Review

Nano Biomed Eng

Innovative Nanomedicine Approaches for Psoriasis: Advancements, Challenges, and Future Directions

Xiangzheng Li[1], Shaowen Liu[1], Yuan He[1,2]

[1] State Key Laboratory of Natural Medicines, School of Basic Medicine and Clinical Pharmacy, China Pharmaceutical University, Nanjing 210009, China

[2] Biological Research Center, Chongqing Innovation Institute, China Pharmaceutical University, Chongqing 401100, China

Corresponding author. E-mail: yuanhe0822@cpu.edu.cn

Received: May 19, 2025; **Revised:** Jun. 20, 2025; **Accepted:** Jun. 23, 2025

Citation: X.Z. Li, S.W. Liu, Y. He. Innovative nanomedicine approaches for psoriasis: advancements, challenges, and future directions. *Nano Biomedicine and Engineering*, 2025, 17(3): 333−345.

http://doi.org/10.26599/NBE.2025.9290132

Abstract

Psoriasis is an autoimmune disease marked by excessive keratinocyte proliferation and aberrant activation of immune cells, resulting in clinical manifestations such as erythema, pruritus, and skin scaling. Although current treatments such as biologics, immunosuppressants, and phototherapy have demonstrated certain therapeutic efficacy, their application remains constrained by systemic side effects, limited drug permeability, and reduced long-term tolerability. Furthermore, the high relapse rate and suboptimal patient compliance contribute to considerable physical and psychological burdens. In recent years, nanomedicines have emerged as a promising therapeutic strategy for psoriasis due to their unique physicochemical properties, including small size, high payload, controllable release, and targeted delivery. By selectively modulating key cellular components, cytokines, and signaling pathways involved in the pathogenesis of psoriasis, nanomedicines have shown potential to achieve targeted, synergistic, and sustained therapeutic effects that are often difficult to attain with conventional formulations. This review aims to summarize recent advances in nanomedicine-based therapies for psoriasis, focusing on diverse therapeutic targets, thereby offering novel perspectives and directions for future development in this field.

Keywords: psoriasis; nanomedicines; liposomes; polymeric and inorganic nanoparticles; biomimetic nanocarriers

Introduction

Psoriasis is an autoimmune skin disease characterized by abnormal keratinocyte proliferation and immune dysregulation. The hyperactivation of the interleukin-23(IL-23)/T helper(Th17) axis has been identified as a central pathogenic mechanism in psoriasis [1]. Current therapeutic strategies mainly include topical therapies (e.g., corticosteroids and vitamin D3 analogs), traditional systemic medications (e.g., methotrexate (MTX) and cyclosporine), and biologics targeting the tumor necrosis factor-α (TNF-α) or IL-17/IL-23 [2, 3]. Despite these therapeutic options, there are still many limitations, such as limited therapeutic efficacy. Traditional topical and systemic medications often exhibit suboptimal efficacy associated with considerable toxicity, while biologics are expensive and susceptible to the loss of secondary response due to immunogenicity [4–6]. Recently, nano-based drug delivery systems have emerged as

promising alternatives to overcome these limitations, such as enhanced drug stability, improved skin-targeting ability, reduced systemic toxicity, and the ability to achieve controlled and sustained release [7]. Currently, nanomedicine for psoriasis treatment encompasses various platforms, including liposomes, polymeric nanoparticles, inorganic nanomaterials, biomimetic nanocarriers, and microenvironment-responsive nanoformulations. These approaches primarily target key pathogenic mediators such as TNF-α, IL-23/IL-17A, antimicrobial peptide LL-37, reactive oxygen species (ROS), etc. This review provides a comprehensive overview of the main therapeutic targets in psoriasis and evaluates the potential applications of nanomedicines in enhancing therapeutic efficacy, minimizing adverse effects, and optimizing treatment strategies. It aims to offer new insights for future research and to highlight the potential of emerging nanomedicine technologies in advancing psoriasis therapy.

Major Therapeutic Targets of Psoriasis for Nanomedicines

Psoriasis is a T cell–mediated inflammatory disease that relies on the interaction between various components in the immune system, with dendritic cells (DCs) and keratinocytes playing crucial roles. The etiology and pathogenesis of psoriasis are multifactorial and complex. Both immunological and genetic studies have identified the IL-23/IL-17A axis as a pivotal pathway in the disease development [8]. Other critical pathways include antiviral signaling pathways, such as toll-like receptor (TLR)/nuclear factor kappa B (NF-κB), janus kinase (JAK)/signal transducer and activator of transcription (STAT), and cyclic GMP-AMP synthase (cGAS)/stimulator of interferon genes (STING) [9–12], along with the expression of pro-inflammatory cytokines (e.g., TNF-α, IL-23, IL-1β) and chemokines (e.g., C–X–C motif ligand 1 (CXCL1), CXCL8, and CXCL10).

External stimuli, such as ultraviolet radiation (UV) and bacterial infections, can cause skin injury, leading to the hyperproduction of keratinocyte-derived ROS and secretion of antimicrobial peptides, such as LL-37 [13, 14]. LL-37, in turn, activates keratinocytes via TLR8 signaling, thereby promoting ROS production and initiating inflammatory pathways, such as NF-κB [15]. LL-37 exerts anti-apoptotic effects, while ROS promotes proliferation, driving abnormal keratinocyte growth and psoriatic lesion formation [13]. Moreover, LL-37-DNA/RNA complexes activate plasmacytoid dendritic cells (pDCs), myeloid dendritic cells (mDCs), and neutrophils, triggering excessive release of inflammatory cytokines, such as interferon-α (IFN-α), TNF-α, and IL-23 [16]. These cytokines amplify local immune responses and exacerbate skin inflammation. Stressed keratinocytes also release chemokines such as CXCL1, CXCL2, and CXCL8, which promote neutrophil recruitment and infiltration, further contributing to disease progression. The IL-23/IL-17A axis serves as the core pathway and a key indicator assessing disease severity. IL-23, primarily secreted by activated mDCs, maintains the differentiation and phenotype of Th17 cells. IL-17A, mainly produced by Th17 cells, induces the production of IL-6 and CXCL8 by macrophages and DCs in the dermis, leading to the recruitment of other immune cells [17]. Moreover, IL-17A drives pathological keratinocyte proliferation [18], fueling further production of pro-inflammatory cytokines and chemokines that exacerbate local skin inflammation. Collectively, the interplay among keratinocytes, dendritic cells, and T cells orchestrates a self-amplifying inflammatory loop that drives psoriasis initiation and progression (Fig. 1).

The pathogenesis of psoriasis involves the complex interplay of multiple signaling pathways, including NF-κB, JAK/STAT, cGAS/STING, and phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt), etc. Elevated levels of phosphorylated NF-κB have been observed in psoriatic lesions, with the canonical pathway playing a significant role in disease development [19]. Notably, TLR4, an upstream regulator of NF-κB, can be activated by lipopolysaccharide from bacteria, thereby exacerbating the progression of psoriasis [12]. The JAK-STAT pathway, essential for intracellular cytokine signaling, is mediated by the JAK family (JAK1, JAK2, JAK3, and tyrosine kinase 2 (TYK2)) and regulates gene transcription through STAT proteins. JAK1 is linked to disease severity [20], and TYK2 deficiency reduces psoriatic features in mice, while TYK2 polymorphisms increase susceptibility [21]. Several JAK inhibitors, including tofacitinib, baricitinib, ruxolitinib, and the selective TYK2 inhibitor deucravacitinib, are approved or offer novel therapeutic options for psoriasis [22, 23]. Within the psoriasis microenvironment, TNF-induced

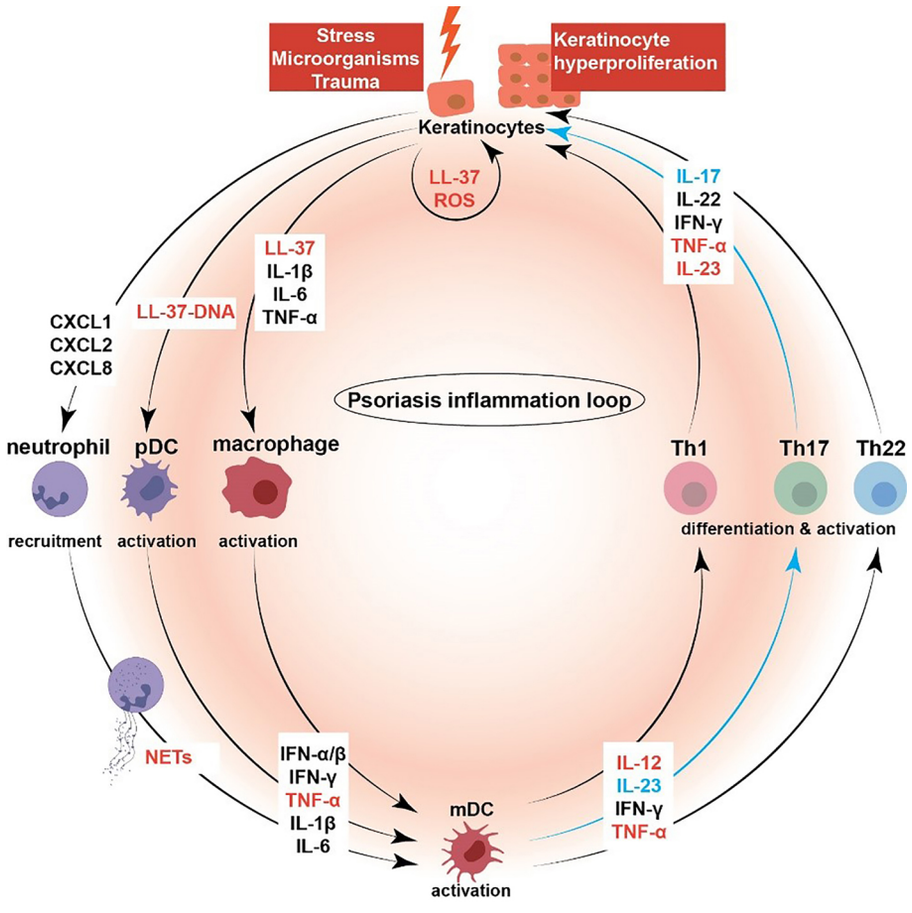

Fig. 1 The pathogenesis of psoriasis. **Initial Triggers:** The cycle begins with external stressors such as stress, microorganisms, and trauma, which activate keratinocytes. **Keratinocyte:** Activated keratinocytes release a variety of cytokines and chemokines, including LL-37, IL-1β, IL-6, TNF-α, CXCL1, CXCL2, and CXCL8. These mediators contribute to the recruitment and activation of immune cells within the skin. **Neutrophils:** Attracted by CXCL1, CXCL2, and CXCL8, neutrophils contribute to the formation of neutrophil extracellular traps (NETs). **pDC:** These cells can be activated by the LL-37-DNA complex and release the interferon cytokines. **Macrophages:** These cells are activated by LL-37, IL-1β, IL-6, and TNF-α, further amplifying the inflammatory response. **mDC:** These cells produce IL-12, IL-23, IFN-γ, and TNF-α, which are crucial for T cell activation. **Th1 Cells:** Activated by IL-12, these cells produce IFN-γ, which contributes to the inflammatory response. **Th17 Cells:** Stimulated by IL-23, these cells produce IL-17A, IL-22, and TNF-α. **Th22 Cells:** These cells are involved in the production of IL-22. In the figure, the color red is used to highlight the research targets of existing nanomedicines. The color blue indicates the core pathways involved in psoriasis.

mitochondrial DNA (mtDNA) activates the cGAS-STING pathway, promoting type I interferon responses [11]. The STING antagonist H-151 alleviates inflammation in imiquimod-induced psoriasis-like models by suppressing IL-17A, IL-23, and IL-6 production, and by reducing M1 macrophage infiltration and Th17 differentiation [10]. The PI3K/Akt pathway contributes to epidermal hyperplasia and immune activation [24]. Akt activation stimulates keratinocyte proliferation by modulating forkhead box O (FOXO) and mTOR signaling, while its negative regulator, PTEN, is downregulated in psoriatic skin [25]. Rapamycin, a mechanistic target of rapamycin complex 1 (mTORC1) inhibitor, has demonstrated therapeutic potential [26]. Together, these pathways orchestrate inflammatory responses and abnormal keratinocyte activity, driving psoriasis pathogenesis. Targeting these signaling pathways and cytokines offers therapeutic strategies for managing the disease (Fig. 2).

Versatile Types of Nanoformulation-based Nanomedicines for Psoriasis Treatment

Nanocarriers loaded with hemotherapeutic or bioactive agents have introduced promising strategies for psoriasis treatment. These nanoformulations, such as liposomes, polymeric nanoparticles, inorganic nanomaterials, biomimetic nanocarriers and

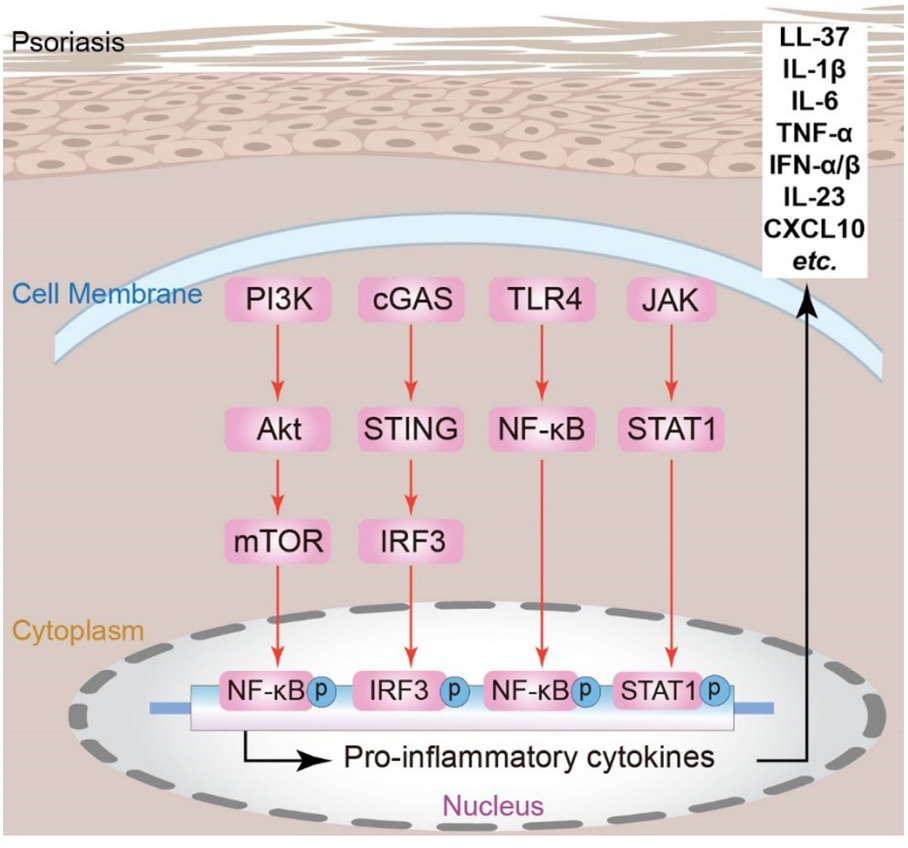

Fig. 2 Intracellular signaling pathways related to psoriasis. In psoriasis, multiple intracellular signaling pathways are activated, including NF-κB, JAK/STAT, cGAS/STING, and PI3K/Akt. The activation of these pathways leads to the phosphorylation of transcription factors like NF-κB, interferon regulatory factor 3 (IRF3), and STAT1, which then translocate to the nucleus to promote the transcription of pro-inflammatory cytokines. This intricate network of signaling pathways drives the inflammatory responses and abnormal keratinocyte activity characteristic of psoriasis.

microenvironment-responsive nanoformulations, offer advantages including low systemic toxicity, enhanced targeting precision, and improved drug stability [27]. However, each nanomaterial exhibits distinct benefits and limitations in psoriasis therapy, as shown in Table 1.

Liposome

Psoriasis, an autoimmune disorder, presents substantial drug delivery challenges. The stratum corneum, as the outermost layer, effectively blocks the invasion of exogenous substances, while tight junctions composed of transmembrane and cytoskeletal proteins serve as a secondary barrier, further hindering drug penetration [33]. In psoriatic lesions, aberrant differentiation and hyperproliferation of keratinocytes further restrict drug permeation [34]. Liposomes, as biocompatible lipid-based nanocarriers, have shown promise in overcoming these barriers owing to their ability to encapsulate poorly soluble drugs and their structural similarity to skin lipids, which facilitates transdermal delivery [35]. For example, Ma et al. developed dendritic lipopeptide liposomes (DLPs) aimed at

Table 1 The characters of various nanomaterials.

Nanocarrier types	Characters	Examples
Liposome	Biocompatible, enhanced drug penetration, load drugs of low solubility	Dendritic lipopeptide [28]
Polymeric	Biocompatible, biodegradable, low toxicity, sustained release, enhanced drug accumulation	PLGA-tipped microneedles [29]
Inorganic	Biodegradable, multiple function (e.g., thermal sensitive, biomimetic enzyme activity)	Thermosensitive hydrogels loaded with Au nanorods [30]
Membrane-camouflaged nanoformulation	Biocompatible, low systemic toxicity, immune evasion, homologous-targeting, enhanced drug penetration	Keratinocyte membrane camouflaged pH-sensitive micelle [31]
Responsive nanoformulation	Low systemic toxicity, stimuli-responsive drug release	H_2O_2 and GSH-sensitive nanocarrier [32]

facilitating the transdermal delivery of small interfering RNA (siRNA), which significantly suppresses STAT3 expression [28]. In this research, the precisely designed novel liposome was composed of a dendritic peptide containing lysine or arginine as the hydrophilic head, with the hydrophobic tail constituted of 1, 2-stearoyl-sn-glycerol-3-phosphoethanolamine (DSPE) or oleylamine (OA) derived lipid chains. This dendritic peptide effectively enhances the drug transdermal efficacy, while the lipid chains confer this nanostructure elevated lipophilicity. Finally, the siRNA was released from the core upon penetrating the skin barrier and achieved precise STAT3 knockdown effect. However, whether the long-term administration triggers immune tolerance, skin structure and function disruption remain unclear. Su et al. engineered a glycyrrhizic acid (GA)-based lipid nanocarrier, with chlorin e6 (Ce6) encapsulated in the nanovesicle, by replacing the conventional liposome component of cholesterol with GA. Simultaneously, the catechol-modified quaternary chitosan salt (QCS-C) was coated on the surface of the GA-based nanoparticles to provide sufficient bio-adhesion [36]. Upon laser irradiation, Ce6 generates substantial ROS to trigger the apoptosis of hyperproliferative T cells and keratinocytes in psoriasis, while GA suppresses the inflammation cascade, achieving synergistic therapeutic effects. Despite these advancements, conventional liposomes still face limitations such as low drug-loading capacity, instability, and short systemic circulation. Smart liposome designs hold great potential to address these issues and improve psoriasis treatment outcomes [37].

Liposomes have garnered great attention in recent years due to their potent transdermal drug delivery capacity. This nanocarrier significantly promotes the drug penetration by overcoming the thickened skin barrier and enhances the drug accumulation in the psoriatic skin.

Polymer-based drug delivery

Polymeric nanoparticles are composed of natural (chitosan, alginate, guar gum, etc.) or synthetic polymers, ranging in size from 1 to 1 000 nm and can encapsulate active drugs within their core or on the surface [38]. A litany of natural polymers, such as chitosan, is particularly noted for their biodegradability, biocompatibility, and anti-inflammatory properties [39–41]. Salma et al. designed tacrolimus-loaded chitosan nanoparticles to treat psoriasis and garnered favorable outcomes by enhancing drug accumulation and penetration [42]. Besides, chitosan is typically positively charged, therefore, Liu et al. designed a cell-free DNA (cfDNA)-scavenging strategy-based nanocarrier and utilized biguanide to modify the chitosan, acquiring a catanionic polymer with powerful DNA-binding capacity [43]. Additionally, chitosan has shown potential in promoting hair growth, reinforcing its use in skin-related therapies [44]. Synthetic polymers, particularly poly (lactic-co-glycolic acid) (PLGA), are favored in nanocarrier design due to their superior property of sustained drug release. To address the severe toxicity of MTX in the treatment of psoriasis and limitations of frequent microneedle administration, Moawad et al. developed a phloretin-loaded sustained-release microneedle system [29]. The tips are fabricated by PLGA, and a small amount of polylactic acid (PLA) is added to ensure sufficient mechanical strength. The main body of the microneedle is composed of hyaluronic acid, which dissolves rapidly and then releases the drug-loaded tip. Liu et al. further advanced treatment by designing a PLGA-based nanoplatform targeting impaired macrophages and activated platelets, using macrophage membranes and targeting peptides to modify the nanoplatform, thereby restoring immune function and efferocytosis, which also demonstrated favorable outcomes [45].

Polymer-based nanoformulations show promise for psoriasis treatment due to their material versatility and biodegradability. However, key challenges remain, including penetration barriers posed by psoriatic hyperkeratosis and potential acute toxicity from the burst release of PLGA nanoparticles [46, 47].

Multi-pattern immunomodulation of inorganic-scaffold nanoformulation

Inorganic nanoformulations are typically composed of inorganic materials, such as silica, metal, metal oxide, etc., and have gained considerable attention in biomedical applications. Among these, gold nanoparticles are among the most widely used inorganic materials in the biomedical area, owing to their high biocompatibility, low systemic toxicity, and modifiable properties [48, 49]. These nanoparticles are also endowed with multiple enzyme catalytic activities, enabling them to scavenge ROS,

which robustly contribute to the progression of psoriasis [50, 51]. Chen et al. developed a thermosensitive hydrogel incorporating gold nanorods (GNRs) and MTX. Upon infrared radiation, the GNRs produce heat to trigger the phase transition of the hydrogel, enabling the controlled release of MTX. Additionally, the photothermal effect of GNRs promotes keratinocyte apoptosis [30]. Functionalized gold nanoparticles, such as those modified with azelamide monoethanolamine, significantly enhance skin penetration and anti-inflammatory effects compared to traditional gold nanoparticles by increasing the expression of superoxide dismutase (SOD) and inhibiting matrix metalloproteinase 9 (MMP-9) activity [52]. Similar to gold nanoparticles, platinum (Pt) nanoparticles also exhibited potent catalytic activity, effectively impairing the ROS-triggered inflammatory cascade [53], in the skin microenvironment, such as platinum-doped positively charged carbon dots (Pt-CDs) [54]. The presence of Pt confers this nanoparticle-enhanced DNA-binding capacity by elevating its electropositivity, thus remarkably suppressing the cGAS-STING pathway. Afterwards, the secretion of multiple inflammatory cytokines was inhibited, such as IFN-γ and TNF-α.

Beyond gold nanoparticles, various metal-based nanomedicines have shown promise in psoriasis therapy by reducing systemic toxicity while enhancing therapeutic efficacy. Ag nanoparticle-anchored ZnO nanoparticles (ZnO/Ag), which possess self-therapeutic properties, have been shown to treat psoriasis by suppressing multiple pro-inflammatory cytokines in macrophages and keratinocytes [55]. Lu et al. engineered iron single-atom catalysts to mimic the active sites of antioxidant enzymes, such as catalase and SOD, thus scavenging accumulated ROS and suppressing pro-inflammatory cytokines (IL-17A, TNF-α, IL-12, and IL-23) [56]. These inorganic nanoparticles are safe, promising, and highly efficient methods to treat psoriasis and could be considered as long-term treatment options to prevent recurrence.

Mesoporous silica nanoparticles (MSNs) are another inorganic nanoformulations that have also been demonstrated as successful nanocarriers, ascribing to their superior drug-loading and sustained release capacity [57]. In addition, MSNs could be modified to achieve mechanism-specific treatment for psoriasis. For example, poly (2-(dimethylamino) ethyl methacrylate) (PDMA) grafted hairy silica particles (cSPs) elicited remarkable psoriasis amelioration by eliminating the dermal cfDNA [58].

Inorganic nanoformulations demonstrate exceptional tunability and synergistic potential with physical therapies (e.g., photothermal therapy and enzyme-mimicking catalysis). Their dual capacity to scavenge ROS and disrupt inflammatory cascades positions them as promising candidates for psoriasis intervention.

Biomimetic membrane-camouflaged nanoformulation

Membrane-camouflaged nanocarriers have emerged as novel therapies for multiple diseases, such as skin diseases and cancer [59, 60], due to their superior homologous targeting efficacy and low toxicity. Yang et al. utilized melanoma-derived exosomes as templates by retaining the critical outer membrane protein Ras homolog family member A (RhoA), which plays a crucial role in transdermal drug delivery. Then they engineered exosome-liposome hybrid nanoparticles to enhance biocompatibility and membrane fluidity. Finally, this nanoplatform was loaded with miR-320-3p to suppress Th17-mediated IL-17 signaling pathway [61]. Simultaneously, no significant systemic toxicity was observed, exhibiting superior biocompatibility and safety. Huang et al. developed a hybrid vesicle system through the fusion of grapefruit-derived exosome-like nanovesicles (GEVs) with CC chemokine receptor 6 $(CCR6)^+$ nanovesicles derived from membranes of engineered gingiva-derived mesenchymal stem cells (GMSCs) [62]. Specifically, CX5461-loaded GEVs leverage CCR6-mediated targeting of GMSCs to precisely deliver immunosuppressive therapy to inflamed sites, effectively alleviating psoriatic lesions. Additionally, keratinocyte membrane-coated nanoparticles enable selective keratinocyte targeting, while microneedle integration facilitates sustained epidermal drug delivery, collectively enhancing therapeutic efficacy against psoriasis progression [31]. The application of membrane-camouflaged technology allows the biomimetic nanoparticles to evade immune recognition and specifically target the immune cells to relieve the inflammation [63]. Therefore, biomimetic nanoparticles may serve as a safety and precisely targeted strategy for psoriasis, with excellent therapeutic efficacy, in the future.

The membrane-camouflaged nanoformulations are characterized by their superior homologous-targeting effect, allowing the precise therapy targeting the diseased cells and inflammation amelioration, while avoiding systemic toxicity.

Microenvironment-responsive drug release

Psoriasis is an inflammatory disorder characterized by elevated levels of ROS and a relatively low pH within the skin microenvironment. These changes are partly attributed to the overproduction of fatty acids and an imbalance between the antioxidant system and increased ROS production [64, 65]. In this respect, boronic esters are ROS-sensitive materials that have already exhibited great promise, due to their high biocompatibility and biosafety [66]. This nanomaterial has been incorporated into ROS-reactive nanocarriers for psoriasis treatment. For instance, a novel microneedle patch was engineered by encapsulating MTX and epigallocatechin gallate (EGCG) within a cross-linked hydrogel via dynamic covalent boronic ester bonds [67]. In the presence of H_2O_2, the hydrogel gradually degrades, releasing MTX and EGCG, which inhibit the hyperproliferation of keratinocytes and improve the inflammatory microenvironment. In another approach, Xin et al. proposed a multifunctional nanoplatform where the MTX-thioketal-lysine (MTX-TK-lys) complexes were assembled with siRNA targeting TNF-α in the core, while poly (ethylene glycol)-polyhistidine (mPEG-pHis) and polyethylene glycol-polylactic acid (mPEG-PLA) were strategically coated on the surface. This design enabled the oxidative stress-triggered, sequential release of MTX and siRNA, aiming to restore immune homeostasis. Additionally, the nanoplatform absorbed elevated levels of LL-37, S100 calcium-binding protein A8 (S100A8), and S100 calcium-binding protein A9 (S100A9), which are detrimental to psoriasis patients [68]. Tan et al. designed a dual-responsive nanocarrier of H_2O_2 and glutathione (GSH) to deliver CRISPR Cas9 and cytosolic protein for the psoriasis treatment [32]. This nanoparticle was fabricated on polyamidoamine dendrimer scaffold, which was functionalized with 4-nitrophenyl 4-benzyl carbonate (NBC) and lipoic acid (LA) moieties. The phenylboronate moiety facilitates H_2O_2-dependent protein delivery, while the LA linker undergoes GSH-mediated reductive cleavage to achieve controlled drug liberation. This dual-stimuli-actuated delivery paradigm demonstrated enhanced bioavailability as well as mitigated off-target cytotoxicity. Li et al. utilized zeolitic imidazolate framework-9 (ZIF-9), which could be gradually degraded in the acidic microenvironment, as the scaffold to encapsulate adenosine monophosphate (AMP) and biomineralize the AMP catabolic enzyme on the outer layer [69]. After degradation, the released drugs effectively ameliorate psoriasis, including suppressing DCs, supporting regulatory T cells (Tregs), and inhibiting the secretion of pro-inflammatory cytokines, such as TNF-α, IL-17A, IL-23, IL-6, etc.

These nanoformulations achieve precise drug delivery targeting the inflammatory microenvironment. Their microenvironment-responsive design enables real-time detection of pathological changes, offering potential for preventing disease recurrence.

Several studies have shed light on the clinical transformation of the nanoformulations in the treatment of psoriasis. For example, a random clinical trial has demonstrated that the cyclosporine liposomes significantly reduced the dermatological scores by approximately 83%, by the eighth week, in compared to the cyclosporine ointment [70]. Curcumin nanoparticles could serve as an adjuvant therapy to improve the serum lipid levels in patients with moderate-to-severe psoriasis treated with oral acitretin [71], thereby helping to mitigate psoriasis progression. A fluidized spanlastic nanovesicle encapsulating tazarotene acquired promising outcomes in patients with psoriasis [72]. However, most studies have remained in the pre-clinical investigation, necessitating further clinical evaluation of these nano-based formulations.

The development of innovative nanoformulations offers a promising approach to achieve superior drug delivery and restore immune homeostasis. These innovative nanocarriers overcome the limitations of conventional formulations by achieving stimuli-triggered sustained release with spatiotemporal precision. Furthermore, the smart design of customized nanoplatforms enables disease-directed therapeutic strategies, where combinational approaches integrating immunomodulation, oxidative stress regulation, and targeted drug delivery, synergistically achieve highly efficient management of psoriasis (Fig. 3).

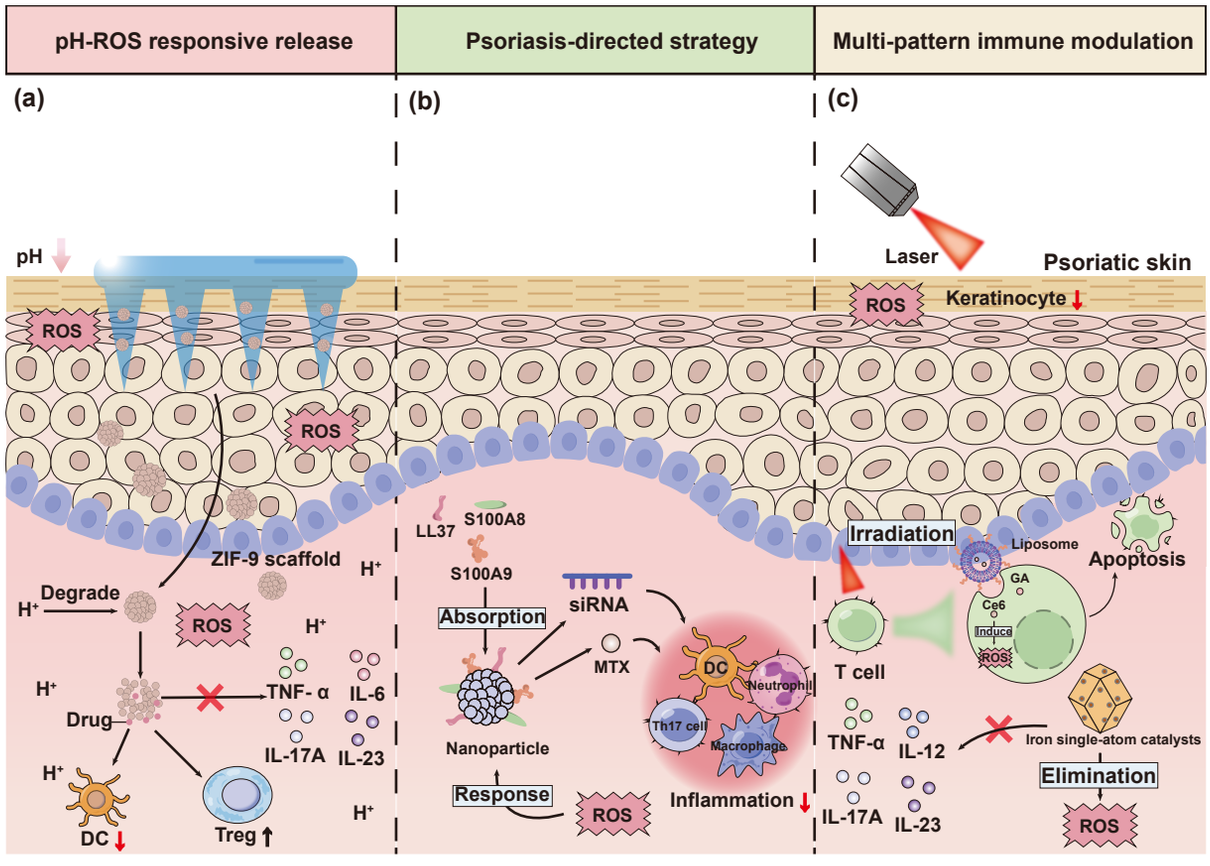

Fig. 3 The immune modulation of nanomedicine for psoriasis treatment. **(a)** the psoriatic skin is characterized by low pH and high ROS. Hydrogel microneedles promote the transdermal delivery of ZIF-9-scaffold nanoparticles, which were degraded by the acidic microenvironment, releasing anti-inflammatory drugs to suppress DC proliferation, enhance Treg-mediated immunosuppression and downregulate multiple inflammatory cytokines, such as TNF-α, IL-6, IL-17A, and IL-23. **(b)** nanoparticles that are capable of eliminating disease-specific proteins highly expressed in psoriasis, such as LL37, S100A8, S100A9, and releasing siRNA and MTX in a ROS-dependent manner, which subsequently inhibit the inflammation cascade. **(c)** liposomes precisely deliver photosensitizer, Ce6, into T cells to promote T cell apoptosis by producing substantial ROS upon laser irradiation, as well as inhibiting keratinocytes hyperproliferation, synergizing with GA to collectively mitigate psoriasis progression. Iron single-atom catalysts with biomimetic enzyme activity significantly scavenge ROS and suppress multiple pro-inflammatory cytokines, such as TNF-α, IL-12, IL-17A, and IL-23, in the skin microenvironment.

Other Potential Therapeutic Targets of Psoriasis for Nanomedicines

Targeting the JAK/STAT pathway is a novel therapeutic strategy for psoriasis. JAK inhibitors, such as tofacitinib and upadacitinib, have demonstrated efficacy and safety in treating psoriasis and other autoimmune diseases, though the development of nanotherapeutics for these inhibitors remains limited. Future research should focus on reducing adverse effects such as immune suppression and infection risk. Recently, the use of siRNA-based nanomedicine to silence STAT3 is a promising gene therapy, though still experimental [73]. So far, there are no clinical trial reports for using siRNA to treat psoriasis. The main challenge is the deficiency of effective transdermal delivery of siRNA, with ongoing research exploring methods like electroporation, ultrasound, cell-penetrating peptides, and nanocarriers. As previously mentioned, rapamycin holds potential for psoriasis treatment by inhibiting the PI3K/Akt signaling pathway. Recent studies have shown that rapamycin encapsulated in lipid-polymer conjugate hybrid nanoparticles (RPMN) and incorporated into a carbopol-based hydrogel system (RPMNGel) can be used to treat psoriasis [74]. In a mouse model of imiquimod-induced psoriasis, RPMNGel exhibited superior drug accumulation, deeper penetration, and slower diffusion compared to the free drug gel, proving excellent efficacy in psoriasis treatment [74].

Targeting chemokine receptors, rather than chemokines themselves, offers a more precise

therapeutic approach by directly modulating receptor-expressing cells and minimizing off-target effects. One notable example involves the use of cationic lipid-assisted polymeric nanoparticles (CLAN) to deliver a plasmid co-expressing CXCL9 and α-programmed death-ligand 1 (αPD-L1) under tumor-specific promoters. This strategy enhances T-cell recruitment and activation within the tumor microenvironment, leading to improved antitumor immune responses [75]. Another promising approach utilizes a chemically synthesized C–X–C receptor 4 (CXCR4) antagonist peptide, E5, encapsulated within polyethylene glycol–glycol-phosphatidyl-ethanolamine (PEG-PE) micelles (M-E5). This formulation effectively targets CXCR4 on acute myeloid leukemia (AML) cells, disrupting the CXCL12/CXCR4 axis, inhibiting chemoresistance, and enhancing the efficacy of chemotherapeutic agents [76]. These findings highlight the therapeutic potential of receptor-targeted nanomedicines in modulating chemokine signaling pathways, offering valuable insights for psoriasis treatment.

In the treatment of psoriasis, the translation of nanomedicines faces multiple scientific challenges. The activated immune system under inflammatory conditions can accelerate the phagocytic clearance of nanoparticles through the aggregation of immune cells such as macrophages [77], and if nanomaterials have insufficient biodegradability, they are prone to accumulate in inflammatory-related organs (e.g., liver, kidney) or normal tissues, leading to toxicity. Some nanomaterials (e.g., metal oxide nanoparticles) may also stimulate immune cells (e.g., macrophages, neutrophils) in inflammatory sites, inducing cytokine storms and exacerbating inflammatory responses [78]. For chronic inflammatory diseases requiring long-term administration, the long-term metabolic pathways of nanomaterials and potential accumulation toxicity (e.g., oxidative stress, tissue fibrosis) lack standardized evaluation methods [79]. Furthermore, psoriasis-like animal models fail to fully mimic the pathological complexity of human diseases in terms of immune cell subtypes and tissue microenvironment, leading to the failure of preclinical data extrapolation. Additionally, the lack of standardized detection methods for dynamic biomarkers of inflammatory diseases (e.g., serum inflammatory factors, histopathological scores) makes it difficult to accurately evaluate the targeting efficiency and pharmacodynamics of nanomedicines.

Conclusions

Nanomedicine holds significant promise for psoriasis therapy by improving drug bioavailability, targeting precision, and therapeutic safety. While the TNF-α/IL-23/IL-17 axis remains the primary therapeutic focus, emerging targets including cGAS-STING, JAK-STAT, PI3K-Akt signaling, and chemokine networks offer additional intervention points. Current nanocarrier platforms, such as spanning liposomal, polymeric, inorganic, biomimetic membrane-coated, and stimuli-responsive systems, each present unique pharmacological advantages and development challenges for clinical translation.

Psoriasis, a chronic inflammatory skin condition, requires tailored nanocarriers that optimize drug delivery and oxidative stress modulation. In summary, liposomes exhibit high similarity to skin components, enabling them to promote transdermal drug absorption. Additionally, the unique vesicle structure allows them to encapsulate both lipophilic and hydrophilic drugs, protecting them from exogenous degradation and prolonging the drug circulation. However, there are still potential limitations behind the liposomes. The particle size of small liposomes makes it rather difficult to encapsulate sufficient drugs into the system and the instability of liposomes, such as the hydrolysis of ester bonds and peroxidation of unsaturated acyl chains, may lead to undesired drug leakage and aggregation [80]. The addition of cholesterol or polyethylene glycol (PEG) has been proven to enhance the stability and blood circulation of liposomes [81, 82]. Polymeric nanoparticles have attracted great attention in recent years due to their excellent biodegradability. Drugs could be encapsulated in the core or absorbed on the surface in the form of polymeric nanoparticles or nanocapsules [38]. Compared to liposomes, the hard structure and insufficient fluidity make it difficult for polymeric nanoparticles to penetrate the stratum corneum. However, polymeric nanoparticles are prone to accumulate in the hair follicle, thereby penetrating deep into the skin and forming a drug reservoir [83–85]. Therefore, polymeric nanoparticles may be beneficial to the follicular drug delivery in dermatological treatment. Besides, polymers exhibit superior biodegradability, representing an ideal material for controlled release of drugs. Inorganic

nanoparticles are characterized by small particle size, large specific surface area, and structural stability, but are resistant to degradation. Besides, inorganic nanoparticles have demonstrated the property of multifunctionality. For example, the inorganic nanoparticles could serve as the delivery vehicles for photosensitizers, eliminating the hyperproliferation of keratinocytes through the photothermal conversion [30]. Concurrently, the specific surface modification could confer them with enzymatic activity, scavenging ROS in the skin microenvironment [51]. However, the inorganic nanoparticles themselves or the released metal ions during degradation may induce immune dysregulation, necessitating further consideration for the application of these nanocarriers [86]. Finally, the membrane-camouflaged nanoformulation and microenvironment-responsive nanoformulation are based upon the above materials, the membrane coated on the surface, and the application of microenvironment-responsive material could enable the precise transportation of drugs, which enhances the therapeutic efficacy and minimizes the toxic effect.

Nano-based therapies have emerged as a transformative approach for psoriasis treatment, offering enhanced skin penetration, tunable physicochemical properties, and superior biocompatibility. While these attributes collectively address key therapeutic challenges, prudent nanomaterial selection requires careful benefit-risk assessment. Ongoing efforts to optimize these platforms for clinical translation hold significant promise for improving patient outcomes.

CRediT Author Statement

Xiangzheng Li: writing original draft, review, and editing. **Shaowen Liu**: writing–review and editing. **Yuan He**: supervision–oversight and leadership responsibility for the writing planning, and execution.

Acknowledgements

This review was supported by the Chongqing Science and Technology Development Foundation (CSTB 2024NSCQ- KJFZZDX0033).

Conflict of Interests

The authors declare no conflict of interest.

Ethical Approvals

There are no ethical concerns in this review.

References

[1] C.E.M. Griffiths, A.W. Armstrong, J.E. Gudjonsson, et al. *The Lancet*, 2021, 397(10281): 1301–1315. https://doi.org/10.1016/S0140-6736(20)32549-6

[2] A.W. Armstrong, C. Read. Pathophysiology, clinical presentation, and treatment of psoriasis: A review. *JAMA*, 2020, 323(19): 1945−1960. https://doi.org/10.1001/jama.2020.4006

[3] M. Lebwohl, P.T. Ting, J.M. Koo. Psoriasis treatment: Traditional therapy. *Annals of the Rheumatic Diseases*, 2005, 64(Suppl 2): ii83−ii86. https://doi.org/10.1136/ard.2004.030791

[4] M. Lebwohl. Combining the new biologic agents with our current psoriasis armamentarium. *Journal of the American Academy of Dermatology*, 2003, 49(2): 118−124. https://doi.org/10.1016/S0190-9622(03)01144-7

[5] T.L. Timis, I.A. Florian, D.R. Mitrea, et al. Mind-body interventions as alternative and complementary therapies for psoriasis: A systematic review of the English literature. *Medicina*, 2021, 57(5): 410. https://doi.org/10.3390/medicina57050410

[6] M. Kassir, L. Kircik, J. Weinberg, et al. Treatment of nail psoriasis. *Journal of Drugs in Dermatology*, 2022, 21(2): 146−150. https://doi.org/10.36849/jdd.4969

[7] F.D. Asl, M. Mousazadeh, S. Taji, et al. Nano drug-delivery systems for management of AIDS: Liposomes, dendrimers, gold and silver nanoparticles. *Nanomedicine*, 2023, 18(3): 279−302. https://doi.org/10.2217/nnm-2022-0248

[8] T.M. Liu, S. Li, S.N. Ying, et al. The IL-23/IL-17 pathway in inflammatory skin diseases: From bench to bedside. *Frontiers in Immunology*, 2020, 11: 594735. https://doi.org/10.3389/fimmu.2020.594735

[9] M. Nogueira, L. Puig, T. Torres. JAK inhibitors for treatment of psoriasis: Focus on selective TYK2 inhibitors. *Drugs*, 2020, 80(4): 341−352. https://doi.org/10.1007/s40265-020-01261-8

[10] Y.H. Pan, Y.P. You, L. Sun, et al. The STING antagonist H-151 ameliorates psoriasis *via* suppression of STING/NF-κB-mediated inflammation. *British Journal of Pharmacology*, 2021, 178(24): 4907−4922. https://doi.org/10.1111/bph.15673

[11] J. Willemsen, M.T. Neuhoff, T. Hoyler, et al. TNF leads to mtDNA release and cGAS/STING-dependent interferon responses that support inflammatory arthritis. *Cell Reports*, 2021, 37(6): 109977. https://doi.org/10.1016/j.celrep.2021.109977

[12] Y.X. Ma, Y.Y. Liu, Y. Zhong, et al. Oroxylin A attenuates psoriasiform skin inflammation by direct targeting p62 (sequestosome 1) *via* suppressing M1 macrophage polarization. *British Journal of Pharmacology*, 2024, 181(24): 5110−5132. https://doi.org/10.1111/bph.17349

[13] H. Sigurgrimsdottir, E.O. Bjornsdottir, J.H. Eysteinsdottir, et al. Keratinocytes secrete multiple inflammatory and immune biomarkers, which are regulated by LL-37, in a psoriasis mimicking microenvironment. *Scandinavian Journal of Immunology*,

2021, 94(6): e13096. https://doi.org/10.1111/sji.13096
[14] J. Wang, J. Ke, X. Wu, et al. Astragaloside prevents UV-induced keratinocyte injury by regulating TLR4/NF-κB pathway. *Journal of Cosmetic Dermatology*, 2022, 21(3): 1163−1170. https://doi.org/10.1111/jocd.14174
[15] S. Miura, S. Garcet, X. Li, et al. Cathelicidin antimicrobial peptide LL37 induces toll-like receptor 8 and amplifies IL-36γ and IL-17C in human keratinocytes. *Journal of Investigative Dermatology*, 2023, 143(5): 832−841.e4. https://doi.org/10.1016/j.jid.2022.10.017
[16] D. Badal, D. Dayal, G. Singh, et al. Role of DNA-LL37 complexes in the activation of plasmacytoid dendritic cells and monocytes in subjects with type 1 diabetes. *Scientific Reports*, 2020, 10(1): 8896. https://doi.org/10.1038/s41598-020-65851-y
[17] S. Xu, X.T. Cao. Interleukin-17 and its expanding biological functions. *Cellular & Molecular Immunology*, 2010, 7(3): 164−174. https://doi.org/10.1038/cmi.2010.21
[18] Z.Y. Yu, Q. Yu, H. Xu, et al. IL-17A promotes psoriasis-associated keratinocyte proliferation through ACT1-dependent activation of YAP–AREG axis. *Journal of Investigative Dermatology*, 2022, 142(9): 2343−2352. https://doi.org/10.1016/j.jid.2022.02.016
[19] X. Zhou, Y.D. Chen L., Cui, e tal. Advances in the pathogenesis of psoriasis: From keratinocyte perspective. *Cell Death & Disease*, 2022, 13: 81. https://doi.org/10.1038/s41419-022-04523-3
[20] H.R. Nada, D.A. El Sharkawy, M.F. Elmasry, et al. Expression of Janus Kinase 1 in vitiligo & psoriasis before and after narrow band UVB: A case-control study. *Archives of Dermatological Research*, 2018, 310(1): 39−46. https://doi.org/10.1007/s00403-017-1792-6
[21] M. Ishizaki, R. Muromoto, T. Akimoto, et al. Tyk2 is a therapeutic target for psoriasis-like skin inflammation. *International Immunology*, 2014, 26(5): 257−267. https://doi.org/10.1093/intimm/dxt062
[22] S. Słuczanowska-Głąbowska, A. Ziegler-Krawczyk, K. Szumilas, et al. Role of Janus kinase inhibitors in therapy of psoriasis. *Journal of Clinical Medicine*, 2021, 10(19): 4307. https://doi.org/10.3390/jcm10194307
[23] A.W. Armstrong, M. Lebwohl, R.B. Warren, et al. Deucravacitinib in plaque psoriasis: Four-year safety and efficacy results from the Phase 3 POETYK PSO-1, PSO-2 and long-term extension trials. *Journal of the European Academy of Dermatology and Venereology*, 2025, 39(7): 1336−1351. https://doi.org/10.1111/jdv.20553
[24] L. Mercurio, C. Albanesi, S. Madonna. Recent updates on the involvement of PI3K/AKT/mTOR molecular cascade in the pathogenesis of hyperproliferative skin disorders. *Frontiers in Medicine*, 2021, 8: 665647. https://doi.org/10.3389/fmed.2021.665647
[25] Y. Teng, Y.B. Fan, J.W. Ma, et al. The PI3K/Akt pathway: Emerging roles in skin homeostasis and a group of non-malignant skin disorders. *Cells*, 2021, 10(5): 1219. https://doi.org/10.3390/cells10051219
[26] H.R. Kim, J.C. Kim, S.Y. Kang, et al. Rapamycin alleviates 2, 3, 7, 8-tetrachlorodibenzo-p-dioxin-induced aggravated dermatitis in mice with imiquimod-induced psoriasis-like dermatitis by inducing autophagy. *International Journal of Molecular Sciences*, 2021, 22(8): 3968. https://doi.org/10.3390/ijms22083968
[27] F. Qu, R. Geng, Y.J. Liu, et al. Advanced nanocarrier- and microneedle-based transdermal drug delivery strategies for skin diseases treatment. *Theranostics*, 2022, 12(7): 3372−3406. https://doi.org/10.7150/thno.69999
[28] X.L. Ma, R. Cong, X. Cui, et al. Dendritic lipopeptide-based transdermal siRNA delivery systems for effective non-invasive therapy in psoriasis. *Journal of Controlled Release*, 2025, 381: 113581. https://doi.org/10.1016/j.jconrel.2025.113581
[29] F. Moawad, Y. Ruel, N. Rezaei, et al. Microneedles with implantable tip-accumulated therapeutics for the long-term management of psoriasis. *Small*, 2024, 20(51): e2405927. https://doi.org/10.1002/smll.202405927
[30] H. Chen, J.M. Xu, Y.X. Jiang, et al. Controlled delivery of MTX from thermosensitive hydrogels using Au nanorods for enhanced therapeutics of psoriasis *via* improving stratum corneum penetration. *Small*, 2025, 21(9): e2410566. 10.1002/smll.202410566
[31] Q. Jing, H. Ruan, J.Q. Li, et al. Keratinocyte membrane-mediated nanodelivery system with dissolving microneedles for targeted therapy of skin diseases. *Biomaterials*, 2021, 278: 121142. https://doi.org/10.1016/j.biomaterials.2021.121142
[32] E.C. Tan, T. Wan, Q. Pan, et al. Dual-responsive nanocarriers for efficient cytosolic protein delivery and CRISPR-Cas9 gene therapy of inflammatory skin disorders. *Science Advances*, 2024, 10(16): eadl4336. https://doi.org/10.1126/sciadv.adl4336
[33] K. Bäsler, S. Bergmann, M. Heisig, et al. The role of tight junctions in skin barrier function and dermal absorption. *Journal of Controlled Release*, 2016, 242: 105−118. https://doi.org/10.1016/j.jconrel.2016.08.007
[34] A. Orsmond, L. Bereza-Malcolm, T. Lynch, et al. Skin barrier dysregulation in psoriasis. *International Journal of Molecular Sciences*, 2021, 22(19): 10841. https://doi.org/10.3390/ijms221910841
[35] G. Bozzuto, A. Molinari. Liposomes as nanomedical devices. *International Journal of Nanomedicine*, 2015: 975. https://doi.org/10.2147/ijn.s68861
[36] L.J. Su, Y.X. Zhu, X.B. Li, et al. Topical adhesive spatio-temporal nanosystem co-delivering chlorin e6 and HMGB1 inhibitor glycyrrhizic acid for *in situ* psoriasis chemo-phototherapy. *Acta Pharmaceutica Sinica B*, 2025, 15(2): 1126−1142. https://doi.org/10.1016/j.apsb.2024.12.020
[37] L.M. Sun, H.M. Liu, Y.Q. Ye, et al. Smart nanoparticles for cancer therapy. *Signal Transduction and Targeted Therapy*, 2023, 8(1): 418. https://doi.org/10.1038/s41392-023-01642-x
[38] A. Zielińska, F. Carreiró, A.M. Oliveira, et al. Polymeric nanoparticles: Production, characterization, toxicology and ecotoxicology. *Molecules*, 2020, 25(16): 3731. https://doi.org/10.3390/molecules25163731
[39] A. Kumar, A. Vimal, A. Kumar. Why Chitosan?From properties to perspective of mucosal drug delivery. *International Journal of Biological Macromolecules*, 2016, 91: 615−622. https://doi.org/10.1016/j.ijbiomac.2016.05.054
[40] J. Rathee, S. Malhotra, M. Pandey, et al. Recent update on nanoemulsion impregnated hydrogel: A gleam into the revolutionary strategy for diffusion-controlled delivery of therapeutics. *AAPS PharmSciTech*, 2023, 24(6): 151. https://doi.org/10.1208/s12249-023-02611-x
[41] C. Muanprasat, V. Chatsudthipong. Chitosan oligosaccharide: Biological activities and potential therapeutic applications. *Pharmacology & Therapeutics*, 2017, 170: 80−97. https://doi.org/10.1016/j.pharmthera.2016.10.013
[42] S.A. Fereig, G.M. El-Zaafarany, M.G. Arafa, et al. Tacrolimus-loaded chitosan nanoparticles for enhanced skin deposition and management of plaque psoriasis. *Carbohydrate Polymers*, 2021, 268: 118238. https://doi.org/10.1016/j.carbpol.2021.118238
[43] Z.H. Liu, Y. Wang, Y.H. Zhang, et al. Biguanide chitosan microneedles with cell-free DNA scavenging ability for psoriasis therapy. *Bioactive Materials*, 2024, 33: 497−505. https://doi.org/10.1016/j.bioactmat.2023.11.015
[44] K. Azuma, R. Koizumi, H. Izawa, et al. Hair growth-promoting activities of chitosan and surface-deacetylated

chitin nanofibers. *International Journal of Biological Macromolecules*, 2019, 126: 11−17. https://doi.org/10.1016/j.ijbiomac.2018.12.135

[45] H.Z. Liu, M.Y. Huang, J.Y. Lyu, et al. Enhance efferocytosis and block the macrophages-platelets feedback loop for targeted treatment of psoriasis. *ACS Nano*, 2025, 19(12): 11774−11791. https://doi.org/10.1021/acsnano.4c13533

[46] R. Schutzman, N.Q. Shi, K.F. Olsen, et al. Mechanistic evaluation of the initial burst release of leuprolide from spray-dried PLGA microspheres. *Journal of Controlled Release*, 2023, 361: 297−313. https://doi.org/10.1016/j.jconrel.2023.06.016

[47] Z.B. Lin, L. Xi, S.K. Chen, et al. Uptake and trafficking of different sized PLGA nanoparticles by dendritic cells in imiquimod-induced psoriasis-like mice model. *Acta Pharmaceutica Sinica B*, 2021, 11(4): 1047−1055. https://doi.org/10.1016/j.apsb.2020.11.008

[48] N. Kim, Y.G. Jeong, S. Lee, et al. Ameliorated skin inflammation through the synergistic effect of gold nanorod-dexamethasone and photothermal therapy. *ACS Applied Materials & Interfaces*, 2024, 16(10): 12217−12231. https://doi.org/10.1021/acsami.3c16919

[49] C. Saweres-Argüelles, I. Ramírez-Novillo, M. Vergara-Barberán, et al. Skin absorption of inorganic nanoparticles and their toxicity: A review. *European Journal of Pharmaceutics and Biopharmaceutics*, 2023, 182: 128−140. https://doi.org/10.1016/j.ejpb.2022.12.010

[50] J.M. Xu, H. Chen, H.S. Qian, et al. Advances in the modulation of ROS and transdermal administration for anti-psoriatic nanotherapies. *Journal of Nanobiotechnology*, 2022, 20(1): 448. https://doi.org/10.1186/s12951-022-01651-y

[51] C.Y. Zhou, L. Zhang, Z.S. Xu, et al. Self-propelled ultrasmall AuNPs-tannic acid hybrid nanozyme with ROS-scavenging and anti-inflammatory activity for drug-induced liver injury alleviation. *Small*, 2023, 19(19): e2206408. https://doi.org/10.1002/smll.202206408

[52] H. Zhao, H. Zhao, Y. Tang, et al. Skin-permeable gold nanoparticles with modifications azelamide monoethanolamine ameliorate inflammatory skin diseases. *Biomarker Research*, 2024, 12(1): 118. https://doi.org/10.1186/s40364-024-00663-0

[53] D. Pedone, M. Moglianetti, E. De Luca, et al. Platinum nanoparticles in nanobiomedicine. *Chemical Society Reviews*, 2017, 46(16): 4951−4975. https://doi.org/10.1039/c7cs00152e

[54] Z.B. Zhang, D.T. Zhou, Z. Li, et al. A nanoinhibitor targeting cGAS-STING pathway to reverse the homeostatic imbalance of inflammation in psoriasis. *Angewandte Chemie* (*International Edition*), 2024, 63(2): e202316007. https://doi.org/10.1002/anie.202316007

[55] J.M. Xu, H. Chen, Z.Y. Chu, et al. A multifunctional composite hydrogel as an intrinsic and extrinsic coregulator for enhanced therapeutic efficacy for psoriasis. *Journal of Nanobiotechnology*, 2022, 20(1): 155. https://doi.org/10.1186/s12951-022-01368-y

[56] X.Y. Lu, L. Kuai, F. Huang, et al. Single-atom catalysts-based catalytic ROS clearance for efficient psoriasis treatment and relapse prevention *via* restoring ESR1. *Nature Communications*, 2023, 14(1): 6767. https://doi.org/10.1038/s41467-023-42477-y

[57] J. Li, Z.G. Yuan, S.Y. Shi, et al. Microneedle patches incorporating zinc-doped mesoporous silica nanoparticles loaded with betamethasone dipropionate for psoriasis treatment. *Journal of Nanobiotechnology*, 2024, 22(1): 706. https://doi.org/10.1186/s12951-024-02986-4

[58] Y.Z. Yan, H.Y. Liang, X.L. Liu, et al. Topical cationic hairy particles targeting cell free DNA in dermis enhance treatment of psoriasis. *Biomaterials*, 2021, 276: 121027. https://doi.org/10.1016/j.biomaterials.2021.121027

[59] D.D. Su, M.C. Li, Y.D. Xie, et al. Gut commensal bacteria Parabacteroides goldsteinii-derived outer membrane vesicles suppress skin inflammation in psoriasis. *Journal of Controlled Release*, 2025, 377: 127−145. https://doi.org/10.1016/j.jconrel.2024.11.014

[60] R.H. Fang, W.W. Gao, L.F. Zhang. Targeting drugs to tumours using cell membrane-coated nanoparticles. *Nature Reviews Clinical Oncology*, 2023, 20(1): 33−48. https://doi.org/10.1038/s41571-022-00699-x

[61] J.R. Yang, J.J. Zhu, S. Lu, et al. Transdermal psoriasis treatment inspired by tumor microenvironment-mediated immunomodulation and advanced by exosomal engineering. *Journal of Controlled Release*, 2025, 382: 113664. https://doi.org/10.1016/j.jconrel.2025.113664

[62] R.F. Huang, B. Jia, D.D. Su, et al. Plant exosomes fused with engineered mesenchymal stem cell-derived nanovesicles for synergistic therapy of autoimmune skin disorders. *Journal of Extracellular Vesicles*, 2023, 12(10): e12361. https://doi.org/10.1002/jev2.12361

[63] J.X. Xu, M.J. Wu, J. Yang, et al. Multimodal smart systems reprogramme macrophages and remove urate to treat gouty arthritis. *Nature Nanotechnology*, 2024, 19(10): 1544−1557. https://doi.org/10.1038/s41565-024-01715-0

[64] E.C. Dobrică, M.A. Cozma, M.A. Găman, et al. The involvement of oxidative stress in psoriasis: A systematic review. *Antioxidants*, 2022, 11(2): 282. https://doi.org/10.3390/antiox11020282

[65] D. Mijaljica, J.P. Townley, D.J. Klionsky, et al. The origin, intricate nature, and role of the skin surface pH (pHSS) in barrier integrity, eczema, and psoriasis. *Cosmetics*, 2025, 12(1): 24. https://doi.org/10.3390/cosmetics12010024

[66] A. Stubelius, S. Lee, A. Almutairi. The chemistry of boronic acids in nanomaterials for drug delivery. *Accounts of Chemical Research*, 2019, 52(11): 3108−3119. https://doi.org/10.1021/acs.accounts.9b00292

[67] D.H. Bi, F. Qu, W.Y. Xiao, et al. Reactive oxygen species-responsive gel-based microneedle patches for prolonged and intelligent psoriasis management. *ACS Nano*, 2023, 17(5): 4346−4357. https://doi.org/10.1021/acsnano.2c08979

[68] X.F. Xin, Y. Zhou, Y.F. Lyu, et al. Disease-specific corona mediated co-delivery of MTX and siRNA-TNFα by a polypeptide nanoplatform with antigen-scavenging functions in psoriasis. *Journal of Controlled Release*, 2023, 364: 326−342. https://doi.org/10.1016/j.jconrel.2023.10.035

[69] X.D. Li, M.L. Chen, X.N. He, et al. Biomineralized *in situ* catalytic nanoreactor integrated microneedle patch for on demand immunomodulator supply to combat psoriasis. *Theranostics*, 2024, 14(17): 6571−6586. https://doi.org/10.7150/thno.101845

[70] R. Kumar, S. Dogra, B. Amarji, et al. Efficacy of novel topical liposomal formulation of cyclosporine in mild to moderate stable plaque psoriasis: A randomized clinical trial. *JAMA Dermatology*, 2016, 152(7): 807−815. https://doi.org/10.1001/jamadermatol.2016.0859

[71] A.R. Bilia, M.C. Bergonzi, B. Isacchi, et al. Curcumin nanoparticles potentiate therapeutic effectiveness of acitrein in moderate-to-severe psoriasis patients and control serum cholesterol levels. *Journal of Pharmacy and Pharmacology*, 2018, 70(7): 919−928. https://doi.org/10.1111/jphp.12910

[72] E. Elmowafy, R.I. El-Gogary, M.H. Ragai, et al. Novel antipsoriatic fluidized spanlastic nanovesicles: *in vitro* physicochemical characterization, *ex vivo* cutaneous retention and exploratory clinical therapeutic efficacy. *International Journal of Pharmaceutics*, 2019, 568:

118556. https://doi.org/10.1016/j.ijpharm.2019.118556
[73] F.Y. Zhao, J.N. Zhao, K. Wei, et al. Targeted siRNA therapy for psoriasis: Translating preclinical potential into clinical treatments. *ImmunoTargets and Therapy*, 2024, 13: 259−271. https://doi.org/10.2147/itt.s458800
[74] R. Keshari, R. Bagale, S. Rath, et al. Transcutaneous delivery of disease-specific PI3K/Akt/mTOR inhibitor-based hybrid nanoparticles in hydrogel system for the management of psoriasis: Insights from *in vivo* studies. *International Journal of Pharmaceutics*, 2025, 672: 125325. https://doi.org/10.1016/j.ijpharm.2025.125325
[75] Y. Wang, S.K. Zhou, Y. Wang, et al. Engineering tumor-specific gene nanomedicine to recruit and activate T cells for enhanced immunotherapy. *Nature Communications*, 2023, 14(1): 1993. https://doi.org/10.1038/s41467-023-37656-w
[76] J. Meng, Y.Y. Ge, H.Y. Xing, et al. Synthetic CXCR4 antagonistic peptide assembling with nanoscaled micelles combat acute myeloid leukemia. *Small*, 2020, 16(31): e2001890. https://doi.org/10.1002/smll.202001890
[77] W. Ngo, S. Ahmed, C. Blackadar, et al. Why nanoparticles prefer liver macrophage cell uptake *in vivo*. *Advanced Drug Delivery Reviews*, 2022, 185: 114238. https://doi.org/10.1016/j.addr.2022.114238
[78] A.A. Aljabali, M.A. Obeid, R.M. Bashatwah, et al. Nanomaterials and their impact on the immune system. *International Journal of Molecular Sciences*, 2023, 24(3): 2008. https://doi.org/10.3390/ijms24032008
[79] X.T. Zhou, J.Q. Liao, Z.P. Lei, et al. Nickel-based nanomaterials: A comprehensive analysis of risk assessment, toxicity mechanisms, and future strategies for health risk prevention. *Journal of Nanobiotechnology*, 2025, 23(1): 211. https://doi.org/10.1186/s12951-025-03248-7
[80] D.E. Large, R.G. Abdelmessih, E.A. Fink, et al. Liposome composition in drug delivery design, synthesis, characterization, and clinical application. *Advanced Drug Delivery Reviews*, 2021, 176: 113851. https://doi.org/10.1016/j.addr.2021.113851
[81] S.C. Semple, A. Chonn, P.R. Cullis. Influence of cholesterol on the association of plasma proteins with liposomes. *Biochemistry*, 1996, 35(8): 2521−2525. https://doi.org/10.1021/bi950414i
[82] A. Gabizon, R. Shiota, D. Papahadjopoulos. Pharmacokinetics and tissue distribution of doxorubicin encapsulated in stable liposomes with long circulation times. *Journal of the National Cancer Institute*, 1989, 81(19): 1484−1488. https://doi.org/10.1093/jnci/81.19.1484
[83] C.Y. Ushirobira, L.A.F. Afiune, M.N. Pereira, et al. Dutasteride nanocapsules for hair follicle targeting: Effect of chitosan-coating and physical stimulus. *International Journal of Biological Macromolecules*, 2020, 151: 56−61. https://doi.org/10.1016/j.ijbiomac.2020.02.143
[84] J.H. Al Mahrooqi, V.V. Khutoryanskiy, A.C. Williams. Thiolated and PEGylated silica nanoparticle delivery to hair follicles. *International Journal of Pharmaceutics*, 2021, 593: 120130. https://doi.org/10.1016/j.ijpharm.2020.120130
[85] E. Kahraman, S. Güngör, Y. Özsoy. Potential enhancement and targeting strategies of polymeric and lipid-based nanocarriers in dermal drug delivery. *Therapeutic Delivery*, 2017, 8(11): 967−985. https://doi.org/10.4155/tde-2017-0075
[86] R. Mohammapdour, H. Ghandehari. Mechanisms of immune response to inorganic nanoparticles and their degradation products. *Advanced Drug Delivery Reviews*, 2022, 180: 114022. https://doi.org/10.1016/j.addr.2021.114022