

HYDROGEL BASED THERAPEUTICS FOR PSORIASIS: ADVANCES IN DRUG DELIVERY AND TARGETED THERAPY

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ABSTRACT

Hydrogel-based therapy can improve skin retention, reduce inflammation, and provide medications for psoriasis. Biocompatibility, high water content, and modulable physicochemical properties make hydrogels the best delivery method for corticosteroids, immunomodulators, biologics, natural phytochemicals, nucleic acids, and nanoparticle-containing therapies. They reduce systemic side effects and boost efficacy. stimuli-responsive, nanocomposite, and multifunctional hydrogel systems release drugs efficiently and site-specifically, penetrate the psoriatic skin barrier, and regulate inflammatory pathways. Modern delivery methods can improve adherence, lower dosages, and focus on treatment. Despite promising preclinical and clinical evidence, long-term stability, regulatory approval, clinical translation, and large-scale production remain challenges. Hydrogel-based medication delivery improves psoriasis treatment due to safety, efficacy, and patient-centeredness.

Keywords: *Psoriasis; Hydrogel-based therapeutics; Targeted drug delivery; Controlled drug release; Topical drug delivery; Stimuli-responsive hydrogels; Nanocomposite hydrogels; Transdermal delivery; Skin inflammation; Precision medicine.*

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1. INTRODUCTION

Chronic immune-mediated inflammatory skin condition psoriasis is characterized by pro-inflammatory cytokines, immune cell infiltration, and excessive keratinocyte proliferation and differentiation. Approximately 2-3% of the global population suffers with psoriasis, a chronic skin disorder that affects their social, psychological, and physical well- Immunological dysregulation, environmental stresses, and genetic vulnerability induce the IL-23/IL-17 axis, which causes the disease. Plaque psoriasis, with its erythematous, distinct plaques and silvery-white scales, is the most common kind. Systemic immunosuppressants, topical corticosteroids, vitamin D analogs, phototherapy, and biologics improve disease treatment. Unfortunately, unpleasant effects, patient noncompliance, frequent dosing, and epidermal barrier medication absorption restrict prolonged therapy's efficacy.

The epidermis' stratum corneum blocks drug distribution. Lotions, ointments, and gels have low drug retention, irregular drug release, and short residence times, limiting their therapeutic efficacy. Hydrogels are employed in drug delivery systems because their three-dimensional hydrophilic polymeric networks can absorb large volumes of water without losing structural integrity. Hydrogels mimic biological tissues to moisturize skin and improve patient comfort due to their biocompatibility, moisture retention, and flexibility. Encapsulating small-molecule medicines, biologics, nucleic acids, peptides, and nanoparticles can increase sustained and localized drug delivery while lowering systemic exposure and treatment-related toxicity due to their changeable physicochemical properties.

2. PATHOGENESIS OF PSORIASIS

Psoriasis, a chronic inflammatory dermatosis, is caused by a complicated interaction between inherited predisposition, environmental conditions, and the immune system. Insufficient epidermal differentiation, keratinocyte proliferation, and immunological activation cause thicker, erythematous, scaly plaques.

Disparities between innate and adaptive immune responses, notably the IL-23/Th17 immunological axis, cause the disease to start and worsen.

Genetic Susceptibility

Genetics greatly affect psoriasis development and expression. The PSORS1 gene on chromosome 6p21.3 in the HLA-Cw6 region is primarily linked to the condition. This chromosomal region may affect intracellular signaling pathways, such as NF- κ B and STAT3, and antigen presentation. These mechanisms cause and maintain psoriatic epidermal inflammation.

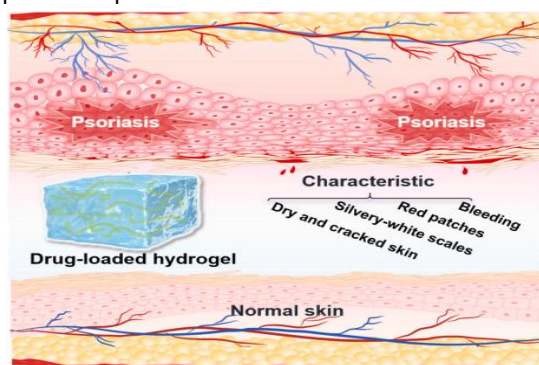


Fig1. Architecture of a psoriatic lesion (top) and a non-psoriatic lesion (bottom).

Environmental Triggers

Plasmacytoid dendritic cells release IL-23 when streptococcal infections and skin lesions damage the epidermal barrier. Th17 and Th1 cells are stimulated by IL-23 to start the IL-23/IL-17 signaling cascade. Inflammatory cytokines like TNF- α , IL-17A, and IL-22 speed epidermal turnover from 28 days to 3-4 days, causing erythema and psoriatic lesions.

Disruptions in lipid metabolism, enhanced ROS generation, metabolic reprogramming with glucose transporter-1 overexpression and lactate buildup, and altered exosomal microRNA expression, particularly miR-381-3p, all contribute to illness progression. Memory T cells in the tissue undergo chronic inflammation and disease.

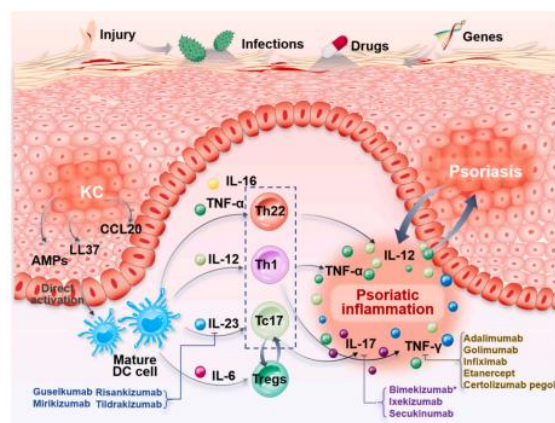


Fig. 2. Pathogenesis of psoriasis.

Current Treatment

Systemic, topical, and biologic medicines treat psoriasis. The main topicals are calcitriol and tacrolimus. Systemic treatment includes cyclosporine A, acitretin, and apremilast, while biologic medicines target inflammatory mediators such TNF- α , IL-12/23, IL-17, and IL-23. Despite their inability to treat localized lesions as topicals, patient adherence concerns, formulation restrictions, and systemic toxicity, biologics have improved disease treatment.

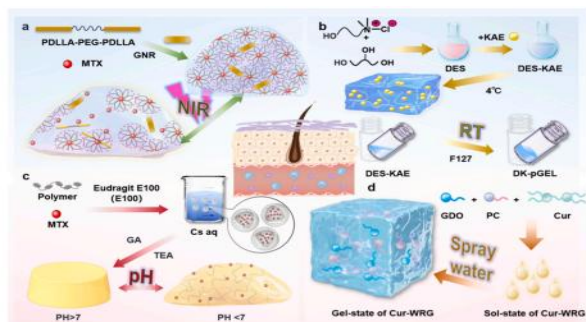


Fig. 3. treatment of psoriasis with responsive hydrogels.

- Photothermal response:** Thermosensitive hydrogels were produced by encasing MTX with PDLLA-PEG-PDLLA and GNRs. Wiley has permission to reproduce.
- Temperature response:** The hydrogel can be injected below 25 °C and solidifies upon contact with the epidermis. Reprinting is permitted by the American Chemical Society.
- pH response:** Hydrogels are created by encasing MTX in pH-sensitive Eudragit E100 polymeric nanoparticles using a pH-dependent nanocarrier method. Reproduced with MDPI permission.
- Water response:** Smart polymers that are "water-triggered" thicken quickly when sprayed. Use is permitted by Elsevier.

3. HYDROGEL DESIGN

Hydrogel-based drug delivery devices are appealing for the treatment of psoriasis due to their biocompatibility, high water content, and capacity to distribute medication continuously and under control. Hydrogels are the optimal choice for targeted therapy due to their superior drug retention, epidermal penetration, and systemic adverse effect profiles in comparison to topical formulations.

Overview

As an alternative to topical therapy, hydrogel formulations enhance the drug's controlled release, penetration, and residence time. By integrating pharmaceutical principles with materials engineering, these methods improve the management of psoriasis.

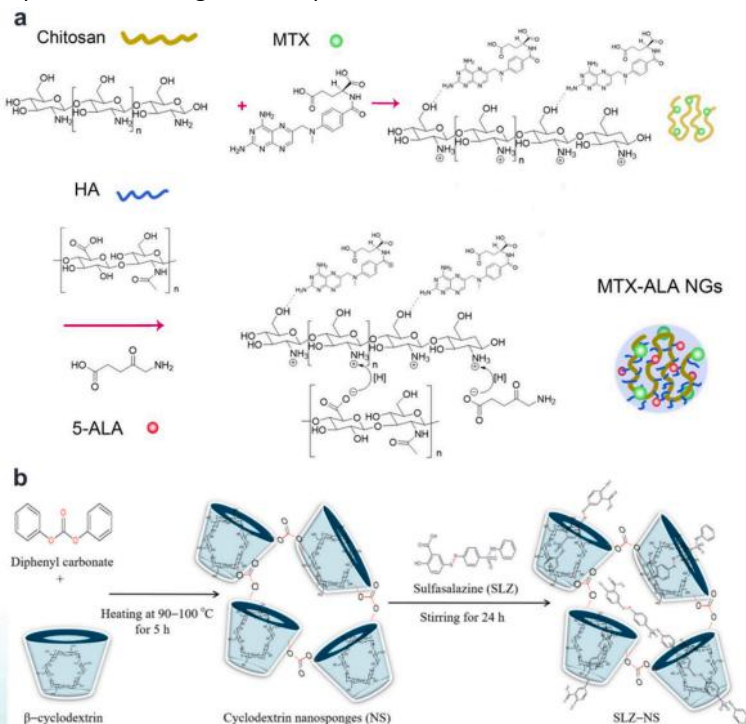


Fig. 6. Nano-hydrogels

Materials

Hydrogels are produced using either natural or synthetic polymers, contingent upon the desired drug-release profile and the pathophysiology of psoriasis. A hydrogel system's biocompatibility, responsiveness, and mechanical characteristics are all determined by the polymer.

- **Natural Polymers:** Hyaluronic acid, cellulose, and chitosan are employed due to their biodegradable, biocompatible, anti-inflammatory, and moisturizing properties. These materials enable adaptive drug delivery and skin regeneration.
- **Synthetic Polymers:** Carbomers, polyethylene glycol, and polyacrylamide are synthetic polymers that can endure mechanical stress, preserve structural integrity, and release medications over time. They are adaptable in their approach to psoriasis therapy.

Crosslinking

Chemical or physical crosslinking is the process by which hydrogels are produced. Physical crosslinking generates self-healing gels that are reversible, while chemical crosslinking enhances the mechanical strength and drug retention at the lesion site.

Stimuli-Responsive Hydrogels

Psoriatic lesions contain hydrogels that are stimuli-responsive and can respond to fluctuations in temperature, pH, moisture, and reactive oxygen species (ROS). Enhanced therapeutic efficacy and reduced systemic exposure are potential results of regulated and site-specific drug release.

4. ADVANCED HYDROGEL DESIGN

Newer hydrogel combinations make medications more deeply absorbed, maintain them in the body longer, and distribute them to psoriatic lesions, improving their therapeutic efficacy. These solutions avoid the issues with standard topical formulations, improve therapeutic efficacy, and reduce systemic toxicity by using advanced materials and engineering.

Ionic Liquid Hydrogels

Ionic liquid (IL) hydrogels are functional systems consisting of ionic liquids and polymer networks. Ionic liquids increase skin permeation and drug delivery by breaking up the stratum corneum's thick lipid structure through hydrogen bonding and ion-pair interactions. Some IL hydrogels improve medication penetration and release over time. Their safety, efficacy, and clinical usage for psoriasis treatment need more study.

Eutectogels

Eutectogels are water-based gel systems made from deep eutectic solvents (DESSs) and polymer matrices. Drug-eluting systems' mechanical characteristics and biocompatibility let non-water-soluble drugs diffuse through the skin. Electrostatic and hydrogen connections make cross-linking in these mixes eco-friendly. Despite these benefits, additional research is needed to determine how they affect skin microbiology, barrier integrity, and large-scale production security.

Nano-Hydrogels

Nano-hydrogels enable drugs enter and stay in psoriatic skin by combining hydrogel structures with nanoscale drug transporters. Physical or covalent crosslinking with polyelectrolytes or cyclodextrin derivatives creates these systems. Nano-hydrogels can encapsulate hard-to-dissolve medicines, sustain drug release, make drug buildup simpler, and improve therapy for psoriasis.

5. THERAPEUTIC ADVANTAGES OF HYDROGELS

Hydrogel-based medication delivery systems improve topical psoriasis treatment by avoiding formulation issues. Their three-dimensional polymeric networks reduce drug exposure, provide controlled and long-lasting drug release, increase skin penetration, and prolong drug retention in the lesion site. These qualities improve patient compliance, dose reduction, and treatment efficacy.

Sustained Release

Hydrogels maintain therapeutic medication concentrations in psoriatic lesions through regulated and continuous release. Their cross-linked polymer networks reduce localized pain, drug administration, and drug

elimination. Sustained-release hydrogels improve therapy by keeping the medicine at the target site and encouraging patients to follow their treatment plan.

Enhanced Skin Penetration

Drugs penetrate the stratum corneum better in hydrogels that stay close to the skin and contain nanocarriers, ionic liquids, or other chemicals. These strategies reduce medicine absorption and side effects while enhancing medicine concentration in psoriatic lesions.

Stimuli-Responsive Drug Delivery

Stimuli-responsive hydrogels react to damaging psoriatic lesion changes including temperature, pH, moisture, and ROS. Making site-specific and regulated medication release easy improves treatment accuracy and lowers drug exposure to non-target areas.

Improved Therapeutic Efficacy

Complex hydrogel systems such nano-hydrogels, microneedle hydrogels, and ionic liquid hydrogels stabilize pharmaceuticals, prolong their absorption, and help them reach their targets. These properties boost anti-inflammatory actions, reduce hyperproliferating keratinocytes, and improve psoriasis treatment.

6. CONCLUSION

Hydrogel-based treatments may be a new and effective technique to treat psoriasis since they avoid some of the issues with topical and systemic treatments. Therapeutic medications treat psoriatic lesions with minimal side effects. Biocompatibility, regulated and sustained medication release, skin penetration, and pathological stimulus response are improved. Smart hydrogels, nano-hydrogels, ionic liquid hydrogels, eutectogels, and microneedle-assisted systems make pharmaceuticals easier to absorb and work better. Future hydrogel formulations should be faster due to biomaterials engineering and targeted drug delivery advances. Despite challenges including mass production, safety, and clinical use, they will treat psoriasis safely, more effectively, and more patient-friendly.

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