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Review Article

Topical Hydrogel Delivery Systems for Skin Diseases: A Scientific Review

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ABSTRACT

Topical hydrogel-based delivery systems have emerged as a versatile and effective platform for the treatment of various skin diseases due to their high water content, biocompatibility, and ability to provide controlled drug release. These semi-solid systems offer a moist environment that promotes wound healing and enhances drug permeation through the skin. This review outlines the classification, physicochemical properties, and mechanisms of drug release, preparation methods, and recent advancements in hydrogel-based delivery systems. It also highlights their application in managing inflammatory, infectious, and chronic dermatological conditions such as psoriasis, atopic dermatitis, acne, fungal infections, and skin cancers. The integration of stimuli-responsive polymers and nanotechnology into hydrogels is also discussed, emphasizing their potential in personalized medicine and advanced dermatotherapy.

KEYWORDS: Topical Hydrogel, Polymer, applications, characteristics.

INTRODUCTION

Skin diseases, ranging from chronic inflammatory conditions to microbial infections and neoplastic disorders, affect millions of individuals globally and significantly impact quality of life. Topical drug delivery remains a preferred route for treating dermatological conditions due to its non-invasive nature and localized effect. However, conventional topical formulations like creams and ointments often suffer from poor skin retention, low drug penetration, and greasy textures[1,2].

Hydrogels are hydrophilic polymer networks capable of retaining large amounts of water, offer a promising alternative. Their unique physicochemical characteristics make them suitable for sustained drug release, improved skin adherence, and enhanced patient compliance. Over the past decade, topical hydrogel systems have gained prominence in treating a variety of skin disorders. Topical hydrogels are three-dimensional polymeric networks with the ability to retain large amounts of water, making them ideal carriers for dermal and transdermal drug delivery. Their high water content offers a cooling, soothing effect upon application and helps maintain skin hydration, making them especially useful for skin diseases[3-5].

Unlike traditional semisolid systems like ointments or creams, hydrogels are non-greasy, spread easily, and allow better patient comfort and compliance. Their tunable physicochemical properties make them suitable for a wide range of therapeutic agents including small molecules, peptides, and nanoparticles[6,7].

This review provides an overview of the classification, physicochemical characteristics, drug release mechanisms, and preparation techniques of hydrogel-based delivery systems. It also explores recent advancements in the field and emphasizes their therapeutic applications in treating a range of dermatological conditions, including inflammatory, infectious, and chronic skin disorders such as psoriasis, atopic dermatitis, acne, fungal infections, and skin cancers.

Structure and Composition of Hydrogels

Hydrogels are three-dimensional, cross-linked polymeric networks that can absorb and retain significant quantities of water or biological fluids. Their structure allows for: High permeability to oxygen and nutrients; Non-occlusive yet moisture-retentive properties; Minimal irritation and superior skin feel. Topical hydrogels are typically composed of:

a. **Polymers:** Natural (e.g., chitosan, hyaluronic acid, alginate) or synthetic (e.g., polyvinyl alcohol [PVA], polyethylene glycol [PEG], carbopol).
b. **Cross-linkers:** Used to form a stable network structure.
c. **Active agents:** Drugs, herbal extracts, antimicrobials, etc.
d. **Water:** The main component, often making up >90% of the system[8-10].

Types of Hydrogels

Hydrogels are classified based on origin, cross-linking type, polymer composition, and stimuli-responsiveness:

Based on Source

a. **Natural:** Alginate, gelatin, hyaluronic acid, chitosan.
b. **Synthetic:** Polyvinyl alcohol (PVA), polyethylene glycol (PEG), polyacrylic acid (PAA).

Based on Cross-linking

a. **Physical:** Hydrogen bonding, ionic interactions, freeze-thawing.
b. **Chemical:** Covalent cross-linking via agents like glutaraldehyde.

Stimuli-Responsive Hydrogels

Respond to pH, temperature, enzymes, or light, enabling "smart" drug release[11,12].

Drug Release Mechanisms

Drug delivery from hydrogels to the skin primarily involves:

a. **Diffusion:** Passive movement of drug molecules through the hydrated polymer matrix.
b. **Swelling-controlled release:** The gel swells upon contact with skin moisture, triggering drug release.
c. **Stimuli-responsive release:** Controlled release in response to environmental triggers (e.g., increased temperature in inflamed skin).

These mechanisms allow sustained, localized, and targeted delivery — particularly important in treating chronic and inflammatory skin conditions[13].

Preparation Techniques

Hydrogel preparation methods vary depending on the desired application and drug properties:

a. **Free Radical Polymerization:** Widely used for synthetic hydrogels.
b. **Ionic Cross-linking:** Common for polysaccharide-based hydrogels like alginate.
c. **Freeze-Thaw Cycling:** Used to physically cross-link PVA hydrogels.
d. **Click Chemistry and Photopolymerization:** Employed for in situ gelling systems.

The choice of technique influences the hydrogel's porosity, mechanical strength, and drug-loading efficiency[14-16].

Applications in Skin Diseases

Hydrogels can be engineered to deliver anti-inflammatory, antimicrobial, antifungal, and antineoplastic agents. Their ability to conform to the skin and provide sustained release enhances therapeutic outcomes in various conditions:

Psoriasis and Atopic Dermatitis

Hydrogels loaded with corticosteroids, calcineurin inhibitors, or herbal agents provide localized action while minimizing systemic exposure. Incorporation of anti-inflammatory agents like tacrolimus into hydrogels has shown improved efficacy and reduced irritation[17].

Acne Vulgaris

Antibacterial agents such as clindamycin and benzoyl peroxide have been successfully incorporated into hydrogel matrices for controlled release, improved skin penetration, and reduced irritation[18].

Fungal Infections

Hydrogels containing antifungal agents (e.g., ketoconazole, clotrimazole) enhance drug solubility and residence time in infected skin layers[17,18].

Wound Healing and Ulcers

Hydrogels facilitate autolytic debridement, maintain a moist environment, and promote angiogenesis. Incorporation of growth factors or silver nanoparticles enhances healing in chronic wounds[19].

Skin Cancer

Hydrogels are used for localized delivery of chemotherapeutic agents (e.g., 5-fluorouracil, imiquimod) with minimal systemic toxicity. Thermo-sensitive and pH-responsive systems are under investigation for improved targeting[20].

Drug Delivery Systems (DDS)

Hydrogels offer controlled and localized drug release through environmental stimuli such as pH-sensitive Hydrogels: Respond to gastrointestinal pH variations; Thermo-sensitive Hydrogels: React to body temperature for on-demand delivery. These allow for: Sustained release of high-concentration drugs; gastroretentive drug systems; protein, enzyme, and vaccine delivery[21].

Wound Healing

Hydrogels maintain a moist environment, promote autolytic debridement, and facilitate healing by enabling oxygen transfer and preventing bacterial contamination[20,21].

Biosensors

Hydrogels can immobilize enzymes, antibodies, or DNA strands, offering a biocompatible interface for detecting analytes. They are employed in diagnostics, environmental monitoring, and point-of-care testing. Living sensors incorporate microorganisms for environmental pollutant detection[22].

Tissue Engineering

Due to their similarity to extracellular matrix (ECM), hydrogels serve as scaffolds for cell growth and differentiation. They support the regeneration of skin, cartilage, bone, and even vascular tissues[23].

Environmental Applications

Hydrogels with functional groups (e.g., –COOH, $–SO_3H$) can adsorb heavy metals and dyes from industrial wastewater. However, large-scale application remains economically challenging[24].

Recent Advancements

Nanotechnology in Hydrogel Systems

Nanoparticles (NPs), liposomes, and micelles incorporated into hydrogels offer enhanced drug loading and penetration:

Nano-hydrogel composites: Combine the controlled release of hydrogels with the high surface area and targeting abilities of nanoparticles.

Lipid-based hydrogels: Improve skin permeation of poorly soluble drugs.

Smart Hydrogels

These hydrogels respond to environmental stimuli for site-specific and time-controlled drug release. Examples include: pH-responsive hydrogels for acne and wound environments; thermo-responsive gels that solidify at body temperature for better retention.

Biopolymer-Based Hydrogels

Natural polymers like chitosan and hyaluronic acid offer excellent biocompatibility and inherent bioactivity, making them ideal for wound healing and anti-aging formulations[25,26].

Advantages and Limitations

Advantages

a. Improved skin adherence and retention
b. Controlled and localized drug release
c. Non-greasy and patient-friendly
d. Can accommodate hydrophilic and hydrophobic drugs
e. Reduced systemic side effects[27-30]

Limitations

a. Limited permeation for large or poorly soluble molecules
b. Stability concerns for certain drugs
c. Potential for microbial contamination if not preserved properly
d. Difficulties in scaling up production for stimuli-responsive systems[27-30]

Future Perspectives

The integration of 3D printing, gene therapy, and CRISPR technology with hydrogel systems is a promising direction for personalized dermatological treatments. Development of multi-functional hydrogels that combine anti-inflammatory, antimicrobial, and regenerative capabilities will further enhance their utility in managing complex skin disorders.

Additionally, regulatory approval and standardization of hydrogel formulations for clinical use remain crucial steps in advancing their commercial viability.

Conclusion

Topical hydrogel delivery systems offer a significant advancement in the management of skin diseases by improving drug retention, reducing systemic side effects, and enhancing patient compliance. Their tunable properties, combined with advances in nanotechnology and stimuli-responsive polymers, position them at the forefront of innovative dermatological therapeutics. Continued interdisciplinary research is needed to overcome current limitations and unlock their full clinical potential.

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