Frontiers in Bioscience Landmark

Front. Biosci. (Landmark Ed) **2025**; 30(3): 27910
https://doi.org/10.31083/FBL27910

Review

Emerging Therapeutic Agents and Nanotechnology-Driven Innovations in Psoriasis Management

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Academic Editor: Xin Han
Submitted: 4 November 2024 Revised: 5 December 2024 Accepted: 10 December 2024 Published: 19 March 2025

Abstract

Psoriasis has been a rising concern for over a decade, imposing significant challenges to individuals and society. Traditional topical therapy is non-targeted and acts systemically, with associated side effects. This increases the global burden both socially and economically. This review covers the evolution of drug molecules and nanotechnology-based approaches for the topical treatment of psoriasis, a chronic inflammatory skin disorder with no known etiology. Nanotechnology-based approaches offer promising solutions by reducing side effects, providing targeted delivery, protecting drug molecules from degradation, enhancing skin retention, and providing controlled release. Researchers have investigated the incorporation of various conventional and non-conventional therapeutic agents into nanocarriers for psoriasis treatment. The current understanding of the disease and its treatment using various therapeutic agents combined with novel formulation strategies will reduce the duration of treatment and improve the quality of life in psoriatic disease conditions.

Keywords: psoriasis; topical drugs; delivery systems; inflammatory cytokines; nanotechnology

1. Introduction

The management of psoriasis, a chronic inflammatory skin disorder, requires innovative therapeutic approaches to overcome the limitations of traditional treatments. Natural agents are widely valued for their diverse biological effects and low side-effect profiles. A comprehensive approach integrating a healthy lifestyle, natural medicines, emerging drugs, and nanotechnology offers promising advancements. The integrative approach not only enhances treatment efficacy but also contributes to reducing the overall burden of psoriasis, improving patient outcomes and quality of life [1,2]. Psoriasis is a chronic inflammatory skin disease characterized by hyperplasia and hyperkeratosis. In psoriasis, the skin undergoes various changes, manifesting as itchiness, redness, inflammation, scaliness, and emergence of skin lesions (Fig. 1) [3]. The prevalence of psoriasis varies, ranging from 0.27% to 11.4%, depending on genetic factors, sex, age, environment, ethnicity, and geography. It affects approximately 64.6 million people worldwide [4]. Psoriasis can affect the skin, nails, scalps, and joints. It is also associated with various comorbidities such as cardiovascular diseases, cancer, diabetes, anxiety, and depression. Common inflammatory pathways, genetic susceptibility, cellular mediators, and risk factors have been hypothesized to play contributory roles. Psoriasis affects quality of life at the physical, psychological, and social levels, resulting in poor mental health, reduced productivity, and even social exclusion [5].

Psoriasis is an autoimmune condition that is triggered by the activation of T lymphocytes. Activated T lymphocytes increase the infiltration of inflammatory cytokines in the dermis and marginally in the systemic circulation, thereby increasing the proliferation of keratinocytes and epidermal cell turnover [6]. One-third of patients with psoriasis have a genetic background. Various factors such as infection, stress, metabolic syndrome, obesity, and diabetes can also trigger it. These triggers can damage the skin, leading to a repair response in which skin keratinocytes undergo excessive proliferation without adequate differentiation. This abnormal process results in an impaired skin barrier and the formation of scaly plaques [7].

Management of psoriasis involves a multifaceted approach including adopting a healthy lifestyle and integrating therapeutic interventions. Key lifestyle modifications include effective stress management, regular physical activity, smoking cessation, avoiding alcohol consumption, maintaining an active skincare routine, dietary modification to reduce systemic inflammation, and utilizing therapeutic agents—essential components of a comprehensive management strategy [8,9].

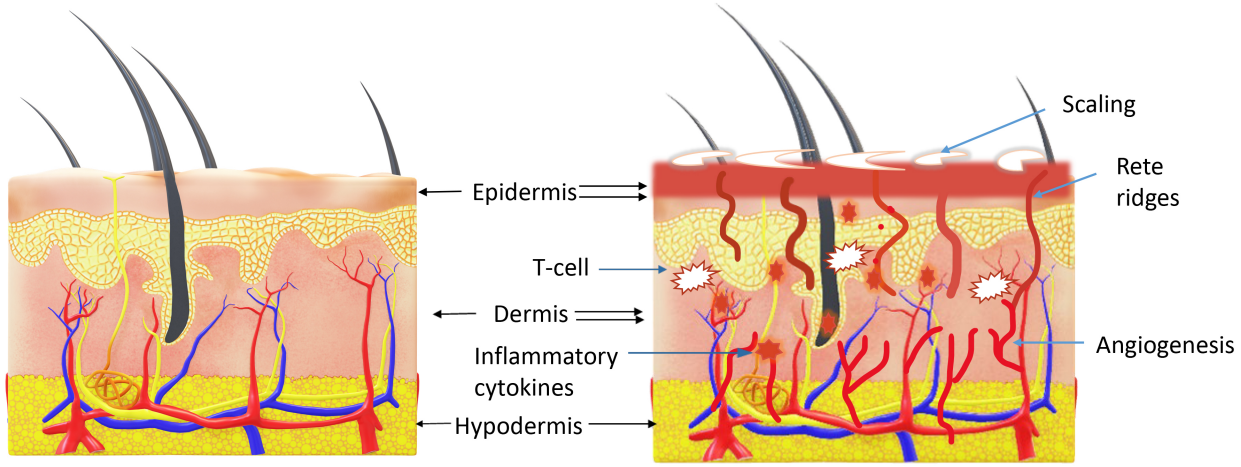

Fig. 1. Comparison of the structure of normal skin and psoriatic skin. Normal skin is represented by single arrows, highlighting its organized structure. Psoriatic (diseased) skin is represented by double arrows, with unique features indicated by blue-colored arrows. In psoriatic skin, there is visible redness, scaling, and significantly increased epidermal thickness. In the dermis, psoriatic skin exhibits increased infiltration of inflammatory cytokines, accumulation of T cells, and increased angiogenesis, contributing to the disease's characteristic symptoms. Drawn using Powerpoint.

Many review articles have described various topical nanotechnology-based formulations and therapeutic agents available for the management of psoriasis [6,10,11]. However, study on emerging topical therapeutic agents are still required. Unlike previous reviews, it critically evaluates the integration of emerging and conventional therapies with nanocarriers. The present study attempts to provide insights into the existing state of research on topical therapeutics effective for psoriasis and proposes directions for future research. Using the query "TITLE-ABS-KEY (topical AND "drug delivery" AND psoriasis) AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English"))", Scopus and PubMed were retrieved at the mid of 2024. A total of 512 articles were retrieved by mid-2024, of which 207 duplicates were removed, leaving 305 articles for review. A total of 132 studies were scanned from 305 articles to confirm that only the relevant studies of interest were selected. After reviewing the title, abstract, and keywords, 156 articles were removed, and 37 were removed after reading the full text. A total of 112 articles were selected for this study.

2. Pathophysiology of Psoriasis

Psoriasis is a multifactorial disease triggered by stress-induced keratinocyte damage due to various factors. Its pathophysiology involves multiple components, including immune cells, genetic predispositions, antimicrobial peptides, and non-coding RNAs (Fig. 2). Psoriasis is an immune-driven condition characterized by T lymphocyte activation. Dendritic cells, which function as antigen-presenting cells (APCs), initiate an immune response by generating interleukin -12 (IL-12) and interleukin -23 (IL-23), prompting the activation of T helper 1 (Th1) and T helper 17 (Th17) cells. Th1 cells generate tumor necrosis factor-α (TNF-α) and interferon-γ (IFN-γ), whereas Th17 cells produce IL-22, IL-17A, and IL-17F. These inflammatory cytokines play pivotal roles in stimulating keratinocyte proliferation (Fig. 3). TNF-α specifically contributes to an increase in inflammatory cell infiltration.

Additionally, Langerhans cells serve as mediators in activating distinct types of T cells such as natural killer (NK) cells and NK-T cells. Th1 and Th2 utilize the Janus kinase/signal transducers and activators of transcription (JAK-STAT) pathway to perform their functions. In contrast, Th17 cells operate through the activator 1 (ACT1) adapter protein and nuclear factor kappa B (NF-κB) signaling mechanism. Macrophages produce TNF-α and vascular endothelial growth factor (VEGF), which further increases inflammation and blood vessel growth. T-cell activation increases keratinocyte proliferation, and keratinocytes produce various growth factors and cytokines, which increase proliferation and inflammation [12]. Chemokine receptors, such as the C–X–C motif chemokine receptor (CXCR) superfamily, play an important role in initiating the innate immune response by activating and migrating immune cells. CXCRs are important for tissue healing and pathogen elimination, but their overactivation results in a T-cell-mediated immune response, increased inflammatory response, and psoriasis [13]. Although not as pivotal as T cells, B cells also play a role in the initiation and progression of psoriasis; when triggered by autoantigens, they induce molecular mimicry, influencing B-cell behavior in gastric centers (GCs), producing autoantibodies and proinflammatory cytokines, forming ectopic germinal centers, and dysregulating proliferation of keratinocytes [14].

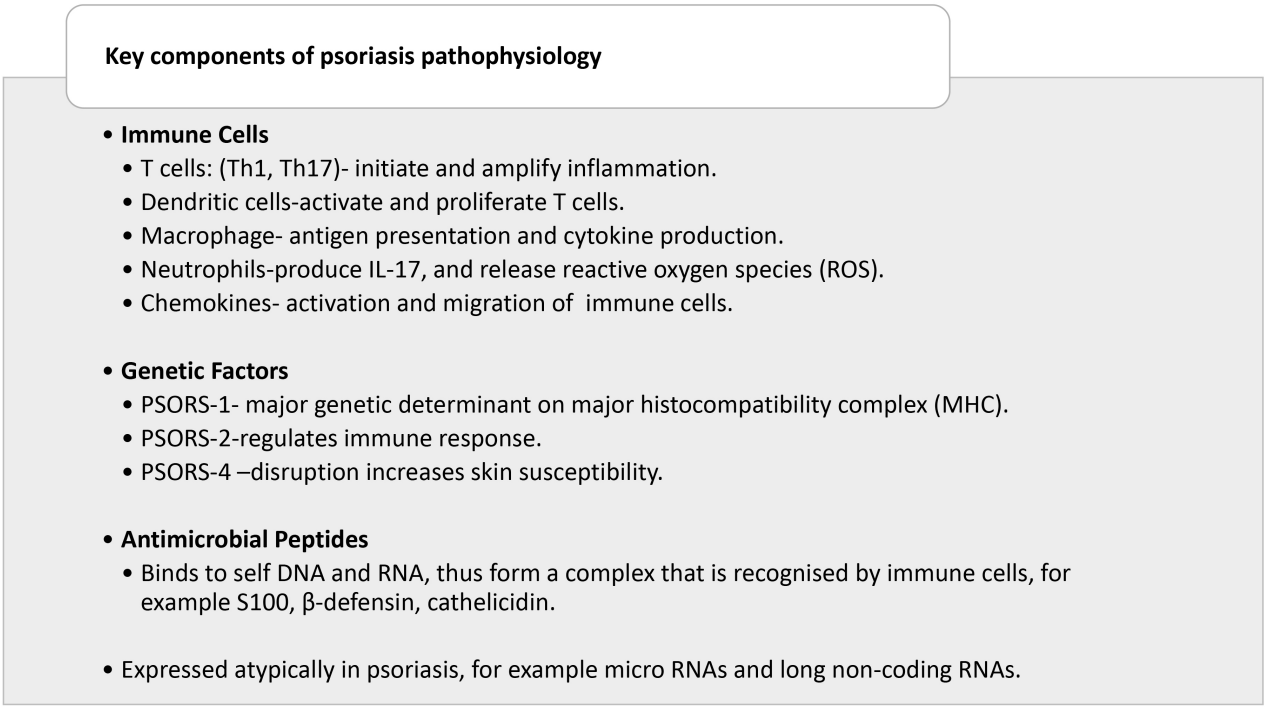

Fig. 2. Key components involved in the pathophysiology of psoriasis. Th1, T helper 1 cells; Th17, T helper 17 cells; IL-17, Interleukin-17; PSORS, Psoriasis-susceptible. Drawn using Powerpoint.

Psoriasis is associated with significant changes in *gene* expression. Psoriasis occurs more frequently in monozygotic twins than in dizygotic twins. It is activated by environmental factors in individuals with genetic predisposition. Approximately 60 psoriasis-susceptible regions have been identified. According to linkage analysis, nine loci known as psoriasis-susceptible (PSOR1-9) are responsible for disease susceptibility. PSORS-1 was the most validated, whereas a weaker linkage was observed in PSORS-2 and PSORS-4. Linkage in the remaining regions was not replicated in independent research. PSORS-1 is the major histocompatibility complex (MHC) locus on chromosome 6p21. The 150 kb region of MHC-1 contains nine genes, of which three, *CCHCR1*, *HLA-C*, and *CDSN*, are significantly related to psoriasis. HLA-C codes for MHC class I receptors that participate in the immune response by acting as an antigen for CD8+ lymphocytes. In the *PSORS-2* locus, the mutation in CARD14 is responsible for the phenotype of plaque and pustular psoriasis. PSORS-4 is located on the 1q21 chromosome; it stretches the epidermal differentiation cluster (EDC). Absence of the *EDC* gene is associated with psoriasis [15].

Antimicrobial peptides (AMPs) are 12–50 amino acid long, amphiphilic molecules. Keratinocytes, T cells, dendritic cells, and neutrophils secrete antimicrobial peptides such as S100, β-defensin, and cathelicidin. They activate the innate immune response to induce inflammation in psoriasis patients. Plasmacytoid dendritic cells (DCs) and neutrophils are critical components of the innate immune system. Antimicrobial peptides enhance the affinity between damage-associated self-DNA and self-RNA and their corresponding receptors. This heightened interaction subsequently amplifies keratinocyte interferon secretion and activates plasmacytoid dendritic cells. Consequently, this process actively stimulates and intensifies the inflammatory responses. Neutrophils release neutrophil extracellular traps (a complex of IL-33 and self-DNA), thereby inducing Th17 activation. Activated myeloid dendritic cells release inflammatory cytokines IL-12, IL-17, and IL-23. Antimicrobial peptides also increase the production of Th1 and Th17 cells. Therefore, AMPs play a vital role in psoriatic inflammation by activating the innate immune response [16,17].

Non-coding RNAs such as microRNAs (mRNAs) and long non-coding RNAs (lncRNAs) also play a role in the pathogenesis of psoriasis. More than 250 mRNA were atypically expressed in psoriatic lesions. Some mRNAs were upregulated, whereas others were downregulated. For example, mRNA miR-31 is upregulated; therefore, deletion of miR-31 alleviates inflammation and hyperplasia of keratinocytes. Conversely, miR-14a/b is highly expressed in psoriatic lesions and negatively regulates keratinocyte proliferation—so it has a protective effect. Genetic deficiency of miR-14a exacerbates psoriatic inflammation. lncRNAs control gene expression at both the transcriptional and post-transcriptional levels. In psoriasis, the non-protein-coding RNA induced by stress (PRINS), a type of lncRNA, is significantly overexpressed in the epidermis of affected patients. PRINS is activated by stress and its si-

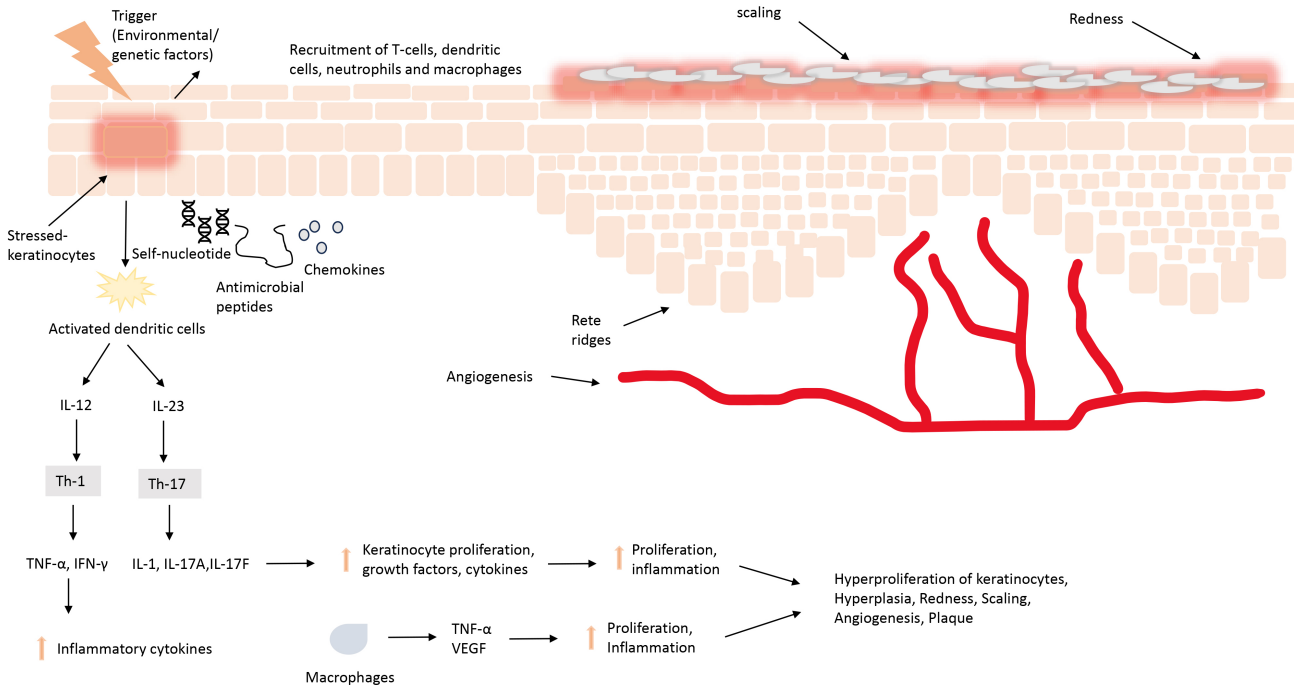

Fig. 3. The pathophysiology of psoriatic skin involves stress-induced activation of keratinocytes, which, when combined with self-nucleotides, antimicrobial peptides, and various chemokines, leads to the activation of dendritic cells. Abbreviations: IL, interleukin; Th, T helper cells, TNF-α, tumor necrosis factor- α, IFN-γ, interferon-γ; VEGF, vascular endothelial growth factor. This activation subsequently promotes the release of Th1 and Th17 cells, leading to the release of inflammatory cytokines. This cascade promotes angiogenesis, keratinocyte differentiation, and proliferation, intensifying the secretion of inflammatory cytokines and sustaining a cycle that exacerbates inflammation and tissue damage. Drawn using Powerpoint.

lencing decreases keratinocyte viability under stress conditions. However, the lncRNA maternally expressed gene 3 (*MEG3*) is downregulated in psoriatic skin. MEG3 suppresses keratinocyte proliferation and enhances apoptosis by targeting miR-21 and increasing Caspase 8 expression [18].

3. Treatment of Psoriasis

The available treatments for psoriasis aim to alleviate symptoms and improve the patient's quality of life, as psoriasis is a chronic disease with no cure and requires long-term treatment. This creates economic challenges for the healthcare and pharmaceutical industries [19]. Treatment of psoriasis consists of combinations of therapeutic agents to address complications of psoriasis depending on the severity of the disease, patient-specific factors, and the presence of co-morbidities. The therapeutic agents alleviate symptoms, improve skin health, and enhance the quality of life for patients. Broadly, therapeutic approaches can be categorized into topical treatments, systemic therapies, and advanced biologics. While topical treatments remain the cornerstone for managing mild to moderate psoriasis, systemic therapies and biologics are pivotal for severe cases. Topical agents are the first-line treatment for mild to moderate cases. Topical agents include corticosteroids, vitamin D derivatives, retinoids, anthralin, and salicylic acid (SA). Potent and super potent corticosteroids are as effective as vitamin D derivatives and can be combined with keratolytic agents, such as salicylic acid, to treat thick scaling. Vitamin D derivatives can be used alone or with corticosteroids but should not be used with keratolytics or phototherapy [3]. Systemic agents are used to treat moderate-to-severe psoriasis. Systemic agents include the following: retinoids, such as acitretin; immunosuppressants, such as methotrexate and tacrolimus; and immunomodulators, such as cyclosporin. These agents can cause serious side effects, such as nephrotoxicity, hepatotoxicity, and increased risk of infection. Therefore, these agents are unsuitable for long-term treatment. Retinoids are teratogenic and should not be used for women of childbearing age [20]. Phototherapy is used in moderate-to-severe psoriasis; it includes narrow- and broad-band Ultraviolet B (UV-B) and Ultraviolet A (UV-A) therapy with or without psoralen. Challenges associated with phototherapy include the limited number of centers available, frequent visits, cost, and increased risk of skin cancer [21]. Biologicals are a relatively new treatment approved by the US FDA (United States Food and Drug Administration) and are used to treat moderate to severe pso-

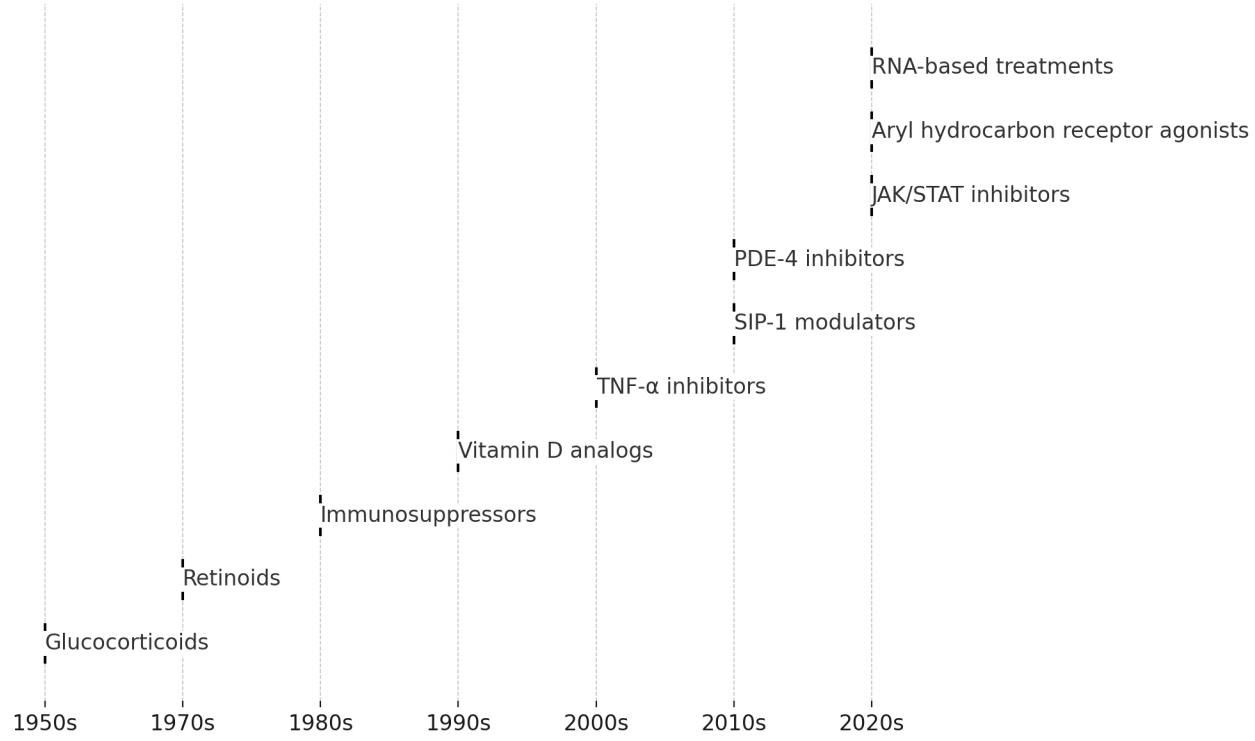

Fig. 4. Historical evolution of psoriasis treatment. Created using Draw.io.

riasis but are costly and lack long-term safety data. Biological agents included TNF-α inhibitors (infliximab, etanercept, and adalimumab), IL-12/23 inhibitors (ustekinumab), IL-17 inhibitors (ixekizumab, secukinumab), and IL-23 inhibitors (guselkumab, risankizumab, and tildrakizumab). Biologicals suppress the immune response, increasing the risk of infection and cancer [21,22]. Although there are many therapeutic agents available for the treatment of psoriasis, they are associated with side effects and limitations in their long-term efficacy. There remains an urgent need for the development of novel therapeutic agents that specifically target the molecular pathways underlying psoriasis. These agents should offer greater specificity for the disease, minimize adverse effects, and provide sustained effectiveness over extended treatment periods, thereby improving overall patient outcomes. Emerging drugs, such as aryl hydrocarbon receptor (AhR) agonists, offer a novel approach to treating psoriasis by regulating keratinocyte function. These drugs help to restore normal skin barrier function, which is often compromised in psoriatic skin [23]. RNA-based approaches hold significant promise for the future of psoriasis treatment. These technologies offer the potential for highly specific, targeted therapies that directly address the underlying molecular mechanisms driving the disease [24]. Numerous natural compounds are under investigation for their potential to complement existing treatments. Many of these compounds, including antioxidants from plant extracts, have demonstrated the ability to reduce oxidative stress, a key factor in the inflammation and skin damage seen in psoriasis. By mitigating oxidative damage, these natural agents can act as adjuvant therapies, potentially enhancing the effectiveness of conventional treatments like corticosteroids or biologicals [2]. Their ability to synergize with standard therapies offers a multi-faceted approach to treatment, potentially improving therapeutic outcomes, reducing side effects, and providing a more holistic approach to disease management.

4. Topical Therapeutics in Psoriasis and Their Mechanism of Action

Topical treatment is effective in most patients with psoriasis, and only 20% require systemic therapy [25]. Glucocorticoids, the primary drugs used for treating psoriasis, were first introduced in the 1950s, followed by the development of immunosuppressants and retinoids. Treatment has advanced significantly with the approval of vitamin D analogs in the 1990s, followed by the introduction of TNF-α inhibitors in the 2000s, marking a major leap in targeted biological therapies. RNA-based treatments are still under investigation and no drugs have been approved to date. Fig. 4 illustrates the historical evolution of psoriasis treatments. This review focuses on drugs, ranging from those in the initial investigational stages to those already approved. Drugs that are currently in the pipeline, undergoing clinical trials, or recently approved by the US FDA are discussed in detail elsewhere [26].

4.1 Glucocorticoids

Glucocorticoids are the first-line treatment, either alone or in combination. It has multiple functions, including antimitotic, anti-inflammatory, immunomodulatory, and vasoconstrictive effects. Therefore, it helps to reduce redness, swelling, scaling, and itching in psoriatic lesions. Glucocorticoids are chemically derived from androgens and pregnanes. Glucocorticoids consist of four lipophilic rings, which enable them to bind to glucocorticoid receptors [27]. Topical glucocorticoids were introduced in the 1950s and are still preferred for psoriasis management. Four classes of glucocorticoids are used to treat psoriasis: low potency (LPG), mid potency (MPG), high potency (HPG), and super high potency (SHPG). Low- and mid-potency glucocorticoids are used in folds, whereas high- and super-high-glucocorticoids are used on the exterior surfaces. Glucocorticoids act via two pathways, genomic and non-genomic. In the genomic pathway, cortisol binds to the glucocorticoid receptor, resulting in receptor dimerization and binding with the glucocorticoid responsive element (GRE), causing transcription of anti-inflammatory genes such as tyrosine aminotransferase (*TAT*), *IL-10*, antagonizing *IL-1*, and promoting dual-specificity protein phosphatase 1 (*DUSP-1*). Glucocorticoids also negatively regulate the expression of proinflammatory genes, such as cytokines, adhesion molecules, growth factors, nitric oxide, and autocoids. The non-genomic pathway does not involve *de novo* protein synthesis, so it rapidly affects binding to the glucocorticoid receptor, and a second messenger comes into action. It alters the activation and response of target cells such as T cells, platelets, and monocytes [27,28].

4.2 Vitamin D3 Analogs (VDA)

The active form of VDA is calcitriol or 1,25$(OH)_2$D3, whereas other synthetic analogs include calcipotriol, calcitriol, maxacalcitol, and tacalcitol. The first topical treatment for VDA was calcipotriol, which was introduced in Europe in 1987 and approved by the US FDA in 1993. It reverses epidermal dysregulation and hyperproliferation and induces apoptosis. In psoriasis, reduced vitamin D receptor expression is correlated with lower tight junction protein levels, which disrupts the skin barrier. Tight junctions are essential for keratinocyte adhesion and permeability and regulate cell differentiation through interactions with nuclear and cytoplasmic proteins. Vitamin D3 promotes keratinocyte terminal differentiation and inhibits proliferation, although the exact mechanism remains unclear. It also has immunomodulatory effects. It acts on cells involved in immunologic reactions, such as macrophages, lymphocytes, and Langerhans cells [29–32].

4.3 Immunosuppressors

Methotrexate is generally used as a systemic agent, but numerous topical formulations have been reported in the literature. It was introduced as a chemotherapeutic agent in the 1950s for treating cancer and autoimmune diseases, with its use in psoriasis beginning in the 1960s. Methotrexate (MTX) is a folic acid analog and antagonist. It binds to folic acid reductase with a much higher affinity than folic acid. It inhibits the synthesis of tetrahydrofolate and pyrimidine, which are required to synthesize DNA base pairs, leading to reduced DNA replication and inhibition of RNA and protein synthesis. It reduces epidermal cell proliferation and lymphocyte number [20].

Cyclosporine, a calcineurin inhibitor, was initially used as an immunosuppressant in organ transplants to prevent rejection, introduced for psoriasis treatment in the 1980s, and received FDA approval in 1997. The mechanism of action of cyclosporine is immunosuppression by binding with cyclophilin and inhibition of calcineurin, which is required for the transduction of calcium-dependent signals from T lymphocytes to cytokine promoters. It inhibits the proliferation of CD4+ helper T cells and keratinocytes. It regulates the immune system by explicitly inhibiting T-cell overproduction and impairing the function of antigen-presenting Langerhans cells. Whether taken orally or topically, cyclosporin has an affinity for skin cells. Cyclosporine reduced cell infiltration and epidermal thickness. It can be administered via a systemic or topical route; however, systemic treatment causes various side effects, which can be reduced with the use of topical formulations [20,33,34]. Other topical calcineurin inhibitors used for the treatment of psoriasis include tacrolimus and pimecrolimus. They exert an antipsoriatic effect by inhibiting the proliferation of T lymphocytes and dysregulation of mast cells. They do not affect fibroblasts and endothelial cells or cause skin atrophy [35].

4.4 Retinoids

Retinoids can be administered via both systemic and topical routes. Etretinate is a synthetic analog of retinoic acid approved by the FDA for oral use in the treatment of severe psoriasis in 1986. It is a metabolite of etretinate, has a shorter half-life, and is preferred as a systemic agent for managing psoriasis [36]. Tretinoin and isotretinoin are topical and systemic agents, respectively, whereas adapalene and tazarotene are topical agents. Retinoids are teratogenic when administered systemically. Retinoids have anti-hyperproliferative potential. They modulate T lymphocyte responses, inhibit chemotactic responses, activate polymorphonuclear leukocytes, and increase Langerhans cells. They also stimulate natural killer lymphocytes and induce the migration of inhibitory factor-related proteins (MRP-8) by inhibiting IFN-γ via retinoid receptor activation [37].

4.5 Sphingosine-1-Phosphate Receptor 1 (S1P1) Modulator

Fingolimod was the first SIP1 modulator approved by the US FDA in 2010 for oral treatment of multiple sclerosis. Owing to its success in modulating the immune response, its potential in treating autoimmune diseases, including psoriasis, has been explored [38]. AKP-11 is a highly selective sphingosine-1-phosphate receptor modulator. SIP is a lipid that binds to G protein-coupled S1P receptors and modulates cell proliferation, cell differentiation, and proinflammatory cytokine production, thus helping maintain skin barrier function. The topical formulation of AKP-11 has been used in clinical trials for psoriasis treatment [39,40]. Similarly, HWG-35D, a sphingosine kinase 2 inhibitor, is beneficial for psoriasis. Sphingosine kinase increases the phosphorylation of sphingosine phosphate and its inhibition blocks Th17 differentiation into CD4+ T lymphocytes. The topical application of HWG-35D (a novel sphingosine kinase 2 inhibitor) normalized the systemic and local immune responses induced by imiquimod (IMQ) treatment [40].

4.6 Aryl Hydrocarbon Receptor Agonist

Tapinarof is the first aryl hydrocarbon inhibitor that received US FDA approval on May 23, 2022, to treat mild, moderate, and severe psoriasis. Tapinarof is a secondary metabolite obtained from the Gram-negative bacterium, *Photorhabdus luminescens*. The binding of tapinarof to the aryl hydrocarbon receptor leads to the translocation of the receptor from the cytoplasm to the nucleus after dimerization with the aryl hydrocarbon nuclear translocator, activating different genes. Aryl hydrocarbon signaling regulates Th17 and Th22 differentiation and IL-17 and IL22 expression. Tapinarof regulates keratinocyte function by inducing the expression of skin barrier genes. Therefore, it helps normalize the skin barrier disrupted by psoriasis. It reduces epidermal oxidative stress by directly scavenging reactive oxygen species and increasing the expression of antioxidant enzyme genes [23,41].

4.7 Antimicrobial Peptides

Omiganan is a 12-amino-acid, antimicrobial cationic peptide active against many Gram-negative and Gram-positive microbes and fungi. It inhibits the activation of toll-like receptors (TLRs) on dendritic cells and other immune cells. This inhibition prevents the downstream inflammatory cascade that contributes to psoriasis. It also possesses anti-inflammatory properties. The liposomal gel formulation of omiganan substantially reduced psoriatic lesions by reducing the levels of proinflammatory cytokines [42]. Thiostrepton is a naturally occurring antimicrobial peptide that inhibits the activation of toll-like receptors 7-9 (TLR7-9) in dendritic cells. In psoriasis, these receptors are activated and contribute to the inflammatory response. Thiostrepton mitigates this activation through two primary mechanisms: the inhibition of proteasome function and endosome acidification. In mouse models, thiostrepton ameliorates psoriasis-like inflammation induced by imiquimod and LL37 [43].

4.8 Phosphodiesterase 4 (PDE-4) Inhibitors

PDE is expressed in keratinocytes and immune cells. It mediates the inflammatory response by hydrolyzing cyclic adenosine monophosphate (cAMP). Inhibition of PDE-4 increases intracellular cAMP concentrations, which activates various downstream pathways. This process inhibits the inflammatory response by suppressing the production of inflammatory cytokines and activating anti-inflammatory mediators [44]. Apremilast was the first PDE-4 inhibitor to receive US FDA approval in March 2014 for the treatment of plaque psoriasis and psoriatic arthritis. Apremilast acts as an anti-inflammatory drug by inhibiting various proinflammatory cytokines involved in the pathogenesis of psoriasis, such as TNF-α, IL-6, and IL-10 [45]. Roflumilast is another highly potent PDE-4 inhibitor approved by the US and FDA in 2022 for the treatment of chronic plaque psoriasis. Blocking PDE-4 activity increases cAMP concentration, which reduces inflammatory cytokines in psoriatic skin [46,47]. PF-07038124 is a potent PDE-4 inhibitor currently undergoing clinical trials for psoriasis treatment. It works by inhibiting cytokines IL-4 and IL-13. According to previous reports, it exhibits minimal to no adverse effects or application site reactions [26,48].

4.9 Herbal Drugs

Many herbal drugs have been explored for their antipsoriatic activity for a long time. Curcumin has shown antipsoriatic activity, as reported in many clinical and preclinical research. Curcumin has an inhibitory effect on IL-22-induced signal transducer and activator of transcription 3 (STAT3) phosphorylation. It also inhibits vesicular endothelial growth factor (VEGNF-κBF), thus reducing vascular proliferation. It decreases the secretion of inflammatory cells and blocks the NF-κB, mitogen-activated protein kinase (MAPK), and Janus kinase–signal transducer and activator of transcription (JAK-STAT) signaling pathways [49]. Other herbal drugs, such as lavender oil, rosmarinic acid, and Rosa species (R. canina, R. damascena, and R. Cairo) have anti-inflammatory and antioxidant properties [50,51]. Berberine, an alkaloid obtained from *Mahonia aquifolium* has antipsoriatic activity due to its ability to suppress keratinocyte growth, inhibit DNA and protein synthesis by inhibiting enzyme reverse transcriptase, and inhibit cell proliferation in psoriasis. It also exhibits anti-inflammatory properties by inhibiting cyclooxygenase, lipoxygenase, and cytokines [52]. Silibinin, an active *Silybum marianum constituent*, exerts an antipsoriatic effect by inhibiting phosphorylation signals and cell proliferation [53]. *Commiphora mukul* and quercetin-loaded lipospheres for antipsoriatic activity have also been reported.

Commiphora mukul has anti-inflammatory properties and inhibits TNF-α and IFs. Quercetin has antioxidant, anti-inflammatory, and antiproliferative properties [54]. Celastrol is a pentacyclic triterpene extracted from *Tripterygium wilfordii* Hook f. and has anti-inflammatory, antioxidant, and anti-tumor properties. It inhibits Th17 cell differentiation, pSTAT3 activation, and downregulates the NF-κB pathway [55]. Erianin, a phytochemical isolated from *Dendrobium chrysotoxum Lindl* inhibits keratinocyte proliferation and angiogenesis [56]. Various active ingredients of *Psoralea corylifolia* have been reported to be beneficial for the treatment of psoriasis [57–59]. Ursolic acid, a pentacyclic triterpenoid, can be extracted from many plants, including bearberry, thyme, lemon balm, lavender, and sage. Ursolic acid inhibits the COX-2 and NF-κB signaling pathways, downregulates proinflammatory cytokines such as IL-17, and provides anti-inflammatory effects in psoriasis. It also exhibits antioxidant activity [60,61]. Retinyl palmitate oil is a stable and natural source of retinoids, whereas dead seawater (DSW) has a high salt composition—both of which are beneficial in many skin diseases, including psoriasis [62].

4.10 Nutraceuticals

Nutraceuticals have both nutritional and medicinal properties [63]. Oleuropein, a nutraceutical product obtained from olive leaves, has anti-inflammatory and antioxidant properties, and its microemulsion formulation was found to be better than the marketed formulation Dermovate in patients with psoriasis, as reported by the authors [64]. (-)-epigallocatechin-3-gallate (EGCG), a catechin found in green tea, induces the expression of keratinocyte differentiation markers and has immunoregulatory and antiangiogenic properties [65].

4.11 Biologicals

4.11.1 TNF-α Inhibitors

TNF-α is a vital cytokine that increases the proliferation of cytokines. Capsaicin inhibits TNF-α by inhibiting NF-κB, substance P, and causes inhibition of cutaneous and axon-reflex vasodilation [66]. Etanercept, a fusion protein, acts as a TNF-α and TNF-β inhibitor, but has a significant molecular weight. It is generally administered subcutaneously, but an ablative fractional laser (Er: YAG laser+etanercept) can deliver etanercept to the epidermis and dermis layer of the skin with low transdermal permeation [67,68]. Etanercept received US FDA approval in 2004 for moderate-to-severe plaque psoriasis or psoriatic arthritis [69].

4.11.2 Janus Kinase/Signal Transducers and Activators of Transcription (JAK/STAT) Inhibitors

JAK inhibitors target specific proinflammatory cascades in psoriasis. Cytokines, such as IL-6, IL-12, IL-22, and IL-23, play a role in the development of psoriasis. They bind to type I and II receptors, which depend on JAKs for signal transduction. Upon the binding of cytokines to their receptor, receptors undergo conformational changes and activate and recruit two JAK proteins. Upon activation, JAK alters the receptor, allows binding of STAT proteins, and results in phosphorylation, dimerization, and translocation to the nucleus to change gene expression. There were four JAK and seven STAT proteins. Inhibition of each subtype of JAK can disrupt various downstream signaling pathways, making it an effective treatment for reducing inflammation in psoriasis [70]. Deucravacitinib is an oral drug approved by the US Food and FDA for the treatment of moderate-to-severe psoriasis. It is a tyrosine kinase 2 (TYK2) inhibitor, a member of the JAK family of inhibitors [71]. Topical JAK inhibitors include tofacitinib, ruxolitinib, and baraticinib. Baraticinib inhibits JAK1 and JAK2 activities by disrupting the production of downstream signaling molecules and proinflammatory mediators. Tofacitinib targets JAK1 and JAK3, whereas ruxolitinib inhibits JAK1 and JAK2. JAK inhibitors prevent the phosphorylation and activation of JAK, inhibiting dimerization and activation of STAT to move from the cell to the nucleus to influence DNA transcription and gene expression. Tofacitinib inhibits the expression of various interleukins, such as IL-16 and IL-23, thus suppressing Th17 differentiation. It also inhibits IL-15 expression, which increases keratinocyte apoptosis. Ruxolitinib suppresses the phosphorylation of STAT3, resulting in reduced expression of IFN-γ [72,73]. Alantolactone, a sesquiterpene, is a STAT3 inhibitor that deactivates the STAT3 pathway and restricts the recruitment of immune cells [74].

4.12 Endogenous Peptide Hormones

α-Melanocyte-stimulating hormone (α-MSH) has anti-inflammatory properties. It downregulates inflammatory cytokines, such as IL-2/4/6/13 and TNF-α, and upregulates the immunosuppressive cytokine IL-10 [75]. Likewise, the endogenous peptide diacerein, used in the treatment of osteoarthritis, inhibits the production of IL-1, IL-1β, IL-12, and TNF-α, and is also a promising agent in the treatment of psoriasis [76]. Bilirubin is an endogenous antioxidant with anti-inflammatory activity. Bilirubin-loaded nanoparticles cross the stratum corneum and internalize into antigen-presenting cells (APCs) and keratinocytes, scavenging excess ROS and inhibiting IL-17-producing T cells [77].

4.13 RNA-Based Treatments

There is a change in the expression of various genes in psoriasis, and RNA-based treatments have been explored. RNA-based treatments are still in an investigational state. Although advances in delivery mechanisms and more targeted approaches have increased the interest in these treatments, they are still not widely approved or used in clinical practice for the treatment of psoriasis. Microinterfer-

ing RNAs (miRNAs) play vital roles in cell differentiation, proliferation, apoptosis, and immune responses. miRNA is highly expressed in psoriatic skin, and topical treatment with biomimetic reconstituted high-density lipoprotein nanogel of miRNA-210-antisense improved the psoriatic symptoms and reversed the immune disorder in the imiquimod-induced mouse model [24]. Similarly, elastic liposomal carriers of RNA interference (RNAi) downregulate human beta-defensin 2, a psoriasis marker, in a psoriatic tissue model [78]. Spherical nucleic acid nanoparticle conjugates (SNA-NCs) of short interfering RNA (siRNA) significantly reduce gene effects and cell proliferation [79].

4.14 Miscellaneous

Anthralin inhibits keratinocyte proliferation. It accumulates in the mitochondria and impairs the energy supply. It also interferes with DNA replication and slows cell division [80]. Tamoxifen, a selective estrogen receptor modulator, inhibits keratinocyte viability and induces an immune shift from Th1 to Th2. It releases anti-inflammatory cytokines such as IL-4, IL-10, and IL-13. Squalene-integrated nanostructured lipid carriers increased the moisture and lipid content of the skin and reduced the Psoriasis Area and Severity Index (PASI) score and proinflammatory cytokine levels [81]. Leflunomide, a disease-modifying antirheumatic drug, exerts an antipsoriatic effect by slowing lymphocyte proliferation. Leflunomide rapidly metabolizes to teriflunomide and inhibits dihydroorotate dehydrogenase, a rate-limiting enzyme in pyrimidine synthesis in lymphocytes, thus modulating DNA synthesis [82]. Pentoxifylline is a hemorheological agent. It inhibits TNF-α and suppresses IL-1, IFN-γ, Th1, and Th2 cells. Additionally, it acts as a vasodilator [83]. Ilomastat belongs to the hydroxamic acid category of reversible metallopeptidase inhibitors (RMIs). A curcumin-based ionic hydrogel loaded with ilomastat improved psoriatic skin lesions in mice by significantly reducing the expression of inflammatory cytokines, collagen-I, and metalloprotease 8 [84]. Fenoldopam mesylate is a highly selective dopamine receptor D1 agonist that is used in the treatment of hypertension. It is also effective in treating psoriasis because of its antiproliferative potential. It binds to dopamine receptor D1 of activated T cells and kills them while having a minimal effect on normal T cells. Glycerin-based carbopol gel of fenoldopam was effective in an imiquimod-induced mouse model [85,86]. A comprehensive table summarizing drugs currently in clinical trials for psoriasis has been previously documented in the literature [26]. In this review, we provide a concise comparison of the key drugs available for psoriasis management, highlighting their mechanisms of action and effect in Table 1 (Ref. [20,23,24,27,28,30,33,37,38,40,42,43,45,46,49,52,64–67,72,75,77,79–82]).

5. Traditional Topical Formulations

Traditional topical formulations, such as creams, lotions, ointments, and gels, offer various benefits but have drawbacks. They may lead to itching, pain, inflammation, and local irritation and can be linked to erythema edema caused by drugs or excipients in the formulation [87]. Molecules with a small molecular weight can pass through the systemic circulation, which may be desired for the systemic delivery of therapeutic agents. However, when a local effect is required, the systemic absorption of the drug molecule may lead to undesirable side effects. For example, long-term use of super-potency corticosteroids may cause hypothalamus-pituitary-adrenal axis (HPA) suppression in young children [88]. Creams and ointments can be greasy, sticky, and have unpleasant odors. They may also be less effective and contain high drug concentrations, potentially affecting patient compliance. Creams, ointments, lotions, and gels exhibit imprecise and unpredictable drug delivery, and drugs do not remain at the site of action for the required period [89].

Nanotechnology plays an important role in overcoming the limitations of the conventional dosage forms. Nanocarriers increase the dermal retention of the drug, deliver the drug at the target site, and reduce the dose, thereby reducing side effects, and increasing patient compliance and acceptability [11]. Agarwal *et al.* [90] reported that the tolerability, efficacy, stability, and acceptability of liposomal gel formulations of dithranol increased in patients with plaque psoriasis compared to traditional cream formulations in an open-label trial. The co-delivery of clobetasol propionate and calcipotriol nanoemulsion loaded in the gel has high retention in the viable epidermis and dermis, negligible skin irritation despite high penetration, and controlled release, as reported by the authors [91]. These are just a few examples that demonstrate the added value of nanotechnology. Given their importance, the following sections provide a detailed overview of nano-based and other technical advances in drug delivery systems for the topical treatment of psoriasis.

6. Advances in Topical Drug Delivery Systems

Psoriasis is an immune-mediated skin condition that requires drugs targeting cells in the epidermis and dermis, including dendritic cells, Langerhans cells, keratinocytes, T lymphocytes, and mast cells. The stratum corneum of the skin is a barrier that limits drug entry to molecules $<$500 Da [92]. In psoriasis, increased epidermal thickness complicates drug delivery Nanocarriers address this challenge via intercellular, transcellular, or appendageal routes. They enhance skin hydration, modify drug properties, mimic skin lipid structures, and utilize permeation enhancers, facilitating drug penetration into deeper skin layers. Additionally,

Table 1. Comparison between different drugs available for management of psoriasis.

Drug Class	Examples	Mechanism of Action	Effect	Reference
Glucocorticoids	Clobetasol propionate, halobetasol propionate, betamethasone dipropionate	Anti-inflammatory, immunosuppressive, and vasoconstriction by binding glucocorticoid receptors and regulating proinflammatory gene expression.	Reduces redness, swelling, and scaling of psoriatic lesions.	[27,28]
Vitamin D3 Analogs	Calcitriol, calcipotriol, maxacalcitol	Promotes keratinocyte differentiation, inhibits proliferation, and modulates immune response.	Reverses dysregulated epidermal differentiation and inhibits keratinocyte proliferation.	[30]
Immunosuppressors	Methotrexate, cyclosporine	Methotrexate inhibits DNA synthesis, cyclosporine suppresses T-cell activity and immune response.	Reduces epidermal cell turnover and inflammation; decreases cell infiltration and epidermal thickness	[20,33]
Retinoids	Acitretin, tazarotene, adapalene	Modulates T-cell response and keratinocyte proliferation, and has anti-inflammatory effects.	Reduces hyperkeratosis and normalizes keratinocyte function.	[37]
S1P Receptor Modulators	Fingolimod, AKP-11, HWG-35D	Modulates immune response by binding sphingosine-1-phosphate receptors and reducing cytokine production and cell proliferation.	Maintains skin barrier function and reduces inflammatory response.	[38,40]
Aryl Hydrocarbon Receptor Agonist	Tapinarof	Regulates keratinocyte function, reduces oxidative stress, and modulates immune responses by activating AhR signaling pathways.	Normalizes skin barrier function, reduces oxidative stress, and inhibits proinflammatory cytokines	[23]
Antimicrobial Peptides	Omiganan, thiostrepton	Inhibits proinflammatory pathways and toll-like receptors on immune cells.	Reduces proinflammatory cytokines and ameliorates inflammation in psoriatic lesions.	[42,43]
PDE-4 Inhibitors	Apremilast, roflumilast	Increases cAMP levels, which in turn suppresses inflammatory cytokine production.	Reduces inflammatory cytokines (TNF-α, IL-6), improving psoriatic symptoms.	[45,46]
Herbal Drugs	Curcumin, berberine	Inhibits proinflammatory cytokines (IL-22, TNF-α), VEGF, and NF-κB signaling; modulates keratinocyte growth and cell proliferation.	Decreases inflammation, blocks cell proliferation, and improves psoriatic lesions.	[49,52]
TNF-α Inhibitors	Capsaicin, etanercept	Blocks TNF-α, preventing the cytokine from inducing inflammatory responses and promoting cell proliferation.	Reduces inflammation and improves clinical symptoms of psoriasis.	[66,67]
JAK/STAT Inhibitors	Tofacitinib, ruxolitinib, baraticinib	Targets JAK/STAT signaling, which is crucial in inflammatory pathways.	Reduces cytokine production, keratinocyte apoptosis, and inflammation in psoriatic lesions	[72]
Nutraceuticals	Oleuropein, EGCG (green tea extract)	Anti-inflammatory and antioxidant effects; supports skin health and immune function.	Supports other treatments.	[64,65]
Endogenous Peptides	α-MSH, bilirubin	α-MSH downregulates proinflammatory cytokines and bilirubin scavenges ROS and inhibits IL-17-producing cells.	Reduces inflammatory cytokines, scavenges ROS, and normalizes immune responses in psoriasis.	[75,77]
RNA-Based Treatments	miRNA-210, siRNA	Modulates gene expression related to inflammation, cell proliferation, and keratinocyte activity through RNA interference mechanisms.	Reduces inflammation and keratinocyte hyperproliferation in psoriatic models.	[24,79]
Miscellaneous	Anthralin, tamoxifen, leflunomide	Inhibits keratinocyte proliferation and induces a shift from Th1 to Th2 immune response; also induces anti-inflammatory cytokines like IL-4, IL-10.	Reduces skin cell proliferation and inflammation, and improves psoriatic symptoms.	[80–82]

Abbreviations: α-MSH, α -melanocyte stimulating hormone; cAMP- cyclic adenosine monophosphate; VEGF, vascular endothelial growth factor ; NF-κB, nuclear factor-kappa B; IL- interleukines; TNF-α, tumor necrosis factor-α; ROS, reactive oxygen species; JAK/STAT, Janus kinase/signal transducer and activator of transcription, Th, T helper cells; S1P, sphingosine-1-phosphate; EGCG, (-)-epigallocatechin-3-gallate.

nanocarriers enable controlled and sustained drug release from the formulations [87]. A detailed discussion on nanotechnology-based delivery systems and the role of the physicochemical properties of nanocarriers in enhancing drug delivery is not included in this review, as it has been comprehensively addressed in other studies [6,11,93–95]. Unlike other reviews, this review adopts a comprehensive and integrative approach, focusing on both emerging therapeutic agents and nanotechnology-based drug delivery systems. While existing reviews have addressed the limitations of conventional therapies and provided broad overviews of topical or systemic treatments, this review uniquely emphasizes the integration of nanotechnology and emerging therapeutics, and the exploration of new therapeutic agents.

6.1 Vesicles

Liposomes are bi-layered vesicles of cholesterol, phospholipids, and fatty acids that encapsulate both hydrophilic and hydrophobic drugs. Liposome lipid composition enables drug delivery via skin. Lipid bilayer vesicles containing large concentrations of ethanol, known as ethosomes, increase permeation to deeper layers of the skin by opening new channels [25,96]. Ethosomes containing anthralin demonstrated significantly superior results in enhancing the PASI, scoring 81.84% compared with liposomes (68.66%) in clinical trials involving patients with psoriasis [80]. Transferosomes, also known as deformable liposomes, have an aqueous core that is surrounded by lipids and amphiphilic surfactants. The elasticity of transferases is due to the presence of edge activators, along with phospholipids, which destabilize the lipid bilayer [97,98]. Transethosomes have the combined properties of transferosomes and ethosomes, and are composed of phospholipids, edge activators, ethanol, and water. They can pass through the stratum corneum and enhance drug delivery to the dermis [25]. Rahangdale and Pandey prepared a topical transethosome formulation of the anti-inflammatory and PDE-4 inhibitor drug apremilast using sodium cholate, Lipiod S 100, and ethanol and incorporated it into 1% carbopol gel. An *ex vivo* permeation study on rat skin demonstrated that the drug penetrates the dermis layer where psoriasis originates, indicating its accessibility for therapeutic action [99]. Niosomes are non-ionic surfactant-based vesicular drug delivery systems. Niosomes are composed of an aqueous core surrounded by a surfactant macromolecule bilayer and cholesterol. Niosomes are osmotically active, less immunogenic, more stable, and less expensive [96]. Ceramide-based liposomes are known as cerosomes. These are composed of sphingolipids. Sphingolipids are natural lipids that make up 45–50% of the intercellular lipids of the stratum corneum and thus increase drug permeation and retention in the skin [100]. Lipospheres are lipid-based nanocarriers with a solid hydrophobic core surrounded by a phospholipid layer that acts as a stabilizer. Lipospheres are easy to prepare and have a low cost, stability, and high aqueous dispersibility. Lipospheres are favored for topical use in psoriasis because of their superior penetration across skin layers. Tacrolimus and curcumin-based liposomes reduced TNF-α, IL-17, and IL-22 levels compared to those in the imiquimod group [101]. Thymoquinone in liposome formulations showed effective skin penetration and gradual drug release. *In vivo*, the results indicated substantial improvements in phenotypic and histopathological features, coupled with a significant decrease in IL-17 and TNF-α levels in psoriatic skin compared to thymoquinone solution [102]. Cubosomes are bicontinuous cubic liquid crystalline systems composed of amphiphilic lipids, stabilizers, and water that can entrap hydrophilic, lipophilic, and amphiphilic drugs. Cubosomes have structural similarities to the skin, thus increasing the penetration of drug molecules. They can also retain moisture in the skin, providing additional benefits for psoriasis treatment [103]. Rapamycin, an immunosuppressant, was efficiently encapsulated in cubosomes using phytantriol, pluronic F127, ethanol, and water. The formulation exhibited a 95% encapsulation efficiency and sustained release for 14 days. Microneedles incorporating this formulation integrated into poly(vinylpyrrolidone) and poly (vinyl alcohol) demonstrated successful skin penetration and localized drug delivery in a skin-mimicking agarose gel. Rapamycin-loaded cubosome-like particles demonstrated antiproliferative effects on natural killer cells *in vitro* [104].

6.2 Nano and Microemulsions

Nanoemulsions are colloidal isotropic drug delivery systems, similar to regular emulsions. They have oil and aqueous phases as dispersed or continuous phases, stabilized by surfactants, but at low concentrations, and the size of droplets ranges from 20 to 500 nm. Microemulsions are similar to nanoemulsions, but the droplet size range is 5–100 nm, and they are thermodynamically stable [6,96]. A cyclosporin microemulsion containing isopropyl myristate, Tween 80, and isopropyl alcohol was formulated to achieve droplet sizes below 50 nm. The local drug depot allowed sustained release of viable skin for 24 h. An *ex vivo* permeation study using goat skin demonstrated that a cyclosporine microemulsion gel significantly enhanced the permeability of cyclosporine compared with a traditional cyclosporine suspension [105].

6.3 Solid Lipid Nanoparticles (SLNs)/Nanostructure Lipid Carriers (NLCs)

SLNs, which are solid at body and room temperature, encapsulate hydrophilic and lipophilic drugs. They feature a lipid core stabilized by a surfactant, which enhances drug penetration through the stratum corneum. SLNs also increase contact with the skin, leading to enhanced skin hydration owing to their occlusive nature. The topical SLN formulation of retinoid acitretin showed an encapsulation efficiency of 89 $\pm$ 1.8%, polydispersity index (PDI) of

0.488, and zeta potential of –17.2 mV. Aciterin-containing SLN in gel showed even skin distribution with 1.75 times more penetration than a drug in gel [106]. NLCs consist of liquid lipids embedded in solid lipids, offer a more lipid matrix, and have better encapsulation efficiency and stability. NLCs have better adhesion properties but low viscosity [25,95]. Fluocinolone acetonide NLC, prepared via a modified microemulsion method, enhanced the *in vitro* drug distribution due to increased drug solubility in the lipid matrix, resulting in limited systemic distribution compared to a plain fluocinolone acetonide suspension [107].

6.4 Micelles

Micelles are colloidal drug delivery systems composed of self-assembled amphiphilic molecules with a core-shell structure above the critical micelle concentration (CMC). Micelles enclose hydrophobic drugs in a nonpolar core, and the polar shell faces the aqueous medium. The small size of micelles mediates crossing the stratum corneum and increases drug deposition in a viable layer of the skin [6,108].

6.5 Dendrimers

Dendrimers are spheroidal, multivalent, hyperbranched, three-dimensional structures with active end groups. Dendrimers are biocompatible, increase the solubility of drugs, form prodrugs (drug-polymer conjugates), control the release of drugs, and increase the skin permeation of topically applied drugs [95].

6.6 Polymeric Carrier

Polymeric nanoparticles incorporate drugs into a polymeric matrix, releasing them through diffusion, erosion, or swelling. Microspheres (1–1000 µm) ensure controlled drug release, osmotically driven by polymer properties, drug amount, or drug-to-polymer ratio. Polymeric nanoparticles (10–100 nm) include nanospheres with dispersed drugs and nanocapsules with a core-shell structure for drug storage [98]. Coal tar-loaded PLGA nanoparticles exhibited a high drug loading of 92%, with a permeability study on the Strat-M membrane indicating 97% local drug accumulation within 24 h. The study also observed improved washability and reduced staining capacity of coal tar compared with crude coal tar [109].

6.7 Metallic Nanoparticles

Metallic nanoparticles are inert particles that are small in size and reactive against living cells [95]. Various metallic nanoparticles such as zinc oxide, silver, gold, and silica have been reported. They increase the permeation of drugs through the skin and exhibit anti-inflammatory properties [110,111]. Methotrexate-loaded gold nanoparticles exhibited 70–80% loading efficiency, proved non-toxic to keratinocytes, demonstrated enhanced penetration in the epidermis and dermis of methotrexate from methotrexate-loaded gold nanoparticles compared to methotrexate alone, and displayed increased drug permeability through mouse skin [112].

6.8 Colloidal Carrier

Colloidal carriers offer many advantages such as high stability, high drug load, solubilization of poorly soluble drugs, and sustained release. Nanosponges (200–500 nm) can entrap hydrophobic and hydrophilic drugs and enhance cutaneous drug retention. Microsponges (size range 5–300 µm) provide prolonged contact time of the drug with the skin. It increases epidermal drug content while preventing absorption into the systemic circulation [113]. The microsponges of clobetasol propionate provide high encapsulation efficiency and a zero-order drug release pattern. *In vivo* drug efficacy research showed better antipsoriatic effects and reduced side effects compared to plain clobetasol propionate gel [114]. Cyclodextrin nanosponges of dithranol showed marked improvement in the antipsoriatic activity of the drug compared to the untreated group [115].

6.9 Microneedles

Microneedles, a non-invasive drug delivery system, penetrate the thick stratum corneum of the skin and enhance drug retention in the epidermis and dermis. Dissolvable microneedles improve drug delivery by dissolving them after their insertion into the skin [116]. Lu *et al*. [117] prepared a novel black phosphorus (BP)-loaded hydrogel inverse opal microneedle with photo and thermal responsive capability. The microneedle was composed of BP-loaded N-isopropyl acrylamide (NIPAM)/poly (ethylene glycol) diacrylate (PEGDA) inverse opal hydrogel scaffold and gelatin/agarose filled scaffold for drug loading. It was fabricated via nanoparticle assembly, and reversed-phase replication with micro-molding, which enables hydrophobic drug loading and photothermal responsive controlled drug delivery. This method enables good medication administration and efficiently improves psoriatic skin conditions by lowering the synthesis of inflammatory cytokines and epidermal hyperplasia in mice compared with calcipotriol ointment treatment. The dissolving microneedle array significantly increased the skin deposition of tofacitinib citrate (835 µg/cm^2) compared with the control cream (143.98 µg/cm^2) [73].

6.10 Technology-Assisted Drug Delivery

Various technical advances have also been explored to enhance drug delivery to the skin in psoriatic conditions. The increased epidermal thickness in psoriasis makes drug delivery via the topical route difficult, despite it being the preferred method for treating this condition. Skin pretreatment with a fractional laser using an Er: YAG laser device creates micropores and causes minimum coagulation, increasing drug penetration through the skin [67]. Iontophoresis uses a mild electric field to

Table 2. Topical delivery of various drug molecules in nano-formulations.

Drug	Class	Nanocarrier	Advantages	Reference
Clobetasol propionate	SHPG	Cyclodextrin nanosponge (CDNS)	Better payload, controlled release, reduced side effects, improved effectiveness	[113]
		SLN	High skin permeation and deposition	[124]
		Microsponge	Absence of burst release, sustained release	[114]
		Polymeric nanoparticles	Delayed and high drug release, fewer side effects	[125]
Desoximetasone	SHPG	Niosomes	Reduced drug dose, dose frequency	[126]
Betamethasone	HPG	Hydrogel	Sustained release, cooling effect	[127]
Betamethasone 17-valerate	HPG	SLN	Controlled release, epidermis/dermis targeting	[128]
Mometasone furoate	HPG	Aspasomes	Prolonged release, skin smoothening	[129]
Triamcinolone acetonide	MPG	Transferosomes	Skin penetration and distribution, controlled release	[130]
Fluocinolone acetonide	MPG	Microemulsion and fractional laser	High efficiency, sustained release	[131]
		NLC	Increased skin permeation and retention	[107]
		Polypeptide drug conjugate	Drug permeation in epidermis, controlled release	[132]
		SLN	Increased skin distribution, low systemic absorption	[133]
Hydrocortisone	LPG	Electrospun nanofibers	100% drug release, no cytotoxicity	[134]
		Microemulsion	Retention in the skin and low penetration through the skin	[135]
		NLC	Protection against degradation, no fast-release	[136]
Calcipotriol	VDA	Liposomes	Increased skin penetration and deposition	[137]
Methotrexate	Immuno-suppressant	ZnO/Ag hybrid mesoporous microspheres	Self-therapeutic ability, sustained release, enhanced drug delivery	[110]
		Liquid crystals with lamellar phase	Extensive remodeling of skin microstructure- increased hair follicles, congestion of blood vessels	[138]
		Fractional CO_2 laser-assisted delivery for nail psoriasis	Reduced subungual hematoma and pain compared to intralesional injection	[120]
		Transdermal patch	Sustained release, better skin permeation	[139]
		ROS-responsive methotrexate prodrug nanoassemblies microneedle	Significant epidermal penetration, suppression of epidermal proliferation	[140]
		Microporation and iontophoresis	High drug delivery to the skin	[141]
		Nanogel	Enhanced transdermal flux	[142]
		Microemulsion	Cutaneous drug distribution	[143]
		Niosomes	High entrapment efficiency, stable	[144]
		NLC	Increased drug deposition, deep skin penetration, prolonged release	[145]
		Gold nanoparticles	Better anti-inflammatory efficacy, reduced proliferation and differentiation of keratinocytes	[146]
		Liposomes	Improved drug retention and penetration in the skin	[147]
		Deformable liposomes	3–4-fold increase in skin permeation, high encapsulation efficiency	[148]
		NLC	High skin penetration, fast drug release	[149]
Cyclosporine	Immuno-suppressant	Ethosomes	Enhanced drug deposition	[150]
		Polymeric micelles	Enhanced cutaneous delivery, deep skin penetration	[151]
		Electroporation	High skin penetration, low systemic absorption	[119]
		Iontophoresis	High skin permeation	[123]
		Niosomes	59-fold increase in skin deposition	[152]
		Nanoemulsion	No cytotoxicity and skin irritation, increased hydration	[153]
		Microemulsion	Quick cutaneous uptake. Increase skin accumulation	[154]
		Microemulsion	High skin deposition, low distribution to other organs	[155]

Table 2. Continued.

Drug	Class	Nanocarrier	Advantages	Reference
Tacrolimus	Immuno-suppressant	Polymeric nanoparticles	Increased skin deposition and retention	[156]
		Self-assembled lipid-polymer hybrid nanoparticles	Increased drug loading, high cutaneous deposition	[157]
		NLC	High skin retention and permeation	[158]
		Hydrogel	2-fold increase in skin deposition, high efficiency	[159]
		Microemulsion	Enhanced permeation and deposition, increased cellular uptake	[160]
		Liquid crystalline nanoparticles	Increased skin permeation and retention	[161]
		Polymeric micelles	High deposition in hair follicles	[162]
Tazarotene	Retinoid derivative	SLN	Improved drug release	[163]
		Microemulsion	Higher skin deposition and anti-psoriatic activity, no irritation	[164]
		Magnetically responsive nanofiber patch	On-off response-based drug release, minimum skin irritation	[165]
		Microemulsion	High skin deposition, high efficacy	[166]
Acitretin	Retinoid derivative	Solid dispersion	Increased solubility, increased skin permeation, and hydration	[167]
		Niosomes	Enhanced skin permeation and deposition, less skin irritation	[168]
Retinol	Retinoid derivative	Silicon particles	Slow release, protection against degradation	[169]
Omiganan	Antimicrobial 0eptide	Liposomes	Better permeation, controlled release	[42]
Curcumin	Herbal drug	Nano-emulsion	4.87-fold increase in skin permeation	[170]
		Nano-hydrogel	Protection against degradation, increased skin penetration	[171]
		NLC	3.24-fold improvement in skin permeation, no cytotoxicity	[172]
		Nanogel	Sustained release, good permeation and retention	[173]
		Ethosomes	Targeted delivery, increased skin accumulation	[174]
		Polymeric nanoparticles	Skin penetration, slow release	[175]
		Polymeric nanoparticles	Enhances skin penetration and accumulation, sustained release	[176]
		Nanofibers	Enhanced skin permeation and deposition	[177]
Erianin	Herbal drug	Mesoporous silica nanospheres	High drug retention, low drug penetration in skin	[56]
Capsaicin	Herbal drug	NLC	Increased drug accumulation in skin, no skin irritation	[178]
Babchi oil (Psoralea *corylifolia*)	Herbal drug	Nanogel	2-folds high efficacy	[179]
		Microemulsion	Significant skin permeation	[180]
Methoxsalen	Herbal drug	Microemulsion	10-fold high deposition in the skin, no skin irritation	[181]
		Microemulsion	Increased skin penetration and accumulation	[58]
Celastrol	Herbal drug	Niosomes	Accumulation in skin, enhanced cell uptake	[182]
		Niosomes	Increased water solubility and permeation	[55]
Berberine oleate	Herbal drug	Liquid crystalline nanoparticles	3-fold increase in drug deposition, enhanced permeation	[52]
Rosmarinic Acid	Herbal drug	Transethosomes	Increased solubility, sustained release	[50]
Oleuropein	Nutraceutical	Microemulsion	Better PASI scoring than the marketed formulation	[64]
(-)-epigallocatechin-3-gallate (EGCG)	Nutraceutical	Polymeric nanoparticles	Dose reduction, sustained release	[65]
Bilirubin	Endogenous peptide	Polymeric nanoparticles	Attenuation of oxidative stress in keratinocytes, reduced inflammatory cytokines	[77]
Diacerein	Endogenous peptide	Niosomes	Cutaneous penetration, high entrapment efficiency	[76]
Pentoxifylline	TNF-α inhibitor	Niosomes	Deep skin penetration and deposition	[83]
		NLC	High drug retention	[183]

Table 2. Continued.

Drug	Class	Nanocarrier	Advantages	Reference
Etanercept	TNF-α inhibitor	Ablative fractional laser microporation	Well tolerated, mild local side effects	[67]
		Er: YAG fractional laser ablation	Drug delivery to the epidermis and dermis	[68]
		Thermosensitive hydrogel	Drug delivery to viable epidermis, stable	[184]
Tofacitinib citrate	JAK inhibitors	Microneedle arrays	Enhanced intradermal drug deposition	[73]
Alantolactone	STAT3 inhibitor	Polymeric nanoparticles	Abrogated keratocyte hyperproliferation and inflammation	[74]
Apremilast	PDE4 inhibitor	NLC	Enhanced skin retention by 3-folds, no skin irritation, no cytotoxicity	[185]
		Nanocrystal	2-folds increased aqueous solubility, enhanced skin penetration	[186]
		Microemulsion	No cytotoxicity reduced inflammatory cytokines	[157]
		Transethosomes	Better skin permeation, sustained release	[99]
		NLC	Drug deposition in the skin, sustained release	[45]
SiRNA	IL-6 inhibitor	Polymeric nanoparticle and ablative laser (fractional CO_2 laser and a fully ablative Er: YAG laser)	Low toxicity, up to 3.3-fold skin deposition, and 56% IL-6 knockdown in mice	[187]
	EGF and EGFR knockdown	*Gene*–nanoparticle conjugate	Excellent penetration in skin, *gene* knockdown	[79]
Anthralin	Anthracene derivative	Ethosomes	High permeation, low side effects	[80]
		Liposomes/niosomes	Enhanced skin permeation of liposomes more than niosomes	[90]
		Dendritic nanoparticles	Controlled release, increased skin accumulation	[188]

Abbrevations: SHPG, super high potency glucocorticoids; CDNS, Cyclodextrin nanosponge; SLN, solid lipid nanoparticles; HPG, high potency glucorticoids; MPG, mid potency glucocorticoids; NLC, nanostructured lipid carriers; LPG, low potency glucocrticoids; VDA, vitamin D analogues; ROS, reactive oxygen species; TNF-α, tumor necrosis factor-α; JAK, janus kinase; STAT3, signal transducer and activator of transcription 3; PDE4, phosphodiesterase 4; IL-6, interleukin 6; EGF, epidermal growth factor; EGFR, epidermal growth factor receptor.

move a charged drug from the application site to the target site. The movement occurs because of electron repulsion or convection flow. Iontophoresis increases the transdermal penetration of drugs, depending on ionic strength [118]. Electroporation uses a high voltage of milliseconds to the skin to generate an electric pulse and create pores for transit time. Therefore, it increases drug transport due to electroosmosis and diffusion [119]. Recent clinical studies have shown that fractional CO_2 laser technology for the delivery of methotrexate is a promising, efficacious, and well-tolerated substitute for the conventional method of intralesional injection in the treatment of nail psoriasis [120,121]. There was a significant improvement in the nail bed and Nail Psoriasis Severity Index (NAPSI) scores for combined fractional CO_2 laser and calcipotriol/betamethasone ointment preparation compared to fractional CO_2 laser alone in a clinical trial in 30 patients. NAPSI scores were calculated at the beginning of the study and 3 months after the last laser session. The patients received six laser sessions at 4-month intervals [122]. Wang *et al*. [119] proposed that there is a six-fold increase in the penetration of cyclosporin solution in 40% ethanol compared to passive diffusion using multiple pulse electroporation. Iontophoresis-assisted delivery can also effectively enhance the skin permeation of cyclosporin, particularly when combined with lecithin vesicles [123]. Table 2 (Ref. [42,45,50,52,55,56,58,64,65,67,68,73,74,76,77,79,80,83,90,99,107,110,113,114,119,120,123–188]) provides an overview of various nano-formulations of drugs used in psoriasis treatment. Detailed information on patented nanotechnology-based drug delivery systems can be found in existing literature.

The combination of innovative therapeutic agents with nanotechnology is transforming psoriasis management. It bridges the gap between drug innovation and effective delivery. By using advancements in nanotechnology, the limitations of conventional formulations, such as poor bioavailability, instability, and systemic side effects can be systematically addressed, paving the way for more effective treatment approaches.

7. Challenges and Limitations

Psoriasis is driven by complex immune system dysregulation, leading to inflammation and the rapid turnover

of skin cells. Despite advancements in psoriasis treatment, several needs are still unmet. Traditional topical therapies may lead to poor skin penetration and retention, leading to suboptimal therapeutic outcomes. High costs and accessibility barriers also confine the widespread utilization of these advanced treatments.

Nanotechnology-based therapies are promising, but not without limitations. The industrial scale-up of nanoformulations is challenging due to complex manufacturing processes, regulatory challenges, and the need for precise quality control to ensure reproducibility and stability. Furthermore, the long-term safety and efficacy of nanoformulations require further clinical validation.

Finally, while natural agents and emerging drugs offer potential, their integration into scalable and clinically validated therapeutics still needs extensive research and development. For instance, biologics such as monoclonal antibodies that target specific components of the immune response (like TNF-α inhibitors) have already transformed the management of moderate to severe psoriasis. However, these therapies are expensive and typically require systemic administration, which can lead to significant side effects. The development of cost-effective, patient-friendly solutions that balance efficacy, safety, and accessibility remains a critical goal for advancing psoriasis treatment.

8. Conclusion

Psoriasis is a chronic inflammatory skin condition that affects approximately 2–3% of the global population, posing significant challenges for both those affected and society as a whole. Although the specific mechanism involved in the development of psoriasis is still unclear, it mainly occurs due to abnormal differentiation and hyperproliferation of keratinocytes, leading to many structural and functional alterations in the skin. Conventional drug delivery systems provide insufficient skin penetration and retention and can also lead to systemic drug leaching. Therefore, nanoenabled drug delivery is required. With the increase in the understanding of the pathophysiology of psoriasis and various advances in nanotechnology-based drug delivery systems, it is possible to deliver the drug at the target site and enhance drug permeation and retention in the skin. The potential of many existing and new drug molecules is being explored, and various target sites are being identified. The exploration of both existing and novel drug molecules, along with the identification of new target sites, is underway and has shown potential. Combining possible therapeutic agents and nanotechnology could revolutionize the treatment of psoriasis, offering more efficient management and potentially shortening the treatment duration. Such advancements are likely to improve the quality of life of psoriasis patients. Future research should focus on developing disease-specific drugs and formulation techniques that can be scaled up to the industrial level while remaining safe, cost-effective, and providing more social benefits.

Author Contributions

JU, NH, SP, TK, MN, KYT and MNA designed the study. TK, MN, and KYT wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

The authors extend their appreciation to the Deanship of Research and Graduate Studies at King Khalid University for this work through a Large Research Project.

Funding

The work was supported by the Deanship of Research and Graduate Studies at King Khalid University for funding this work through a Large Research Project under grant number RGP2/580/45.

Conflict of Interest

Sudeep Pukale is a consultant/proctor of Lupin Research Park, the judgments in data interpretation and writing were not influenced by this relationship. All other authors have no conflicts relevant to the contents of this paper to disclose.

References

[1] Patel P, Pal R, Butani K, Singh S, Prajapati BG. Nanomedicine-fortified cosmeceutical serums for the mitigation of psoriasis and acne. Nanomedicine (London, England). 2023; 18: 1769–1793. https://doi.org/10.2217/nnm-2023-0147.

[2] Zeng M, Guo D, Fernández-Varo G, Zhang X, Fu S, Ju S, *et al*. The Integration of Nanomedicine with Traditional Chinese Medicine: Drug Delivery of Natural Products and Other Opportunities. Molecular Pharmaceutics. 2023; 20: 886–904. https://doi.org/10.1021/acs.molpharmaceut.2c00882.

[3] Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. Canadian Family Physician Medecin De Famille Canadien. 2017; 63: 278–285.

[4] AlQassimi S, AlBrashdi S, Galadari H, Hashim MJ. Global burden of psoriasis - comparison of regional and global epidemiology, 1990 to 2017. International Journal of Dermatology. 2020; 59: 566–571. https://doi.org/10.1111/ijd.14864.

[5] Weigle N, McBane S. Psoriasis. American Family Physician. 2013; 87: 626–633.

[6] Jyothi SL, Krishna KL, Ameena Shirin VK, Sankar R, Pramod K, Gangadharappa HV. Drug delivery systems for the treatment of psoriasis: Current status and prospects. Journal of Drug Delivery Science and Technology. 2021; 62: 102364. https://doi.org/10.1016/J.JDDST.2021.102364.

[7] Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk Factors for the Development of Psoriasis. International Journal of Molecular Sciences. 2019; 20: 4347. https://doi.org/10.3390/ijms20184347.

[8] Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker JNWN. Psoriasis. Lancet. 2021; 397: 1301–1315.

[9] Duchnik E, Kruk J, Tuchowska A, Marchlewicz M. The Impact of Diet and Physical Activity on Psoriasis: A Narrative Review of the Current Evidence. Nutrients. 2023; 15: 840. https://doi.org/10.3390/nu15040840.
[10] Petit RG, Cano A, Ortiz A, Espina M, Prat J, Muñoz M, *et al*. Psoriasis: From Pathogenesis to Pharmacological and Nano-Technological-Based Therapeutics. International Journal of Molecular Sciences. 2021; 22: 4983. https://doi.org/10.3390/ijms22094983.
[11] Gomes GS, Frank LA, Contri RV, Longhi MS, Pohlmann AR, Guterres SS. Nanotechnology-based alternatives for the topical delivery of immunosuppressive agents in psoriasis. International Journal of Pharmaceutics. 2023; 631: 122535. https://doi.org/10.1016/j.ijpharm.2022.122535.
[12] Rapalli VK, Waghule T, Gorantla S, Dubey SK, Saha RN, Singhvi G. Psoriasis: pathological mechanisms, current pharmacological therapies, and emerging drug delivery systems. Drug Discovery Today. 2020; 25: 2212–2226. https://doi.org/10.1016/j.drudis.2020.09.023.
[13] Liu W. The Involvement of Cysteine-X-Cysteine Motif Chemokine Receptors in Skin Homeostasis and the Pathogenesis of Allergic Contact Dermatitis and Psoriasis. International Journal of Molecular Sciences. 2024; 25: 1005. https://doi.org/10.3390/ijms25021005.
[14] Noor AAM, Nor AKCM, Redzwan NM. The immunological understanding on germinal center B cells in psoriasis. Journal of Cellular Physiology. 2024; 239: e31266. https://doi.org/10.1002/jcp.31266.
[15] Capon F. The Genetic Basis of Psoriasis. International Journal of Molecular Sciences. 2017; 18: 2526. https://doi.org/10.3390/ijms18122526.
[16] Takahashi T, Yamasaki K. Psoriasis and Antimicrobial Peptides. International Journal of Molecular Sciences. 2020; 21: 6791. https://doi.org/10.3390/ijms21186791.
[17] Morizane S, Gallo RL. Antimicrobial peptides in the pathogenesis of psoriasis. The Journal of Dermatology. 2012; 39: 225–230. https://doi.org/10.1111/j.1346-8138.2011.01483.x.
[18] Zhou X, Chen Y, Cui L, Shi Y, Guo C. Advances in the pathogenesis of psoriasis: from keratinocyte perspective. Cell Death & Disease. 2022; 13: 81. https://doi.org/10.1038/s41419-022-04523-3.
[19] Sala M, Elaissari A, Fessi H. Advances in psoriasis physiopathology and treatments: Up to date of mechanistic insights and perspectives of novel therapies based on innovative skin drug delivery systems (ISDDS). Journal of Controlled Release: Official Journal of the Controlled Release Society. 2016; 239: 182–202. https://doi.org/10.1016/j.jconrel.2016.07.003.
[20] Peters BP, Weissman FG, Gill MA. Pathophysiology and treatment of psoriasis. American Journal of Health-system Pharmacy: AJHP: Official Journal of the American Society of Health-System Pharmacists. 2000; 57: 645–6459; quiz 660–661. https://doi.org/10.1093/ajhp/57.7.645.
[21] Armstrong AW, Read C. Pathophysiology, Clinical Presentation, and Treatment of Psoriasis: A Review. JAMA. 2020; 323: 1945–1960. https://doi.org/10.1001/jama.2020.4006.
[22] Lowes MA, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Nature. 2007; 445: 866–873. https://doi.org/10.1038/nature05663.
[23] Jaleel N, Navya VS, George M. Tapinarof: A Novel Topical Agent For Psoriasis. Indian Dermatology Online Journal. 2023; 14: 916–918. https://doi.org/10.4103/idoj.idoj_309_23.
[24] Feng H, Wu R, Zhang S, Kong Y, Liu Z, Wu H, *et al*. Topical administration of nanocarrier miRNA-210 antisense ameliorates imiquimod-induced psoriasis-like dermatitis in mice. The Journal of Dermatology. 2020; 47: 147–154. https://doi.org/10.1111/1346-8138.15149.
[25] Lee HJ, Kim M. Challenges and Future Trends in the Treatment of Psoriasis. International Journal of Molecular Sciences. 2023; 24: 13313. https://doi.org/10.3390/ijms241713313.
[26] Drakos A, Vender R. A Review of the Clinical Trial Landscape in Psoriasis: An Update for Clinicians. Dermatology and Therapy. 2022; 12: 2715–2730. https://doi.org/10.1007/s13555-022-00840-9.
[27] Uva L, Miguel D, Pinheiro C, Antunes J, Cruz D, Ferreira J, *et al*. Mechanisms of action of topical corticosteroids in psoriasis. International Journal of Endocrinology. 2012; 2012: 561018. https://doi.org/10.1155/2012/561018.
[28] Bos JD, Spuls PI. Topical treatments in psoriasis: today and tomorrow. Clinics in Dermatology. 2008; 26: 432–437. https://doi.org/10.1016/j.clindermatol.2007.10.025.
[29] Segaert S, Ropke M. The biological rationale for use of vitamin d analogs in combination with corticosteroids for the topical treatment of plaque psoriasis. Journal of Drugs in Dermatology: JDD. 2013; 12: e129–e137.
[30] Trémezaygues L, Reichrath J. Vitamin D analogs in the treatment of psoriasis: Where are we standing and where will we be going? Dermato-endocrinology. 2011; 3: 180–186. https://doi.org/10.4161/derm.3.3.17534.
[31] Barrea L, Savanelli MC, Di Somma C, Napolitano M, Megna M, Colao A, *et al*. Vitamin D and its role in psoriasis: An overview of the dermatologist and nutritionist. Reviews in Endocrine & Metabolic Disorders. 2017; 18: 195–205. https://doi.org/10.1007/s11154-017-9411-6.
[32] Fda, Cder. CENTER FOR DRUG EVALUATION AND RESEARCH Approval Package for: ANDA 90-633 CENTER FOR DRUG EVALUATION AND RESEARCH 2010. Available at: https://www.fda.gov (Accessed: 2 October 2024).
[33] Heule F, Laijendecker R, van Joost T. Topical cyclosporin A treatment in psoriasis and other dermatological diseases: Theoretical and practical aspects. The Journal of Dermatological Treatment. 1992; 2: 149–153. https://doi.org/10.3109/09546639209092744.
[34] Fernandes IC, Torres T, Selores M. Maintenance treatment of psoriasis with cyclosporine A: comparison between continuous and weekend therapy. Journal of the American Academy of Dermatology. 2013; 68: 341–342. https://doi.org/10.1016/j.jaad.2012.08.013.
[35] Ermertcan AT, Ozturkcan S. Topical Calcineurin Inhibitors, Pimecrolimus and Tacrolimus. Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry. 2008; 6: 237–243. https://doi.org/10.2174/187152307781368300.
[36] Clark S. Etretinate. XPharm: The Comprehensive Pharmacology Reference (pp. 1–4). Elsevier: the Netherlands. 2007. https://doi.org/10.1016/B978-008055232-3.61730-1.
[37] van de Kerkhof PCM. Update on retinoid therapy of psoriasis in: an update on the use of retinoids in dermatology. Dermatologic Therapy. 2006; 19: 252–263. https://doi.org/10.1111/j.1529-8019.2006.00082.x.
[38] Sharma S, Mathur AG, Pradhan S, Singh DB, Gupta S. Fingolimod (FTY720): First approved oral therapy for multiple sclerosis. Journal of Pharmacology & Pharmacotherapeutics. 2011; 2: 49–51. https://doi.org/10.4103/0976-500X.77118.
[39] Bieber T. Atopic dermatitis: an expanding therapeutic pipeline for a complex disease. Nature Reviews. Drug Discovery. 2022; 21: 21–40. https://doi.org/10.1038/s41573-021-00266-6.
[40] Pinto LM, Chiricozzi A, Calabrese L, Mannino M, Peris K. Novel Therapeutic Strategies in the Topical Treatment of Atopic Dermatitis. Pharmaceutics. 2022; 14: 2767. https://doi.org/10.3390/pharmaceutics14122767.
[41] Prieto K, Duong JQ, Feldman SR. Tapinarof cream for the topical treatment of plaque psoriasis in adults. Expert Review of Clinical Immunology. 2024; 20: 327–337. https://doi.org/10.

1080/1744666X.2023.2296607.
[42] Javia A, Misra A, Thakkar H. Liposomes encapsulating novel antimicrobial peptide Omiganan: Characterization and its pharmacodynamic evaluation in atopic dermatitis and psoriasis mice model. International Journal of Pharmaceutics. 2022; 624: 122045. https://doi.org/10.1016/j.ijpharm.2022.122045.
[43] Lai CY, Yeh DW, Lu CH, Liu YL, Huang LR, Kao CY, *et al*. Identification of Thiostrepton as a Novel Inhibitor for Psoriasis-like Inflammation Induced by TLR7-9. Journal of Immunology (Baltimore, Md.: 1950). 2015; 195: 3912–3921. https://doi.org/10.4049/jimmunol.1500194.
[44] Milakovic M, Gooderham MJ. Phosphodiesterase-4 Inhibition in Psoriasis. Psoriasis (Auckland, N.Z.). 2021; 11: 21–29. https://doi.org/10.2147/PTT.S303634.
[45] Madan JR, Khobaragade S, Dua K, Awasthi R. Formulation, optimization, and in vitro evaluation of nanostructured lipid carriers for topical delivery of Apremilast. Dermatologic Therapy. 2020; 33: e13370. https://doi.org/10.1111/dth.13370.
[46] Pixley JN, Schaetzle T, Feldman SR. A Review of Topical Roflumilast for the Treatment of Plaque Psoriasis. The Annals of Pharmacotherapy. 2023; 57: 966–969. https://doi.org/10.1177/10600280221137750.
[47] Thurston AW, Jr, Osborne DW, Snyder S, Higham RC, Burnett P, Berk DR. Pharmacokinetics of Roflumilast Cream in Chronic Plaque Psoriasis: Data from Phase I to Phase III Studies. American Journal of Clinical Dermatology. 2023; 24: 315–324. https://doi.org/10.1007/s40257-022-00741-9.
[48] Eichenfield LF, Tarabar S, Forman S, García-Bello A, Feng G, Fetterly G, *et al*. Efficacy and Safety of PF-07038124 in Patients With Atopic Dermatitis and Plaque Psoriasis: A Randomized Clinical Trial. JAMA Dermatology. 2024; 160: 156–163. https://doi.org/10.1001/jamadermatol.2023.4990.
[49] Zhang S, Wang J, Liu L, Sun X, Zhou Y, Chen S, *et al*. Efficacy and safety of curcumin in psoriasis: preclinical and clinical evidence and possible mechanisms. Frontiers in Pharmacology. 2022; 13: 903160. https://doi.org/10.3389/fphar.2022.903160.
[50] Rodríguez-Luna A, Talero E, Ávila-Román J, Romero AMF, Rabasco AM, Motilva V, *et al*. Preparation and In Vivo Evaluation of Rosmarinic Acid-Loaded Transethosomes After Percutaneous Application on a Psoriasis Animal Model. AAPS PharmSciTech. 2021; 22: 103. https://doi.org/10.1208/s12249-021-01966-3.
[51] Gavra DI, Endres L, Pető Á, Józsa L, Fehér P, Ujhelyi Z, *et al*. In Vitro and Human Pilot Studies of Different Topical Formulations Containing *Rosa* Species for the Treatment of Psoriasis. Molecules (Basel, Switzerland). 2022; 27: 5499. https://doi.org/10.3390/molecules27175499.
[52] Freag MS, Torky AS, Nasra MM, Abdelmonsif DA, Abdallah OY. Liquid crystalline nanoreservoir releasing a highly skin-penetrating berberine oleate complex for psoriasis management. Nanomedicine (London, England). 2019; 14: 931–954. https://doi.org/10.2217/nnm-2018-0345.
[53] Chavoshy F, Zadeh BSM, Tamaddon AM, Anbardar MH. Delivery and Anti-Psoriatic Effect of Silibinin-Loaded Polymeric Micelles: An Experimental Study in the Psoriatic Skin Model. Current Drug Delivery. 2020; 17: 787–798. https://doi.org/10.2174/1567201817666200722141807.
[54] Mestry M, Rane M, Bajaj A. Commiphora mukul and quercetin loaded liposphere gel: Potential treatment for psoriasis. Indian Journal of Pharmaceutical Education and Research. 2020; 54: 654–667. https://doi.org/10.5530/ijper.54.3.115.
[55] Meng S, Sun L, Wang L, Lin Z, Liu Z, Xi L, *et al*. Loading of water-insoluble celastrol into niosome hydrogels for improved topical permeation and anti-psoriasis activity. Colloids and Surfaces. B, Biointerfaces. 2019; 182: 110352. https://doi.org/10.1016/j.colsurfb.2019.110352.
[56] Mo C, Lu L, Liu D, Wei K. Development of erianin-loaded dendritic mesoporous silica nanospheres with pro-apoptotic effects and enhanced topical delivery. Journal of Nanobiotechnology. 2020; 18: 55. https://doi.org/10.1186/s12951-020-00608-3.
[57] Zhang YT, Shen LN, Wu ZH, Zhao JH, Feng NP. Comparison of ethosomes and liposomes for skin delivery of psoralen for psoriasis therapy. International Journal of Pharmaceutics. 2014; 471: 449–452. https://doi.org/10.1016/j.ijpharm.2014.06.001.
[58] Baroli B, López-Quintela MA, Delgado-Charro MB, Fadda AM, Blanco-Méndez J. Microemulsions for topical delivery of 8-methoxsalen. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2000; 69: 209–218. https://doi.org/10.1016/s0168-3659(00)00309-6.
[59] Lboutounne H, Guillaume YC, Michel L, Makki S, Humbert P, Millet J. Study and development of encapsulated forms of 4, 5′, 8-Trimethylpsoralen for topical drug delivery. Drug Development Research. 2004; 61: 86–94. https://doi.org/10.1002/DDR.10339.
[60] Ahmad A, Abuzinadah MF, Alkreathy HM, Banaganapalli B, Mujeeb M. Ursolic acid rich Ocimum sanctum L leaf extract loaded nanostructured lipid carriers ameliorate adjuvant induced arthritis in rats by inhibition of COX-1, COX-2, TNF-α and IL-1: Pharmacological and docking studies. PloS One. 2018; 13: e0193451. https://doi.org/10.1371/journal.pone.0193451.
[61] Miastkowska M, Kulawik-Pióro A, Lasoń E, Śliwa K, Malinowska MA, Sikora E, *et al*. Topical Formulations Based on Ursolic Acid-Loaded Nanoemulgel with Potential Application in *Psoriasis* Treatment. Pharmaceutics. 2023; 15: 2559. https://doi.org/10.3390/pharmaceutics15112559.
[62] Garcia-Bilbao A, Gómez-Fernández P, Larush L, Soroka Y, Suarez-Merino B, Frušić-Zlotkin M, *et al*. Preparation, characterization, and biological evaluation of retinyl palmitate and Dead Sea water loaded nanoemulsions toward topical treatment of skin diseases. Journal of Bioactive and Compatible Polymers. 2020; 35: 24–38. https://doi.org/10.1177/0883911519885970.
[63] Nasri H, Baradaran A, Shirzad H, Rafieian-Kopaei M. New concepts in nutraceuticals as alternative for pharmaceuticals. International Journal of Preventive Medicine. 2014; 5: 1487–1499.
[64] El-Gogary RI, Ragai MH, Moftah N, Nasr M. Oleuropein as a novel topical antipsoriatic nutraceutical: formulation in microemulsion nanocarrier and exploratory clinical appraisal. Expert Opinion on Drug Delivery. 2021; 18: 1523–1532. https://doi.org/10.1080/17425247.2021.1932813.
[65] Chamcheu JC, Siddiqui IA, Adhami VM, Esnault S, Bharali DJ, Babatunde AS, *et al*. Chitosan-based nanoformulated (-)-epigallocatechin-3-gallate (EGCG) modulates human keratinocyte-induced responses and alleviates imiquimod-induced murine psoriasiform dermatitis. International Journal of Nanomedicine. 2018; 13: 4189–4206. https://doi.org/10.2147/IJN.S165966.
[66] Gupta R, Gupta M, Mangal S, Agrawal U, Vyas SP. Capsaicin-loaded vesicular systems designed for enhancing localized delivery for psoriasis therapy. Artificial Cells, Nanomedicine, and Biotechnology. 2016; 44: 825–834. https://doi.org/10.3109/21691401.2014.984301.
[67] Bauer M, Lackner E, Matzneller P, Al Jalali V, Pajenda S, Ling V, *et al*. Phase I Study to Assess Safety of Laser-Assisted Topical Administration of an Anti-TNF Biologic in Patients With Chronic Plaque-Type Psoriasis. Frontiers in Medicine. 2021; 8: 712511. https://doi.org/10.3389/fmed.2021.712511.
[68] Del Río-Sancho S, Lapteva M, Sonaje K, Böhler C, Ling V, Boehncke WH, *et al*. Targeted cutaneous delivery of etanercept using Er:YAG fractional laser ablation. International Journal of Pharmaceutics. 2020; 580: 119234. https://doi.org/10.1016/j.ijpharm.2020.119234.
[69] Nguyen TU, Koo J. Etanercept in the treatment of plaque psori-

asis. Clinical, Cosmetic and Investigational Dermatology. 2009; 2: 77–84. https://doi.org/10.2147/ccid.s3412.

[70] Megna M, Potestio L, Ruggiero A, Cacciapuoti S, Maione F, Tasso M, *et al*. JAK Inhibitors in Psoriatic Disease. Clinical, Cosmetic and Investigational Dermatology. 2023; 16: 3129–3145. https://doi.org/10.2147/CCID.S433367.

[71] Kingston P, Blauvelt A, Strober B, Armstrong AW. Deucravacitinib: a novel TYK2 inhibitor for the treatment of moderate-to-severe psoriasis. Journal of Psoriasis and Psoriatic Arthritis. 2023; 8: 156–165. https://doi.org/10.1177/24755303231201336.

[72] Hsu L, Armstrong AW. JAK inhibitors: treatment efficacy and safety profile in patients with psoriasis. Journal of Immunology Research. 2014; 2014: 283617. https://doi.org/10.1155/2014/283617.

[73] Cárcamo-Martínez Á, Mallon B, Anjani QK, Domínguez-Robles J, Utomo E, Vora LK, *et al*. Enhancing intradermal delivery of tofacitinib citrate: Comparison between powder-loaded hollow microneedle arrays and dissolving microneedle arrays. International Journal of Pharmaceutics. 2021; 593: 120152. https://doi.org/10.1016/j.ijpharm.2020.120152.

[74] Chen R, Zhai YY, Sun L, Wang Z, Xia X, Yao Q, *et al*. Alantolactone-loaded chitosan/hyaluronic acid nanoparticles suppress psoriasis by deactivating STAT3 pathway and restricting immune cell recruitment. Asian Journal of Pharmaceutical Sciences. 2022; 17: 268–283. https://doi.org/10.1016/j.ajps.2022.02.003.

[75] Shah PP, Desai PR, Boakye CHA, Patlolla R, Kikwai LC, Babu RJ, *et al*. Percutaneous delivery of α-melanocyte-stimulating hormone for the treatment of imiquimod-induced psoriasis. Journal of Drug Targeting. 2016; 24: 537–547. https://doi.org/10.3109/1061186X.2015.1103743.

[76] Moghddam SRM, Ahad A, Aqil M, Imam SS, Sultana Y. Formulation and optimization of niosomes for topical diacerein delivery using 3-factor, 3-level Box-Behnken design for the management of psoriasis. Materials Science & Engineering. C, Materials for Biological Applications. 2016; 69: 789–797. https://doi.org/10.1016/j.msec.2016.07.043.

[77] Keum H, Kim TW, Kim Y, Seo C, Son Y, Kim J, *et al*. Bilirubin nanomedicine alleviates psoriatic skin inflammation by reducing oxidative stress and suppressing pathogenic signaling. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2020; 325: 359–369. https://doi.org/10.1016/j.jconrel.2020.07.015.

[78] Desmet E, Bracke S, Forier K, Taevernier L, Stuart MCA, De Spiegeleer B, *et al*. An elastic liposomal formulation for RNAi-based topical treatment of skin disorders: Proof-of-concept in the treatment of psoriasis. International Journal of Pharmaceutics. 2016; 500: 268–274. https://doi.org/10.1016/j.ijpharm.2016.01.042.

[79] Nemati H, Ghahramani MH, Faridi-Majidi R, Izadi B, Bahrami G, Madani SH, *et al*. Using siRNA-based spherical nucleic acid nanoparticle conjugates for gene regulation in psoriasis. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2017; 268: 259–268. https://doi.org/10.1016/j.jconrel.2017.10.034.

[80] Fathalla D, Youssef EMK, Soliman GM. Liposomal and Ethosomal Gels for the Topical Delivery of Anthralin: Preparation, Comparative Evaluation and Clinical Assessment in Psoriatic Patients. Pharmaceutics. 2020; 12: 446. https://doi.org/10.3390/pharmaceutics12050446.

[81] Sharma A, Upadhyay DK, Sarma GS, Kaur N, Das Gupta G, Narang RK, *et al*. Squalene integrated NLC based gel of tamoxifen citrate for efficient treatment of psoriasis: A preclinical investigation. Journal of Drug Delivery Science and Technology. 2020; 56: 101568. https://doi.org/10.1016/J.JDDST.2020.101568.

[82] Pund S, Pawar S, Gangurde S, Divate D. Transcutaneous delivery of leflunomide nanoemulgel: Mechanistic investigation into physicomechanical characteristics, in vitro anti-psoriatic and anti-melanoma activity. International Journal of Pharmaceutics. 2015; 487: 148–156. https://doi.org/10.1016/j.ijpharm.2015.04.015.

[83] Bhardwaj P, Tripathi P, Pandey S, Gupta R, Khar RK, Patil PR. Improved dermal delivery of pentoxifylline niosomes for the management of psoriasis: Development, optimization and in-vivo studies in imiquimod induced psoriatic plaque model. Journal of Drug Delivery Science and Technology. 2022; 75: 103643. https://doi.org/10.1016/J.JDDST.2022.103643.

[84] Lu B, Zhong Y, Zhang J, Zhang J. Curcumin-Based Ionic Liquid Hydrogel for Topical Transdermal Delivery of Curcumin To Improve Its Therapeutic Effect on the Psoriasis Mouse Model. ACS Applied Materials & Interfaces. 2024; 16: 17080–17091. https://doi.org/10.1021/acsami.3c17091.

[85] Doppalapudi S, Jain A, Khan W, Domb AJ. Fenoldopam mesylate for treating psoriasis: A new indication for an old drug. International Journal of Pharmaceutics. 2020; 573: 118726. https://doi.org/10.1016/j.ijpharm.2019.118726.

[86] Jain H, Bhat AR, Dalvi H, Godugu C, Singh SB, Srivastava S. Repurposing approved therapeutics for new indication: Addressing unmet needs in psoriasis treatment. Current Research in Pharmacology and Drug Discovery. 2021; 2: 100041. https://doi.org/10.1016/j.crphar.2021.100041.

[87] Gupta M, Agrawal U, Vyas SP. Nanocarrier-based topical drug delivery for the treatment of skin diseases. Expert Opinion on Drug Delivery. 2012; 9: 783–804. https://doi.org/10.1517/17425247.2012.686490.

[88] Wood Heickman LK, Davallow Ghajar L, Conaway M, Rogol AD. Evaluation of Hypothalamic-Pituitary-Adrenal Axis Suppression following Cutaneous Use of Topical Corticosteroids in Children: A Meta-Analysis. Hormone Research in Paediatrics. 2018; 89: 389–396. https://doi.org/10.1159/000489125.

[89] Singhvi G, Hejmady S, Rapalli VK, Dubey SK, Dubey S. Nanocarriers for topical delivery in psoriasis. Delivery of Drugs: Volume 2: Expectations and Realities of Multifunctional Drug Delivery Systems (pp. 75–96). Elsevier: the Netherlands. 2020. https://doi.org/10.1016/B978-0-12-817776-1.00004-3.

[90] Agarwal R, Katare OP, Vyas SP. Preparation and in vitro evaluation of liposomal/niosomal delivery systems for antipsoriatic drug dithranol. International Journal of Pharmaceutics. 2001; 228: 43–52. https://doi.org/10.1016/s0378-5173(01)00810-9.

[91] Kaur A, Katiyar SS, Kushwah V, Jain S. Nanoemulsion loaded gel for topical co-delivery of clobitasol propionate and calcipotriol in psoriasis. Nanomedicine: Nanotechnology, Biology, and Medicine. 2017; 13: 1473–1482. https://doi.org/10.1016/j.nano.2017.02.009.

[92] Raina N, Rani R, Thakur VK, Gupta M. New Insights in Topical Drug Delivery for Skin Disorders: From a Nanotechnological Perspective. ACS Omega. 2023; 8: 19145–19167. https://doi.org/10.1021/acsomega.2c08016.

[93] Mohd Nordin UU, Ahmad N, Salim N, Mohd Yusof NS. Lipid-based nanoparticles for psoriasis treatment: a review on conventional treatments, recent works, and future prospects. RSC Advances. 2021; 11: 29080–29101. https://doi.org/10.1039/d1ra06087b.

[94] Singh S, Sharma N, Behl T, Sarkar BC, Saha HR, Garg K, *et al*. Promising Strategies of Colloidal Drug Delivery-Based Approaches in Psoriasis Management. Pharmaceutics. 2021; 13: 1978. https://doi.org/10.3390/pharmaceutics13111978.

[95] Mascarenhas-Melo F, Carvalho A, Gonçalves MBS, Paiva-Santos AC, Veiga F. Nanocarriers for the topical treatment of psoriasis - pathophysiology, conventional treatments, nanotech-

nology, regulatory and toxicology. European Journal of Pharmaceutics and Biopharmaceutics. 2022; 176: 95–107. https://doi.org/10.1016/j.ejpb.2022.05.012.

[96] Shetty K, Sherje AP. Nano intervention in topical delivery of corticosteroid for psoriasis and atopic dermatitis-a systematic review. Journal of Materials Science. Materials in Medicine. 2021; 32: 88. https://doi.org/10.1007/s10856-021-06558-y.

[97] Murphy EC, Schaffter SW, Friedman AJ. Nanotechnology for Psoriasis Therapy. Current Dermatology Reports. 2019; 8: 14–25. https://doi.org/10.1007/s13671-019-0248-y.

[98] Pradhan M, Singh D, Singh MR. Novel colloidal carriers for psoriasis: current issues, mechanistic insight and novel delivery approaches. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2013; 170: 380–395. https://doi.org/10.1016/j.jconrel.2013.05.020.

[99] Rahangdale M, Pandey P. Development and Characterization of Apremilast Transethosomal Gel for Transdermal Delivery. International Journal of Pharmaceutical Sciences and Nanotechnology. 2021;14: 5508–5518. https://doi.org/10.37285/ijpsn.2021.14.3.8.

[100] Yang X, Tang Y, Wang M, Wang Y, Wang W, Pang M, *et al*. Co-delivery of methotrexate and nicotinamide by cerosomes for topical psoriasis treatment with enhanced efficacy. International Journal of Pharmaceutics. 2021; 605: 120826. https://doi.org/10.1016/j.ijpharm.2021.120826.

[101] Jain A, Doppalapudi S, Domb AJ, Khan W. Tacrolimus and curcumin co-loaded liposphere gel: Synergistic combination towards management of psoriasis. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2016; 243: 132–145. https://doi.org/10.1016/j.jconrel.2016.10.004.

[102] Jain A, Pooladanda V, Bulbake U, Doppalapudi S, Rafeeqi TA, Godugu C, *et al*. Liposphere mediated topical delivery of thymoquinone in the treatment of psoriasis. Nanomedicine: Nanotechnology, Biology, and Medicine. 2017; 13: 2251–2262. https://doi.org/10.1016/j.nano.2017.06.009.

[103] Shalaby RA, El-Gazayerly O, Abdallah M. Cubosomal Betamethasone-Salicylic Acid Nano Drug Delivery System for Enhanced Management of Scalp Psoriasis. International Journal of Nanomedicine. 2022; 17: 1659–1677. https://doi.org/10.2147/IJN.S345430.

[104] Ramalheiro A, Paris JL, Silva BFB, Pires LR. Rapidly dissolving microneedles for the delivery of cubosome-like liquid crystalline nanoparticles with sustained release of rapamycin. International Journal of Pharmaceutics. 2020; 591: 119942. https://doi.org/10.1016/j.ijpharm.2020.119942.

[105] Pandey SS, Maulvi FA, Patel PS, Shukla MR, Shah KM, Gupta AR, *et al*. Cyclosporine laden tailored microemulsion-gel depot for effective treatment of psoriasis: In vitro and in vivo studies. Colloids and Surfaces. B, Biointerfaces. 2020; 186: 110681. https://doi.org/10.1016/j.colsurfb.2019.110681.

[106] Mahajan M, Kaur M, Thakur S, Singh A, Shahtaghi NR, Shivgotra R, *et al*. Solid Lipid Nanoparticles as Carrier to Increase Local Bioavailability of Acitretin After Topical Administration in Psoriasis Treatment. Journal of Pharmaceutical Innovation. 2023; 18: 220–237. https://doi.org/10.1007/s12247-022-09635-z.

[107] Pradhan M, Singh D, Murthy SN, Singh MR. Design, characterization and skin permeating potential of Fluocinolone acetonide loaded nanostructured lipid carriers for topical treatment of psoriasis. Steroids. 2015; 101: 56–63. https://doi.org/10.1016/j.steroids.2015.05.012.

[108] Damiani G, Pacifico A, Linder DM, Pigatto PDM, Conic R, Grada A, *et al*. Nanodermatology-based solutions for psoriasis: State-of-the art and future prospects. Dermatologic Therapy. 2019; 32: e13113. https://doi.org/10.1111/dth.13113.

[109] Sunoqrot S, Niazi M, Al-Natour MA, Jaber M, Abu-Qatouseh L. Loading of Coal Tar in Polymeric Nanoparticles as a Potential Therapeutic Modality for Psoriasis. ACS Omega. 2022; 7: 7333–7340. https://doi.org/10.1021/acsomega.1c07267.

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

[111] Crisan D, Scharffetter-Kochanek K, Crisan M, Schatz S, Hainzl A, Olenic L, *et al*. Topical silver and gold nanoparticles complexed with Cornus mas suppress inflammation in human psoriasis plaques by inhibiting NF-κB activity. Experimental Dermatology. 2018; 27: 1166–1169. https://doi.org/10.1111/exd.13707.

[112] Bessar H, Venditti I, Benassi L, Vaschieri C, Azzoni P, Pellacani G, *et al*. Functionalized gold nanoparticles for topical delivery of methotrexate for the possible treatment of psoriasis. Colloids and Surfaces. B, Biointerfaces. 2016; 141: 141–147. https://doi.org/10.1016/j.colsurfb.2016.01.021.

[113] Kumar S, Prasad M, Rao R. Topical delivery of clobetasol propionate loaded nanosponge hydrogel for effective treatment of psoriasis: Formulation, physicochemical characterization, antipsoriatic potential and biochemical estimation. Materials Science & Engineering. C, Materials for Biological Applications. 2021; 119: 111605. https://doi.org/10.1016/j.msec.2020.111605.

[114] Devi N, Kumar S, Prasad M, Rao R. Eudragit RS100 based microsponges for dermal delivery of clobetasol propionate in psoriasis management. Journal of Drug Delivery Science and Technology. 2020; 55: 101347. https://doi.org/10.1016/j.jddst.2019.101347.

[115] Kumar S, Jangir BL, Rao R. A new perspective for psoriasis: Dithranol nanosponge loaded hydrogels. Applied Surface Science Advances. 2022; 12: 100347. https://doi.org/10.1016/j.apsadv.2022.100347.

[116] Men Z, Su T, Tang Z, Liang J, Shen T. Tacrolimus nanocrystals microneedle patch for plaque psoriasis. International Journal of Pharmaceutics. 2022; 627: 122207. https://doi.org/10.1016/j.ijpharm.2022.122207.

[117] Lu M, Zhang X, Cai L, Gan J, Wang J, Wang Y, *et al*. Black phosphorus hydrogel inverse opal microneedle patches for psoriasis treatment. Nano Today. 2024; 54: 102072. https://doi.org/10.1016/j.nantod.2023.102072.

[118] Alvarez-Figueroa MJ, Delgado-Charro MB, Blanco-Méndez J. Passive and iontophoretic transdermal penetration of methotrexate. International Journal of Pharmaceutics. 2001; 212: 101–107. https://doi.org/10.1016/s0378-5173(00)00599-8.

[119] Wang S, Kara M, Krishnan TR. Transdermal delivery of cyclosporin-A using electroporation. Journal of Controlled Release: Official Journal of the Controlled Release Society. 1998; 50: 61–70. https://doi.org/10.1016/s0168-3659(97)00117-x.

[120] Alakad R, Nassar A, Atef H, Eldeeb F. Fractional CO2 Laser-Assisted Delivery Versus Intralesional Injection of Methotrexate in Psoriatic Nails. Dermatologic Surgery. 2022; 48: 539–544. https://doi.org/10.1097/DSS.0000000000003418.

[121] Konisky H, Klinger R, Coe L, Jaller JA, Cohen JL, Kobets K. A focused review on laser- and energy-assisted drug delivery for nail disorders. Lasers in Medical Science. 2024; 39: 39. https://doi.org/10.1007/s10103-024-03992-6.

[122] El Sharkawy DA, El-Komy MHM, Sobhi RM, Abdel Raouf NM, Fahim A. Fractional CO 2 Laser versus Fractional CO 2 Laser Plus Betamethasone/Calcipotriol Ointment in the Treatment of Nail Psoriasis. Dermatologic Surgery. 2023; 49: 570–574. https://doi.org/10.1097/DSS.0000000000003791.

[123] Boinpally RR, Zhou SL, Devraj G, Anne PK, Poondru S, Jasti BR. Iontophoresis of lecithin vesicles of cyclosporin A. Inter-

national Journal of Pharmaceutics. 2004; 274: 185–190. https://doi.org/10.1016/j.ijpharm.2004.01.016.

[124] Madan JR, Khude PA, Dua K. Development and evaluation of solid lipid nanoparticles of mometasone furoate for topical delivery. International Journal of Pharmaceutical Investigation. 2014; 4: 60–64. https://doi.org/10.4103/2230-973X.133047.

[125] Badıllı U, Sen T, Tarımcı N. Microparticulate based topical delivery system of clobetasol propionate. AAPS PharmSciTech. 2011; 12: 949–957. https://doi.org/10.1208/s12249-011-9661-7.

[126] Shah P, Goodyear B, Dholaria N, Puri V, Michniak-Kohn B. Nanostructured Non-Ionic Surfactant Carrier-Based Gel for Topical Delivery of Desoximetasone. International Journal of Molecular Sciences. 2021; 22: 1535. https://doi.org/10.3390/ijms22041535.

[127] Rana K, Pani T, Jha SK, Mehta D, Yadav P, Jain D, *et al*. Hydrogel-mediated topical delivery of steroids can effectively alleviate psoriasis *via* attenuating the autoimmune responses. Nanoscale. 2022; 14: 3834–3848. https://doi.org/10.1039/d1nr06001e.

[128] Zhang J, Smith E. Percutaneous permeation of betamethasone 17-valerate incorporated in lipid nanoparticles. Journal of Pharmaceutical Sciences. 2011; 100: 896–903. https://doi.org/10.1002/jps.22329.

[129] Shinde G, Desai P, Shelke S, Patel R, Bangale G, Kulkarni D. Mometasone furoate-loaded aspasomal gel for topical treatment of psoriasis: formulation, optimization, in vitro and in vivo performance. 2022; 33: 885–896. https://doi.org/10.1080/09546634.2020.1789043.

[130] Yadav K, Singh D, Singh MR. Nanovesicles delivery approach for targeting steroid mediated mechanism of antipsoriatic therapeutics. Journal of Drug Delivery Science and Technology. 2021; 65: 102688. https://doi.org/10.1016/j.jddst.2021.102688.

[131] Vejjabhinanta V, Muangsiri W, Werawatganone P. Fluocinolone Acetonide Microemulsion in Combination with a Fractional Laser for the Treatment of Scalp Psoriasis. AAPS PharmSciTech. 2022; 23: 122. https://doi.org/10.1208/s12249-022-02249-1.

[132] Dolz-Pérez I, Sallam MA, Masiá E, Morelló-Bolumar D, Pérez Del Caz MD, Graff P, *et al*. Polypeptide-corticosteroid conjugates as a topical treatment approach to psoriasis. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2020; 318: 210–222. https://doi.org/10.1016/j.jconrel.2019.12.016.

[133] Pradhan M, Singh D, Singh MR. Development characterization and skin permeating potential of lipid based novel delivery system for topical treatment of psoriasis. Chemistry and Physics of Lipids. 2015; 186: 9–16. https://doi.org/10.1016/j.chemphyslip.2014.11.004.

[134] Hemati Azandaryani A, Derakhshandeh K, Arkan E. Electrospun nanobandage for hydrocortisone topical delivery as an antipsoriasis candidate. 2017; 67: 677–685. https://doi.org/10.1080/00914037.2017.1375493.

[135] Ghorbanzadeh M, Golmohammadzadeh S, Karimi M, Farhadian N. Evaluation of vitamin D3 serum level of microemulsion based hydrogel containing Calcipotriol drug. Materials Today Communications. 2022; 33: 104409. https://doi.org/10.1016/j.mtcomm.2022.104409.

[136] Simioni YR, Perez NS, Barbosa LRS, Perez AP, Schilrreff P, Romero EL, et al. Enhancing the anti-psoriatic activity of vitamin D3 employing nanostructured archaeolipid carriers. Journal of Drug Delivery Science and Technology. 2022; 73: 103455. https://doi.org/10.1016/j.jddst.2022.103455.

[137] Knudsen NØ, Rønholt S, Salte RD, Jorgensen L, Thormann T, Basse LH, *et al*. Calcipotriol delivery into the skin with PEGylated liposomes. European Journal of Pharmaceutics and Biopharmaceutics. 2012; 81: 532–539. https://doi.org/10.1016/j.ejpb.2012.04.005.

[138] Alves CO, Novaes RD, Bernardes MTCP, Gonçalves RV, da Silva LP, Agostini SBN, *et al*. Evaluation of methotrexate-loaded surfactants, ceramides and cholesterol-based lamellar phases as a topical treatment for psoriasis. The Journal of Pharmacy and Pharmacology. 2022; 74: 1342–1352. https://doi.org/10.1093/jpp/rgac006.

[139] Latif MS, Al-Harbi FF, Nawaz A, Rashid SA, Farid A, Mohaini MA, *et al*. Formulation and Evaluation of Hydrophilic Polymer Based Methotrexate Patches: In Vitro and In Vivo Characterization. Polymers. 2022; 14: 1310. https://doi.org/10.3390/polym14071310.

[140] Zhou Y, Yang L, Lyu Y, Wu D, Zhu Y, Li J, *et al*. Topical Delivery of ROS-Responsive Methotrexate Prodrug Nanoassemblies by a Dissolvable Microneedle Patch for Psoriasis Therapy. International Journal of Nanomedicine. 2023; 18: 899–915. https://doi.org/10.2147/IJN.S394957.

[141] Vora D, Garimella HT, German CL, Banga AK. Microneedle and iontophoresis mediated delivery of methotrexate into and across healthy and psoriatic skin. International Journal of Pharmaceutics. 2022; 618: 121693. https://doi.org/10.1016/j.ijpharm.2022.121693.

[142] Panonnummal R, Sabitha M. Anti-psoriatic and toxicity evaluation of methotrexate loaded chitin nanogel in imiquimod induced mice model. International Journal of Biological Macromolecules. 2018; 110: 245–258. https://doi.org/10.1016/j.ijbiomac.2017.10.112.

[143] Amarji B, Garg NK, Singh B, Katare OP. Microemulsions mediated effective delivery of methotrexate hydrogel: more than a tour de force in psoriasis therapeutics. Journal of Drug Targeting. 2016; 24: 147–160. https://doi.org/10.3109/1061186X.2015.1058804.

[144] Zidan AS, Mokhtar Ibrahim M, Megrab NAE. Optimization of methotrexate loaded niosomes by Box-Behnken design: an understanding of solvent effect and formulation variability. Drug Development and Industrial Pharmacy. 2017; 43: 1450–1459. https://doi.org/10.1080/03639045.2017.1318907.

[145] Tripathi P, Kumar A, Jain PK, Patel JR. Carbomer gel bearing methotrexate loaded lipid nanocontainers shows improved topical delivery intended for effective management of psoriasis. International Journal of Biological Macromolecules. 2018; 120: 1322–1334. https://doi.org/10.1016/j.ijbiomac.2018.08.136.

[146] Özcan A, Sahin D, Impellizzieri D, Nguyen TT, Hafner J, Yawalkar N, *et al*. Nanoparticle-Coupled Topical Methotrexate Can Normalize Immune Responses and Induce Tissue Remodeling in Psoriasis. The Journal of Investigative Dermatology. 2020; 140: 1003–1014.e8. https://doi.org/10.1016/j.jid.2019.09.018.

[147] Nagle A, Goyal AK, Kesarla R, Murthy RR. Efficacy study of vesicular gel containing methotrexate and menthol combination on parakeratotic rat skin model. Journal of Liposome Research. 2011; 21: 134–140. https://doi.org/10.3109/08982104.2010.492476.

[148] Trotta M, Peira E, Carlotti ME, Gallarate M. Deformable liposomes for dermal administration of methotrexate. International Journal of Pharmaceutics. 2004; 270: 119–125. https://doi.org/10.1016/j.ijpharm.2003.10.006.

[149] Pinto MF, Moura CC, Nunes C, Segundo MA, Costa Lima SA, Reis S. A new topical formulation for psoriasis: development of methotrexate-loaded nanostructured lipid carriers. International Journal of Pharmaceutics. 2014; 477: 519–526. https://doi.org/10.1016/j.ijpharm.2014.10.067.

[150] Verma DD, Fahr A. Synergistic penetration enhancement effect of ethanol and phospholipids on the topical delivery of cyclosporin A. Journal of Controlled Release: Official Jour-

nal of the Controlled Release Society. 2004; 97: 55–66. https://doi.org/10.1016/j.jconrel.2004.02.028.

[151] Lapteva M, Santer V, Mondon K, Patmanidis I, Chiriano G, Scapozza L, *et al*. Targeted cutaneous delivery of ciclosporin A using micellar nanocarriers and the possible role of inter-cluster regions as molecular transport pathways. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2014; 196: 9–18. https://doi.org/10.1016/j.jconrel.2014.09.021.

[152] Pandey SS, Shah KM, Maulvi FA, Desai DT, Gupta AR, Joshi SV, *et al*. Topical delivery of cyclosporine loaded tailored niosomal nanocarriers for improved skin penetration and deposition in psoriasis: Optimization, ex vivo and animal studies. Journal of Drug Delivery Science and Technology. 2021; 63: 102441. https://doi.org/10.1016/j.jddst.2021.102441.

[153] Musa SH, Razali FN, Shamsudin N, Salim N, Basri M. Novel topical nano-colloidal carrier loaded with cyclosporine: Biological evaluation potentially for psoriasis treatment. Journal of Drug Delivery Science and Technology. 2021; 63: 102440. https://doi.org/10.1016/j.jddst.2021.102440.

[154] Benigni M, Pescina S, Grimaudo MA, Padula C, Santi P, Nicoli S. Development of microemulsions of suitable viscosity for cyclosporine skin delivery. International Journal of Pharmaceutics. 2018; 545: 197–205. https://doi.org/10.1016/j.ijpharm.2018.04.049.

[155] Liu H, Wang Y, Lang Y, Yao H, Dong Y, Li S. Bicontinuous cyclosporin a loaded water-AOT/Tween 85-isopropylmyristate microemulsion: structural characterization and dermal pharmacokinetics in vivo. Journal of Pharmaceutical Sciences. 2009; 98: 1167–1176. https://doi.org/10.1002/jps.21485.

[156] Fereig SA, El-Zaafarany GM, Arafa MG, Abdel-Mottaleb MMA. 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.

[157] Sarango-Granda P, Silva-Abreu M, Calpena AC, Halbaut L, Fábrega MJ, Rodríguez-Lagunas MJ, *et al*. Apremilast Microemulsion as Topical Therapy for Local Inflammation: Design, Characterization and Efficacy Evaluation. Pharmaceuticals (Basel, Switzerland). 2020; 13: 484. https://doi.org/10.3390/ph13120484.

[158] Saha I, Palak A, Rai VK. Relevance of NLC-gel and microneedling-assisted tacrolimus ointment against severe psoriasiform: In vitro dermal retention kinetics, in vivo activity and drug distribution. Journal of Drug Delivery Science and Technology. 2022; 71: 103272. https://doi.org/10.1016/j.jddst.2022.103272.

[159] Gabriel D, Mugnier T, Courthion H, Kranidioti K, Karagianni N, Denis MC, *et al*. Improved topical delivery of tacrolimus: A novel composite hydrogel formulation for the treatment of psoriasis. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2016; 242: 16–24. https://doi.org/10.1016/j.jconrel.2016.09.007.

[160] Wan T, Pan J, Long Y, Yu K, Wang Y, Pan W, *et al*. Dual roles of TPGS based microemulsion for tacrolimus: Enhancing the percutaneous delivery and anti-psoriatic efficacy. International Journal of Pharmaceutics. 2017; 528: 511–523. https://doi.org/10.1016/j.ijpharm.2017.06.050.

[161] Thapa RK, Yoo BK. Evaluation of the effect of tacrolimus-loaded liquid crystalline nanoparticles on psoriasis-like skin inflammation. The Journal of Dermatological Treatment. 2014; 25: 22–25. https://doi.org/10.3109/09546634.2012.755250.

[162] Lapteva M, Mondon K, Möller M, Gurny R, Kalia YN. Polymeric micelle nanocarriers for the cutaneous delivery of tacrolimus: a targeted approach for the treatment of psoriasis. Molecular Pharmaceutics. 2014; 11: 2989–3001. https://doi.org/10.1021/mp400639e.

[163] Sharma S, Kanugo A, Gaikwad J. Design and development of solid lipid nanoparticles of tazarotene for the treatment of psoriasis and acne: a quality by design approach. 2021; 37: 735–744. https://doi.org/10.1080/10667857.2021.1873637.

[164] Nasr M, Abdel-Hamid S, Moftah NH, Fadel M, Alyoussef AA. Jojoba Oil Soft Colloidal Nanocarrier of a Synthetic Retinoid: Preparation, Characterization and Clinical Efficacy in Psoriatic Patients. Current Drug Delivery. 2017; 14: 426–432. https://doi.org/10.2174/1567201813666160513132321.

[165] Andrýsková N, Sourivong P, Babincová M, Šimaljaková M. Controlled Release of Tazarotene from Magnetically Responsive Nanofiber Patch: Towards More Efficient Topical Therapy of Psoriasis. Applied Sciences. 2021; 11: 11022 https://doi.org/10.3390/APP112211022.

[166] K. Sawant K, Mundada P, Sodani D. Physicochemical Characterization and Clinical Evaluation of a Microemulsion System for Topical Delivery of Tazarotene in Psoriasis. Micro and Nanosystems. 2015; 7: 98–107. https://doi.org/10.2174/1876402907666151103210822.

[167] Kendre PN, Borawake N, Jain SP, Vibhute SK, Pote AK. An effort to tailor the solid dispersion loaded, surface-modified, microporous-cryogel formulation of acitretin for the treatment of psoriasis. 2020; 37: 645–654. https://doi.org/10.1080/10667857.2020.1868210.

[168] Abu Hashim II, Abo El-Magd NF, El-Sheakh AR, Hamed MF, Abd El-Gawad AEGH. Pivotal role of Acitretin nanovesicular gel for effective treatment of psoriasis: ex vivo-in vivo evaluation study. International Journal of Nanomedicine. 2018; 13: 1059–1079. https://doi.org/10.2147/IJN.S156412.

[169] Shields CW, 4th, White JP, Osta EG, Patel J, Rajkumar S, Kirby N, *et al*. Encapsulation and controlled release of retinol from silicone particles for topical delivery. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2018; 278: 37–48. https://doi.org/10.1016/j.jconrel.2018.03.023.

[170] Algahtani MS, Ahmad MZ, Ahmad J. Nanoemulsion loaded polymeric hydrogel for topical delivery of curcumin in psoriasis. Journal of Drug Delivery Science and Technology. 2020; 59: 101847. https://doi.org/10.1016/j.jddst.2020.101847.

[171] Filippone A, Consoli GML, Granata G, Casili G, Lanza M, Ardizzone A, *et al*. Topical Delivery of Curcumin by Choline-Calix[4]arene-Based Nanohydrogel Improves Its Therapeutic Effect on a Psoriasis Mouse Model. International Journal of Molecular Sciences. 2020; 21: 5053. https://doi.org/10.3390/ijms21145053.

[172] Rapalli VK, Kaul V, Waghule T, Gorantla S, Sharma S, Roy A, *et al*. Curcumin loaded nanostructured lipid carriers for enhanced skin retained topical delivery: optimization, scale-up, in-vitro characterization and assessment of ex-vivo skin deposition. European Journal of Pharmaceutical Sciences: Official Journal of the European Federation for Pharmaceutical Sciences. 2020; 152: 105438. https://doi.org/10.1016/j.ejps.2020.105438.

[173] Kesharwani P, Jain A, Srivastava AK, Keshari MK. Systematic development and characterization of curcumin-loaded nanogel for topical application. Drug Development and Industrial Pharmacy. 2020; 46: 1443–1457. https://doi.org/10.1080/03639045.2020.1793998.

[174] Zhang Y, Xia Q, Li Y, He Z, Li Z, Guo T, *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: 48–64. https://doi.org/10.7150/thno.29715.

[175] Mao KL, Fan ZL, Yuan JD, Chen PP, Yang JJ, Xu J, *et al*. Skin-penetrating polymeric nanoparticles incorporated in silk fibroin hydrogel for topical delivery of curcumin to improve its therapeutic effect on psoriasis mouse model. Colloids and Surfaces.

B, Biointerfaces. 2017; 160: 704–714. https://doi.org/10.1016/j.colsurfb.2017.10.029.

[176] Sun L, Liu Z, Wang L, Cun D, Tong HHY, Yan R, *et al*. Enhanced topical penetration, system exposure and anti-psoriasis activity of two particle-sized, curcumin-loaded PLGA nanoparticles in hydrogel. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2017; 254: 44–54. https://doi.org/10.1016/j.jconrel.2017.03.385.

[177] Kang NW, Kim MH, Sohn SY, Kim KT, Park JH, Lee SY, *et al*. Curcumin-loaded lipid-hybridized cellulose nanofiber film ameliorates imiquimod-induced psoriasis-like dermatitis in mice. Biomaterials. 2018; 182: 245–258. https://doi.org/10.1016/j.biomaterials.2018.08.030.

[178] Agrawal U, Gupta M, Vyas SP. Capsaicin delivery into the skin with lipidic nanoparticles for the treatment of psoriasis. Artificial Cells, Nanomedicine, and Biotechnology. 2015; 43: 33–39. https://doi.org/10.3109/21691401.2013.832683.

[179] Kumar S, Singh KK, Rao R. Enhanced anti-psoriatic efficacy and regulation of oxidative stress of a novel topical babchi oil (*Psoralea corylifolia*) cyclodextrin-based nanogel in a mouse tail model. Journal of Microencapsulation. 2019; 36: 140–155. https://doi.org/10.1080/02652048.2019.1612475.

[180] Ali J, Akhtar N, Sultana Y, Baboota S, Ahuja A. Antipsoriatic microemulsion gel formulations for topical drug delivery of babchi oil (Psoralea corylifolia). Methods and Findings in Experimental and Clinical Pharmacology. 2008; 30: 277–285. https://doi.org/10.1358/mf.2008.30.4.1185802.

[181] Sah A, Jain SK, Pandey R. Microemulsion based hydrogel formulation of methoxsalen for the effective treatment of psoriasis. Asian Journal of Pharmaceutical and Clinical Research, 2011; 4, 140–145.

[182] Qiu F, Xi L, Chen S, Zhao Y, Wang Z, Zheng Y. Celastrol Niosome Hydrogel Has Anti-Inflammatory Effect on Skin Keratinocytes and Circulation without Systemic Drug Exposure in Psoriasis Mice. International Journal of Nanomedicine. 2021; 16: 6171–6182. https://doi.org/10.2147/IJN.S323208.

[183] Ghate VM, Kodoth AK, Shah A, Vishalakshi B, Lewis SA. Colloidal nanostructured lipid carriers of pentoxifylline produced by microwave irradiation ameliorates imiquimod-induced psoriasis in mice. Colloids and Surfaces. B, Biointerfaces. 2019; 181: 389–399. https://doi.org/10.1016/j.colsurfb.2019.05.074.

[184] Giulbudagian M, Yealland G, Hönzke S, Edlich A, Geisendörfer B, Kleuser B, *et al*. Breaking the Barrier - Potent Anti-Inflammatory Activity following Efficient Topical Delivery of Etanercept using Thermoresponsive Nanogels. Theranostics. 2018; 8: 450–463. https://doi.org/10.7150/thno.21668.

[185] Rapalli VK, Sharma S, Roy A, Singhvi G. Design and dermatokinetic evaluation of Apremilast loaded nanostructured lipid carriers embedded gel for topical delivery: A potential approach for improved permeation and prolong skin deposition. Colloids and Surfaces. B, Biointerfaces. 2021; 206: 111945. https://doi.org/10.1016/j.colsurfb.2021.111945.

[186] Parmar PK, Bansal AK. Novel nanocrystal-based formulations of apremilast for improved topical delivery. Drug Delivery and Translational Research. 2021; 11: 966–983. https://doi.org/10.1007/s13346-020-00809-1.

[187] Lee WR, Chou WL, Lin ZC, Sung CT, Lin CY, Fang JY. Laser-assisted nanocarrier delivery to achieve cutaneous siRNA targeting for attenuating psoriasiform dermatitis. Journal of Controlled Release: Official Journal of the Controlled Release Society. 2022; 347: 590–606. https://doi.org/10.1016/j.jconrel.2022.05.032.

[188] Agrawal U, Mehra NK, Gupta U, Jain NK. Hyperbranched dendritic nano-carriers for topical delivery of dithranol. Journal of Drug Targeting. 2013; 21: 497–506. https://doi.org/10.3109/1061186X.2013.771778.