 24 h before evaluation [18].

**2.6 Pharmaceutical Evaluation of Nano Gel**
The prepared nano gel was evaluated for various physicochemical parameters including appearance, homogeneity, pH, viscosity, spreadability, extrudability, drug content, swelling index, and in vitro drug release. Particle size, polydispersity index (PDI), and zeta potential of the nanoparticles were determined using dynamic light scattering (DLS). Surface morphology was examined by scanning electron microscopy (SEM). Entrapment efficiency (%) was calculated by measuring the amount of unentrapped curcumin using UV-visible spectrophotometry [19].

**2.7 Experimental Animals**
Healthy adult male Wistar albino rats weighing 180–220 g were obtained from the Central Animal House Facility. Animals were housed under standard laboratory conditions (22 ± 2°C; 55 ± 5% relative humidity; 12 h light/12 h dark cycle) with free access to standard pellet diet and water ad libitum. Animals were acclimatized for one week before initiation of the experiment. The experimental protocol was approved by the Institutional Animal Ethics Committee (IAEC), and all procedures were performed according to CPCSEA guidelines [20].

**2.8 Induction of Experimental Psoriasis**
Psoriasis-like dermatitis was induced by topical application of 5% imiquimod cream (62.5 mg/day) on the shaved dorsal skin of rats for seven consecutive days. Daily application of imiquimod resulted in erythema, scaling, epidermal thickening, and inflammatory infiltration closely resembling human plaque psoriasis [21].

**2.9 Experimental Design**
Animals were randomly divided into five groups (n = 6):
**Group I:** Normal Control (vehicle only)
**Group II:** Psoriatic Control (Imiquimod)
**Group III:** Standard Treatment (Clobetasol Propionate 0.05%)
**Group IV:** Aloe vera–Curcuma longa Conventional Gel
**Group V:** Aloe vera–Curcuma longa Nano Gel
Topical treatments were administered once daily for 14 consecutive days following psoriasis induction.

**2.10 Psoriasis Area and Severity Index (PASI)**
Disease severity was evaluated using a modified Psoriasis Area and Severity Index (PASI). Erythema, scaling, and skin thickness were individually scored on a scale of 0–4, where 0 indicated no symptoms and 4 represented very severe symptoms. The cumulative PASI score ranged from 0 to 12 and was recorded on days 0, 3, 7, 10, and 14 [22].

**2.11 Histopathological Examination**
At the end of the experimental period, animals were euthanized, and dorsal skin tissues were excised and fixed in 10% neutral buffered formalin. Samples were processed by routine paraffin embedding, sectioned at 5 µm thickness, and stained with hematoxylin and eosin (H&E). Histological alterations including epidermal thickness, parakeratosis, acanthosis, inflammatory cell infiltration, and dermal edema were examined under a light microscope by a blinded histopathologist [23].

**2.12 RNA Isolation and Quantitative Real-Time PCR**
Total RNA was isolated from skin tissue using TRIzol reagent according to the manufacturer's instructions. RNA purity and concentration were determined spectrophotometrically, and complementary DNA (cDNA) was synthesized using a reverse transcription kit. Quantitative real-time PCR (RT-qPCR) was performed using SYBR Green Master Mix in a real-time PCR system. Relative gene expression levels of IL-17A, IL-23, TNF-α, IL-6, NF-κB, and STAT3 were analyzed using GAPDH as the internal reference gene. Relative expression was calculated by the $2^{-\Delta\Delta Ct}$ method [24].

**2.13 Oxidative Stress Biomarker Analysis**
Skin tissue homogenates were prepared in phosphate-buffered saline and centrifuged at 10,000 rpm for 15 min at 4°C. The supernatant was used for biochemical estimation of malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) using commercially available assay kits according to the manufacturer's instructions [25].

**2.14 Immunohistochemical Analysis**
Immunohistochemical staining was performed to evaluate the protein expression of NF-κB p65 and Ki-67 in skin tissue sections. Following antigen retrieval, endogenous peroxidase activity was blocked, and tissue sections were incubated overnight with primary antibodies. Sections were subsequently incubated with horseradish peroxidase-

conjugated secondary antibodies and visualized using 3,3′-diaminobenzidine (DAB). Immunostained sections were analyzed using ImageJ software for semi-quantitative assessment [26].

### 2.15 Statistical Analysis

All experimental data were expressed as mean ± standard deviation (SD). Statistical analysis was performed using GraphPad Prism version 10.0. Comparisons among multiple groups were carried out using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison post hoc test. A value of $P < 0.05$ was considered statistically significant [27].

## 3. Results

### 3.1 Preliminary Phytochemical Screening

Qualitative phytochemical analysis confirmed the presence of several biologically active secondary metabolites in both Aloe vera and Curcuma longa extracts (Table 1). Aloe vera extract was rich in polysaccharides, flavonoids, phenolic compounds, tannins, glycosides, amino acids, and anthraquinones, whereas Curcuma longa extract predominantly contained curcuminoids, flavonoids, phenolics, terpenoids, and essential oils. Alkaloids were absent in both extracts. The abundance of phenolic and flavonoid constituents suggested strong antioxidant and anti-inflammatory potential, supporting their incorporation into the nanogel formulation.

**Table 1. Preliminary phytochemical screening of plant extracts**

| Phytoconstituent | Aloe vera | Curcuma longa |
|---|---|---|
| Alkaloids | – | – |
| Flavonoids | +++ | +++ |
| Phenolics | +++ | +++ |
| Tannins | ++ | ++ |
| Glycosides | ++ | + |
| Terpenoids | + | +++ |
| Saponins | ++ | + |
| Anthraquinones | ++ | – |
| Polysaccharides | +++ | – |
| Steroids | + | + |
| Proteins | + | – |

Symbols: (+++) abundant; (++) moderate; (+) present; (–) absent.

### 3.2 Total Phenolic and Total Flavonoid Contents

The ethanolic extracts demonstrated high phenolic and flavonoid contents (Table 2). Curcuma longa exhibited significantly higher total phenolic content, whereas Aloe vera showed comparatively greater polysaccharide content. These phytochemicals are known to contribute to antioxidant and anti-inflammatory activities.

**Table 2. Total phenolic and flavonoid contents**

| Parameter | Aloe vera | Curcuma longa |
|---|---|---|
| Total phenolics (mg GAE/g extract) | 128.64 ± 4.12 | **176.92 ± 5.38*** |
| Total flavonoids (mg QE/g extract) | 82.35 ± 2.46 | **121.74 ± 3.51*** |

Values are Mean ± SD (n=3). **P<0.001 vs Aloe vera.**

### 3.3 Characterization of Aloe vera–Curcuma longa Nano Gel

The optimized nano gel possessed desirable physicochemical characteristics (Table 3). Dynamic light scattering analysis revealed a mean particle size of 168.4 ± 7.5 nm with a narrow particle distribution (PDI = 0.236 ± 0.02). The zeta potential was −31.7 ± 2.4 mV, indicating excellent colloidal stability. Entrapment efficiency exceeded 90%, suggesting efficient incorporation of curcumin into the nanoparticulate system.

The nano gel exhibited a smooth appearance, homogeneous consistency, skin-compatible pH, and excellent spreadability, making it suitable for topical administration.

**Table 3. Physicochemical evaluation of optimized nano gel**

| Parameter | Result |
|---|---|
| Appearance | Smooth yellowish gel |
| Homogeneity | Excellent |
| pH | 6.54 ± 0.09 |
| Viscosity (cP) | 27,640 ± 415 |

| | |
|---|---|
| Spreadability (g·cm/s) | 7.94 ± 0.24 |
| Extrudability (g) | 585 ± 18 |
| Drug content (%) | 98.63 ± 1.28 |
| Particle size (nm) | 168.4 ± 7.5 |
| Polydispersity Index | 0.236 ± 0.02 |
| Zeta potential (mV) | −31.7 ± 2.4 |
| Entrapment efficiency (%) | 91.84 ± 2.11 |

**3.4 In Vitro Drug Release**

The nano gel demonstrated sustained drug release over 24 h compared with the conventional gel. Approximately 93.8% of curcumin was released from the nano gel after 24 h, whereas the conventional gel released only 71.6%.

**Table 4. In vitro drug release profile**

| Time (h) | Conventional Gel (%) | Nano Gel (%) |
|---|---|---|
| 1 | 18.4 ±1.2 | 12.6 ±0.8 |
| 2 | 28.7 ±1.6 | 24.3 ±1.1 |
| 4 | 42.9 ±2.0 | 45.8 ±1.9 |
| 8 | 56.4 ±2.2 | 67.5 ±2.4 |
| 12 | 63.2 ±2.5 | 79.8 ±2.8 |
| 24 | 71.6 ±2.7 | 93.8 ±2.6* |

**3.5 Effect on Psoriasis Severity (PASI Score)**

Topical application of imiquimod produced marked erythema, scaling, and skin thickening in the disease control group. Treatment with the Aloe vera–Curcuma longa nano gel significantly reduced psoriasis severity throughout the treatment period. By Day 14, the nano gel reduced the PASI score by approximately **76%**, comparable to the standard treatment and significantly superior to the conventional gel ($P<0.001$).

**Table 5. PASI score during treatment**

| Group | Day 0 | Day 3 | Day 7 | Day 10 | Day 14 |
|---|---|---|---|---|---|
| Normal | 0.0±0.0 | 0.0±0.0 | 0.0±0.0 | 0.0±0.0 | 0.0±0.0 |
| Psoriatic Control | 8.84±0.36 | 9.15±0.42 | 9.43±0.38 | 9.62±0.31 | 9.74±0.27 |
| Standard | 8.81±0.33 | 6.42±0.31 | 4.23±0.24 | 2.14±0.19 | 1.08±0.11 |
| Conventional Gel | 8.80±0.41 | 7.64±0.38 | 5.91±0.31 | 4.32±0.26 | 2.84±0.21 |
| Nano Gel | 8.83±0.35 | 6.81±0.29 | 4.46±0.22 | 2.51±0.17 | 1.36±0.15* |

**3.6 Histopathological Findings**

Normal skin exhibited intact epidermal architecture with well-organized keratinocytes and absence of inflammatory infiltration. The psoriatic control group demonstrated severe acanthosis, hyperkeratosis, parakeratosis, elongated rete ridges, dermal edema, and dense inflammatory cell infiltration.

The standard treatment markedly restored normal epidermal morphology. The conventional herbal gel moderately reduced epidermal hyperplasia and inflammatory infiltration. In contrast, the Aloe vera–Curcuma longa nano gel almost completely normalized epidermal thickness, reduced inflammatory cell infiltration, minimized parakeratosis, and restored normal dermal architecture.

**Table 6. Histopathological score**

| **Group** | **Score** |
|---|---|
| Normal | 0.34±0.12 |
| Psoriatic Control | 7.82±0.42 |
| Standard | 1.22±0.19 |
| Conventional Gel | 2.73±0.28 |
| Nano Gel | 1.54±0.17* |

**3.7 Effect on Inflammatory Cytokine Gene Expression**

RT-qPCR analysis demonstrated significant upregulation of inflammatory cytokine genes in psoriatic skin (Figure 2). The nano gel markedly downregulated IL-17A, IL-23, TNF-α, IL-6, NF-κB, and STAT3 expression compared with the disease control group ($P<0.001$).

Among all treatment groups, the nano gel exhibited the greatest suppression of inflammatory gene expression, approaching values observed in healthy animals.

**Table 7. Relative gene expression (Fold Change)**

| Gene | Normal | Psoriatic | Standard | Conventional | Nano Gel |
|---|---|---|---|---|---|
| IL-17A | 1.00±0.06 | 6.84±0.38 | 1.84±0.15 | 2.93±0.22 | 1.42±0.11* |
| IL-23 | 1.00±0.07 | 5.92±0.34 | 1.76±0.12 | 2.61±0.18 | 1.38±0.09* |
| TNF-α | 1.00±0.05 | 6.21±0.31 | 2.02±0.18 | 3.11±0.21 | 1.56±0.12* |
| IL-6 | 1.00±0.06 | 5.73±0.29 | 1.92±0.14 | 2.86±0.19 | 1.48±0.11* |
| NF-κB | 1.00±0.08 | 5.84±0.32 | 1.74±0.13 | 2.68±0.18 | 1.34±0.10* |
| STAT3 | 1.00±0.06 | 5.39±0.28 | 1.63±0.11 | 2.42±0.17 | 1.29±0.08* |

### 3.8 Oxidative Stress Biomarkers

Psoriatic animals exhibited a marked increase in lipid peroxidation accompanied by depletion of endogenous antioxidant enzymes. Treatment with the nano gel significantly restored antioxidant status by reducing MDA levels and increasing SOD, CAT, and GSH activities ($P<0.001$).

**Table 8. Oxidative stress biomarkers**

| Parameter | Normal | Psoriatic | Standard | Conventional | Nano Gel |
|---|---|---|---|---|---|
| MDA (nmol/mg protein) | 2.15±0.18 | 8.96±0.46 | 3.14±0.22 | 4.62±0.31 | 2.86±0.19* |
| SOD (U/mg protein) | 12.86±0.54 | 5.24±0.33 | 11.36±0.48 | 9.48±0.42 | 11.94±0.51* |
| CAT (U/mg protein) | 67.3±2.4 | 28.6±1.8 | 60.8±2.1 | 52.4±2.3 | 63.5±2.2* |
| GSH (µmol/g tissue) | 8.42±0.31 | 3.15±0.22 | 7.64±0.29 | 6.42±0.27 | 8.01±0.28* |

### 3.9 Immunohistochemical Analysis

Immunohistochemical staining demonstrated intense NF-κB p65 nuclear localization and strong Ki-67 expression in the psoriatic control group, indicating enhanced inflammatory signaling and keratinocyte proliferation. Nano gel treatment markedly reduced NF-κB immunoreactivity and Ki-67-positive cells, suggesting suppression of inflammatory pathways and normalization of epidermal proliferation.

**Table 9. Immunohistochemical expression**

| Group | NF-κB Positive Cells (%) | Ki-67 Positive Cells (%) |
|---|---|---|
| Normal | 8.6±1.2 | 9.3±1.4 |
| Psoriatic Control | 78.4±3.6 | 72.8±3.4 |
| Standard | 21.6±2.1 | 18.7±2.2 |
| Conventional Gel | 34.5±2.8 | 30.8±2.6 |
| Nano Gel | 17.2±1.9* | 15.4±1.8* |

## 4. Discussion

The present investigation demonstrated that the developed Aloe vera–Curcuma longa nano gel possessed favorable pharmaceutical characteristics and produced significant anti-psoriatic activity in the imiquimod-induced experimental model. The formulation effectively improved psoriasis severity, restored normal skin histoarchitecture, suppressed inflammatory cytokine gene expression, enhanced antioxidant defense, and reduced cellular proliferation. These findings suggest that incorporation of Aloe vera and curcumin into a nano-sized delivery system substantially enhanced their therapeutic efficacy through modulation of multiple molecular pathways involved in psoriasis pathogenesis.

Phytochemical screening confirmed the presence of abundant phenolics, flavonoids, polysaccharides, terpenoids, and glycosides in the prepared extracts. These phytoconstituents are recognized for their antioxidant, anti-inflammatory, immunomodulatory, and wound-healing properties. Polyphenols and flavonoids can directly scavenge reactive oxygen species, inhibit lipid peroxidation, and regulate inflammatory transcription factors, whereas Aloe vera polysaccharides contribute to tissue repair and epidermal regeneration. Such multitarget phytochemical composition provides a strong pharmacological basis for the observed therapeutic activity of the nano gel [28,29].

The optimized nano gel exhibited a particle size below 200 nm, a low polydispersity index, high entrapment efficiency, and a negative zeta potential indicative of excellent colloidal stability. Nanometer-sized carriers facilitate closer interaction with the stratum corneum, improve dermal penetration, increase drug retention within epidermal layers, and provide sustained release of encapsulated phytoconstituents. These pharmaceutical characteristics likely contributed to the enhanced biological activity observed with the nano gel compared with the conventional formulation. Recent studies have emphasized that nano-based topical delivery systems overcome the poor aqueous solubility and limited skin permeability of curcumin while improving localized therapeutic concentrations and minimizing systemic exposure [30,31].

A sustained drug-release profile was observed for the optimized nano gel, releasing more than 90% of the incorporated curcumin over 24 h. Controlled release is particularly advantageous in chronic inflammatory skin diseases because it prolongs drug residence time, reduces dosing frequency, and maintains therapeutic concentrations within psoriatic lesions. Sustained topical delivery also minimizes rapid drug loss caused by desquamation and repeated washing of the affected skin, thereby improving overall treatment efficacy [32].

The imiquimod-induced psoriasis model successfully reproduced characteristic clinical manifestations including erythema, scaling, epidermal thickening, and inflammatory infiltration. Treatment with the Aloe vera–Curcuma longa nano gel significantly reduced PASI scores throughout the experimental period, with therapeutic efficacy approaching that of the standard corticosteroid treatment. The superior clinical response compared with the conventional gel indicates that nanotechnology enhanced the bioavailability and pharmacological activity of the incorporated phytoconstituents. Similar observations have been reported for phytochemical-loaded nanocarriers, which exhibit improved topical efficacy through enhanced penetration and controlled release [33].

Histopathological examination further supported the clinical findings. Psoriatic control animals demonstrated marked acanthosis, parakeratosis, elongated rete ridges, dermal edema, and extensive inflammatory cell infiltration, whereas nano gel treatment markedly restored normal epidermal architecture. Reduction in epidermal thickness and inflammatory infiltration suggests effective suppression of keratinocyte hyperproliferation and local immune activation. Restoration of normal skin morphology is considered a critical endpoint for evaluating anti-psoriatic therapies because it reflects both structural and functional recovery of the epidermis [34].

One of the most significant findings of the present study was the marked downregulation of IL-17A, IL-23, TNF-α, IL-6, NF-κB, and STAT3 gene expression following nano gel treatment. The IL-23/IL-17 signaling axis represents the principal immunological pathway responsible for maintaining chronic inflammation in psoriasis. IL-23 promotes differentiation and survival of Th17 lymphocytes, which subsequently produce IL-17A and IL-22, stimulating keratinocyte proliferation and inflammatory cytokine release. Simultaneously, activation of NF-κB and STAT3 further amplifies inflammatory signaling by inducing transcription of numerous cytokines and chemokines. Suppression of these molecular targets indicates that the herbal nano gel interrupts multiple interconnected inflammatory pathways rather than acting through a single mechanism [35,36].

Curcumin is recognized as a pleiotropic phytochemical capable of regulating several intracellular signaling cascades implicated in psoriasis. Previous mechanistic investigations have demonstrated that curcumin inhibits phosphorylation of NF-κB and STAT3, suppresses activation of MAPK pathways, decreases expression of COX-2 and inducible nitric oxide synthase, and reduces production of IL-17A, IL-23, TNF-α, and IL-6. In addition, curcumin modulates keratinocyte proliferation and promotes apoptosis of activated inflammatory cells. The present findings agree with these molecular observations and further indicate that nanoformulation enhances the biological availability of curcumin within psoriatic tissue, resulting in greater suppression of inflammatory gene expression [37].

Aloe vera also contributed substantially to the therapeutic response. In addition to its moisturizing and wound-healing properties, Aloe vera contains acemannan, anthraquinones, sterols, and phenolic compounds that regulate macrophage activation, inhibit oxidative stress, stimulate collagen synthesis, and promote re-epithelialization. Restoration of the epidermal barrier may further reduce penetration of environmental antigens and decrease recurrent immune activation, thereby complementing the anti-inflammatory actions of curcumin. The synergistic interaction between these two medicinal plants probably accounts for the marked improvement observed in both clinical and molecular parameters [38].

Oxidative stress plays a pivotal role in psoriasis by promoting activation of redox-sensitive transcription factors, DNA damage, and inflammatory cytokine production. In the present study, psoriatic animals exhibited elevated malondialdehyde levels together with depletion of endogenous antioxidant enzymes including superoxide dismutase, catalase, and reduced glutathione. Treatment with the nano gel significantly restored antioxidant status, suggesting efficient neutralization of reactive oxygen species and protection against oxidative tissue injury. Improvement of oxidative balance may further contribute to inhibition of NF-κB activation and subsequent reduction of inflammatory cytokine expression [39].

Immunohistochemical analysis revealed marked reduction in NF-κB nuclear localization and Ki-67-positive keratinocytes following nano gel treatment. Ki-67 is an established marker of cellular proliferation and is markedly elevated in psoriatic epidermis because of accelerated keratinocyte turnover. Simultaneous reduction of NF-κB and Ki-67 expression indicates that the formulation effectively suppressed both inflammatory signaling and epidermal hyperproliferation, providing molecular evidence for the histological recovery observed in treated animals [40].

Overall, the present study demonstrates that integrating herbal therapeutics with nanotechnology provides significant advantages over conventional topical formulations. Enhanced penetration, sustained release, improved stability, and simultaneous modulation of oxidative stress, inflammatory cytokines, and proliferative signaling pathways collectively contributed to the superior anti-psoriatic activity of the Aloe vera–Curcuma longa nano gel. These findings support the growing concept that multifunctional herbal nanomedicines may represent an effective

strategy for managing chronic inflammatory skin disorders while minimizing the adverse effects associated with prolonged corticosteroid therapy [41-60].

## 5. Conclusion

The present study demonstrated that the developed Aloe vera–Curcuma longa nano gel exhibited promising anti-psoriatic activity by combining favorable pharmaceutical properties with significant molecular and pharmacological effects. The nano gel effectively reduced psoriasis severity, restored normal skin architecture, attenuated oxidative stress, and significantly downregulated the expression of key inflammatory mediators, including IL-17A, IL-23, TNF-α, IL-6, NF-κB, and STAT3. The enhanced therapeutic efficacy observed with the nanoformulation suggests improved topical delivery and bioavailability of the herbal phytoconstituents. Overall, these findings indicate that the Aloe vera–Curcuma longa nano gel represents a promising herbal nanotherapeutic approach for psoriasis management and warrants further clinical investigation to establish its safety and therapeutic potential in human subjects.

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