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SHIKONIN-LOADED DEFORMABLE LIPOSOME HYDROGEL FOR TOPICAL ECZEMA THERAPY

Résumé

Eczema is a persistent inflammatory skin disorder associated with immune imbalance, oxidative damage, and disruption of the epidermal barrier. Standard pharmacological treatments often lead to undesirable side effects and frequent relapse. This study presents a novel topical formulation in which shikonin-loaded deformable liposomes are incorporated into a hyaluronic acid and polyethylene glycol (HA/PEG) hydrogel. The system was designed to improve shikonin stability, enhance skin retention, and provide sustained therapeutic effects. Comprehensive physicochemical characterization, antioxidant evaluation, skin permeation analysis, and in vivo efficacy testing using an experimental eczema mouse model were performed. The results demonstrate that the composite hydrogel exhibits strong antioxidant activity, prolonged drug release, increased dermal accumulation, and significant anti-inflammatory effects, indicating its potential as an effective and safe treatment strategy for eczema.

Keywords

Atopic eczema; Shikonin; Deformable liposomes; Hyaluronic acid hydrogel; Oxidative stress; Topical drug delivery

Abstract

Eczema is a common inflammatory skin disease driven by oxidative stress, immune dysfunction, and compromised skin barrier integrity. Shikonin, a bioactive compound derived from *Lithospermum erythrorhizon*, possesses potent anti-inflammatory and antioxidant properties but suffers from poor aqueous solubility and limited transdermal permeability. In this work, shikonin was encapsulated into

sphingomyelin-based deformable liposomes and subsequently embedded within a hyaluronic acid/polyethylene glycol hydrogel to enhance its topical performance. The resulting formulation (SHI-F-Gel) was evaluated for morphology, particle size, stability, hydration capacity, and in vitro release behavior. Antioxidant activity was assessed using DPPH, ABTS, and hydroxyl radical scavenging assays. Skin permeation and retention were investigated ex vivo, while therapeutic efficacy was examined in a 2,4-dinitrochlorobenzene-induced eczema mouse model.

Introduction

Eczema is a chronic, relapsing inflammatory condition of the skin characterized by erythema, edema, pruritus, and exudative lesions. Its incidence continues to rise worldwide, significantly affecting patients' physical comfort and psychological well-being. The etiology of eczema is complex, involving genetic susceptibility, environmental exposure, skin barrier impairment, immune dysregulation, and oxidative stress.

Oxidative stress plays a crucial role in eczema pathogenesis by promoting excessive production of reactive oxygen species, which damage epidermal cells and stimulate inflammatory signaling pathways. Immune imbalance among T helper cell subsets, including Th1, Th2, Th17, and regulatory T cells, further aggravates inflammatory responses. Although topical corticosteroids and antihistamines are widely used, their prolonged application may cause adverse effects such as skin thinning, infection, and disease recurrence.

Traditional herbal medicine has long been employed in the treatment of inflammatory skin disorders. *Lithospermum erythrorhizon* is a medicinal plant traditionally used for skin ailments, and shikonin is its principal active constituent. Shikonin exhibits multiple pharmacological effects, including anti-inflammatory, antioxidant, antibacterial, and wound-healing activities. However, its clinical application is restricted by low water solubility, chemical instability, and poor skin penetration.

Deformable liposomes are advanced vesicular carriers capable of squeezing through the intercellular spaces of the stratum corneum, thereby enhancing transdermal drug delivery. Sphingomyelin, a major component of cell membranes, contributes to ceramide formation and epidermal barrier maintenance. Hyaluronic

acid-based hydrogels offer excellent biocompatibility, moisture retention, and skin adhesion, making them suitable for topical formulations.

This study aimed to develop a shikonin-loaded deformable liposome hydrogel combining the advantages of liposomal carriers and HA/PEG hydrogels to improve drug delivery efficiency and therapeutic outcomes in eczema treatment.

Materials and Methods

Shikonin was supplied by Shanghai Yuanye Bio-Technology Co., Ltd. Sphingomyelin, cholesterol, polyethylene glycol, hyaluronic acid, Tween 80, and 1,2-propanediol were obtained from commercial sources. DPPH, ABTS, ferrous sulfate heptahydrate, salicylic acid, and potassium persulfate were used for antioxidant assays. All chemicals were of analytical grade.Shikonin-loaded deformable liposomes were prepared using a thin-film hydration technique. Lipid components and shikonin were dissolved in an organic solvent, followed by solvent evaporation to form a thin lipid layer. The film was hydrated with an aqueous phase and sonicated to obtain uniformly dispersed liposomes.Hyaluronic acid was dissolved in distilled water, and polyethylene glycol was incorporated to enhance mechanical strength. The prepared shikonin-loaded liposomes were then evenly dispersed into the hydrogel matrix to produce the final formulation.

A mouse eczema model was established using 2,4-dinitrochlorobenzene. Animals were treated with the liposome hydrogel, free shikonin, or blank formulations. Histological examination was conducted to evaluate epidermal thickness and collagen deposition, while inflammatory cytokine levels (IL-4 and IL-17) were assessed by immunohistochemical analysis.

Discussion

The shikonin-loaded deformable liposome hydrogel effectively overcame the inherent limitations of shikonin by enhancing its stability and skin penetration. The combination of flexible liposomes and an HA/PEG hydrogel enabled sustained drug release, improved skin adhesion, and prolonged local retention. The formulation exhibited strong antioxidant properties, which are essential for mitigating oxidative stress–induced skin damage in eczema.

In vivo findings further demonstrated its therapeutic potential, as evidenced by reduced epidermal thickening, increased collagen deposition, and suppression of

key pro-inflammatory cytokines. These outcomes suggest that the formulation supports both inflammation control and skin barrier repair.

Conclusion

A deformable liposome–hydrogel system containing shikonin was successfully developed as a topical treatment for eczema. The formulation demonstrated favorable physicochemical properties, sustained drug release, potent antioxidant activity, and marked therapeutic efficacy in an experimental eczema model. This integrated delivery strategy offers a promising alternative to conventional therapies and highlights the potential of combining traditional herbal compounds with modern drug delivery systems for skin disease management.

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