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CURCUMIN IN ATOPIC DERMATITIS THERAPY: MOLECULAR MECHANISMS, FORMULATION CHALLENGES, AND NANO-ENABLED TOPICAL DELIVERY

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ABSTRACT

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin illness characterized by immunological dysregulation, skin barrier dysfunction, oxidative stress, and microbial colonization, leading to erythema, pruritus, and reduced quality of life. Conventional treatments, such as calcineurin inhibitors and corticosteroids, alleviate symptoms but are linked to poor patient compliance, immunosuppression, and long-term side effects. Curcuma longa is the source of curcumin, a naturally occurring polyphenolic chemical with strong anti-inflammatory, antioxidant, immunomodulatory, and antibacterial properties that make it a prospective treatment for AD. However, poor water solubility, chemical instability, low skin penetration, and formulation issues including stains and odor hinder its clinical translation. Nano-enabled topical delivery methods, including nanoemulsions, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), polymeric nanoparticles, nanogels, and vesicular carriers (liposomes, ethosomes, transfersomes), has been developed to address these restrictions. These nano-systems increase the solubility of curcumin, shield it from deterioration, promote epidermal and dermal penetration, offer regulated and prolonged release, and lessen local discomfort and systemic exposure. Evaluation factors such as particle size, zeta potential, encapsulation efficiency, in vitro release, skin permeability, stability, and in vivo efficacy confirm the higher performance of nano-curcumin formulations compared to conventional preparations. This thesis addresses the therapeutic potential of curcumin in AD, stressing the role of nano-enabled administration in increasing

bioavailability, skin retention, and patient compliance. Future research ought to concentrate on well-designed clinical trials, combination therapy with existing anti-AD medications, targeted and personalized nano-delivery techniques, and long-term safety assessments to assist regulatory approval and clinical translation.

KEYWORDS: Curcumin, Atopic dermatitis, Nano-formulations, Topical drug delivery, Solid lipid nanoparticles, Liposomes, Anti-inflammatory therapy.

1. INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin illness marked by extreme pruritus, xerosis, erythema, and eczematous lesions. It often begins in early childhood but can persist or recur throughout adolescence and adulthood, greatly limiting quality of life. AD is seen as a multifaceted disease that results from a complicated interaction between environmental stressors, immunological dysregulation, epidermal barrier malfunction, and genetic predisposition. Mutations in genes encoding skin barrier proteins, including filaggrin, lead to reduced stratum corneum integrity, enhanced transepidermal water loss, and greater penetration of allergens and microbial antigens.[1]

AD is characterized immunologically by a strong T-helper 2 (Th2)-mediated immune response, particularly during the acute phase, with increased levels of cytokines such interleukin-4 (IL-4), IL-5, and IL-13. Chronic lesions may also involve Th1, Th17, and Th22 pathways, contributing to prolonged inflammation and epidermal hyperplasia. Because the condition is atopic, elevated blood IgE levels and eosinophilia are usually seen. Furthermore, colonization of the skin by Staphylococcus aureus causes additional inflammation by producing superantigens and toxins. AD continues to be a significant dermatological and therapeutic problem because of its chronicity, frequent flare-ups, and systemic immunological involvement.[2]

1.1. Limitations of Current Conventional Therapies

Topical corticosteroids, topical calcineurin inhibitors, antihistamines, emollients, and, in extreme situations, systemic immunosuppressants or biologics are the mainstays of contemporary AD treatment. Because of its strong anti-inflammatory and immunosuppressive properties, topical corticosteroids are regarded as the first-line treatment. However, a number of negative side effects, such as skin shrinkage, telangiectasia, striae, hypopigmentation, and suppression of the hypothalamic-pituitary-adrenal (HPA) axis, are linked to prolonged or

improper use. Furthermore, patients with corticosteroid fear frequently have poor adherence and subpar treatment results.[3]

For sensitive areas including the face and intertriginous regions, topical calcineurin inhibitors like tacrolimus and pimecrolimus provide an alternative to corticosteroids. Despite their effectiveness, these medicines may elicit burning sensations, erythema, and pruritus at an application site. Concerns regarding long-term safety and a suspected link with malignancies have also hindered their wider usage. Despite their effectiveness, systemic treatments and more recent biologics are costly, necessitate ongoing monitoring, and may make a person more vulnerable to infections [4]. Collectively, these limitations underline the need for safer, affordable, and easily tolerated treatment solutions for long-term care of AD.

1.2. Rationale for Exploring Phytoconstituents in Atopic Dermatitis Management

In the past few decades, there has been rising scientific interest in the use of phytoconstituents for the management of chronic inflammatory illnesses, including AD. Plant-derived bioactive chemicals possess a wide spectrum of pharmacological actions such as anti-inflammatory, antioxidant, immunomodulatory, antibacterial, and wound-healing properties. Phytoconstituents frequently operate through several molecular targets, in contrast to traditional synthetic medications, providing a comprehensive approach to disease modulation.[5]

The pathogenesis of AD comprises oxidative stress, inflammatory cytokine overproduction, immunological imbalance, and skin barrier dysfunction pathways that can possibly be treated by natural substances. Several herbal extracts and isolated phytochemicals have proven to have the capacity to suppress pro-inflammatory mediators (e.g., TNF-α, IL-1β, IL-6), inhibit nuclear factor-kappa B (NF-κB) signaling, reduce oxidative damage, and reestablish epidermal barrier function. Additionally, phytoconstituents are often associated with fewer side effects, making them attractive candidates for long-term therapy in chronic disorders like AD. As a result, more study is being done to find and validate plant-based substitutes or supplements to current treatments.[6]

1.3. Curcumin as a Promising Natural Anti-Inflammatory Agent

In spite of its strong anti-inflammatory, antioxidant, and immunomodulatory qualities, curcumin, a polyphenolic substance obtained from the rhizomes of Curcuma longa (turmeric), has garnered a lot of attention. Curcumin, which has long been utilized in Chinese

and Ayurvedic medicine, has been thoroughly investigated for its ability to treat a range of autoimmune and inflammatory conditions. Curcumin reduces inflammation at the molecular level by blocking important signaling pathways such as NF-κB, mitogen-activated protein kinases (MAPKs), and Janus kinase/signal transducer and activator of transcription (JAK/STAT).[7]

Curcumin has been demonstrated to modulate both Th2- and Th1-mediated immune responses in the context of atopic dermatitis by suppressing the expression of pro-inflammatory cytokines such IL-4, IL-5, IL-13, TNF-α, and interferon-γ. Reactive oxygen species, which are a major factor in aggravating skin irritation and barrier degradation, are neutralized by its potent antioxidant action. Furthermore, curcumin has antibacterial action against Staphylococcus aureus, decreasing bacterial colonization and accompanying inflammatory responses in AD lesions.[8]

Curcumin has a promising pharmacological profile, but its quick metabolism, low bioavailability, and poor water solubility limit its clinical use. These challenges have prompted research into innovative delivery mechanisms such as nanoparticles, liposomes, and topical formulations to boost its therapeutic efficacy in skin conditions. In conclusion, curcumin offers a promising phytoconstituent for managing symptoms of atopic dermatitis, either as a standalone agent or as an addition to conventional medications, offering a safer and diversified approach to treating chronic skin inflammation.[9]

2. PATHOPHYSIOLOGY OF ATOPIC DERMATITIS

Atopic dermatitis (AD) is a complex, multifactorial inflammatory skin condition resulting from the interplay of epidermal barrier dysfunction, immunological dysregulation, genetic vulnerability, oxidative stress, and microbial colonization. AD is now understood to be a systemic immune-mediated disease with substantial cutaneous symptoms rather than a merely allergic syndrome. A self-sustaining loop of barrier degradation, immunological activation, and inflammation is the cause of AD's chronic and recurrent character.[10]

2.1. Skin Barrier Dysfunction and Filaggrin Deficiency

One of the key pathogenic mechanisms in atopic dermatitis is disruption of the skin barrier function. The stratum corneum prevents excessive transepidermal water loss (TEWL) and serves as the main defense against environmental allergies, irritants, and microbial invasion. This barrier is both physically and functionally weakened in AD, resulting in skin that is dry,

cracked, and irritated.[11]

Filaggrin, a major structural protein expressed by the FLG gene, plays a fundamental role in keratinocyte development, aggregation of keratin filaments, and maintenance of skin moisture. Reduced filaggrin levels, poor cornified envelope production, and a decrease in natural moisturizing factors are the outcomes of loss-of-function mutations in the FLG gene. As a result, TEWL rises, making it possible for allergens and irritants to enter the skin's deeper layers and trigger immunological reactions. Furthermore, a lack of filaggrin changes the pH of the skin, which promotes microbial colonization and the enzymatic breakdown of epidermal lipids, exacerbating inflammation.[12]

2.2. Role of Immune Dysregulation (Th1/Th2/Th17 Imbalance)

One of the main characteristics of atopic dermatitis is immune dysregulation, which is an imbalance between different subsets of T-helper (Th) cells. Increased production of IL-4, IL-5, and IL-13 is indicative of a dominant Th2-mediated immune response during the acute phase of AD. These cytokines increase susceptibility to infections by promoting eosinophil activation, IgE class switching in B cells, and inhibition of antimicrobial peptide synthesis.[13]

As the condition proceeds to a chronic state, a shift toward Th1-mediated responses occurs, with increased production of interferon-γ (IFN-γ), contributing to persistent inflammation and epidermal thickness (lichenification). Additionally, Th17 and Th22 cells are crucial, especially in severe and long-term AD. IL-22 causes epidermal hyperplasia and barrier breakdown, whereas Th17-derived IL-17 encourages keratinocyte activation and neutrophil recruitment. The immunological complexity of AD is highlighted by the presence of Th2, Th1, and Th17 responses, which also explains why the illness manifests differently at different stages.[14]

2.3. Involvement of Inflammatory Mediators and Cytokines

The overproduction of various cytokines, chemokines, and inflammatory mediators produced by keratinocytes, dendritic cells, mast cells, and T lymphocytes drives the inflammatory cascade in atopic dermatitis. Important Th2 cytokines IL-4 and IL-13 reduce the expression of filaggrin, loricrin, and involucrin, which compromises the integrity of the epidermal barrier. These cytokines also block keratinocyte differentiation and antimicrobial peptide production, sustaining inflammation.[15]

Another important mediator that increases inflammatory signaling is tumor necrosis factor-α

(TNF-α), which activates the nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) pathways. IFN-γ, which is mostly linked to Th1 responses, has a role in tissue remodeling and chronic inflammation. When combined, these cytokines provide a pro-inflammatory milieu that maintains keratinocyte failure, immune cell infiltration, and the chronicity of the illness. Elevated blood and tissue levels of each of these mediators correlate closely with disease severity in AD patients.[16]

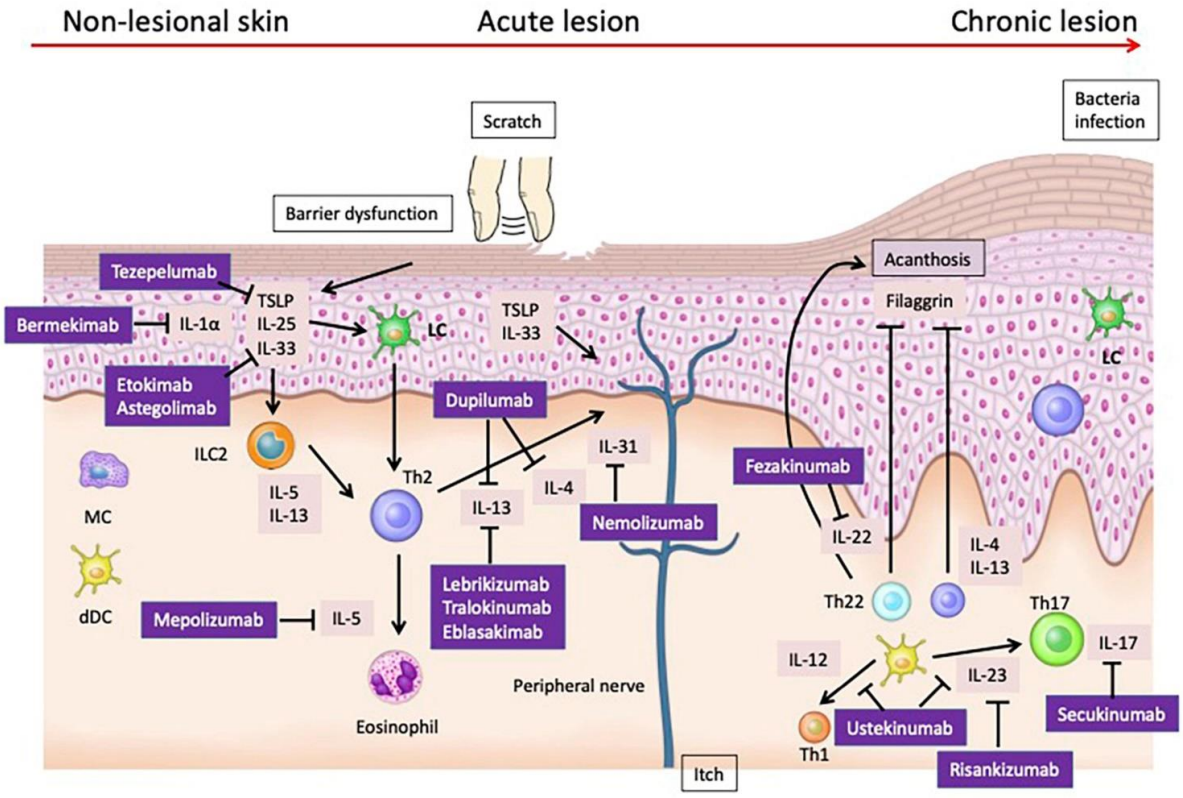

Fig. 1: Pathophysiology of Atopic Dermatitis.[17]

2.4. Oxidative Stress and Microbial Colonization in AD Progressio

The pathophysiology of atopic dermatitis is significantly influenced by oxidative stress. Chronic inflammation increases reactive oxygen species (ROS) generation, which overwhelms the skin's antioxidant defense systems and causes keratinocyte DNA damage, lipid peroxidation, and protein degradation. Oxidative stress increases the generation of cytokines and inflammatory signals by further disrupting the epidermal barrier and activating redox-sensitive transcription factors like NF-κB.[18]

Another important role in the development of AD is microbial colonization, especially by Staphylococcus aureus. Compared to healthy skin, S. aureus colonizes over 90% of AD lesions. Exotoxins and superantigens released by the bacteria directly stimulate T cells and

antigen-presenting cells, hence exacerbating inflammation. Microbial persistence is further aided by decreased production of antimicrobial peptides with the value defensins and cathelicidins, which is mostly caused by Th2 cytokine dominance. Oxidative stress, microbial colonization, and immunological dysregulation work together to produce a vicious cycle that increases the severity and recurrence of illness.[19]

3. CURCUMIN

As a result of its wide range of pharmacological effects, curcumin, a naturally occurring polyphenolic molecule, has attracted a lot of scientific interest. For ages, Ayurvedic and Chinese medicine have utilized curcumin, which is derived from the rhizomes of Curcuma longa L. Modern research has proven many of its traditional uses, notably in the management of inflammatory and immune-mediated illnesses, making it a good option for dermatological applications such as atopic dermatitis.[20]

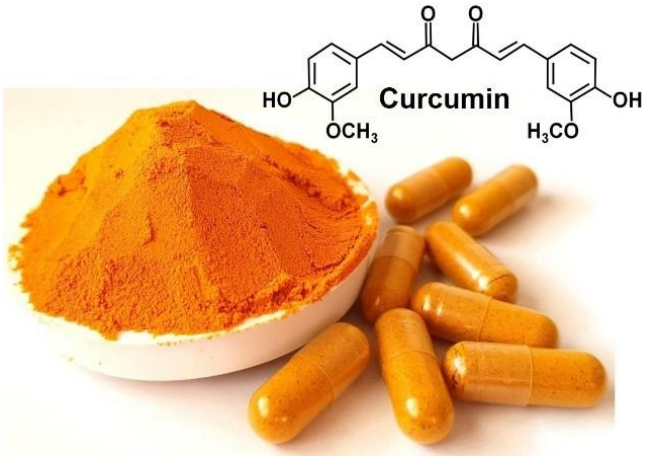

Fig. 2: Curcumin.[21]

3.1. Botanical Source and Chemical Structure of Curcumin

Curcumin is the major bioactive element of turmeric (Curcuma longa L.), a perennial plant belonging to the family Zingiberaceae. Turmeric rhizomes contain around 2–8% curcuminoids, of which curcumin (diferuloylmethane) is the most prevalent and pharmacologically active component, together with demethoxycurcumin and bisdemethoxycurcumin.[22]

Chemically, curcumin is a diarylheptanoid polyphenol with the chemical formula $C_{21}H_{20}O_6$ and a molecular weight of roughly 368.38 g/mol. Its structure is made up of two aromatic o-methoxy phenolic rings joined by a seven-carbon linker that contains an α,β-unsaturated β-diketone moiety. The keto and enol tautomeric forms of curcumin coexist in equilibrium,

with the enol form being more stable and physiologically active. Its antioxidant and anti-inflammatory qualities are further enhanced by the presence of conjugated double bonds and phenolic hydroxyl groups.[23]

3.2. Physicochemical Properties Relevant to Topical Delivery

The physicochemical features of curcumin greatly impact its formulation and distribution, particularly for topical applications. Curcumin is a hydrophobic molecule with extremely low water solubility (~11 ng/mL), which restricts its permeability across biological membranes. It has a log P value of roughly 3.0, suggesting moderate lipophilicity, a feature advantageous for skin penetration across the lipid-rich stratum corneum.[24]

Curcumin degrades quickly due to its weak chemical stability, particularly in alkaline environments and when exposed to light. In pH ranges from acidic to neutral, it is rather stable. For traditional topical preparations, these restrictions provide serious difficulties that frequently lead to low absorption and decreased therapeutic effectiveness.[25] To circumvent these limitations, improved drug delivery technologies such as liposomes, niosomes, solid lipid nanoparticles, nanoemulsions, and polymeric nanoparticles have been extensively intensively investigated. Such technologies boost curcumin's solubility, stability, skin retention, and controlled release, making it more suited for chronic inflammatory skin disorders.[26]

3.3. Pharmacological Activities of Curcumin

- **Antibacterial action:** Curcumin has broad-spectrum antibacterial activity against viruses, fungi, and bacteria. In the context of atopic dermatitis, this characteristic is particularly essential due to the high incidence of Staphylococcus aureus colonization on AD lesions. Curcumin decreases the development of bacterial toxins and superantigens that worsen skin inflammation, breaks down bacterial cell membranes, and prevents biofilm formation. By decreasing microbial burden and avoiding subsequent infections, curcumin helps interrupt the vicious cycle of inflammation and barrier disruption typical of AD.[27]

- **Skin barrier-restorative activity:** By encouraging keratinocyte differentiation and increasing the production of structural proteins including filaggrin, loricrin, and involucrin, curcumin helps restore the function of the skin barrier. It also affects ceramide production and lipid structure within the stratum corneum, resulting to decreased transepidermal water loss (TEWL) and enhanced skin hydration. Restoring barrier integrity is essential for long-

term AD disease treatment because it lowers allergen penetration and the ensuing immunological activation.[28]

- **Anti-pruritic activity:** One of the most upsetting signs of atopic dermatitis is pruritus, which is strongly associated with inflammatory mediators and neural sensitization. It has been demonstrated that curcumin reduces itching by reducing itch-related cytokines like IL-31 and preventing mast cells from releasing histamine. Curcumin also reduces neurogenic inflammation and itch perception by modulating transient receptor potential (TRP) channels involved in sensory nerve activation.[29]

- **Activity related to tissue repair and wound healing:** Prolonged scratching in AD causes fissures, excoriations, and poor wound healing. By encouraging fibroblast proliferation, collagen deposition, angiogenesis, and re-epithelialization, curcumin speeds up the healing of wounds. It also controls growth factors such as transforming growth factor-β (TGF-β) and vascular endothelial growth factor (VEGF), which are needed for tissue healing. This characteristic is particularly effective in minimizing secondary problems and improving skin integrity in persistent AD lesions.[30]

- **Anti-fibrotic and anti-lichenification effects:** Epidermal thickening and lichenification are caused by recurrent inflammation and itching in chronic AD. By preventing fibroblast activation and excessive extracellular matrix deposition, curcumin has anti-fibrotic action. Over an extended period of therapy, it improves lesion shape and lessens skin thickness by suppressing profibrotic mediators and signaling pathways.[31]

- **Anti-allergic activity:** By stabilizing mast cells and basophils, curcumin exhibits notable anti-allergic effects by stopping the production of histamine and other allergic mediators. It inhibits IgE-mediated signaling pathways and lowers eosinophil infiltration into irritated skin. Together, these benefits help to lessen the hypersensitive responses that AD patients frequently experience.[32]

- **Photoprotective and anti-aging effects:** By neutralizing UV-generated free radicals and blocking UV-activated inflammatory pathways, curcumin protects skin from UV-induced damage. It also reduces collagen breakdown by blocking matrix metalloproteinases (MMPs). These characteristics promote general skin health and may increase the advantages of topical curcumin formulations, even if they are not the main treatment aim in AD.[33]

3.4. Safety and Tolerability Profile

Due to its long history of use, regulatory approval, and thorough toxicity testing, curcumin is well known for its exceptional safety profile. Regulatory bodies have designated it as Generally Recognized as Safe (GRAS), which permits its usage as a nutraceutical and food additive. Asian cultures commonly consume 100–200 mg of curcumin daily from turmeric-containing diets; no negative health impacts have been documented, underscoring the long-term dietary safety of turmeric.[34]

- **Preclinical Toxicity Data:** Preclinical toxicity tests have indicated that curcumin displays very low acute and chronic toxicity. Experiments on acute oral toxicity in rats have shown LD²₀ values higher than 2,000 mg/kg, and even at doses as high as 5,000 mg/kg, no fatality was shown in many experiments, suggesting a broad margin of safety. Hematological parameters, liver enzymes, renal function markers, and the histopathological architecture of major organs did not significantly change after repeated oral administration of curcumin at doses ranging from 100 to 1,000 mg/kg/day for up to 90 days in subacute and chronic toxicity studies.[35] Using common tests like the Ames test and chromosomal aberration studies, curcumin has also been assessed for genotoxicity and mutagenicity. Even at high doses, it showed no potential for mutagenicity or carcinogenicity. Studies on developmental and reproductive toxicity also found no teratogenic effects at pharmacologically relevant levels.[36]

- **Clinical Safety Data:** Studies assessing oral curcumin have verified that it is very well tolerated by people. Curcumin is safe at levels between 500 to 8,000 mg/day when taken over weeks to several months, according to many studies. Even at the highest dose of 8 g/day, only a tiny number of subjects (<10%) had moderate gastrointestinal symptoms as nausea, bloating, or diarrhea. Crucially, no hematological abnormalities, hepatotoxicity, nephrotoxicity, or dose-limiting toxicity were seen.[37]

- **Topical Safety and Dermatological Tolerability:** Curcumin has a low irritation and sensitization index when used topically. For curcumin doses up to 1-2% w/w in topical formulations, skin irritation ratings of 0–1 (negligible to mild) have been observed in trials utilizing standardized Draize grading techniques. Studies including repeated treatment over a period of 14–28 days revealed no signs of sensitization, allergic contact dermatitis, or cumulative irritation [38]. Patch test investigations in human volunteers have showed that topical curcumin formulations induce no erythema or only moderate, transitory redness that

disappears within 24 hours. The most often reported topical impact is a transient, reversible, and aesthetically pleasing yellowish discolouration. When curcumin is added to nanoformulations, where surface deposition is minimal, this impact is much diminished.[39]

- **Comparison with Conventional Therapies:** Curcumin does not produce epidermal thinning, telangiectasia, or striae even after extended treatment, in contrast to topical corticosteroids, which may cause skin atrophy after 2-4 weeks of continuous usage. Curcumin does not inhibit keratinocyte proliferation or collagen formation, according to studies assessing indicators of skin integrity. Additionally, curcumin does not generate rebound flares or hypothalamic–pituitary–adrenal (HPA) axis suppression, a concern reported with medium- to high-potency corticosteroids. Calcineurin inhibitors such as tacrolimus typically elicit burning or stinging sensations in 30–50% of patients after beginning medication, but topical curcumin formulations have exhibited local discomfort rates of <5%, indicating greater tolerability.[40]

- **Formulation-Dependent Safety Considerations:** While curcumin is safe by nature, formulation modification is essential for optimizing patient compliance and tolerance. Liposomes, solid lipid nanoparticles, and polymeric nanoparticles are examples of advanced delivery methods that have been demonstrated to improve skin retention, minimize staining by 40–70%, and enable effective therapeutic action at lower doses (usually 0.1–0.5% w/w), further reducing the risk of discomfort.[41]

Curcumin has a broad therapeutic index, good topical tolerance, and low systemic toxicity, according to numerical toxicological and clinical data taken together. Its usefulness for the long-term treatment of chronic inflammatory skin conditions, such as atopic dermatitis, is strongly supported by its ability to be safely delivered at gram-level oral dosages and up to 1-2% topical concentration without noticeable side effects.

4. MOLECULAR MECHANISMS OF CURCUMIN IN ATOPIC DERMATITIS

Utilizing a multi-targeted molecular mechanism that concurrently regulates inflammatory signaling pathways, immunological responses, oxidative stress, epidermal barrier integrity, and microbial colonization, curcumin has therapeutic effects in atopic dermatitis. Given that AD is a disease with intricately linked pathogenic pathways; this pleiotropic mechanism of action is especially beneficial.[42]

4.1. Inhibition of NF-κB and MAPK Signaling Pathways

A key molecular mechanism behind curcumin's anti-inflammatory properties is its capacity to block the nuclear factor-kappa B (NF-κB) signaling pathway. In atopic dermatitis, pro-inflammatory genes encoding cytokines, chemokines, adhesion molecules, and enzymes like COX-2 and iNOS are transcriptionally triggered by NF-κB activation in keratinocytes, dendritic cells, and T lymphocytes. By blocking the phosphorylation and degradation of inhibitor kappa B (IκBα), curcumin inhibits NF-κB activation and stops NF-κB subunits (p65/p50) from translocating to the nucleus. As a result, chronic skin inflammation is attenuated and inflammatory mediator expression is decreased.[44]

Apart from NF-κB, curcumin also inhibits p38 MAPK, c-Jun N-terminal kinase (JNK), extracellular signal-regulated kinase (ERK), and other mitogen-activated protein kinase (MAPK) pathways. In AD, these pathways play a crucial role in immune cell recruitment, keratinocyte activation, and cytokine generation. Curcumin decreases the expression of inflammatory genes, epidermal hyperplasia, and tissue damage linked to persistent AD symptoms by inhibiting MAPK phosphorylation.[45]

4.2. Modulation of Cytokine Expression and Immune Responses

By controlling T-helper cell development and cytokine production, curcumin plays a crucial part in immune response modulation. IgE synthesis, eosinophil activation, and the inhibition of antimicrobial peptides are all facilitated by the overproduction of IL-4, IL-5, and IL-13 in AD, which is caused by a dominant Th2-mediated immune response. Curcumin reduces allergic inflammation and hypersensitivity reactions by downregulating Th2 cytokines.[46]

Curcumin concurrently regulates Th1 and Th17 responses, lowering the overproduction of IFN-γ and IL-17, which fuel chronic inflammation and epidermal thickness. Additionally, curcumin decreases histamine production and inhibits mast cell degranulation, which lessens neurogenic inflammation and itch. Curcumin has a normalizing immunomodulatory effect instead of generalized immunosuppression, which is ideal for long-term AD therapy, by reestablishing the equilibrium between Th1, Th2, and Th17 immunological pathways.[47]

4.3. Antioxidant Mechanisms and Reduction of Oxidative Stress

One of the main causes of the development and course of atopic dermatitis is oxidative stress. Lipid peroxidation, protein oxidation, DNA damage, and further activation of inflammatory signaling pathways are all caused by elevated amounts of reactive oxygen species (ROS) produced during chronic inflammation. Curcumin's conjugated double-bond structure and

phenolic hydroxyl groups directly scavenge reactive nitrogen species (RNS) and ROS, making it a powerful antioxidant.[48]

Superoxide dismutase (SOD), catalase, glutathione peroxidase, and heme oxygenase-1 (HO-1) are examples of endogenous antioxidant enzymes that are upregulated when curcumin stimulates the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway at the molecular level. Curcumin prevents further deterioration of epidermal barrier function, reduces redox-sensitive inflammatory pathways including NF-κB, and shields keratinocytes from oxidative damage by restoring redox equilibrium.[49]

4.4. Effects on Skin Barrier Repair and Keratinocyte Function

Atopic dermatitis is characterized by skin barrier failure, which is intimately linked to decreased structural protein expression and compromised keratinocyte development. Curcumin increases keratinocyte differentiation and proliferation, which aids in the restoration of the epidermal barrier. It has been demonstrated to increase the expression of important barrier-related proteins, including as involucrin, loricrin, and filaggrin, which are frequently downregulated in AD as a result of Th2 cytokine dominance.[50]

Additionally, curcumin improves lipid structure and promotes ceramide production in the stratum corneum, which lowers transepidermal water loss (TEWL). Curcumin also supports proper epidermal turnover and wound healing by controlling growth factor expression and calcium signaling in keratinocytes. All of these actions work together to restore the integrity of the barrier lessen the penetration of allergens, and lower immunological activation.[51]

4.5. Antimicrobial Action against *Staphylococcus aureus*

Staphylococcus aureus colonization of AD lesions contributes significantly to the worsening of the disease by generating superantigens and exotoxins that increase immunological activation. Strong antibacterial action is demonstrated by curcumin against S. aureus, including those that are resistant to methicillin (MRSA). Bacterial cell membrane rupture, protein synthesis inhibition, quorum sensing suppression, and biofilm development are all part of its antibacterial action.[52]

Crucially, curcumin also limits T-cell hyperactivation and cytokine storm in AD lesions by lowering the expression of superantigens produced from S. aureus. Curcumin helps break the inflammatory feedback loop between microorganisms and host immune responses by

lowering bacterial colonization and avoiding secondary infections. Its antibacterial effect also happens without encouraging antibiotic resistance, which is a big benefit over traditional antimicrobial treatments.[53]

5. FORMULATION CHALLENGES OF CURCUMIN FOR TOPICAL APPLICATION

The practical translation of curcumin for topical application is severely hampered by a number of formulation-related issues, despite its strong pharmacological actions and superior safety profile. These difficulties are mostly related to its negative physicochemical characteristics, low stability, restricted skin penetration, and problems with patient acceptance. To fully use curcumin's therapeutic potential in the treatment of atopic dermatitis, these restrictions must be addressed.

5.1. Poor Aqueous Solubility and Chemical Instability

Curcumin's relatively low water solubility (about 10–20 ng/mL) limits its absorption into traditional aqueous creams, gels, and lotions, making it one of the most severe formulation problems. In the end, low solubility limits therapeutic efficacy by causing inadequate drug loading, uneven drug distribution, and decreased thermodynamic reactivity at the skin's surface.[54]

Curcumin is not only poorly soluble but also chemically unstable, especially in alkaline environments, when exposed to light, and at high temperatures. Inactive degradation products are produced as an outcome of its quick hydrolytic and photodegradation. This instability can result in a substantial loss of medication efficacy during storage and usage in topical preparations, when contact to environmental conditions is unavoidable. Therefore, to maintain curcumin's action, stabilizing techniques such encapsulation, antioxidant inclusion, and light protection are required.[55]

5.2. Low Skin Penetration and Rapid Degradation

Curcumin's large molecular weight (~368 Da), crystalline structure, and strong intermolecular interactions prevent effective penetration into the stratum corneum, despite its moderate lipophilicity (log P = 3.0). Consequently, only a tiny portion of curcumin administered topically can reach deeper layers of the epidermis and dermis, where inflammatory processes in atopic dermatitis take place.

Additionally, curcumin's effective concentration at the target location is decreased by

oxidative and enzymatic degradation once it reaches the skin's surface. Because of its quick breakdown and removal from the skin, it must be applied often and at greater dosages, which might affect patient compliance. These drawbacks emphasize the necessity of controlled-release and permeation-enhancing delivery strategies.[56]

5.3. Limited Bioavailability at the Target Site

One major issue with topical treatment is curcumin's low bioavailability at the site of action. Stability, limited penetration, and poor solubility all contribute to subtherapeutic medication levels in inflammatory skin tissues. Insufficient drug accumulation jeopardizes treatment results in atopic dermatitis, because inflammation is frequently restricted to certain epidermal and dermal areas.[57]

Furthermore, rather of evenly dispersing across the deeper layers of skin, curcumin tends to build up superficially in the stratum corneum. To properly regulate immune cells, cytokine signaling, and oxidative stress that occurs inside the viable epidermis and dermis, this superficial localization might not be enough. As a result, formulation techniques need to minimize systemic absorption while maximizing skin retention and localized administration.

5.4. Issues Related to Staining, Odor, and Patient Compliance

An important consideration in the long-term treatment of chronic diseases such atopic dermatitis is patient acceptance. Because curcumin may discolor skin, clothes, and bedding, its bright yellow hue is a serious cosmetic problem. Regular usage is typically discouraged by this staining effect, especially in exposed regions like the hands, neck, and face.

Furthermore, curcumin has a unique smell that comes from turmeric, which some patients may find disagreeable. Compliance problems are made worse by the requirement for frequent reapplication because of the poor stability and bioavailability. Traditional curcumin formulations' poor appearance and difficulty can drastically lower patient adherence, which limits clinical efficacy.[58]

5.5. Need for Advanced Formulation Strategies

The advancement of sophisticated topical drug delivery methods that can enhance curcumin's solubility, stability, skin penetration, and patient acceptance is imperative in light of the aforementioned difficulties. These formulation obstacles may be overcome by cutting-edge strategies including liposomes, niosomes, solid lipid nanoparticles, nanoemulsions, polymeric

nanoparticles, and microneedle-assisted delivery. In order to improve therapeutic efficacy and patient compliance, such methods can prevent curcumin from degrading, improve penetration and skin retention, lessen staining, and permit regulated drug release.[59]

6. NANO-ENABLED TOPICAL DELIVERY SYSTEMS FOR CURCUMIN

Curcumin's poor solubility, instability, minimal skin penetration, and restricted bioavailability at the target location severely restrict its therapeutic use in atopic dermatitis. By facilitating the effective topical administration of curcumin, developments in nanotechnology have offered creative solutions to these problems. Because they minimize systemic exposure and side effects while enabling focused, prolonged, and localized therapeutic activity, nano-enabled delivery methods are especially ideally suited for AD.

6.1. Rationale for Nanotechnology-Based Delivery in Atopic Dermatitis

The chronic inflammatory skin condition known as atopic dermatitis mostly affects the dermal and epidermal layers. Sustained medication concentrations at the site of inflammation, immune response regulation, epidermal barrier function restoration, and microbial colonization decrease are all necessary for effective treatment. Due to inadequate drug penetration and quick drug loss from the skin's surface, conventional topical formulations frequently fall short of these goals.[60]

Delivery methods based on nanotechnology provide a logical solution to these problems by increasing curcumin's solubility, shielding it from enzymatic and chemical deterioration, and facilitating its entry into deeper layers of the skin. In order to promote more medication deposition in inflammatory tissues, nanocarriers can be designed to interact positively with the compromised skin barrier in AD. Additionally, regulated and site-specific medication distribution is made possible by nanotechnology, which is essential for managing AD over the long term without resulting in systemic toxicity.[61]

6.2. Advantages of Nano-Carriers in Topical Therapy

Compared to traditional formulations, nano-carriers which mean liposomes, niosomes, solid lipid nanoparticles (SLNs), nanostructured lipid carriers (NLCs), polymeric nanoparticles, and nanoemulsions provide a number of benefits. Their vast surface area and tiny particle size (usually 10–300 nm) improve medication solubilization and skin contact.

By protecting curcumin from light, oxygen, and moisture, its encapsulation in nanocarriers

enhances its chemical stability. Additionally, nano-carriers provide homogenous medication distribution and increased drug loading, guaranteeing steady therapeutic efficacy. Furthermore, lipid-based nanocarriers have outstanding occlusive and biocompatibility qualities that promote medication penetration and skin hydration a crucial factor in AD, which is characterized by xerosis and barrier failure.[62]

6.3. Enhanced Skin Permeation and Controlled Drug Release

Improved skin penetration is one of the main advantages of topical administration afforded by nanotechnology. Through intercellular lipid channels, follicular routes, or damaged barrier areas typical of AD lesions, nanocarriers can enter the stratum corneum. Better integration and deeper penetration are made possible by lipid-based nanocarriers, which closely mimic the lipid matrix of the stratum corneum.

Additionally, nanocarriers offer prolonged and regulated drug release, sustaining curcumin's therapeutic concentrations throughout time. This lowers peak-related discomfort and lessens the requirement for frequent application. In AD, where ongoing regulation of inflammation and immunological responses is necessary to avoid disease flare-ups, controlled release is especially helpful. Research has indicated that as compared to traditional formulations, nanoformulated curcumin exhibits noticeably greater skin retention and longer-lasting anti-inflammatory benefits.[63]

6.4. Reduction of Systemic Exposure and Side Effects

Localizing medication activity inside the skin while restricting systemic absorption is a key benefit of topical administration methods provided by nanotechnology. Nanocarriers reduce the possibility of systemic adverse effects by improving skin retention and decreasing transdermal penetration into the systemic circulation. This is especially crucial when treating atopic dermatitis over the long term, as continuous therapy is frequently needed.[64]

By avoiding systemic immunosuppression and related side effects, nano-formulated curcumin provides a safer treatment profile than systemic medicines and strong topical corticosteroids. Additionally, tailored administration improves safety and tolerability by enabling the use of lower medication dosages to produce the intended therapeutic effect. By encapsulating curcumin inside the carrier matrix, nano-enabled devices further improve patient compliance by reducing aesthetic problems like stains and odor.[65]

7. TYPES OF NANO-BASED CURCUMIN FORMULATIONS

Numerous topical nano-based delivery strategies have been proposed to address curcumin's physicochemical and biological constraints. The composition, structure, drug release behavior, skin penetration mechanism, and clinical appropriateness of these systems vary. Choosing the best formulation approach for atopic dermatitis requires a logical grasp of each nanosystem.

7.1. Nanoemulsions and Microemulsions

Oil, water, surfactant, and co-surfactant make up nanoemulsions and microemulsions, which are colloidal dispersion systems with droplet sizes usually between 20 and 200 nm. Because curcumin is lipophilic, it dissolves in the oil phase, greatly increasing its apparent solubility and dispersion in topical preparations.

While microemulsions are thermodynamically stable and develop spontaneously under the right circumstances, nanoemulsions are kinetically stable entities. By breaking down lipid bilayers and raising drug thermodynamic activity at the skin's surface, both mechanisms improve curcumin's penetration into the stratum corneum. Additionally, nanoemulsions in AD have a moisturizing action that reduces xerosis. However, microemulsions' high surfactant content may irritate sensitive atopic skin with extended usage.[66]

7.2. Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs)

Solid lipids stabilized by surfactants make up solid lipid nanoparticles (SLNs), which typically have particle diameters between 50 and 300 nm. Curcumin is embedded or molecularly distributed inside the solid lipid matrix, allowing for regulated drug release and protection against chemical deterioration. SLNs reduce transepidermal water loss and improve skin hydration by forming an occlusive layer on the skin's surface, which is a significant advantage in AD.

A combination of solid and liquid lipids makes up nanostructured lipid carriers (NLCs), a second-generation lipid nanoparticle system. A typical drawback of SLNs is drug ejection during storage, which is avoided by this defective lipid matrix, which also boosts drug loading capacity.In comparison to SLNs, NLCs have shown better skin retention and longer curcumin release, which makes them more appealing for long-term treatment of chronic inflammatory skin conditions.[67]

7.3. Polymeric Nanoparticles and Nanogels

Biodegradable polymers like chitosan, PLGA, or alginate are used to create polymeric nanoparticles, which usually have particle diameters between 100 and 400 nm. These technologies offer outstanding physical stability and exact control over the kinetics of medication release. Curcumin-loaded polymeric nanoparticles allow for prolonged release inside the dermal and epidermal layers while shielding the medication from environmental deterioration.

Three-dimensional, nanoscale, crosslinked polymer networks that can absorb a lot of water are called nanogels. Curcumin-loaded nanogels offer high drug loading, improved skin penetration, and superior moisturizing qualities by combining the benefits of hydrogels with nanoparticles. Because of their calming, non-greasy properties and capacity to release curcumin in reaction to skin variables like pH or inflammation, nanogels are very helpful in AD.[68]

7.4. Liposomes, Ethosomes, and Transfersomes

Particle sizes of liposomes, which are vesicular structures made up of phospholipid bilayers encasing an aqueous core, usually range from 50 to 500 nm. Curcumin's solubility and skin affinity can be improved by incorporating it into the lipid bilayer. Liposomes minimize negative effects by reducing systemic absorption and improving medication localization in the epidermis.

Ethosomes are modified liposomes with high ethanol content (20–40%) that improves skin penetration and membrane fluidity. Transfersomes are ultra-deformable vesicles that can fit through the stratum corneum's small intercellular gaps because they have edge activators. Compared to traditional liposomes, ethosomes and transfersomes both have better penetration into deeper skin layers, which makes them especially useful for delivering curcumin to inflammatory tissues in AD. To prevent irritation in atopic skin that is already damaged, ethanol-containing solutions might need to be carefully optimized.[69]

7.5. Comparative Evaluation of Different Nano-Systems

For topical curcumin administration, each nano-based formulation has unique benefits and drawbacks. Although nanoemulsions offer superior solubilization and formulation simplicity, they may be irritated by surfactants. Both SLNs and NLCs provide better stability, skin hydration, and controlled release; however, NLCs often perform better than SLNs in terms of long-term stability and drug loading. Although they offer considerable formulation flexibility

and controlled release, polymeric nanoparticles and nanogels may need intricate production procedures. Although their physical stability and expense may present difficulties, vesicular systems like liposomes, ethosomes, and transfersomes are very biocompatible and efficient in improving skin penetration.[70]

Since they can improve skin retention, restore barrier function, provide sustained drug release, and reduce systemic exposure, lipid-based nanocarriers (NLCs and SLNs) and deformable vesicular systems (ethosomes and transfersomes) are thought to be the most appropriate therapeutic options for atopic dermatitis. Therefore, the severity of the condition, the target skin layer, safety concerns, and patient compliance should all be taken into account when choosing a suitable nano-system.

Table 1: Comparative Evaluation of Nano-Based Curcumin Formulations for Topical Application in Atopic Dermatitis.

Nano-System	Typical Particle Size (nm)	Composition	Advantages	Limitations	Suitability for Atopic Dermatitis
Nanoemulsions	20–200	Oil, water, surfactant and co-surfactant	Nanoemulsions enhance the solubility of curcumin and improve its dispersion and penetration through the stratum corneum while also providing a moisturizing effect to the skin	These systems are kinetically stable and require relatively high concentrations of surfactants, which may cause irritation upon prolonged use	Suitable for mild atopic dermatitis when formulated with mild and skin-compatible surfactants
Microemulsions	10–100	Oil, water, surfactant and co-surfactant	Microemulsions are thermodynamically stable systems that improve drug thermodynamic activity and enhance skin permeation of curcumin	The high surfactant and co-surfactant content may lead to skin irritation, limiting long-term use in sensitive skin	Limited suitability for atopic dermatitis due to irritation potential[72]
Solid Lipid Nanoparticles (SLNs)	50–300	Solid lipids stabilized by surfactants	SLNs protect curcumin from chemical degradation and provide controlled drug release while forming an occlusive film that reduces transepidermal water loss	Drug loading capacity is limited and drug expulsion may occur during storage	Highly suitable for atopic dermatitis due to hydration enhancement and barrier repair[73]
Nanostructured Lipid Carriers (NLCs)	80–250	Mixture of solid and liquid lipids with surfactants	NLCs offer higher drug loading, improved physical stability, prolonged skin retention and sustained release of curcumin	Formulation design is more complex compared to SLNs	Most suitable nano-carrier for chronic atopic dermatitis therapy
Polymeric Nanoparticles	100–400	Biodegradable polymers such as chitosan, PLGA or	These systems provide precise control over drug release kinetics and protect curcumin from	Manufacturing processes are complex and polymer-related	Suitable for long-term management of atopic dermatitis when

		alginate	environmental degradation	toxicity must be carefully evaluated	biocompatible polymers are used
Nanogels	50–300	Crosslinked hydrophilic polymer networks	Nanogels provide excellent moisturizing properties, improved skin penetration and stimuli-responsive drug release	Stability and mechanical strength may be limited	Highly suitable for atopic dermatitis due to soothing effect and improved patient compliance
Liposomes	50–500	Phospholipid bilayer vesicles	Liposomes enhance epidermal localization of curcumin and reduce systemic absorption due to their biocompatibility	Physical instability and limited penetration into deeper skin layers are major challenges	Suitable for mild to moderate atopic dermatitis[74]
Ethosomes	100–400	Phospholipids with high ethanol content	Ethosomes enhance membrane fluidity and improve penetration of curcumin into deeper skin layers	Ethanol may cause irritation in compromised atopic skin	Suitable with careful optimization for moderate to severe atopic dermatitis
Transfersomes	100–300	Phospholipids with edge activators	Transfersomes are highly deformable and penetrate deeply through the stratum corneum delivering curcumin efficiently to inflamed tissues	High formulation cost and stability issues may limit large-scale use	Highly suitable for targeted delivery in severe atopic dermatitis[75]

8. EVALUATION PARAMETERS FOR NANO-CURCUMIN TOPICAL FORMULATIONS

To guarantee the physicochemical stability, cutaneous safety, therapeutic effectiveness, and appropriateness of nano-curcumin topical formulations for the treatment of atopic dermatitis, a thorough investigation is necessary. Particle characterisation, in vitro and in vivo performance, stability evaluation, and safety profile are all included in the evaluation parameters.

8.1. Particle Size, Zeta Potential, and Encapsulation Efficiency

One important factor affecting medication release, skin penetration, and formulation stability is particle size. Particle sizes in nano-curcumin topical formulations typically fall between 50 to 300 nm, which is thought to be ideal for cutaneous administration and improved follicular penetration. Dynamic light scattering (DLS) is frequently used to measure particle size and size distribution; homogenous particle dispersion is indicated by polydispersity index (PDI) values less than 0.3.[76]

Zeta potential is a crucial measure of colloidal stability and represents the surface charge of nanoparticles. Because of the electrostatic repulsion between particles, formulas with zeta potential values larger than ±30 mV are often regarded as physically stable. Slightly positive zeta potential values improve skin retention for chitosan-based or lipid-based systems by enhancing contact with the negatively charged skin surface.

The percentage of curcumin that is effectively entrapped inside the nano-carrier system is known as the encapsulation efficiency. To improve therapeutic efficacy and reduce drug loss, high encapsulation efficiency is preferred. Depending on the carrier type and formulation technique, nano-curcumin formulations usually show encapsulation efficiencies between 70% and 95%. Ultracentrifugation or dialysis methods are frequently used to separate the free medicine from the encapsulated drug in order to assess encapsulation efficiency.[77]

8.2. In Vitro Drug Release and Skin Permeation Studies

Curcumin's release kinetics from nano-carriers is assessed by in vitro drug release investigations. Dialysis membrane methods are often used in these investigations in appropriate release medium, which can include phosphate buffer saline (pH 5.5 or 7.4) with solubilizing agents. For extended anti-inflammatory effect in atopic dermatitis, nano-curcumin formulations often show a biphasic release pattern, with an initial burst release accompanied by sustained drug release over 12–48 hours.

Franz diffusion cells with removed animal or human cadaver skin are commonly used for skin permeation and retention investigations. Compared to standard formulations, nano-curcumin formulations have been demonstrated to greatly improve curcumin penetration, with claimed improvements in skin retention of two to six times. These investigations shed light on the capacity of nano-systems to minimize systemic absorption while localizing the medication inside the dermal and epidermal layers.[78]

8.3. Stability Studies

The physical and chemical stability of nano-curcumin topical formulations during storage is evaluated by stability tests. According to ICH recommendations, parameters such particle size, zeta potential, drug concentration, pH, and visual appearance are tracked over time under various storage settings, usually 25 ± 2 °C/60 ± 5% RH and 40 ± 2 °C/75 ± 5% RH.

Over the course of three to six months, a stable formulation should show less than 10% volatility in both drug content and particle size. Since nano-encapsulation shields the medication from oxidative and photodegradation, curcumin encapsulated in nano-carriers exhibits better chemical stability than free curcumin.[79]

8.4. In Vivo Efficacy and Skin Irritation Studies

To validate the potential for therapy of nano-curcumin formulations in atopic dermatitis, in vivo effectiveness studies are crucial. Animal models such as DNFB- or DNCB-induced atopic dermatitis in mice or rats are frequently used in these investigations. Reduction of erythema, edema, skin thickness, pruritus, and histological alterations are among the parameters assessed. When compared to traditional curcumin formulations, nano-curcumin formulations have shown notable decreases in inflammatory indicators and the severity of skin lesions.

Investigations on skin irritation and sensitization are carried out to assess topical formulations' safety. Erythema and edema scores are evaluated after topical treatment using tests like the Draize skin irritation test. Irritation ratings for nano-curcumin formulations are often less than 1, suggesting that they are either non-irritating or just slightly irritating. Nano-curcumin formulations are suitable for long-term usage in atopic dermatitis since they do not damage the skin's barrier or promote skin atrophy like corticosteroids do.[80]

9. REGULATORY, SAFETY, TRANSLATIONAL CONSIDERATIONS AND FUTURE PERSPECTIVES OF NANO-CURCUMIN IN ATOPIC DERMATITIS

Safety, Regulatory, and Manufacturing Challenges: Long-term dermal exposure, nanoparticle penetration, and possible accumulation inside skin layers are safety issues that need to be carefully considered, despite the fact that nano-curcumin topical formulations offer substantial therapeutic benefits. Due to the lack of clear international rules addressing nano-specific quality features, toxicity evaluation, and phytoconstituent standardization, the regulatory clearance process for herbal nano-products is still complicated.[81] Additionally, maintaining constant particle size, encapsulation effectiveness, and product stability during large-scale production are issues associated with the scale-up and manufacture of nano-formulations. Successful industrial translation requires addressing these safety and regulatory issues in addition to strong quality control procedures.[82]

Clinical Translation, Combination Therapy, and Patient Acceptance: To demonstrate the long-term safety, therapeutic effectiveness, and superiority of nano-curcumin formulations over traditional formulations, carefully planned preclinical and clinical trials are necessary [83]. In chronic conditions like atopic dermatitis, where formulation features like non-greasy texture, low staining, pleasant odor, and simplicity of application greatly affect adherence, patient satisfaction is critical. Furthermore, using nano-curcumin in conjunction with currently available anti-atopic medications like calcineurin inhibitors or corticosteroids may have synergistic therapeutic advantages, lower dosage requirements, and fewer side effects, all of which might enhance therapy results.[84]

Future Research Approaches and Personalized Nano-Therapeutics: The creation of targeted and customized nano-delivery systems that take into account individual differences in skin barrier function, immune response, and disease severity should be the main focus of future investigations. Cutting-edge nano-carriers with stimuli-responsive and regulated medication release show potential for enhancing therapeutic precision and site-specific delivery.[85] International regulatory harmonization, real-world clinical assessments, and long-term toxicity studies are also required to guarantee the safe commercialization of nano-curcumin formulations. The conversion of nano-curcumin from experimental formulations to clinically feasible and patient-friendly treatments for atopic dermatitis will be made easier by filling in these research gaps.[86]

10. CONCLUSION

In addition to its diverse pharmacological actions, which include strong anti-inflammatory, antioxidant, immunomodulatory, and antibacterial effects, curcumin has considerable therapeutic potential in atopic dermatitis. It is a viable natural alternative or supplement to traditional therapy due to its capacity to affect important molecular pathways implicated in AD, including NF-κB, MAPK, Th1/Th2/Th17 balance, oxidative stress, and skin barrier repair. Curcumin is well tolerated and has few side effects, which makes it appropriate for long-term treatment of chronic inflammatory skin disorders, according to preclinical and early clinical research.

A key tactic to get beyond curcumin's intrinsic drawbacks such as its poor solubility, low stability, restricted skin penetration, and certain cosmetic problems like staining—is the use of nano-enabled topical delivery methods. In order to maximize therapeutic efficacy while avoiding systemic exposure, lipid-based nanoparticles, deformable vesicles, polymeric

nanoparticles, and nanogels improve skin retention, offer controlled release, and increase patient compliance. All things considered, nano-formulated curcumin has great potential for clinical application in atopic dermatitis, providing a secure, efficient, and patient-friendly substitute for traditional topical medications. To fully realize its potential in standard dermatological treatment, more research and well planned clinical trials will be necessary.

REFERENCES

1. Raghav A, Negi S, Masiwal V, Mascarenhas-Melo F, Lohani A. Nanotechnology in skin care: Opportunities and challenges. Nanodermatology, 2026 Jan 1; 3-22.
2. Suddikattu B, Tiwari V, Tiwari A, Marisetti AL, Sharma A, Chhikara A, Dahiya S. Exploring innovative therapeutic strategies for psoriasis treatment using bioactive compounds. Discover Pharmaceutical Sciences, 2025 Dec; 1(1): 1-38.
3. Brar GS, Nandy SK, Sharma A, Siddiqui AJ, Sharma L. Antimicrobial and Anti-Infective Potential of Herbal Creams in Dermatology: Efficacy, Safety, and Challenges in Skin Infection Management. Infection and Drug Resistance, 2025 Dec 31: 6289-311.
4. Xue Y, Wang T, Liu JP, Chen Q, Dai XL, Su M, Cheng YH, Chu CC, Ren YQ. Recent Trends in the Development and Application of Nano-Antioxidants for Skin-Related Disease. Antioxidants, 2024 Dec 28; 14(1): 27.
5. Patel P, Pal R, Butani K, Singh S, Prajapati BG. Nanomedicine-fortified cosmeceutical serums for the mitigation of psoriasis and acne. Nanomedicine, 2023 Oct 1; 18(24): 1769-93.
6. Kuwar UC, Pradhan M, Dhote NS, Patel R, Sinha A, Jain P, Ajazuddin. Novel approaches and applications of nanotechnology in the delivery of topical drugs for psoriasis via nanocarriers. Current Nanoscience, 2025 Jul; 21(4): 658-84.
7. Garg N, Dhankhar S, Chauhan S, Beniwal S. Bioactive-Based Nanocarriers for Dermal Diseases. Bioactive-Based Nanotherapeutics, 2025 Aug 13; 115-50.
8. Yihan W, Jinjin D, Yingqi W, Guanai M, Xiwu Z. Advances in plant essential oils and drug delivery systems for skincare. Frontiers in Pharmacology, 2025 Apr 17; 16: 1578280.
9. Jain AK, Jain S, Abourehab MA, Mehta P, Kesharwani P. An insight on topically applied formulations for management of various skin disorders. Journal of Biomaterials Science, Polymer Edition, 2022 Nov 23; 33(18): 2406-32.
10. Patel R, Yadav BK, Patel G. Progresses in nano-enabled platforms for the treatment of vaginal disorders. Recent Patents on Nanotechnology, 2023 Sep 1; 17(3): 208-27.

11. Wang Y, Jinjin D, Wang Y, Guanai M, Zhang X. Advances in plant essential oils and drug delivery systems for skincare. Frontiers in Pharmacology, 2025 Apr 1; 16: 1578280.
12. Khairnar P, Phatale V, Shukla S, Tijani AO, Hedaoo A, Strauss J, Verana G, Vambhurkar G, Puri A, Srivastava S. Nanocarrier-integrated microneedles: Divulging the potential of novel frontiers for fostering the management of skin ailments. Molecular Pharmaceutics, 2024 Apr 25; 21(5): 2118-47.
13. Palshetkar A, Mehendale P, Pingale P, Desai N. Topical drug delivery for psoriasis using nanocarriers. Nanocarrier Drug Delivery Systems: Therapeutic and Diagnostic Medicine, 2024 Sep 3; 307.
14. Manickam V, Sundar V, Panchangam RL, Amiti, S KA, Tamizhselvi R. Nanotechnology in delivery and targeting of phytochemicals. InNanopharmaceuticals: Principles and Applications. Cham: Springer International Publishing, 2020 Jul 15; 2: 211-264.
15. Braithwaite MC, Tyagi C, Tomar LK, Kumar P, Choonara YE, Pillay V. Nutraceutical-based therapeutics and formulation strategies augmenting their efficiency to complement modern medicine: An overview. Journal of Functional Foods, 2014 Jan 1; 6: 82-99.
16. Gao Y, Xu T, Wang Y, Hu Y, Yin S, Qin Z, Yu H. Pathophysiology and treatment of psoriasis: from clinical practice to basic research. Pharmaceutics, 2025 Jan 3; 17(1): 56.
17. Nnamani PO, Onokala OB, Owodeha-Ashaka K, Cardoso-Daodu IM, Ilomuanya M, Mbah CC, Attama AA. Liposomes and nanoliposomes as potential nano-enabled platforms for enhanced bioavailability of phytoconstituents. Advances in novel phytopharmaceuticals., 2024 Dec 19; 99-133.
18. Li J, Zhang YL, Jin T, Jin Z, Zhu M, Qing G, Zhang J, Wang Z, Mu Y, Li J, Hua Q. Advanced Pharmaceutical Nanotechnologies Applied for Chinese Herbal Medicines. Advanced Science, 2025; e00167.
19. Rode K, Rajankar N, Aalhate M, Mahajan S, Maji I, Gupta U, Singh PK. Hydrogels as delivery systems in herbal medicine. Formulating Pharma-, Nutra-, and Cosmeceutical Products from Herbal Substances: Dosage Forms and Delivery Systems, 2025 Aug 26; 323-53.
20. Mishra S, Jayronia S, Tyagi LK, Kohli K. Targeted Delivery Strategies of Herbal-Based Nanogels: Advancements and Applications. Current Drug Targets., 2023 Dec 1; 24(16): 1260-70.
21. De S, Gopikrishna A, Keerthana V, Girigoswami A, Girigoswami K. An overview of nanoformulated nutraceuticals and their therapeutic approaches. Current Nutrition & Food Science, 2021 May 1; 17(4): 392-407.

22. Sharma D, Pukale S, Gupta SM. Natural and synthetic agents targeting angiogenesis, oxidative stress, and inflammation in psoriasis. InTargeting Angiogenesis, Inflammation, and Oxidative Stress in Chronic Diseases, 2024 Jan 1; 109-129. Academic Press.
23. Das MK, editor. Nanocosmeceuticals: Innovation, Application, and Safety. Academic Press, 2022 Aug 23.
24. Almoshari Y. Novel hydrogels for topical applications: An updated comprehensive review based on source. Gels., 2022 Mar 10; 8(3): 174.
25. Shadab A, Ansari AF. Adaptive Nanocarriers: A New Era in Transdermal Delivery with Transferosomes. Journal of Drug Delivery & Therapeutics., 2025 Nov 1; 15(11).
26. Jacob S, Nair AB, Shah J, Sreeharsha N, Gupta S, Shinu P. Emerging role of hydrogels in drug delivery systems, tissue engineering and wound management. Pharmaceutics, 2021 Mar 8; 13(3): 357.
27. Tidke VN, Dumda AK, Rawat S, Tigote RM. Therapeutic Potential of Nanoemulsion Systems: A Multifunctional Platform for Drug Delivery and Targeting. PEXACY International Journal of Pharmaceutical Science., 2024 Nov 18; 3(11): 1-32.
28. Amisha, Singh D, Kurmi BD, Singh A. *Recent Advances in Nanocarrier-based Approaches to Atopic Dermatitis and Emerging Trends in Drug Development and Design.* Current Drug Delivery, 2024 Aug 1; 21(7): 932–60.
29. Arun Raj R, Murali A. *Formulation and evaluation of curcumin loaded transferosomal nasal in-situ gel for Alzheimer's disease.* Res Rev AJ Drug Formul Dev Prod., 2019; 6(2): 19–31.
30. Atia HA, Shahien MM, Ibrahim S, Ahmed EH, Elariny HA, Abdallah MH. *Plant-Based Nanovesicular Gel Formulations Applied to Skin for Ameliorating the Anti-Inflammatory Efficiency.* Gels., 2024 Aug 10; 10(8): 525.
31. Balasubramanyam P, Sudheer P, Sreeharsha N, Nair AB, Ramachandra DP. *Transfersomes Mediated Transdermal Delivery of Curcumin: In Vitro and In Vivo Evaluation.* Pharmaceutical Sciences, 2025 Mar 31; 31(2): 203–15.
32. Bodnár K, Fehér P, Ujhelyi Z, Bácskay I, Józsa L. *Recent approaches for the topical treatment of psoriasis using nanoparticles.* Pharmaceutics., 2024 Mar 25; 16(4): 449.
33. Dabhadkar M, Kulkarni M. *Novel drug delivery systems in topical treatment of atopic dermatitis.* Naunyn-Schmiedeberg's Archives of Pharmacology., 2025 Mar 13: 1–22.
34. Dixena B, Madhariya R, Panday A, Ram A, Jain AK. *Overcoming skin barrier with transfersomes: opportunities, challenges, and applications.* Current Drug Delivery., 2025 Mar; 22(2): 160–80.

35. Esposito E, Nastruzzi C, Sguizzato M, Cortesi R. *Nanomedicines to treat skin pathologies with natural molecules.* Current Pharmaceutical Design., 2019 Jun 1; 25(21): 2323–37.
36. Farooqui RK, Kaurav M, Kumar M, Sudheesh MS, Pandey RS. *Permeation enhancer nanovesicles mediated topical delivery of curcumin for the treatment of hyperpigmentation.* Journal of Liposome Research., 2022 Oct 2; 32(4): 332–9.
37. Garg T. *Current nanotechnological approaches for an effective delivery of bio-active drug molecules in the treatment of acne.* Artificial Cells, Nanomedicine, and Biotechnology., 2016 Jan 2; 44(1): 98–105.
38. Gupta V, Sanyogita KM, Manigauha A. *Novel formulation of aloe vera and quercetin in the management of dermal disease: Eczema.* J Pharm Drug Res., 2021; 4(2): 480–7.
39. Kant S, Kaur H, Mishra AK, Challa RR, Vallamkonda B, Popli P, Swami R. *Harmonizing Nature and Technology: Lipidic Nano-phytotherapeutics in the Management of Atopic Dermatitis.* Revista Brasileira de Farmacognosia., 2024 Oct; 34(5): 948–68.
40. Katiyar D, Kumar A, Bansal P, Prakash S, Rao NR. *Recent Trends in Topical Herbal Nanotherapeutics for Psoriasis.* In: Recent Advances in Pharmaceutical Innovation and Research. Singapore: Springer Nature Singapore, 2023 Sep 12; 559–80.
41. Kaur PR, Garg V, Bawa PA, Sharma RO, Singh SK, Kumar BI, Gulati MO, Pandey NK, Narang RA, Wadhwa SH, Mohanta SO. *Formulation, systematic optimization, in vitro, ex vivo and stability assessment of transethosome based gel of curcumin.* Asian J Pharm Clin Res., 2018; 11(2): 41–7.
42. 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 Jun 8; 24(5): 134.
43. Kumari S, Goyal A, Sönmez Gürer E, Algın Yapar E, Garg M, Sood M, Sindhu RK. *Bioactive loaded novel nano-formulations for targeted drug delivery and their therapeutic potential.* Pharmaceutics., 2022 May 19; 14(5): 1091.
44. Kushwaha P, Saxena S, Shukla B. *A recent overview on dermatological applications of liposomes.* Recent Patents on Nanotechnology, 2021 Dec 1; 15(4): 310–21.
45. Lalan M, Shah P, Barve K, Parekh K, Mehta T, Patel P. *Skin cancer therapeutics: nano-drug delivery vectors—present and beyond.* Future Journal of Pharmaceutical Sciences., 2021 Aug 30; 7(1): 179.
46. Omidian H, Wilson RL, Chowdhury SD. *Enhancing therapeutic efficacy of curcumin: advances in delivery systems and clinical applications.* Gels., 2023 Jul 25; 9(8): 596.

47. Paiva-Santos AC, Silva AL, Catarina G, Peixoto D, Pereira-Silva M, Mahdi Z, Filipa MM, Castro R, Veiga F. *Ethosomes as nanocarriers for the development of skin delivery formulations.* Pharmaceutical Research., 2021 Jun 1; 38(6): 947–70.
48. Pandey P, Satija S, Wadhwa R, Mehta M, Purohit D, Gupta G, Prasher P, Chellappan DK, Awasthi R, Dureja H, Dua K. *Emerging trends in nanomedicine for topical delivery in skin disorders: current and translational approaches.* Dermatol Ther., 2020 May 1; 33(3): e13292.
49. Patil TS, Gujarathi NA, Aher AA, Pachpande HE, Sharma C, Ojha S, Goyal SN, Agrawal YO. *Recent advancements in topical anti-psoriatic nanostructured lipid carrier-based drug delivery.* International Journal of Molecular Sciences., 2023 Feb 3; 24(3): 2978.
50. Sana E, Zeeshan M, Ain QU, Khan AU, Hussain I, Khan S, Lepeltier E, Ali H. *Topical delivery of curcumin-loaded transfersomes gel ameliorated rheumatoid arthritis by inhibiting NF-κβ pathway.* Nanomedicine., 2021 Apr 1; 16(10): 819–37.
51. Sarotsumpan P, Chiu IH, Wu PC, Khong NM, Liew CV, Chutoprapat R. *Development and Evaluation of Trans-Resveratrol-Loaded Transfersomes: Role of Cholesterol in Formulation Design for Dermal Delivery.* Nanotechnology, Science and Applications., 2025 Dec 31: 359–75.
52. Shinde G, Desai P, Shelke S, Patel R, Bangale G, Kulkarni D. *Mometasone furoate-loaded aspasomal gel for topical treatment of psoriasis: formulation, optimization, in vitro and in vivo performance.* Journal of Dermatological Treatment., 2022 Feb 17; 33(2): 885–96.
53. Shree D, Patra CN, Acharjya SK, Sahoo BM. *Applications of herbal drug delivery through a targeted approach using vesicular carriers.* Current Nanomedicine (Formerly: Recent Patents on Nanomedicine)., 2022 Mar 1; 12(1): 2–16.
54. Simrah, Hafeez A, Usmani SA, Izhar MP. *Transfersome, an ultra-deformable lipid-based drug nanocarrier: an updated review with therapeutic applications.* Naunyn-Schmiedeberg's Archives of Pharmacology., 2024 Feb; 397(2): 639–73.
55. Tuntiyasawasdikul S, Sripanidkulchai B. *Curcuma comosa loaded transfersomal gel for transdermal application: formulation, in vitro and in vivo evaluation.* Drug Development and Industrial Pharmacy., 2021 Nov 2; 47(11): 1824–34.
56. Imam SS. The future of non-invasive ways to treat cancer. Int J Pharm Sci & Res., 2021; 12(8): 4684-96.

57. Imam SS, Agarwal S. A Pragmatic Approach To Treat Lung Cancer Through Loading Theaflavin -3,3'-Digallate And Epigallocatechin Gallate In Spanlastic. Asian J Pharm Clin Res., 2021 Nov 7; 14(11): 1-8.
58. Imam SS, Imam ST, Mdwasifathar, Kumar R, Ammar MY. Interaction Between Ace2 And Sars-Cov2, And Use Of EGCG And Theaflavin To Treat Covid 19 In Initial Phases. International Journal of Current Pharmaceutical Research., 2022 Mar; 14(2): 5-10.
59. Imam SS, Sharma R. Natural compounds promising way to treat Lung Cancer. International Journal of Pharmaceutical Research and Applications., 2023; 8(2): 552- 558.
60. Imam SS, Sharma S, Kumari D, Khan S, Pathak P, Katiyar D. An Expedient Approach to Treat Asthma through Non-Steroidal, Natural Transferosomes Aerosol System. Innovare journal of medical sciences., 2022; 10(6): 7-11.
61. Imam SS, Imam ST, Agarwal S, Kumar R, Ammar MY, Athar MW, Akthar A. Lung Cancer Therapy Using Naturally Occurring Products and Nanotechnology. Innovare journal of medical sciences., 2022; 10(4): 1-5.
62. Imam ST, Imam SS. The Cream which relieves the pain of Menstrual cramps without interfering with the Hormones or Period Cycle. Research Journal of Pharmacy and Technology., 2023; 16(3): 1239-6.
63. Imam SS. Topical Formulation Constituted with Transferosomes for the Treatment Of Non-Melanoma Skin Cancer. Asian J Pharm Clin Res., 2023 May 7; 16(5): 27-32.
64. IMAM SS. NANOPARTICLES: THE FUTURE OF DRUG DELIVERY. Int J Curr Pharm Sci., 2023 Nov. 15; 15(6): 8-15.
65. Imam SS, Mehdi S, Mansuri A. A COMPREHENSIVE REVIEW ON THE PHARMACOLOGICAL POTENTIAL OF RED GINSENG OIL, TEA TREE OIL AND HEMP SEED OIL. European Journal of Biomedical., 2024; 11(4): 167-77.
66. Imam SS. Sublingual Tablets Amalgamated with Nano-particles and natural products to treat Oral Cancer., 2024; 17(5): 2056-62.
67. Imam SS, Mehdi S. Factors Affecting Pharmaceutical Pricing In India. INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES., 2024; 2(4): 1367-1384. DOI: 10.5281/zenodo.11314004.
68. Mehdi S, Tabrez UZ, Imam SS. Management of Green Pharmaceuticals. International Journal of Pharmaceutical Sciences And Research., 2024; 15(7): 1951-1962. DOI: 10.13040/IJPSR.0975-8232.15(7).1951-62.
69. Imam SS. EVALUATING THE IMPACT OF US TARIFFS AND EVOLVING GLOBAL TRADE POLICIES ON PHARMACEUTICAL PRICING, MARKET

PENETRATION, AND THE SUPPLY OF GENERIC MEDICINES FROM INDIA TO THE WORLD. Journal of Pharmacoeconomics and Pharmaceutical Management., 2025 Nov 7; 11(2): 27-34.

70. Imam SS. Pharmaceutical Marketing Management in India. Journal of Pharmacoeconomics and Pharmaceutical Management., 2024 Oct 23; 10(2): 37-48.
71. Singh A, Fatima Z, Srivastava D. A Comprehensive Review on Polyphenols based Nanovesicular System for Topical Delivery. Current Drug Delivery., 2025 Mar; 22(2): 123-39.
72. Wollina U, Tirant M, Vojvodic A, Lotti T. *Treatment of psoriasis: novel approaches to topical delivery.* Open Access Macedonian Journal of Medical Sciences., 2019 Aug 30; 7(18): 3018.
73. Wollina U, Tirant M, Vojvodic A, Lotti T. *Treatment of Psoriasis: Novel Approaches to Topical Delivery.* Open Access Maced J Med Sci., 2019 Sep 30; 7(18): 3018–25.
74. Zoabi A, Touitou E, Margulis K. *Recent advances in nanomaterials for dermal and transdermal applications.* Colloids and Interfaces., 2021 Mar 18; 5(1): 18.
75. Fonseca-Santos B, Silva PB, Rigon RB, Sato MR, Chorilli M. Formulating SLN and NLC as innovative drug delivery systems for non-invasive routes of drug administration. Current medicinal chemistry., 2020 Jul 1; 27(22): 3623-56.
76. Shah S, Patel AA, Prajapati BG, Alexander A, Pandya V, Trivedi N, Pandey P, Patel SG, Patel RJ. Multifaceted nanolipidic carriers: a modish stratagem accentuating nose-to-brain drug delivery. Journal of Nanoparticle Research., 2023 Jul; 25(7): 150.
77. Ngoepe MP, Battison A, Mufamadi S. Nano-enabled chronic wound healing strategies: Burn and diabetic ulcer wounds. Journal of Biomedical Nanotechnology., 2022 Sep 1; 18(9): 2081-99.
78. Chopra H, Tsagkaris C, Matthews L, Gautam RK, Kamal MA. Novel approaches for the application of herbs for skin care. Current Pharmaceutical Biotechnology., 2023 Jan 1; 24(1): 164-87.
79. Setapar SH, Ahmad A, Jawaid M, editors. Nanotechnology for the preparation of cosmetics using plant-based extracts. Elsevier, 2022 Feb 18.
80. Paul A, Sarkar R, Yadav DK, Koli P, Kundu A, Saha S. Characterization of Nanocomposites for Curcumin. InHandbook of Nanoencapsulation, 2023 Apr 5; 83-111. CRC Press.
81. Malhotra S, Jindal S, Bala R, Madaan R. Liposome as a Potential Drug Delivery System in Addressing Skin Diseases: A Review. Current Drug Therapy, 2025 Apr; 20(3): 332-44.

82. Kundu A, Saha S. Anindita Paul, Rohan Sarkar, Dinesh Kumar Yadav, Pushpendra Koli. Handbook of Nanoencapsulation: Preparation, Characterization, Delivery, and Safety of Nutraceutical Nanocomposites., 2023 Apr 5: 83.
83. Pukale SS, Mittal A, Chitkara D. Topical application of vitamin D3-loaded hybrid nanosystem to offset imiquimod-induced psoriasis. AAPS PharmSciTech., 2021 Sep 24; 22(7): 238.
84. Afzal O, Altamimi AS, Nadeem MS, Alzarea SI, Almalki WH, Tariq A, Mubeen B, Murtaza BN, Iftikhar S, Riaz N, Kazmi I. Nanoparticles in drug delivery: from history to therapeutic applications. Nanomaterials., 2022 Dec 19; 12(24): 4494.
85. Gupta J, Sultana S, Sharma V. Advancements in Nanotechnology for Targeted Drug Delivery in Chronic Obstructive Pulmonary Disease. Current Materials Science., 2025 Nov 4.
86. Singh D, Bainsal N, Bisht N. Macromolecular Biomaterials Endowed Strategies for Synergistic Treatment of Psoriasis: Recent Advancements and Future Prospects. Journal of Macromolecular Science, Part B., 2025 May 4; 64(5): 555-76.