Clinical, Cosmetic and Investigational Dermatology

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Mechanisms and Research Advances in Drug Delivery Systems for Psoriasis and Atopic Dermatitis

Xiaoqing Yan*, Yusong Shi*, Jiguang Yang

Medical Aesthetics Department, Jinan Dermatosis Prevention and Control Hospital, Jinan, 250000, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jiguang Yang, Email woshi992024@126.com

Abstract: Inflammatory skin diseases, including psoriasis and atopic dermatitis (AD), are distinguished by their chronic nature, high rates of recurrence, and intricate immune mechanisms, severely compromising patients' physical and mental health. The stratum corneum's innate barrier property contributes to the low bioavailability of conventional topical formulations, while prolonged systemic administration entails substantial systemic toxicity concerns. There is an urgent clinical need for novel therapeutic strategies that balance high transdermal efficacy with safety. The Drug Delivery Systems (DDS) overcome physical barriers through distinct structural and material mechanisms, ranging from lipid fusion and stratum corneum hydration to the minimally invasive construction of physical microchannels. Furthermore, these systems enable precise accumulation and on-demand release of drugs at the target site via stimuli-responsive and biomimetic strategies. This review summarizes the research progress and mechanisms of action for these novel delivery platforms, with a focus on psoriasis and atopic dermatitis. The article provides a theoretical basis for the advancement of the DDS from the management of symptoms to the provision of precise cures by outlining these advancements.

Keywords: psoriasis, AD, drug delivery system, nanotechnology, intelligent delivery mechanism

Introduction

The skin, the largest organ of the human body, serves as the primary line of defense against physical injury, chemical stimuli, and microbial invasion,[1] while also playing a critical role in maintaining the body's fluid and electrolyte balance and regulating body temperature.[2] Inflammatory skin diseases are a category of disorders characterized by immune dysregulation, impairment of the skin barrier, and chronic inflammation[3] This group encompasses a range of prevalent and challenging-to-treat conditions, including psoriasis,[4] atopic dermatitis (AD),[5] acne vulgaris,[6] and seborrheic dermatitis,[7] representing a significant global challenge in dermatology, this review focuses specifically on psoriasis, AD, and acne vulgaris, as these three diseases serve as the primary clinical models for evaluating novel drug delivery systems. The global prevalence of psoriasis is estimated to be approximately 2–3%,[8] whereas the incidence of AD reaches up to 15–20% in children and 3–7% in adults.[9] The pathogenesis of these diseases is multifaceted, involving a combination of genetic susceptibility, environmental triggers, immune system dysfunction, and compromised physical barrier function of the skin.[10,11] Current clinical management predominantly relies on topical medications and systemic administration. However, the dense stratum corneum effectively hinders the passive diffusion of most drug molecules, impeding the achievement of therapeutic concentrations at the lesion site and limiting the efficacy of long-term topical treatments.[12]

Advancements in nanotechnology, biomaterials science, and microelectromechanical systems technology have facilitated the development of drug delivery systems (DDS), which offer revolutionary solutions for the precision treatment of inflammatory skin diseases. DDS encompasses a variety of forms, including lipid-based nanocarriers,[13] polymeric systems,[14] and transdermal enhancement technologies.[15] In comparison with conventional formulations, DDS exhibit numerous substantial advantages. The nanoscale effect, lipid fusion, or physical perforation enables DDS to effectively overcome the stratum corneum barrier, thereby enhancing the transdermal penetration efficiency of poorly soluble drugs and

https://doi.org/10.2147/CCID.S611342
Received: 23 March 2026
Accepted: 28 June 2026
Published: 9 July 2026

biomacromolecules.[16,17] The active targeted delivery of drugs to specific cells or structures at the lesion site is achieved by DDS through the use of surface-modified ligands or particle size effects.[18,19] Furthermore, the application of smart, responsive materials enables on-demand drug release in response to changes in the skin microenvironment, thereby enhancing local therapeutic efficacy while substantially reducing systemic toxicity and side effects.[20,21]

Despite these theoretical advantages, the clinical management of inflammatory skin diseases remains hindered by significant translational barriers. Furthermore, while existing reviews have extensively cataloged DDS based on their material compositions, there remains a distinct need for a comprehensive analysis of how these platforms specifically interact with and alter the pathological microenvironment. To bridge this gap, this review differentiates itself by fundamentally focusing on the mechanistic interplay between advanced delivery platforms and skin biology. We selected lipid-based nanocarriers, polymeric systems, microneedle systems, and biomimetic carriers for detailed discussion. This article summarizes recent advances in DDS for the treatment of inflammatory skin conditions, with a focus on elucidating their mechanisms of action. It explores the manner in which DDSs intervene in disease progression through strategies such as physical permeation enhancement, modulating cellular responses, microenvironment responsiveness, and biomimetic repair. The objective of this study is to critically assess the practical utility of DDS in enhancing bioavailability and therapeutic efficacy, thereby providing a robust theoretical foundation that informs the successful clinical translation of next-generation dermatological therapeutics.

Primary DDSs

The advent of DDS has integrated achievements in nanotechnology, polymer science, and bioengineering to overcome the limitations of traditional topical therapies. While various delivery platforms exist, we specifically selected lipid-based nanocarriers, polymers/hydrogels, microneedles, and biomimetic systems for detailed discussion in this review. These four categories represent the predominant strategies—ranging from lipid fusion and microenvironmental response to physical perforation and biological camouflage, currently employed to breach the skin barrier and modulate local immunity, showing the highest potential for clinical translation. Based on their constituent materials and delivery mechanisms, these systems can be categorized into four main types (Figure 1).

Lipid-Based Nanocarriers

Lipid-based nanocarriers represent the most extensively researched and clinically translatable class of DDS. The composition of lipid-based nanocarriers is primarily phospholipids, triglycerides, and analogous components. Their structural similarity to skin intercellular lipids results in exceptional biocompatibility.[22] Lipid-based nanocarriers have evolved from first-generation liposomes to second-generation solid lipid nanoparticles (SLNs) and nanostructured lipid carriers (NLCs). This transition was primarily aimed at overcoming the inherent limitations of traditional liposomes, such as poor physical stability, low drug-loading capacity, and susceptibility to drug leakage during storage. By incorporating solid lipid matrices, SLNs and NLCs effectively address these issues, enhancing physical stability and drug loading capacity while also forming occlusive films on the skin to reduce moisture loss.[23,24] Transfersomes modified with edge activators exhibit remarkable deformability, adapting to the mechanical structure of intercellular spaces within the stratum corneum.[25] The stratum corneum is breached by the deep penetration achieved through adaptive compression and permeation, thereby enhancing transdermal drug delivery efficiency.[26] Despite these significant advantages, lipid-based nanocarriers still face several critical limitations. First-generation liposomes are frequently prone to physical instability and drug leakage during long-term storage. While SLNs and NLCs partially address these stability issues, they exhibit inherent loading constraints, particularly for highly hydrophilic macromolecules. Additionally, the transition of lipid matrices to more stable crystalline forms during storage can lead to unexpected drug expulsion.[27] Furthermore, transitioning from laboratory formulation to industrial-scale production remains a major bottleneck. The scale-up process is often complicated by the strict requirements for maintaining reproducible particle size distributions, entrapment efficiencies, and batch-to-batch stability.

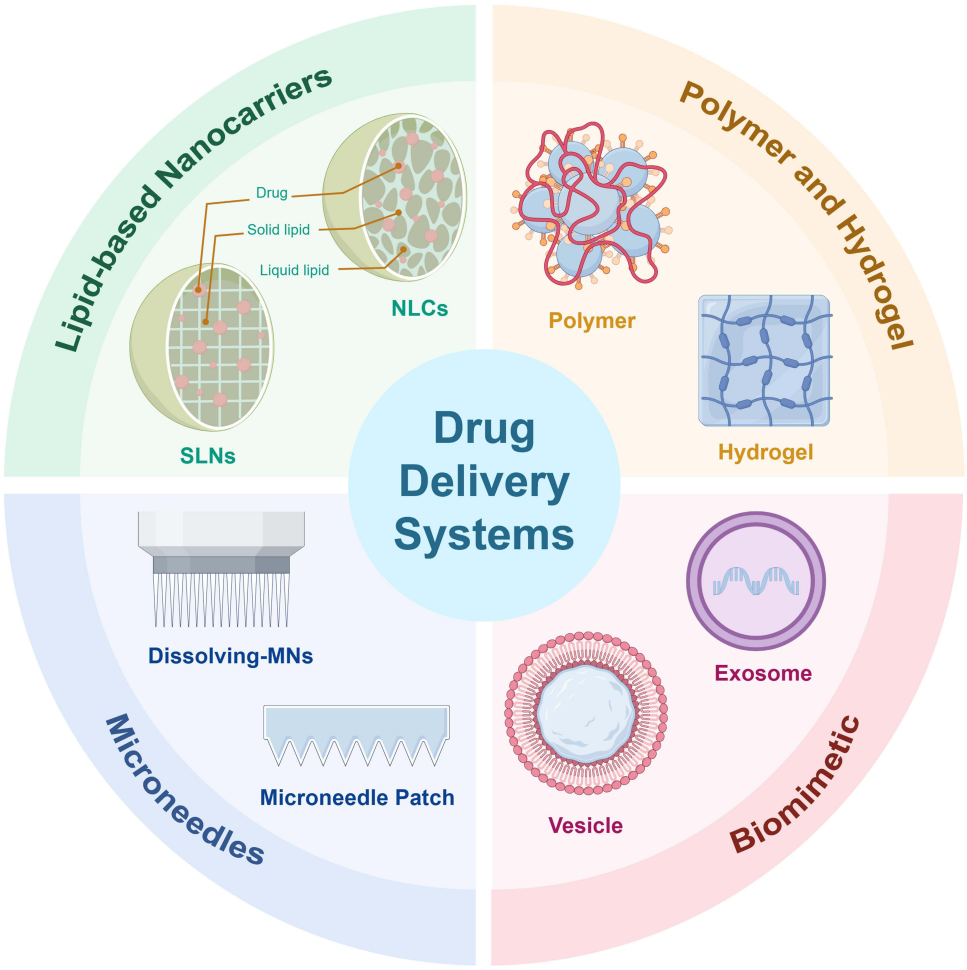

Figure 1 The classification of primary DDS. This schematic provides a conceptual overview of the four major delivery platforms, lipid-based nanocarriers, polymeric systems and hydrogels, microneedle systems, and biomimetic carriers.

Polymeric Systems and Hydrogels

These materials demonstrate exceptional modifiability and environmental responsiveness. Polymeric micelles employ amphiphilic block copolymers to self-assemble into core-shell structures, thereby effectively solubilizing hydrophobic drugs.[28] Dendrimers demonstrate properties that facilitate modification and targeted ligands due to their multivalent surfaces.[29] Hydrogels, particularly nanogels, possess a three-dimensional network structure similar to the extracellular matrix,[30] exhibit strong bioadhesion, and capacity to respond to pH changes, temperature increases, or reactive oxygen species (ROS) accumulation in the skin's inflammatory microenvironment, enabling on-demand drug release.[31]

Microneedle Systems

Microneedles (MNs) constitutes a minimally invasive physical transdermal delivery technology. MNs utilize micron-scale needle arrays to perforate the stratum corneum, thereby forming reversible microchannels on the skin surface.[32] The delivery of drugs to the epidermis or dermis without engaging pain-sensing nerves.[33] This technology is suitable for transdermal delivery of antibodies, nucleic acids, and protein-based biomolecules.[34] Furthermore, the incorporation of dissolving microneedles and hydrogel microneedles not only facilitates instantaneous drug delivery but also enables sustained release or fluid absorption through matrix design.[17,35]

Biomimetic Carriers

Inspired by natural biological processes, drug delivery systems (DDS) based on native biomembrane structures have become a prominent area of research in recent years. While sharing common biomimetic advantages, these systems can be categorized into mammalian-derived exosomes, plant-derived extracellular vesicles, and cell membrane-coated nanoparticles based on their origins and structural paradigms.[36] Mammalian-derived exosomes are natural nanoscale lipid bilayer vesicles secreted by cells, which inherently participate in intercellular communication. The complex surface proteins facilitate exceptional biocompatibility and deep penetration into the stratum corneum, effectively delivering anti-inflammatory nucleic acids and proteins directly to target keratinocytes or resident immune cells.[37] Plant-derived extracellular vesicles offer a highly scalable, cost-effective alternative free of zoonotic risks. Beyond functioning as inert carriers, these vesicles are intrinsically rich in bioactive lipids, specific RNAs, and anti-inflammatory phytochemicals, which can act synergistically with loaded therapeutic agents to promote tissue repair.[38] Conversely, membrane-coated nanoparticles utilize isolated native cell membranes—such as those derived from neutrophils or red blood cells—to encapsulate synthetic nanoparticle cores effectively, combining the tunable drug-loading capacity of synthetic carriers with the biological functions of endogenous cells.[39] The native membrane coating preserves crucial membrane proteins, enabling these nanocarriers to evade immune clearance, home in on inflammatory skin lesions via receptor-mediated interactions, and effectively participate in reshaping the local immune microenvironment.[40] The preservation of native biological interfaces ensures low immunogenicity, high structural stability, and an extended circulation half-life, making them promising for advanced inflammatory skin disease therapy.

Comparative Analysis of DDSs

While each DDS platform demonstrates distinct capabilities in overcoming the stratum corneum and modulating the inflammatory microenvironment, they present divergent profiles regarding safety, manufacturability, and clinical applicability. Lipid-based nanocarriers offer exceptional biocompatibility and scaling feasibility, yet often struggle with long-term physical stability. Polymeric systems provide highly tunable, stimuli-responsive release profiles, though their synthetic nature may elicit local immunogenicity upon repeated application. Microneedle systems uniquely enable the macromolecular delivery of biologics via physical microchannels, but their application is constrained by payload capacity and the requirement for precise insertion techniques. Biomimetic carriers, while offering immune-evasion and specific cellular modulation, face the steepest translational barriers due to complex, low-yield extraction processes and stringent regulatory definitions. A critical comparison of these platforms, highlighting their penetration mechanisms, key advantages, and limitations, is summarized in Table 1.

Application of DDS in Inflammatory Skin Diseases

The pathophysiology of inflammatory skin diseases is intricate, involving immune dysregulation, impaired skin barrier function, and alterations in the local microenvironment. The precision therapy achieved by DSS is accomplished through the implementation of several strategies, including enhanced physical penetration, drug dissolution and stabilization, active

Table 1 Critical Comparison of Primary DDSs

DDS	Penetration Mechanism	Key Advantages	Limitations
Lipid-based Nanocarriers	Hydration occlusion, lipid fusion, adaptive deformation	High biocompatibility; restores lipid barrier; simple synthesis.	Drug leakage; lipid polymorphism during storage; poor hydrophilic
Polymeric Systems and Hydrogels	Matrix swelling, responsive-release	Highly tunable structural and responsive properties; high stability.	Potential local toxicity
Microneedle Systems	Physical perforation of stratum corneum	Painless macromolecular delivery; rapid onset; bypasses chemical enhancers.	Low drug loading capacity; strict requirements for mechanical strength; risk of minor local erythema.
Biomimetic Carriers	Receptor-mediated internalization, immune evasion	Exceptional target; synergistic anti-inflammatory effects; escapes phagocytosis.	Complex extraction/purification; low yield; batch-to-batch inconsistency.

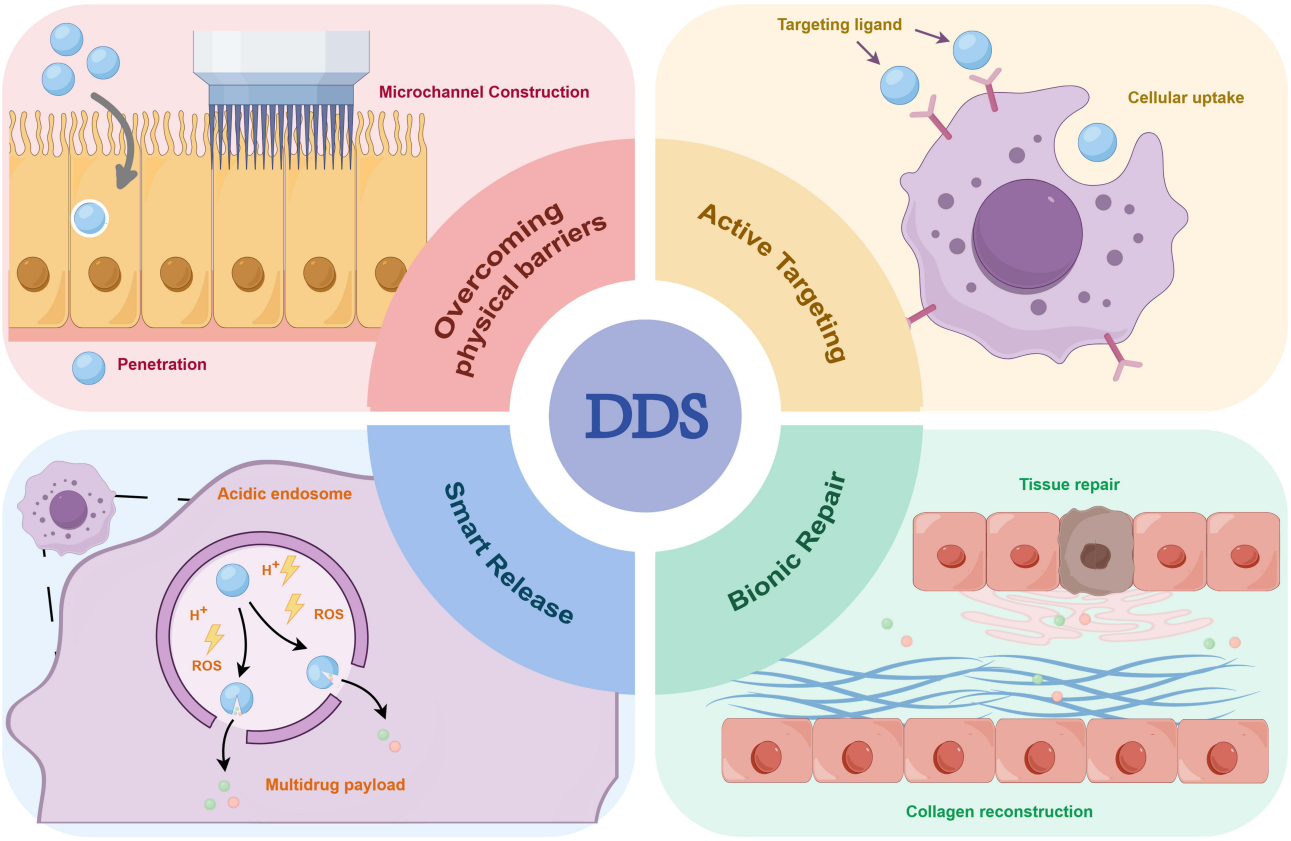

Figure 2 Overview of multiple treatment strategies employed by DDS. The illustration depicts the broad therapeutic interventions enabled by these platforms, including overcoming physical barriers, microenvironment-responsive smart release, modulating specific cellular responses, and biomimetic tissue repair.

targeted delivery, microenvironment-responsive release, and genetic regulation (Figure 2). A summary of representative recent studies in Table 2.

Overcoming Physical Barriers

The stratum corneum, the outermost layer of the skin, functions as a dense barrier structure that provides substantial protection against external aggressors. However, this barrier also restricts the passive diffusion of most therapeutic agents, thus constituting the principal factor limiting the bioavailability of topical medications.[32] The DDS achieves

Table 2 Summary of Representative Recent Studies on DDS for Inflammatory Skin Diseases

DDS	Formulation Type	Target Disease	Mechanism & Primary Outcomes	Ref
Lipid-based	Transfersomes	General Inflammation	Enhanced stratum corneum penetration via adaptive deformation; significantly reduced pro-inflammatory cytokines.	[16]
Lipid-based	Nanostructured Lipid Carriers (NLCs)	Psoriasis	Synergistic immunomodulatory and antioxidant effects; restored physical barrier hydration.	[41]
Polymeric	pH-Responsive Nanogels	AD/Dermatitis	Controlled drug release triggered by the acidic inflammatory microenvironment; minimized systemic exposure.	[21]
Microneedles	Trilayer Dissolving MNs	Psoriasis	Physical microchannel creation for deep epidermal delivery; rapid dissolution for high local drug concentration.	[17]
Biomimetic	Neutrophil Membrane-coated Liposomes	Psoriasis/AD	Camouflaged delivery recognized by dendritic cells; enhanced uptake via efferocytosis to reshape the immune microenvironment.	[42]

https://doi.org/10.2147/CCID.S611342

highly effective penetration of the stratum corneum barrier through rheological modification, lipid fusion effects, and minimally invasive physical perforation.

Hydration and Fusion Effects

Conventional rigid liposomes struggle to penetrate the dense stratum corneum.[43] The application of engineered transfersomes, comprising edge-activated agents such as sodium cholic acid and polysorbate, has been demonstrated to yield membrane flexibility and deformability that is notably superior. Transfersomes possess the capacity to traverse the pores in the stratum corneum with a diameter that is considerably smaller than their own.[44] The delivery of macromolecular anti-inflammatory drugs to the deep layers of the epidermis and dermis is achieved without compromising the integrity of the skin barrier.[16] Ethosomes are designed to utilize the physicochemical properties of ethanol to penetrate the stratum corneum lipid bilayer. This interaction enhances lipid chain fluidity and induces a transient, reversible disruption in the organization of stratum corneum lipids.[45] The presence of ethanol increases the flexibility of the vesicle membrane, rendering it more deformable and susceptible to fusion with skin lipids.[46] This mechanism of transfersomes and ethosomes significantly enhances the transdermal efficiency and skin retention of poorly soluble phytochemicals, such as resveratrol, thereby facilitating the deep penetration of hydrophobic drug molecules.[47] Furthermore, invasomes, which contains terpenoid compounds, enhances drug delivery flux by disrupting the tight packing of stratum corneum lipids. In a study on acne therapy, El-Nabarawi et al reported that invasomes achieved skin drug deposition levels several times higher than those of conventional alcoholic solutions, thereby significantly improving the topical bioavailability of the administered agents.[48]

In contrast to the penetration mechanism of flexible vesicles, SLNs and NLCs utilize a solid lipid matrix to form a dense monolayer occlusive film on the skin surface.[49] This occlusive effect significantly reduce transepidermal water loss and increase stratum corneum hydration.[50] This hydration leads to keratinocyte swelling, resulting in the enlargement of intercellular spaces and the promotion of drug permeation.[51] The distinctive disordered lattice structure of NLCs can accommodate elevated concentrations of hydrophobic drugs (such as methotrexate and luteolin) while impeding drug leakage during storage.[52] In the psoriasis treatment, this effect not only enhances drug bioavailability but also utilizes the carrier's film-forming properties to physically repair the damaged barrier and reduce the entry of external irritants.[53,54] Furthermore, Almeida et al synthesized SLNs utilizing fatty acid-rich entomological lipids. The exogenous replenishment of the skin's lipid-deficient matrix with these natural components not only reinstates barrier integrity but also facilitates lipid homeostasis.[55]

Physical Microchannel Construction

The efficacy of drugs with highly hydrophilic, extremely large molecular weights, or requiring rapid onset of action, relying solely on chemical osmotic enhancers, often proves ineffective. MNs based on physical microchannels utilize micron-scale needle tips to puncture the stratum corneum, establishing microchannels in the epidermis and superficial dermis, and directly entering the active epidermis or dermis.[56] Dissolvable MNs (dMNs) employ biodegradable polymeric materials as their matrix. Upon skin insertion, the polymeric matrix undergoes rapid dissolution or degradation triggered by the interstitial fluid, subsequently releasing the encapsulated therapeutic nanoparticles.[57] For instance, Dai et al engineered triple-layered DMNs loaded with calcipotriol nanospray for the management of psoriasis. These dMNs leverage the rapid dissolution properties at the microneedle tips to deliver the drug directly into the depths of psoriatic lesions, thereby significantly enhancing local drug concentration.[17] Furthermore, Shen et al developed hydrogel microneedles capable of sustained drug release. This MNs remain intact after insertion into the skin, ensuring continuous delivery of loaded berberine hydrochloride liposomes while simultaneously absorbing inflammatory exudate at the lesion site to improve the local microenvironment.[35]

MNs demonstrate unique advantages in gas therapy. The biconical microneedles have been engineered to facilitate the intradermal delivery of magnesium hydride, a water-sensitive hydrogen source. Upon exposure to interstitial fluid, the particles undergo a sustained hydrolysis reaction, generating molecular hydrogen in situ, overcoming the challenge of hydrogen's tendency to dissipate, and ensuring a prolonged therapeutic window within the target tissue.[58] Inspired by local occlusion injections, Zhao et al developed a patch that delivers tacrolimus into the skin via hyaluronic acid microneedles to form a reservoir, achieving sustained high local drug concentrations.[59] Furthermore, for highly insoluble drugs, microneedle delivery has been shown to achieve equivalent anti-inflammatory effects with a mere 10% of the oral dosage, significantly reducing hepatic and renal toxicity.[60]

Active Targeting

The pathological changes associated with inflammatory skin diseases extend beyond impairment of the barrier function to include the upregulation of specific cell surface receptors, abnormal infiltration of immune cells, and disruption of the microbiome.[61] DDS achieves active targeting of lesions through surface functionalization, leveraging ligand-receptor interactions, thereby reshaping the immune microenvironment.

CD44 Receptor-Mediated Epidermal Targeting

The CD44 receptor is a transmembrane glycoprotein that exhibits significantly elevated expression in keratinocytes and infiltrating lymphocytes within AD and psoriatic lesions, while maintaining low expression in normal skin.[62] In consequence, hyaluronic acid, as the natural high-affinity ligand for CD44, emerges as the material of choice for designing targeted delivery systems.

Hyaluronic acid-modified carriers delivering curcumin or methotrexate can specifically recognize and adhere to the surfaces of diseased cells that highly express CD44.[18] This facilitates the accumulation of the drug at the site of skin lesions and more effectively suppresses the expression of key inflammatory factors, such as TNF-α and IL-17, thereby significantly reducing drug diffusion into surrounding healthy tissues.[63] Furthermore, Li et al achieved active targeting of inflammatory cells by utilizing a method incorporating the use of a conjugate comprising chitosan-functionalized graphene oxide, which was conjugated with fluorescently labeled peptides and TLR4 antibodies, enabling the visual monitoring of inflammation through the analysis of fluorescence signals.[64]

Macrophages and Dendritic Cells Targeting

Improving the immune microenvironment of the dermis is also key to treating inflammatory skin diseases. Dendritic cells and macrophages play a pivotal role in the pathogenesis of psoriasis and AD.[65] Targeting the phagocytic properties of these cells, designing nanocarriers with specific surface charges or modified specific ligands can achieve immunomodulation. Sulfated polyglycerol dendritic macromolecules selectively accumulate within the immediate vicinity of inflamed tissue sites, facilitating the targeted delivery of JAK inhibitors, which effectively impede the STAT signaling pathway.[66]

Inspired by the principles of biomimetics, Ye et al engineered a camouflaged nanocarrier by encapsulating liposomes within apoptotic neutrophil membranes, preserving the “eat me” signals that are naturally present on the surface of such cells. During the natural process of apoptosis, these signals (primarily externalized phosphatidylserine) facilitate direct binding to specific scavenger receptors on phagocytes. Consequently, this biomimetic platform is specifically recognized by dendritic cells and internalized via the MERTK/AXL receptor pathways. This interaction triggers a natural and highly efficient phagocytic clearance mechanism, which significantly improves the cellular uptake of the nanocarriers, offering a potent strategy for targeted immunomodulation.[42] Thermosensitive hydrogels integrated with ionic liquids and cyclodextrins exhibit phase transition upon exposure to scalp temperature, trapping minoxidil and finasteride at the hair follicle site to enhance local drug concentration and reduce systemic side effects associated with transvascular drug absorption.[19] Expanding on targeted intervention strategies, Abid et al employed polymeric micelles to achieve site-specific accumulation of antimicrobial agents within the hair follicle, thus achieving targeted elimination of *Propionibacterium acnes* residing in the deep follicular compartments.[67]

Microenvironment Response and Smart Release

Inflammatory skin diseases are frequently accompanied by alterations in the microenvironment, including oxidative stress, pH changes, and alterations in specific enzyme activities.[5] DDS employs these pathological features as trigger switches to achieve smart response-driven release or directly eliminate harmful substances.

ROS-Response

Elevated levels of ROS represent a critical factor to wound healing in inflammatory skin diseases. The frozen MNs loaded with chlorophyll-cerium dioxide nanocomposites leverage the reversible redox cycle between Ce^{3+} and Ce^{4+} ions to mimic the activity of superoxide dismutase and catalase, efficiently catalyzing ROS decomposition and blocking inflammatory cascade reactions.[68] To address the complex pathophysiology of periorbital dermatitis, Mu et al engineered

ROS-responsive MNs patches utilizing epigallocatechin gallate (EGCG) as a functional crosslinking agent. Upon encountering elevated levels of ROS, it releases the immunosuppressant cyclosporine A while concurrently consuming ROS through the potent antioxidant properties of EGCG, facilitating the concurrent anti-inflammatory effect and the release of therapeutic drugs.[69]

pH-Response

The pH levels of inflamed skin regions frequently deviate from those of normal tissue. Nano-gels constructed from pH-sensitive biomaterials maintain stability within physiological pH ranges, while they undergo swelling or degradation in inflammatory microenvironments, enabling rapid release of loaded drugs for on-demand delivery.[70] This pH-responsive mechanism ensures high-concentration drug release at the lesion site while maintaining low release in healthy skin, reducing unnecessary drug exposure. Chitosan-based pH-responsive nanogels exhibit significantly increased swelling rates under inflammatory pH conditions by adjusting crosslinking density, triggering the rapid release of drug. Conversely, at a neutral pH level, the nanogels remain in a contracted state to reduce the amount of drug that is wasted.[21] Tang et al engineered a self-assembled hydrogel utilizing Schiff base linkages to cross-link carboxymethyl chitosan with oxidized hyaluronic acid. The controlled degradation of this hydrogel in acidic microenvironments under low pH conditions, resulting in a significant acceleration in drug release.[71]

Photothermal-Response

Phototherapy stands as a pivotal treatment for inflammatory skin conditions, and its integration with nanotechnology facilitates enhanced precision in therapeutic intervention. Yu et al modified dendritic mesoporous silica with photosensitizing groups; upon exposure to UV irradiation of a specific wavelength, the photosensitizing groups underwent isomerization to release Eri, enabling precise temporal and spatial treatment of psoriatic plaques.[72] Furthermore, the injectable photothermal hydrogel developed by Zhu et al generates heat under near-infrared light irradiation to ablate melanoma tissue and promote drug release, rendering it suitable for treating melanoma and associated skin inflammation.[73]

Bionic Repair and Multidrug Co-Delivery

For diseases such as AD, for which impaired barrier function is a hallmark, the administration of anti-inflammatory treatment alone frequently proves inadequate for achieving a cure. The DSS employs biomimetic design to replicate skin components and integrates a multi-drug synergistic strategy, achieving integrated therapeutic and restorative effects.

Bionic Repair

Exosomes and plant-derived exosome-like nanovesicles exhibit low immunogenicity and high stability due to their natural phospholipid bilayer structure and surface proteins.[74] Plant-derived vesicles are rich in bioactive lipids and phytochemicals, capable of penetrating biological barriers to regulate melanin production and inflammatory responses.[40] Engineered extracellular vesicle mimics are more effectively taken up by target cells than free drugs, inhibiting mast cell degranulation and IgE production to control allergic inflammation at its immunological source.[75] Furthermore, loading anti-inflammatory drugs into exosome structures can significantly modify the drug's pharmacokinetic characteristics, enhancing anti-inflammatory activity.[76] At the microscopic level, layered sol-gel liquid crystals mimic the layered lipid matrix between stratum corneum cells at the microscopic level.[77] Liquid crystals composed of natural oils, which are abundant in fatty acids, serve a role as reservoirs for corticosteroids. Additionally, their matrix components function as intrinsic replenishers of lipids, significantly reducing transepidermal water loss.[78,79]

Multidrug Co-Delivery

The intricate pathophysiological mechanisms of skin diseases frequently necessitate a multifaceted approach. The employment of an ionic liquid delivery system, selected through the utilization of machine learning algorithms, facilitates the concurrent delivery of STAT3-inhibiting peptides and catalase, enhancing the therapeutic efficacy of psoriasis treatment.[80] For acne caused by microbiome imbalance and inflammation, the biphasic self-locking microneedle patch rapidly releases antibacterial agents to eliminate *Propionibacterium acnes* while delivering sustained-release anti-inflammatory agents to control tissue damage.[81] Alam et al developed NLC gels loaded with tacrolimus and thymoquinone; this co-loading of both

agents in NLC not only enhanced transdermal efficiency but also achieved significantly superior efficacy compared to monotherapy in psoriasis models through complementary immunomodulatory and antioxidant mechanisms, without observable systemic toxicity.[41] Furthermore, DDS has facilitated the integration of drug therapy with physical therapy. Ramez et al investigated the combined therapy of methotrexate micelles with an arrayed erbium laser, which resulted in a significant reduction in the treatment cycle for psoriasis.[82]

Discussion

In summary, the treatment of inflammatory skin diseases has long been hindered by challenges such as poor drug penetration and significant side effects. Conventional therapeutic strategies frequently encounter difficulties in achieving an optimal balance between efficacy and safety. The application of DDS offers a potential solution to these limitations.

The DDS effectively overcome the barrier function of the stratum corneum, significantly enhancing the bioavailability of poorly soluble drugs and macromolecular biopharmaceuticals.[17,47,83] The contemporary generation of nanocarriers transcends the confines of mere inert transport vehicles.[78] Instead, they synergize with their loaded drugs to produce therapeutic effects by supplementing physiological lipids to repair barriers, utilizing antioxidant materials to scavenge ROS, or mimicking apoptotic cells to induce immune tolerance.[42,68] Nevertheless, nanoparticle carriers constructed from chemically synthesized precursors have the potential to trigger protein crown formation at damaged skin sites or be recognized as foreign bodies by the immune system, which could lead to an exacerbation of existing local inflammatory responses.[84] In the future, the development of nanoparticle carriers based on biomimetic principles is expected to be a major area of research.[85,86] For instance, the utilization of plant-derived exosome-like nanovesicles or endogenous cell membrane camouflage techniques holds promise for achieving efficient delivery while minimizing immunogenicity.

Intelligent delivery systems that are responsive to ROS, pH, or enzymes enable on-demand drug release based on dynamic changes in the microenvironment of skin lesions.[21,70] Notwithstanding, the clinical translation of such systems faces significant challenges due to patient biological heterogeneity. Microenvironment parameters vary considerably across individuals and even across different disease stages in the same patient, potentially leading to response failure or unintended drug release by smart carriers. Predictive models based on humanized data, established using machine learning algorithms, have the potential to assist in the design of carriers that are more sensitive to microenvironmental changes.[80] Concurrent integration of 3D printing technology facilitates the customized production of personalized patches or microneedle arrays, which are tailored to different lesion morphologies and thicknesses, thereby advancing the treatment of inflammatory skin diseases toward precision medicine.

Driven by a more profound understanding of the molecular landscape underlying inflammatory skin disease, the therapeutic focus is shifting from downstream anti-inflammatory approaches to upstream gene intervention and microenvironment regulation. Technologies such as tetrahedral framework nucleic acids (tFNA) facilitate the transdermal delivery of siRNAs and CRISPR/Cas9 gene editing tools, which has led to the emergence of new hope for the treatment of genetically influenced diseases, such as psoriasis.[87,88] Concurrently, co-delivery strategies incorporating prebiotics or phages offer novel approaches to restoring skin microbiome balance. In the context of addressing the challenges associated with deep tissue delivery, integrated systems that combine physical permeation enhancement with molecular carriers are poised to emerge as the optimal solution. The creation of macroscopic pathways through physical pore formation, in conjunction with the utilization of nanocarriers for cellular-level targeting, facilitates the precise molecular-level correction of intractable skin disorders while ensuring long-term safety.

While advanced DDS demonstrate exceptional preclinical efficacy, their clinical translation is significantly impeded by manufacturing and regulatory hurdles. Formulation stability remains a primary concern, as sophisticated nanocarriers are often susceptible to lipid polymorphism, premature drug leakage, and nanoparticle aggregation during prolonged storage. Furthermore, transitioning from laboratory-scale synthesis to industrial manufacturing frequently compromises batch-to-batch reproducibility. Maintaining consistent particle size distributions, precise encapsulation efficiencies, and structural integrity at a large scale is technically demanding. From a regulatory perspective, microenvironment-responsive and biomimetic platforms frequently straddle the definitions of chemical drugs, biologics, and medical devices. The current absence of standardized evaluation protocols for these highly complex systems, coupled with the strict requirement for extensive long-term safety data in human skin, creates substantial regulatory bottlenecks that inevitably delay clinical approval and commercialization.

Conclusion

Drug delivery systems (DDS) have demonstrated profound potential in preclinical models of psoriasis and atopic dermatitis by effectively overcoming the stratum corneum barrier and enabling precise, on-demand drug accumulation. By integrating microenvironment-responsive elements, these platforms shift the therapeutic paradigm from passive permeation to active, molecular-level intervention. Despite these advancements, significant gaps remain between laboratory innovation and broad clinical application. Moving forward, several critical challenges must be addressed to realize the full translational potential of DDS. First, a major gap exists between murine models and human biological heterogeneity; future research must prioritize the use of advanced, humanized 3D skin equivalents to more accurately predict human efficacy and safety. Second, the clinical translation of sophisticated platforms—particularly microenvironment-responsive and biomimetic systems—is severely bottlenecked by manufacturing scalability and batch-to-batch reproducibility. Developing robust, standardized engineering processes and purification protocols is a realistic and urgent research direction. Finally, from a regulatory standpoint, next-generation biomimetic and responsive platforms blur the traditional definitions of chemical drugs, medical devices, and biologics. Establishing clear, standardized regulatory frameworks and long-term dermatological toxicity guidelines is imperative. Ultimately, addressing these translational and regulatory hurdles, combined with the integration of machine learning for rational carrier design, will catalyze the evolution of dermatological therapies from temporary symptom management to precision microbiome remodeling and gene regulation.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analyzed in this study.

Author Contributions

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

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Zareie P, Weiss ES, Kaplan DH, Mackay LK. Cutaneous T cell immunity. *Nat Immunol*. 2025;26(7):1014–1022. doi:10.1038/s41590-025-02145-3
2. Choi MS, Chae YJ, Choi JW, Chang JE. Potential therapeutic approaches through modulating the autophagy process for skin barrier dysfunction. *Int J Mol Sci*. 2021;22(15):7869. doi:10.3390/ijms22157869
3. Zhang L, Chai R, Tai Z, et al. Noval advance of histone modification in inflammatory skin diseases and related treatment methods. *Front Immunol*. 2023;14:1286776. doi:10.3389/fimmu.2023.1286776
4. Sieminska I, Pieniawska M, Grzywa TM. The immunology of psoriasis-current concepts in pathogenesis. *Clin. Rev. Allergy Immunol*. 2024;66(2):164–191.
5. Hülpüsch C, Rohayem R, Reiger M, Traidl-Hoffmann C. Exploring the skin microbiome in atopic dermatitis pathogenesis and disease modification. *J Allergy Clin Immunol*. 2024;154(1):31–41. doi:10.1016/j.jaci.2024.04.029
6. Layton AM, Ravenscroft J. Adolescent acne vulgaris: current and emerging treatments. *Lancet Child Adolesc Health*. 2023;7(2):136–144. doi:10.1016/S2352-4642(22)00314-5
7. Polaskey MT, Chang CH, Daftary K, Fakhraie S, Miller CH, Chovatiya R. The global prevalence of seborrheic dermatitis: a systematic review and meta-analysis. *JAMA dermatol*. 2024;160(8):846–855. doi:10.1001/jamadermatol.2024.1987
8. Armstrong AW, Blauvelt A, Callis Duffin K, et al. Psoriasis. *Nat. Rev. Dis. Primers*. 2025;11(1):45. doi:10.1038/s41572-025-00630-5
9. Guttman-Yassky E, Renert-Yuval Y, Brunner PM. Atopic dermatitis. *Lancet*. 2025;405(10478):583–596. doi:10.1016/S0140-6736(24)02519-4
10. Petit RG, Cano A, Ortiz A, et al. Psoriasis: from pathogenesis to pharmacological and nano-technological-based therapeutics. *Int J Mol Sci*. 2021;22(9):4983. doi:10.3390/ijms22094983

11. Souto EB, Dias-Ferreira J, Oliveira J, et al. Trends in atopic dermatitis-from standard pharmacotherapy to novel drug delivery systems. *Int J Mol Sci*. 2019;20(22):5659. doi:10.3390/ijms20225659
12. Souto EB, Cano A, Martins-Gomes C, Coutinho TE, Zielińska A, Silva AM. Microemulsions and Nanoemulsions in Skin Drug Delivery. *Bioengineering*. 2022;9(4):158. doi:10.3390/bioengineering9040158
13. Khan MS, Mohapatra S, Gupta V, et al. Potential of lipid-based nanocarriers against two major barriers to drug delivery-skin and blood-brain barrier. *Membranes*. 2023;13(3):343. doi:10.3390/membranes13030343
14. Sabbagh F, Kim BS. Recent advances in polymeric transdermal drug delivery systems. *J Control Release*. 2022;341:132–146. doi:10.1016/j.jconrel.2021.11.025
15. Gaikwad SS, Zanje AL, Somwanshi JD. Advancements in transdermal drug delivery: a comprehensive review of physical penetration enhancement techniques. *Int J Pharm*. 2024;652:123856. doi:10.1016/j.ijpharm.2024.123856
16. Barone A, Cristiano MC, Cilurzo F, et al. Ammonium glycyrrhizate skin delivery from ultradeformable liposomes: a novel use as an anti-inflammatory agent in topical drug delivery. *Colloids Surf. B*. 2020;193:111152. doi:10.1016/j.colsurfb.2020.111152
17. Dai X, Permana AD, Li M, et al. Calcipotriol nanosuspension-loaded trilayer dissolving microneedle patches for the treatment of psoriasis: in vitro delivery and in vivo antipsoriatic activity studies. *Mol Pharmaceut*. 2024;21(6):2813–2827. doi:10.1021/acs.molpharmaceut.3c01223
18. Zhang Y, Xia Q, Li Y, et al. CD44 assists the topical anti-psoriatic efficacy of curcumin-loaded hyaluronan-modified ethosomes: a new strategy for clustering drug in inflammatory skin. *Theranostics*. 2019;9(1):48–64. doi:10.7150/thno.29715
19. Liu Z, Li X, Xiong S, et al. Co-delivery of minoxidil and finasteride via ionic liquid and cyclodextrin-assisted in situ thermosensitive hydrogel for synergistic treatment of androgenic alopecia. *Int J Pharm*. 2025;671:125263. doi:10.1016/j.ijpharm.2025.125263
20. Zhu DD, Lim RYD, Poh YL, Li DS, Raghavan S, Chen P. Transdermal hydrogen therapy for psoriasis using cavity-embedded double-conical microneedles. *J Control Release*. 2025;388(Pt 1):114313. doi:10.1016/j.jconrel.2025.114313
21. Suhail M, Chiu IH, Ullah A, et al. Formulation and in vitro assessment of polymeric ph-responsive nanogels of chitosan for sustained delivery of madecassoside. *ACS omega*. 2024;9(17):19345–19352. doi:10.1021/acsomega.4c00461
22. Antonara L, Triantafyllopoulou E, Chountoulesi M, Pippa N, Dallas PP, Rekkas DM. Lipid-based drug delivery systems: concepts and recent advances in transdermal applications. *Nanomaterials*. 2025;15(17):1326. doi:10.3390/nano15171326
23. Salvi VR, Pawar P. Nanostructured lipid carriers (NLC) system: a novel drug targeting carrier. *J Drug Delivery Sci Technol*. 2019;51:255–267. doi:10.1016/j.jddst.2019.02.017
24. Musielak E, Feliczak-Guzik A, Nowak I. Synthesis and potential applications of lipid nanoparticles in medicine. *Materials*. 2022;15(2):682. doi:10.3390/ma15020682
25. Gupta R, Kumar A. Transfersomes: the ultra-deformable carrier system for non-invasive delivery of drug. *Curr. Drug Deliv*. 2021;18(4):408–420. doi:10.2174/1567201817666200804105416
26. Simrah, Hafeez A, Usmani SA, Izhar MP, Izhar MP. Transfersome, an ultra-deformable lipid-based drug nanocarrier: an updated review with therapeutic applications. *Naunyn-Schmiedeberg's Arch Pharmacol*. 2024;397(2):639–673. doi:10.1007/s00210-023-02670-8
27. Peng TX, Liang DS, Guo F, et al. Enhanced storage stability of solid lipid nanoparticles by surface modification of comb-shaped amphiphilic inulin derivatives. *Colloids Surf. B*. 2019;181:369–378. doi:10.1016/j.colsurfb.2019.05.061
28. Türk H, Shukla A, Alves Rodrigues PC, Rehage H, Haag R. Water-soluble dendritic core-shell-type architectures based on polyglycerol for solubilization of hydrophobic drugs. *Chemistry*. 2007;13(15):4187–4196. doi:10.1002/chem.200601337
29. Choudhury H, Pandey M, Mohgan R, et al. Dendrimer-based delivery of macromolecules for the treatment of brain tumor. *Biomater. Adv*. 2022;141:213118. doi:10.1016/j.bioadv.2022.213118
30. Farjadian F, Mirkiani S, Ghasemiyeh P, et al. Smart nanogels as promising platform for delivery of drug, gene, and vaccine; therapeutic applications and active targeting mechanism. *Eur. Polym. J*. 2024;219:113400. doi:10.1016/j.eurpolymj.2024.113400
31. Cao H, Wang M, Ding J, Lin Y. Hydrogels: a promising therapeutic platform for inflammatory skin diseases treatment. *J Mat Chem B*. 2024;12(33):8007–8032. doi:10.1039/D4TB00887A
32. Xu P, Xiao W, Xu K, et al. Potential strategy of microneedle-based transdermal drug delivery system for effective management of skin-related immune disorders. *Eur. J. Pharm. Biopharm*. 2024;195:114148. doi:10.1016/j.ejpb.2023.11.013
33. Karim Z, Karwa P, Hiremath SRR. Polymeric microneedles for transdermal drug delivery- a review of recent studies. *J Drug Delivery Sci Technol*. 2022;77:103760. doi:10.1016/j.jddst.2022.103760
34. Zheng Y, Ye R, Gong X, et al. Iontophoresis-driven microneedle patch for the active transdermal delivery of vaccine macromolecules. *Microsys Nanoeng*. 2023;9:35. doi:10.1038/s41378-023-00515-1
35. Shen S, Shen W, Wang L, et al. Berberine hydrochloride-loaded liposomes-in-hydrogel microneedles achieve the efficient treatment for psoriasis. *Mater Today Bio*. 2025;32:101795. doi:10.1016/j.mtbio.2025.101795
36. Yin G, Wang H, Liu Y, et al. Mammalian, plant, and gut microbiota-derived extracellular vesicles as emerging therapeutics for bone diseases. *Front Bioeng Biotechnol*. 2026;14:1825617. doi:10.3389/fbioe.2026.1825617
37. Xu H, Zhang J, Li M. Cargo-driven extracellular vesicles as pharmaceutical nanocarriers: a pharmaceutics-oriented comparison of animal exosomes and plant-derived exosome-like nanoparticles. *Int J Pharm X*. 2026;11:100530. doi:10.1016/j.ijpx.2026.100530
38. Imran M, Jha LA, Hasan N, et al. "Nanodecoys" - Future of drug delivery by encapsulating nanoparticles in natural cell membranes. *Int J Pharm*. 2022;621:121790. doi:10.1016/j.ijpharm.2022.121790
39. Han WJ, He Z, Xing JW, et al. Cell membrane-coating nanotechnology: an integrated strategy against the multifactorial pathogenesis of periodontitis. *Biomaterials*. 2026;332:124139. doi:10.1016/j.biomaterials.2026.124139
40. Liu H, Dong T, Dong C, et al. Plant-derived exosome-like nanovesicles: a novel therapeutic perspective for skin diseases. *J Nanobiotechnol*. 2025;23(1):640. doi:10.1186/s12951-025-03715-1
41. Alam M, Rizwanullah M, Ahmad S, et al. Co-delivery of tacrolimus and thymoquinone topically by nanostructured lipid carrier gel for enhanced efficacy against psoriasis. *AAPS Pharm Sci Tech*. 2025;26(4):90. doi:10.1208/s12249-025-03074-y
42. Ye K, He Y, Jian D, et al. Apoptotic neutrophil membrane-modified nanoparticles promote wound healing by enhancing efferocytotic capacity of dendritic cells. *J Control Release*. 2025;386:114127. doi:10.1016/j.jconrel.2025.114127
43. Lohakare NS, Bhamare VG, Chavan ND, Shelar SD, Mahajan HD, Amrutkar RD. Ethosome: an innovative perspective of drug delivery. *Pharm. Nanotechnol*. 2025;13(4):712–725. doi:10.2174/0122117385303596240513053014

44. Natsheh H, Touitou E. Phospholipid vesicles for dermal/transdermal and nasal administration of active molecules: the effect of surfactants and alcohols on the fluidity of their lipid bilayers and penetration enhancement properties. *Molecules*. 2020;25(13):2959. doi:10.3390/molecules25132959
45. Hameed H, Faheem S, Khan MA, Hameed A, Ereej N, Ihsan H. Ethosomes: a potential nanovesicular carrier to enhancing the drug delivery against skin barriers. *J. Microencapsul*. 2024;41(3):204–225. doi:10.1080/02652048.2024.2326085
46. Paiva-Santos AC, Silva AL, Guerra C, et al. Ethosomes as nanocarriers for the development of skin delivery formulations. *Pharm Res*. 2021;38(6):947–970. doi:10.1007/s11095-021-03053-5
47. Wu PS, Li YS, Kuo YC, Tsai SJ, Lin CC. Preparation and evaluation of novel transfersomes combined with the natural antioxidant resveratrol. *Molecules*. 2019;24(3):600. doi:10.3390/molecules24030600
48. El-Nabarawi MA, Shamma RN, Farouk F, Nasralla SM. Dapsone-loaded invasomes as a potential treatment of acne: preparation, characterization, and in vivo skin deposition Assay. *AAPS Pharm Sci Tech*. 2018;19(5):2174–2184. doi:10.1208/s12249-018-1025-0
49. Viegas C, Patrício AB, Prata JM, Nadhman A, Chintamaneni PK, Fonte P. Solid lipid nanoparticles vs. nanostructured lipid carriers: a comparative review. *Pharmaceutics*. 2023;15(6):1593. doi:10.3390/pharmaceutics15061593
50. Garcês A, Amaral MH, Sousa Lobo JM, Silva AC. Formulations based on solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) for cutaneous use: a review. *Eur. J. Pharm. Sci*. 2018;112:159–167. doi:10.1016/j.ejps.2017.11.023
51. Ogawa-Fuse C, Morisaki N, Shima K, et al. Impact of water exposure on skin barrier permeability and ultrastructure. *Contact Dermatitis*. 2019;80(4):228–233. doi:10.1111/cod.13174
52. Javed S, Mangla B, Almoshari Y, Sultan MH, Ahsan W. Nanostructured lipid carrier system: a compendium of their formulation development approaches, optimization strategies by quality by design, and recent applications in drug delivery. *Nanotechnol Rev*. 2022;11(1):1744–1777. doi:10.1515/ntrev-2022-0109
53. Hatem S, El-Kayal M. Novel anti-psoriatic nanostructured lipid carriers for the cutaneous delivery of luteolin: a comprehensive in-vitro and in-vivo evaluation. *Eur. J. Pharm. Sci*. 2023;191:106612. doi:10.1016/j.ejps.2023.106612
54. Agrawal YO, Mahajan UB, Mahajan HS, Ojha S. Methotrexate-loaded nanostructured lipid carrier gel alleviates imiquimod-induced psoriasis by moderating inflammation: formulation, optimization, characterization, in-vitro and in-vivo studies. *Int J Nanomed*. 2020;15:4763–4778. doi:10.2147/IJN.S247007
55. Almeida C, Roque R, Vieira J, et al. Lipid extract from Black Soldier Fly larvae: a high value excipient for solid lipid nanoparticles tailored to tackle atopic dermatitis. *Int J Pharm*. 2024;667(Pt B):124929. doi:10.1016/j.ijpharm.2024.124929
56. Das M, Parhi R. Nanocarriers and their integrated microneedle systems-mediated drug delivery for the treatment of moderate-severe dermatological diseases: recent progress, applications and future perspectives. *J Drug Delivery Sci Technol*. 2025;106:106748.
57. Braz Gomes K, D'Souza B, Vijayanand S, Menon I, D'Souza MJ. A dual-delivery platform for vaccination using antigen-loaded nanoparticles in dissolving microneedles. *Int J Pharm*. 2022;613:121393. doi:10.1016/j.ijpharm.2021.121393
58. Wang Y, Rong F, Sun X, et al. Microneedle-mediated transdermal H2S gas therapy for psoriasis. *Polym Chem*. 2025;16(18):2117–2127. doi:10.1039/D4PY01431F
59. Zhao Z, Wang H, Yao L, et al. Efficient local delivery of FK506 using blocking patches in psoriasis. *J Colloid Interface Sci*. 2023;630(Pt A):676–687. doi:10.1016/j.jcis.2022.09.146
60. Xue X, Zhang P, Cao Y, et al. Costunolide nanosuspension loaded in dissolvable microneedle arrays for atopic dermatitis treatment. *Int J Pharm*. 2025;675:125566. doi:10.1016/j.ijpharm.2025.125566
61. Upadhyay PR, Seminario-Vidal L, Abe B, Ghobadi C, Sims JT. Cytokines and epidermal lipid abnormalities in atopic dermatitis: a systematic review. *Cells*. 2023;12(24):2793. doi:10.3390/cells12242793
62. Lugović-Mihić L, Novak-Bilić G, Vučić M, Japundžić I, Bukvić I. CD44 expression in human skin: high expression in irritant and allergic contact dermatitis and moderate expression in psoriasis lesions in comparison with healthy controls. *Contact Dermatitis*. 2020;82(5):297–306. doi:10.1111/cod.13463
63. Zhang P, Tang J, Cheng L, et al. Hyaluronic acid modified liposomes with enhanced transdermal delivery of methotrexate for psoriasis treatment. *Colloids Surf. B*. 2025;247:114457. doi:10.1016/j.colsurfb.2024.114457
64. Li Y, Yang Y, Shao Y, et al. Chitosan functionalized graphene oxide nanocomposites for fluorescence imaging of apoptotic processes and targeted anti-inflammation study. *Carbohydr. Polym*. 2021;269:118345. doi:10.1016/j.carbpol.2021.118345
65. Behr NJ, Pierre S, Ickelsheimer T, et al. High content imaging shows distinct macrophage and dendritic cell phenotypes for psoriasis and atopic dermatitis. *Sci Rep*. 2025;15(1):18904. doi:10.1038/s41598-025-99727-w
66. Zabihi F, Cherri M, Guo X, et al. Topical delivery of tofacitinib in dermatology: the promise of a novel therapeutic class using biodegradable dendritic polyglycerol sulfates. *Pharmaceuticals*. 2024;17(1):77. doi:10.3390/ph17010077
67. Abid F, Savaliya B, Parikh A, et al. Nanotechnology and narasin: a powerful combination against acne. *Nanoscale*. 2023;15(33):13728–13739. doi:10.1039/D3NR01789C
68. Du S, Fu X, Luo X, et al. Frozen-microneedles with novel cerium dioxide nanocomposites for effective relief of irritant contact dermatitis. *Colloids Surf. B*. 2025;256(Pt 2):115044. doi:10.1016/j.colsurfb.2025.115044
69. Mu J, Ding X, Song Y, et al. ROS-Responsive Microneedle Patches Enable Peri-Lacrimal Gland Therapeutic Administration for Long-Acting Therapy of Sjögren's Syndrome-Related Dry Eye. *Adv. Sci*. 2025;12(16):e2409562. doi:10.1002/advs.202409562
70. Qin J, Zhu Y, Zheng D, Zhao Q. pH-sensitive polymeric nanocarriers for antitumor biotherapeutic molecules targeting delivery. *Bio-Des Manuf*. 2021;4(3):612–626. doi:10.1007/s42242-020-00105-4
71. Tang X, Liu Y, Yuan H, Gao R. Development of a self-assembled hydrogels based on carboxymethyl chitosan and oxidized hyaluronic acid containing tanshinone extract nanocrystals for enhanced dissolution and acne treatment. *Pharmaceuticals*. 2022;15(12):1534. doi:10.3390/ph15121534
72. Yu H, Liu Y, Zheng F, Chen W, Wei K. Erianin-loaded photo-responsive dendrimer mesoporous silica nanoparticles: exploration of a psoriasis treatment method. *Molecules*. 2022;27(19):6328. doi:10.3390/molecules27196328
73. Zhu B, Zou K, Huang Y, et al. Injectable and self-healing photothermal hydrogel with pH/photothermal dual-responsive mesoporous polydopamine for synergistic melanoma therapy. *Int J Biol Macromol*. 2026;335(Pt 1):149336. doi:10.1016/j.ijbiomac.2025.149336

74. Langellotto MD, Rassu G, Serri C, Demartis S, Giunchedi P, Gavini E. Plant-derived extracellular vesicles: a synergetic combination of a drug delivery system and a source of natural bioactive compounds. *Drug Delivery Transl Res*. 2025;15(3):831–845. doi:10.1007/s13346-024-01698-4
75. Kim YS, Go G, Yun CW, et al. Topical Administration of Melatonin-Loaded Extracellular Vesicle-Mimetic Nanovesicles Improves 2,4-Dinitrofluorobenzene-Induced Atopic Dermatitis. *Biomolecules*. 2021;11(10):1450. doi:10.3390/biom11101450
76. Tran PHL, Wang T, Yin W, et al. Development of a nanoamorphous exosomal delivery system as an effective biological platform for improved encapsulation of hydrophobic drugs. *Int J Pharm*. 2019;566:697–707. doi:10.1016/j.ijpharm.2019.06.028
77. Kayali I, Suhery T, Friberg SE, Simion FA, Rhein LD. Lyotropic liquid crystals and the structural lipids of the stratum corneum. *J Pharmaceut Sci*. 1991;80(5):428–431. doi:10.1002/jps.2600800506
78. Vitek M, Medoš Ž, Lavrič Z, et al. Highly biocompatible lamellar liquid crystals based on hempseed or flaxseed oil with incorporated betamethasone dipropionate: a bioinspired multi-target dermal drug delivery system for atopic dermatitis treatment. *Int J Nanomed*. 2024;19:13687–13715. doi:10.2147/IJN.S488684
79. Vitek M, Matjaž MG. Clinical application of hempseed or flaxseed oil-based lyotropic liquid crystals: evaluation of their impact on skin barrier function. *Acta Pharm*. 2024;74(2):301–313. doi:10.2478/acph-2024-0014
80. Zeng M, Deng P, Yang Q, et al. Machine learning-guided composite ionic liquid-based system for dual-drug delivery targeting redox homeostasis and STAT3-PI3K axis in psoriasis therapy. *Bioact. Mater.* 2026;58:107–122. doi:10.1016/j.bioactmat.2025.11.034
81. Park J, Kim J, Fakhraei Lahiji S, Kim YH. Dual-phase antibacterial and anti-inflammatory self-locking microarray patches for the effective treatment of acne vulgaris. *ACS Appl. Mater. Interfaces*. 2025;17(32):45438–45447. doi:10.1021/acsami.5c07718
82. Ramez SA, Soliman MM, Fadel M, et al. Novel methotrexate soft nanocarrier/fractional erbium YAG laser combination for clinical treatment of plaque psoriasis. *Artif. Cells Nanomed. Biotechnol*. 2018;46(sup1):996–1002. doi:10.1080/21691401.2018.1440236
83. Jin Y, Liu Y, Wang Y, et al. Preparation of curcumin nanocomposite drug delivery system and its therapeutic efficacy on skin injury. *Gels*. 2025;11 (9):727. doi:10.3390/gels11090727
84. Choi JK, Park JY, Lee S, et al. Greater plasma protein adsorption on mesoporous silica nanoparticles aggravates atopic dermatitis. *Int J Nanomed*. 2022;17:4599–4617. doi:10.2147/IJN.S383324
85. Guo R, Zhang Z, Zhang S, et al. Innovative nanocarriers: synthetic and biomimetic strategies for enhanced drug delivery. *Mater Today Bio*. 2025;34:102180. doi:10.1016/j.mtbio.2025.102180
86. Miao Y, Wang K, Liu X, et al. Multifunctional biomimetic liposomal nucleic acid scavengers inhibit the growth and metastasis of breast cancer. *Biomater. Sci*. 2025;13(9):2475–2488. doi:10.1039/D4BM01721H
87. Zhang M, Qin X, Gao Y, et al. Transcutaneous Immunotherapy for RNAi: a Cascade-Responsive Decomposable Nanocomplex Based on Polyphenol-Mediated Framework Nucleic Acid in Psoriasis. *Adv Sci*. 2023;10(33):e2303706. doi:10.1002/advs.202303706
88. Zeng A, Liu Y, Wang P, Cao Y, Guo W. Using siRNA-Based Anti-Inflammatory Lipid Nanoparticles for Gene Regulation in Psoriasis. *Int J Nanomed*. 2025;20:4519–4533. doi:10.2147/IJN.S504639