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Hydrogel-Based Transdermal Drug Delivery Systems of *Centella asiatica* Extract: A Promising Optimized Strategy for Atopic Dermatitis Therapy

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Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by severe itching, dry skin, impaired epidermal barrier function, and dysregulated immune responses, including predominant Th2, Th17, and Th22 cytokine signalling. While topical therapies remain the cornerstone of treatment, conventional formulations often face challenges such as limited skin penetration, suboptimal delayed release, poor patient compliance, and variable efficacy. This narrative review explores the potential of hydrogel-based transdermal drug delivery systems (TDDS) as an optimized strategy for the treatment of atopic dermatitis, with a focus on the incorporation of *Centella asiatica* extract, known for its anti-inflammatory, skin barrier protective, and wound-healing properties. A narrative literature review was conducted in various scientific databases, covering the pathophysiology of AD, transdermal delivery mechanisms via hydrogels, skin permeability enhancement, and the pharmacological activities of *Centella asiatica* extract (including its key triterpenoids such as asiatic acid, asiaticoside, and madecassoside). Priority was given to studies on hydrogel formulations, sustained release profiles, and anti-inflammatory effects in skin models. Hydrogel-based TDDS offer advantages such as improved drug permeability through the stratum corneum, enhanced hydration (essential for dry AD skin), improved stability of bioactive compounds, and controlled/prolonged release directly into the affected skin layers. *Centella asiatica* extract demonstrates potent anti-inflammatory effects by modulating NF-κB, MAPK pathways and cytokine production (by reducing TNF-α, IL-6, IL-1β, and Th2-related mediators), while promoting collagen synthesis, antioxidant activity, and skin barrier repair, properties well suited to the management of AD. Its incorporation into hydrogels facilitates superior transdermal absorption and targeted delivery compared to conventional creams or ointments, which may improve therapeutic outcomes and compliance. Hydrogel-based transdermal delivery of *Centella asiatica* extract represents a promising, optimized approach to overcome limitations of traditional topical treatments for atopic dermatitis, offering enhanced anti-inflammatory efficacy, skin hydration, and sustained action. This strategy leverages the extract's multifaceted bioactivities for more effective, patient-friendly therapy. Further preclinical and clinical studies are essential to validate formulation stability, skin permeation kinetics, and long-term efficacy/safety in AD patients.

Keywords: atopic dermatitis, *Centella asiatica* extract, hydrogel, inflammation, transdermal drug delivery

Introduction

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder driven by a dysfunctional epidermal barrier and dysregulated immune responses, prominently featuring overactivation of T-helper (Th)2, Th17, and Th22 pathways. These lead to excessive production of cytokines such as Interleukin (IL)-4, IL-13 (Th2), IL-17 (Th17), and IL-22 (Th22), which perpetuate inflammation, pruritus, epidermal hyperplasia, and barrier impairment, manifesting as intense itching, erythema, dryness, and scaling.[1] A

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key downstream signaling hub in AD pathogenesis is the Janus Kinase (JAK)-Signal Transducer and Activator of Transcription (STAT) pathway, through which many of these cytokines transmit signals to amplify inflammatory cascades, including further cytokine release, immune cell recruitment, and disruption of skin barrier proteins (e.g., filaggrin). Inhibiting JAK-STAT signaling has proven effective in reducing AD symptoms, as evidenced by approved JAK inhibitors.[2] Conventional treatments, such as emollients for barrier support and topical corticosteroids for inflammation control, remain first-line for mild-to-moderate AD. However, they often suffer from limitations including poor patient adherence due to greasiness/messiness (leading to clothing staining), imprecise dosing, variable penetration through the impaired barrier, and risks of side effects with prolonged use (e.g., skin atrophy from steroids).[3]

Transdermal drug delivery systems (TDDS), particularly hydrogel-based patches, address these gaps by providing painless, occlusive application that enhances skin hydration (critical for AD's xerosis), ensures controlled and sustained release of actives, improves bioavailability via diffusion across the stratum corneum into lesional tissue, minimizes systemic exposure, and offers better dosing accuracy and cosmetic acceptability which avoiding messiness and enabling discreet, long-term wear.[4] *Centella asiatica* extract (and its key triterpenoids, including asiatic acid, madecassoside, and asiaticoside) offers a multifaceted natural therapeutic profile ideally suited to AD's dual pathophysiology of barrier defect and immune dysregulation. The extract demonstrates robust anti-inflammatory effects by modulating pathways such as Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), Mitogen-Activated Protein Kinase (MAPK)/Extracellular Signal-Regulated Kinase (ERK), and JAK/STAT (including JAK/STAT3), leading to reduced production of pro-inflammatory cytokines (e.g., Tumor Necrosis Factor (TNF)-α, IL-1β, IL-6, IL-4, IL-13, IL-17, IL-23) and Immunoglobulin (Ig)E, decreased mast cell infiltration, and suppression of inducible Nitric Oxide Synthase (iNOS)/Cyclooxygenase (COX)-2 expression. Concurrently, it promotes barrier repair and wound healing by stimulating fibroblast/keratinocyte proliferation, migration, collagen synthesis (types I and III), and extracellular matrix production, directly countering AD's epidermal damage and impaired recovery. While individual components (e.g., asiatic acid) excel in in vitro wound-healing models (e.g., enhancing HDF proliferation, migration, and extracelullar matrix (ECM) synthesis), and the extract shows efficacy in AD animal models (e.g., reducing dermatitis severity via NF-κB inhibition and cytokine downregulation), conventional topical formulations limit optimal delivery due to poor penetration and short contact time in inflamed, excoriated skin.[5]

The integration of Centella asiatica extract into hydrogel-based TDDS patches represents a novel, synergistic, and potentially breakthrough strategy. Hydrogels provide an ideal matrix: their high water content mimics and augments the skin's natural hydration, facilitating enhanced permeation of hydrophilic/hydrophobic triterpenoids across the disrupted AD barrier; they enable sustained, localized release over hours to days for prolonged anti-inflammatory and reparative action; and they combine moisturization with targeted delivery, addressing both immune hyperactivity (via pathway modulation, including potential JAK/STAT effects) and barrier dysfunction in a single, patient-friendly system. This overcomes limitations of separate conventional topicals (e.g., inconsistent dosing, suboptimal absorption) and synthetic JAK inhibitors (e.g., potential systemic risks), offering a natural, multi-target approach with improved compliance, reduced irritation, and possibly superior outcomes in barrier restoration and symptom control.[6] This article therefore aims to discuss the potential of *Centella asiatica* extract-loaded hydrogel patches as an optimized, innovative therapeutic modality for atopic dermatitis, bridging pathophysiology-driven needs with advanced delivery to achieve more effective, sustained, and tolerable management.

Result and Disscusion

Pathophysiology and Current Therapies of Atopic Dermatitis

Atopic dermatitis also known as atopic eczema, is a chronic, relapsing inflammatory skin disease affecting 15–20% of children and 1–3% of adults worldwide.[7] It presents clinically as eczematous lesions with intense pruritus, erythema, scaling, and excoriations, often following an age-specific distribution (e.g., facial/extensor surfaces in infants, flexural areas in children/adolescents, and hands/face in adults). Persistent inflammation frequently leads to lichenification (skin thickening) and secondary bacterial superinfections, most commonly by *Staphylococcus aureus* colonization, which exacerbates flares and perpetuates the itch-scratch cycle.[8] The pathogenesis of AD is multifactorial and complex, involving a vicious cycle of impaired epidermal barrier function, dysregulated immune

responses, genetic predisposition, and environmental triggers[1]. Central to barrier impairment is dysfunction of the stratum corneum (the outermost epidermal layer composed of anucleate corneocytes embedded in a lipid matrix) and tight junctions, which regulate paracellular permeability of water, solutes, and allergens. Homeostasis of the stratum corneum critically depends on filaggrin (FLG), a protein essential for maintaining hydration, regulating trans-epidermal water loss (TEWL), supporting epidermal cornification, and organizing epidermal structure. FLG mutations or reduced expression (the strongest genetic risk factor for AD) lead to decreased FLG activity, elevated skin pH, and hyperactivation of serine proteases such as kallikreins (KLK)-5, KLK7, KLK14). These KLKs promote excessive corneocyte desquamation and cleave protease-activated receptor 2 (PAR2) on keratinocytes, triggering the release of thymic stromal lymphopoietin (TSLP), IL-1α, and IL-1β. TSLP acts as a key "alarm" cytokine, initiating Th2-skewed inflammation by activating dendritic cells and promoting further cytokine production.[9]

Environmental factors further compromise the barrier in susceptible individuals, including prenatal exposures, microbial dysbiosis (e.g., reduced skin microbiome diversity), extreme climates, hard water, air pollution, tobacco smoke, irritants, and allergens. These disrupt keratinocytes, increase allergen penetration, enhance microbial signalling, and amplify immune activation, resulting in elevated cytokine and chemokine production. Genetic polymorphisms in immune mediators (e.g., IL-4, IL-13, IL-18, IL-22, IL-31, Chemokine Ligand (CCL)5, Cluster of Differentiation (CD)14) reinforce this dysregulation. Immune imbalance features predominant activation of Th2, Th17, and Th22 pathways, with variable Th1 contributions in chronic lesions. Key cytokines include: Th2 cytokines (IL-4, IL-5, IL-13, IL-31) drive IgE class switching, mast cell/eosinophil activation, pruritus (especially IL-31 via sensory nerves), and barrier disruption (e.g., IL-4/IL-13 suppress FLG and tight junction proteins). Th22 cytokines, particularly IL-22, play a significant role in the chronic phase of atopic dermatitis by promoting epidermal hyperplasia (the excessive proliferation of keratinocytes that leads to skin thickening) and driving the development of chronic lichenification, the characteristic leathery, accentuated skin markings seen in long-standing lesions. Th17 cytokines, especially IL-17, contribute to the inflammatory process in specific AD phenotypes. Their involvement is particularly notable in certain patient subgroups, such as Asian populations or pediatric cases, where Th17-driven inflammation adds to the overall immune dysregulation and amplifies skin inflammation beyond the dominant Th2 responses.[10]

A pivotal intracellular hub integrating these signals is the JAK–STAT pathway. Many AD-relevant cytokines (IL-4, IL-5, IL-13, IL-31, IL-22, TSLP, and others like IFN-γ in chronic phases) bind type I/II cytokine receptors, recruiting and activating JAK proteins (JAK1, JAK2, JAK3, TYK2). Activated JAKs phosphorylate STAT proteins (STAT1–6, with key roles for STAT6 in Th2 responses, STAT3 in IL-6/IL-22/IL-31 signalling, and STAT5 in pruritus/barrier effects), leading to dimerization, nuclear translocation, and transcription of pro-inflammatory genes. This pathway sustains immune cell recruitment, keratinocyte dysfunction, barrier impairment, and itch transduction via peripheral nerves which making it a central driver of both acute flares (Th2-dominant) and chronic persistence. Current first-line therapies focus on basic skincare (gentle cleansing, emollients to restore barrier and reduce TEWL, trigger avoidance) and topical corticosteroids (or calcineurin inhibitors like tacrolimus/pimecrolimus) for mild-to-moderate AD.[2] These provide anti-inflammatory effects with minimal systemic absorption and easy discontinuation but have notable limitations: greasiness/messiness leading to poor adherence and clothing staining, imprecise dosing, suboptimal penetration in thickened or excoriated skin, and risks of local side effects (e.g., skin atrophy, striae) with prolonged use.[3]

For moderate-to-severe or refractory AD, advanced targeted therapies include biologics (e.g., dupilumab, tralokinumab, lebrikizumab targeting IL-4/IL-13 signalling) and JAK inhibitors (topical: ruxolitinib cream for mild-to-moderate; systemic: upadacitinib, abrocitinib, baricitinib for moderate-to-severe). JAK inhibitors block multiple cytokine signals simultaneously (e.g., IL-4/IL-13 via JAK1/TYK2 which activates STAT6; IL-31 via JAK1/JAK2 which activates STAT3/5), offering rapid itch relief, robust lesion clearance, and efficacy in corticosteroid-refractory cases. However, systemic JAK inhibitors carry potential risks (e.g., infections, thromboembolism, malignancy signals in some populations), while topical options improve localized control with lower systemic exposure[11]. Despite these advances, challenges persist: variable long-term efficacy, access/cost barriers, need for better pediatric formulations, and incomplete response in some patients, highlighting the demand for novel, natural,

multi-target, patient-friendly strategies that address both barrier and immune defects without significant risks.

Principle of Transdermal Drug Delivery Systems and Hydrogels in Dermatology

Transdermal drug delivery systems (TDDS) are pharmaceutical formulations designed to deliver active ingredients into the systemic circulation via the skin, with the amount delivered being controlled. With this type of drug delivery, the skin serves as the entry route, allowing the drugs to bypass the gastrointestinal tract and avoid first-pass metabolism in the liver. As a result, transdermal administration can maintain a more stable drug concentration in the bloodstream compared to conventional oral or injectable dosage forms and improve patient compliance. This sustained delivery is particularly valuable in AD, where patients frequently require repeated applications of topical treatments but often experience poor adherence due to the greasiness, messiness, and discomfort associated with applying creams or ointments to already inflamed and intensely pruritic skin.[12]

TDDS patches can be designed in several forms, including reservoir systems in which the drug is held in a central compartment separated by a rate-controlling membrane, matrix systems in which the drug is uniformly dispersed throughout a polymer network, and drug-in-adhesive systems in which the active ingredient is incorporated directly into the adhesive layer that contacts the skin. For atopic dermatitis, matrix and drug-in-adhesive designs are most commonly used because they produce flexible, conformable patches that adhere securely to affected body sites, such as flexural areas, without restricting movement or causing additional discomfort during daily activities.[13, 14]

Hydrogel-based TDDS are especially well suited to the needs of atopic dermatitis therapy. Hydrogels consist of three-dimensional, cross-linked polymer networks that contain a very high proportion of water (typically more than 70–90%) which gives them a soft, moist texture that closely resembles natural tissue. This high-water content allows hydrogels to function as effective occlusive or semi-occlusive dressings that hydrate the stratum corneum, directly counteracting the severe xerosis and elevated trans-epidermal water loss that characterize AD lesions.[15]

By restoring moisture to the skin, hydrogels help repair the compromised epidermal barrier, promote keratinocyte differentiation, and support the replenishment of intercellular lipids that are often deficient in AD. In the context of atopic dermatitis, the already impaired skin barrier (resulting from filaggrin deficiency, elevated skin pH, and increased protease activity) permits greater penetration of active compounds into lesioned skin compared with healthy skin. However, this same impairment also causes inconsistent drug absorption, rapid clearance from scratched or excoriated areas, and a higher risk of local irritation.[16] Hydrogel-based TDDS overcome many of these difficulties by providing controlled and sustained release of therapeutic agents, which reduces the need for frequent reapplication, minimizes fluctuations in drug concentration that can trigger flares, and delivers the active ingredient steadily to the inflamed dermis and epidermis. At the same time, the inherent moisturizing properties of the hydrogel matrix deliver dual benefits in a single application: continuous hydration to improve barrier function alongside targeted delivery of anti-inflammatory or antipruritic compounds to suppress Th2-, Th17-, and Th22-driven immune responses.[16,17]

Hydrogels also enhance patient comfort and treatment adherence. Their cooling, non-greasy sensation upon application, ease of placement and removal, and reduced potential for irritation make them far more acceptable than traditional ointments or creams, especially for children and adults who find conventional topicals burdensome on pruritic or excoriated skin.[18] In addition, hydrogels can incorporate a wide range of hydrophilic and hydrophobic compounds ensuring better stability, solubility, and targeted action against key AD mediators such as cytokines, reactive oxygen species, or itch-signaling pathways.[17]

Despite these advantages, several challenges specific to atopic dermatitis must be addressed when developing hydrogel-based TDDS. Acute inflamed lesions permit excessive drug penetration, which may lead to local irritation or uneven dosing, while chronic lichenified areas can resist diffusion and require the inclusion of permeation enhancers or advanced technologies such as microneedles.[19] Prolonged occlusion from patch wear can increase the risk of maceration, bacterial overgrowth (particularly Staphylococcus aureus colonization), or folliculitis, especially in humid climates or intertriginous sites.[12] Formulation issues also arise, including the need to maintain long-term stability of the hydrogel matrix, prevent phase separation when loading lipophilic or sensitive actives, ensure strong yet residue-free adhesion on damaged skin, and achieve consistent release profiles in the fluctuating microenvironment of AD lesions (which can vary in pH, moisture, and mechanical disruption from scratching).[14]

Overall, hydrogel-based transdermal drug delivery systems represent a highly promising and patient-centered approach for managing atopic dermatitis. By combining advanced moisturization with precise, sustained delivery of anti-inflammatory agents, these systems address many of the practical limitations of conventional topical therapies, such as poor adherence, imprecise dosing, and suboptimal penetration, while simultaneously targeting both the barrier dysfunction and the immune dysregulation that drive the disease.[20-24]

Pharmacology of Centella asiatica and Asiatic Acid

Centella asiatica an herbaceous plant in the Apiaceae family, is widely distributed in Southeast Asian countries such as Malaysia and Indonesia. The utilization of this plant in the treatment of a wide range of ailments has spanned millennia. *Centella asiatica* a medicinal plant in Indian medicine, has been traditionally employed to treat various dermatological conditions, including leprosy, lupus, ulcers, eczema, and psoriasis. A comprehensive review of the phytochemicals present in this plant reveals the presence of flavonoids, sterols, eugenol, and pentacyclic triterpenoids. Numerous studies have demonstrated that asiatic acid constitutes the primary wound healing agent in *Centella asiatica*[4].

Asiatic acid has been demonstrated to possess a multitude of pharmacological effects, including but not limited to: anti-inflammatory, anti-depressant, hepatoprotective, neuroprotective, wound-healing, and antitumor properties. Moreover, asiatic acid has been demonstrated to enhance the proliferation of HDFs, as evidenced by an observed increase in the rate of migration and attachment of HDFs and keratinocytes, along with a 20% improvement in wound healing[5].

As evidenced, *Centella asiatica* extract has anti-inflammatory effects that are achieved through cellular mechanisms, which include the inhibition of pro-inflammatory cytokines and the JAK/STAT pathway in models of atopic dermatitis[6]. As shown in **Figure 1** the therapeutic effect of *Centella asiatica* has been demonstrated to reduce the production of nitric oxide (NO), iNOS, COX-2, IL-2, IL-6, IL-10, and TNF-α, which are characteristic of allergies. Furthermore, the results indicate that Centella asiatica extract possesses the potential to manifest anti-inflammatory effects by targeting the JAK/STAT pathway, thereby serving as a promising therapeutic option for patients afflicted with atopic dermatitis. *Centella asiatica* extract (CAE) and its bioactive constituent, asiatic acid (Aa), demonstrated a reduction in wound area and accelerated healing by increasing collagen synthesis, cell proliferation, fibroblast division, and re-epithelialization during the proliferation and remodeling phases of wound healing. CAE and Aa have also been demonstrated to play a role in the inflammatory phase by inhibiting immune cell recruitment, reducing the synthesis of pro-inflammatory cytokines (TNF-α, IL-6, and IL-1β) and growth factors (Transforming Growth Factor (TGF)-β, Platelet-Derived Growth Factor (PDGF), and Vascular Endothelial Growth Factor (VEGF)). Furthermore, Aa has been observed to impede the escalation of serum concentrations of IL-17/IL-23.[4]

Conceptual Design of a Centella asiatica–Based Hydrogel Patch for Atopic Dermatitis

Hydrogels can be loaded with diverse compounds to stimulate the wound healing process. Polyvinyl alcohol-based hydrogels capable of secreting nitric oxide have been developed for the treatment of diabetic foot ulcers. Nitric oxide has been identified as a potential agent that can enhance the wound healing process and improve tissue quality. Another compound that has the potential to be used in hydrogels is *Centella asiatica* extract. *Centella asiatica* leaf and root extracts have been demonstrated to possess wound healing and fibroblast proliferation activities.[20] The preparation of *Centella asiatica* hydrogel involved the dissolution of polyvinyl alcohol (PVA) with a concentration of 8% in deionized water for a duration of one hour within a heated vessel, accompanied by constant agitation using a magnetic stirrer. Subsequently, 5% polyethylene glycol (PEG) was incorporated, and the solution was autoclaved at 121°C for a duration of 15 minutes. After cooling, the asiaticoside-rich fraction is dissolved into the prepared PVA/PEG hydrogel base, and the mixture undergoes five consecutive freeze-thaw cycles to physically cross-link the polymer network, resulting in a stable, elastic hydrogel matrix.[20, 22] This PVA/PEG hydrogel containing an asiaticoside-rich fraction was developed and evaluated primarily for general wound healing applications, rather than specifically for atopic dermatitis. However, the formulation could be adapted for use in atopic dermatitis lesions by optimizing drug loading.

Research Gaps and Future Directions

Despite preclinical studies having demonstrated promising effects of *Centella asiatica* in models of atopic dermatitis, and hydrogel-based transdermal delivery systems offering well-documented advantages in dermatology (including

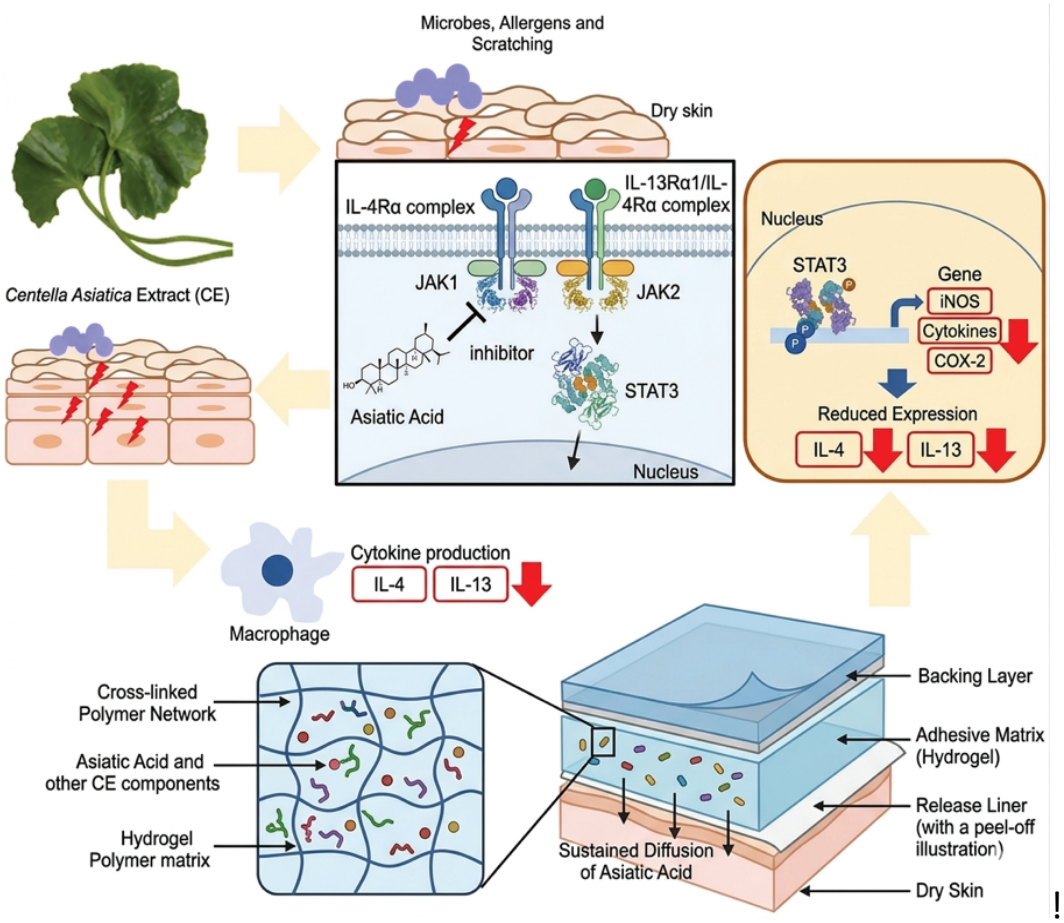


Figure 1. The mechanism of action of *Centella asiatica* in reducing pro-inflammatory cytokines in atopic dermatitis patients.

excellent moisture retention, prolonged drug release and targeted local drug delivery), there remain some significant gaps in the research. These gaps include the lack of specific clinical trials evaluating hydrogel patches containing *Centella asiatica* extract in atopic dermatitis, comprehensive pharmacokinetic data (including permeability dynamics and bioavailability in inflammatory tissue), optimised formulation specifications (such as the ideal extract concentration and triterpenoid composition), long-term stability and safety profiles, and rigorous comparative studies with current standard treatments or JAK inhibitors. Future research should focus on several critical areas: in vitro and ex vivo experiments using skin models that replicate the conditions of atopic dermatitis to assess transdermal behaviour; randomised controlled clinical trials assessing therapeutic success using standardised measures such as SCORAD scores, itch ratings, indicators of barrier function (e.g. trans-epidermal water loss and filaggrin expression), and relevant biomarkers of the JAK–STAT pathway; direct mechanistic confirmation of the modulation of the JAK-STAT signalling pathway in samples or models of human atopic dermatitis; and practical assessments of scalability for the development of user-friendly, economically viable patch products suitable for broad clinical application. In summary, this hydrogel-based strategy represents significant breakthrough potential, as it is a natural, precisely targeted and multi-targeted therapeutic approach that effectively combines the central pathophysiology of atopic dermatitis (impaired skin barrier and overactive immune response) with modern innovations in drug delivery, thereby potentially offering greater efficacy and better patient acceptance than conventional topical treatments.

Conclusion

The integration of asiatic acid from *Centella asiatica* extract into a hydrogel-based TDDS patch holds considerable promise as a more effective and optimized therapeutic strategy for atopic dermatitis. By combining sustained release, enhanced skin hydration, and targeted modulation of inflammatory pathways (including potential effects on JAK–STAT signaling), this approach has the potential to overcome many limitations of conventional topical treatments, such as poor adherence, inconsistent dosing, and suboptimal penetration in lesional skin. However, this concept is currently hypothetical and requires rigorous validation. Future work should prioritize in vitro permeation studies using AD-mimetic skin models, preclinical testing in appropriate atopic dermatitis animal models, detailed pharmacokinetic and stability assessments, and ultimately well-designed clinical trials to confirm efficacy, safety, and real-world benefits before any clinical application can be considered.

Authors' Contribution

MQ was responsible for the conceptualization of the topic, the execution of the literature search and selection. AUD and LA responsible to synthesis of the findings, and the composition of the manuscript.

Conflict of Interest

The authors declare that they have no conflict of interest related to the research, authorship, or publication of this article.

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References

1. Edslev SM, Agner T, Andersen PS. Skin Microbiome in Atopic Dermatitis. Acta Derm Venereol. 2020;100(12):adv00164. doi: 10.2340/00015555-3514.
2. Chovatiya R, Paller AS. JAK inhibitors in the treatment of atopic dermatitis. J Allergy Clin Immunol. 2021;148(4):927-940. doi: 10.1016/j.jaci.2021.08.009.
3. Vaz MB, Vitorino C, Sousa JJS. Safe-by-design development of a topical patch for drug delivery. Braz J Pharm Sci. 2020;56.
4. Diniz LRL, Calado LL, Duarte ABS, de Sousa DP. Centella asiatica and Its Metabolite Asiatic Acid: Wound Healing Effects and Therapeutic Potential. Metabolites. 2023 ;13(2):276. doi: 10.3390/metabo13020276.
5. He Z, Hu Y, Niu Z, Zhong K, Liu T, Yang M, Ji L, Hu W. A review of pharmacokinetic and pharmacological properties of asiaticoside, a major active constituent of Centella asiatica (L.) Urb. J Ethnopharmacol. 2023;302(Pt A):115865. doi: 10.1016/j.jep.2022.115865.
6. Tungsukruthai S, Pochairach R, Krajarng A, Jumpa ngern P, Tungsukruthai P. The Investigation of The Network Pharmacology and Mechanism of Action of Centella asiatica Extract on The Atopic Dermatitis Model. Pharmacognosy J. 2023;15(5):881–890.
7. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66 Suppl 1:8-16. doi: 10.1159/000370220.
8. Huang IH, Chung WH, Wu PC, Chen CB. JAK-STAT signaling pathway in the pathogenesis of atopic dermatitis: An updated review. Front Immunol. 2022:8;13:1068260. doi: 10.3389/fimmu.2022.1068260.
9. Rerknimitr P, Otsuka A, Nakashima C, Kabashima K. The etiopathogenesis of atopic dermatitis: barrier disruption, immunological derangement, and pruritus. Inflamm Regen. 2017;37:14. doi: 10.1186/s41232-017-0044-7.
10. Chovatiya R, Silverberg JI. Pathophysiology of Atopic Dermatitis and Psoriasis: Implications for Management in Children. Children. 2019;6(10):108. doi: 10.3390/children6100108.
11. Nakashima C, Yanagihara S, Otsuka A. Innovation in the treatment of atopic dermatitis: Emerging topical and oral Janus kinase inhibitors. Allergol Int. 2022 Jan;71(1):40-46. doi: 10.1016/j.alit.2021.10.004.
12. Parga AD, Doshi N, Bhat RM, Vu T, Sraa K, Casagrande S, Borra R. Transdermal Drug Delivery Systems in Atopic Dermatitis: A Review of Vehicle Innovation and Skin Barrier Challenges. Cureus. 2025;17(10):e94120. doi: 10.7759/cureus.94120.
13. Jung H, Kim MK, Lee JY, Choi SW, Kim J. Adhesive

Hydrogel Patch with Enhanced Strength and Adhesiveness to Skin for Transdermal Drug Delivery. Adv Funct Mater. 2020 Oct 1;30(42). doi: 10.1002/adfm.202004407

14. Alex M, Alsawaftah NM, Husseini GA. State-of-All-the-Art and Prospective Hydrogel-Based Transdermal Drug Delivery Systems. Applied Sciences. 2024;14(7):2926.
15. Cao H, Duan L, Zhang Y, Cao J, Zhang K. Current hydrogel advances in physicochemical and biological response-driven biomedical application diversity. Signal Transduct Target Ther. 2021;6(1):426.
16. Wan L, Wang M, Song Y, Sun G, Zhang R, Chen Z, et al. Multifunctional hydrogel for the treatment of atopic dermatitis: current advances and translational challenges. European Journal of Pharmaceutical Sciences. 2025; 214:107288.
17. Rao H, Tan JBL. Polysaccharide-based hydrogels for atopic dermatitis management: A review. Carbohydr Polym. 2025; 349:122966.
18. Harrison IP, Spada F. Hydrogels for Atopic Dermatitis and Wound Management: A Superior Drug Delivery Vehicle. Pharmaceutics. 2018;10(2):71.
19. Liu S, Deng T, Cheng H, Lu J, Wu J. Advances in Transdermal Drug Delivery Systems and Clinical Applications in Inflammatory Skin Diseases. Pharmaceutics. 2025;17(6):746.
20. Sh Ahmed A, Taher M, Mandal UK, Jaffri JM, Susanti D, Mahmood S, et al. Pharmacological properties of Centella asiatica hydrogel in accelerating wound healing in rabbits. BMC Complement Altern Med. 2019 Aug 14;19(1).
21. Barbosa AI, Torres T, Lima SAC, Reis S. Hydrogels: A Promising Vehicle for the Topical Management of Atopic Dermatitis. Adv Ther (Weinh). 2021;4(7).
22. Ahmed ASh, Mandal UK, Taher M, Susanti D, Jaffri JMd. PVA-PEG physically cross-linked hydrogel film as a wound dressing: experimental design and optimization. Pharm Dev Technol. 2018;23(8):751–60.