Microsponge-Based Topical Gels: Advances in Controlled Drug Delivery for Psoriasis Skin

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Abstract

Psoriasis is a chronic, inflammatory skin disorder marked by excessive keratinocyte proliferation, immune system dysfunction, and persistent skin lesions. Traditional topical treatments often face limitations such as poor skin penetration, short duration of action, and frequent application, which can affect patient compliance and therapeutic success. Microsponge-based topical gels have emerged as an innovative drug delivery system capable of overcoming these challenges. These formulations utilize porous, polymer-based microstructures that enable controlled and sustained release of active agents directly at the site of inflammation. This review focuses on the recent advances in microsponge technology for psoriasis treatment, discussing formulation techniques, advantages over conventional carriers, incorporation of herbal and synthetic drugs, and evaluation parameters. Despite certain limitations such as scale-up difficulties and drug loading constraints, microsponge-based gels hold significant promise as an effective and patient-friendly strategy for long-term psoriasis management.

Keywords: Psoriasis, Microsponge technology, Topical gels, Controlled drug delivery, Skintargeted therapy, Herbal actives, Sustained release systems.

1. Introduction

1.1 Overview of Psoriasis

Psoriasis is a lifelong immune-mediated inflammatory skin disease, associated with morbidities such as psoriatic arthropathy, psychological, cardiovascular and hepatic diseases. In 2014, the World Health Organization recognised psoriasis as a serious non-communicable disease and highlighted the distress related to misdiagnosis, inadequate treatment and stigmatisation of this disease.[1] The Global Burden of Disease Study estimated that psoriasis accounted for 5.6 million all-age disability-adjusted life-years (DALYs) in 2016; at least three-fold that of inflammatory bowel disease.[2]

1.2 Challenge in Psoriasis treatment

1.2.1 Chronic and Relapsing Nature

Psoriasis is marked by frequent flare-ups and remissions, necessitating long-term treatment strategies. This chronic course often leads to patient fatigue and poor adherence.[3]

1.2.2 Limited Skin Penetration of Topical Drugs

Thickened psoriatic plaques (hyperkeratosis) hinder drug absorption, reducing the effectiveness of topical agents such as corticosteroids and vitamin D analogs.[4]

1.2.3 Adverse Effects of Long-term Therapies

Long-term use of systemic drugs (e.g., methotrexate, cyclosporine) or biologics can lead to organ toxicity, immunosuppression, or loss of efficacy due to antibody formation.[5]

1.2.4 High Cost of Biologics

Biologic agents are highly effective but are expensive, limiting their accessibility to many patients, particularly in low- and middle-income countries.[6]

1.2.5 Psychological and Quality of Life Burden

Psoriasis is associated with depression, anxiety, and low self-esteem, which can negatively impact treatment outcomes and compliance.[7]

1.2.6 Resistance and Treatment Failure

Over time, patients may develop resistance or stop responding to treatments, requiring frequent treatment modifications or switching therapies.[8]

1.3 Need for Advanced topical drug delivery

Topical therapy remains the first-line treatment for mild to moderate psoriasis due to its localized action and reduced systemic side effects. However, conventional topical formulations such as creams and ointments often fail to provide adequate therapeutic outcomes due to multiple limitations, necessitating the development of advanced drug delivery systems.

1.3.1 Limitations of Conventional Topical Formulations

Poor skin penetration: Thick psoriatic plaques (hyperkeratosis) act as a barrier, limiting drug absorption. Rapid clearance: Drugs may be wiped or washed off easily, reducing contact time. Low patient compliance: Greasy, sticky formulations reduce user satisfaction and adherence. Dose fluctuations: Inconsistent application can lead to under or over-dosing.[9]

1.3.2 Rationale for Advanced Delivery Systems

Advanced drug delivery systems such as microsponge gels, liposomes, niosomes, solid lipid nanoparticles (SLNs), and nanoemulsions offer several advantages:

- Improved drug penetration into the deeper skin layers.
- Controlled and sustained drug release, reducing dosing frequency.

- Minimized local irritation and systemic side effects.
- Enhanced stability of sensitive drugs like herbal extracts (e.g., liquorice).
- Improved patient compliance through better aesthetics and ease of use.[10]

1.3.3 Microsponge-Based Systems: A Promising Solution -

Microsponge technology has emerged as a versatile carrier for topical applications. These porous, polymeric microspheres:

- Allow encapsulation of both hydrophilic and lipophilic drugs.
- Provide sustained release, reducing the need for frequent application.
- Improve targeted delivery and minimize systemic absorption.
- Are non-irritant and compatible with herbal actives like liquorice, which is beneficial in psoriasis due to its anti-inflammatory and antioxidant properties.[11]

1.4 Role of Microsponges in dermatology

1.4.1 Introduction to Psoriasis and Dermatological

Challenges - Psoriasis is a chronic, inflammatory, and immune-mediated skin disease affecting around 2–3% of the global population. It is characterized by erythematous plaques, scaling, and keratinocyte hyperproliferation, making drug delivery through the skin highly challenging due to the thickened stratum corneum.

Conventional topical treatments, though first-line for mild to moderate psoriasis, often face limitations like poor skin penetration, short residence time, and frequent application requirements, necessitating novel drug delivery systems.[12]

1.4.2 Overview of Microsponge Drug Delivery System

Microsponge technology is a polymeric, porous, and microscopic spherical structure that can entrap both hydrophilic and lipophilic drugs. These sponges act as reservoirs, releasing the drug in a controlled and sustained manner, making them ideal for dermatological applications.

Key Features:

- High loading capacity
- Controlled and sustained release
- Non-irritant and non-toxic
- Improved drug stability
- Better skin adhesion[13]

1.4.3 Benefits of Microsponge in Psoriasis Management

Microsponge-based gels and creams offer several advantages in the treatment of psoriasis.

Enhanced Penetration: Porous structure facilitates deep dermal absorption.

Reduced Irritation: Controlled drug release prevents local irritation from concentrated drug exposure.

Improved Efficacy: Constant therapeutic levels are maintained.

Patient Compliance: Better aesthetics and reduced application frequency.[14]

1.4.4. Herbal Integration: Microsponge with Liquorice Extract

Herbal compounds such as liquorice extract (Glycyrrhiza glabra) have shown antiinflammatory and antioxidant potential in psoriasis. However, poor skin permeability and stability limit their efficacy. Encapsulating such actives in microsponge systems enhances bioavailability, protects the phytoconstituents, and improves therapeutic results.[15]

1.4.5. Future Prospects and Clinical Relevance

Microsponge systems are a promising tool for next-generation topical therapies in dermatology, especially for chronic skin diseases like psoriasis. Ongoing research on biodegradable polymers, herbal integration, and patient-friendly formulations may pave the way for commercial products that offer enhanced safety, stability, and efficacy.[16]

2. Pathophysiology of Psoriasis

2.1 Etiology and Immunological Aspects

Psoriasis is a chronic immune-mediated skin disorder with multifactorial origins involving genetic susceptibility and environmental triggers. Genes such as HLA-Cw6, IL23R, and CARD14 are strongly associated with psoriasis and regulate immune responses.[17] External factors like streptococcal infections, trauma (Koebner phenomenon), stress, medications, smoking, and obesity may trigger or worsen symptoms.[18]

The IL-23/Th17 immune axis plays a central role in disease progression. Dendritic cells produce cytokines like IL-12 and IL-23, promoting the differentiation of Th1 and Th17 cells. These T cells release cytokines including IFN-γ, TNF-α, IL-17, and IL-22, leading to keratinocyte activation, hyperproliferation, and inflammation.[17,19] Keratinocytes themselves contribute to inflammation by releasing cytokines and antimicrobial peptides.[18]Additionally, Treg cell dysfunction and NF-κB pathway activation support chronic immune activation and lesion persistence.

Understanding these mechanisms is essential for developing targeted therapies and advanced delivery systems such as microsponge-based topical gels, which can improve local drug action while minimizing systemic effects.[20]

2.2 Histological features of Psoriatic Skin

Psoriatic skin shows distinct histological alterations, primarily due to abnormal keratinocyte turnover and chronic inflammation. The epidermis becomes thickened (acanthosis) with elongated rete ridges, caused by rapid cell proliferation. Parakeratosis (nuclei retention in the stratum corneum) and loss of the granular layer indicate defective skin maturation. The dermis exhibits dilated capillaries and immune cell infiltration, mainly T cells and dendritic cells, which drive inflammation. Neutrophil clusters, known as Munro’s microabscesses, are often seen in the stratum corneum, reflecting active disease. [21]

2.3 Conventional Therapies and Limitations

The management of psoriasis has traditionally relied on three main treatment approaches: topical agents, systemic medications, and phototherapy. Each method targets different aspects of the disease pathophysiology, including immune dysregulation, epidermal hyperproliferation, and inflammation. However, despite their clinical utility, these conventional therapies present notable limitations, especially in chronic or recalcitrant cases.

2.3.1 Topical Therapies

Topical medications remain the first-line choice for mild to moderate psoriasis. These include: Corticosteroids: anti-inflammatory agents that suppress cytokine expression and keratinocyte proliferation.

Vitamin D analogues (e.g., calcipotriol): normalize keratinocyte growth and differentiation.
Coal tar and salicylic acid: used to reduce scaling and plaque thickness.
While effective in the short term, long-term use of topical corticosteroids may lead to skin thinning, irritation, tachyphylaxis and barrier dysfunction. Moreover, penetration through thick psoriatic plaques is poor, limiting therapeutic effectiveness at deeper layers of the skin where inflammation persists.[22,23]

2.3.2 Systemic Therapies

Moderate to severe psoriasis may require systemic treatments such as:

Methotrexate: Inhibits DNA synthesis, reducing keratinocyte turnover and immune activation.

Cyclosporine: Suppresses T-cell function.

Acitretin: A retinoid that modulates epidermal differentiation.

However, these drugs are associated with significant systemic side effects, including hepatotoxicity, nephrotoxicity, bone marrow suppression, and teratogenicity. Their nonspecific action often affects healthy tissues, demanding regular monitoring and limiting longterm use.[24]

2.3.3 Phototherapy

Ultraviolet (UV) light, particularly narrowband UVB (NB-UVB) and psoralen UVA (PUVA), helps reduce inflammation and slow keratinocyte proliferation. However, limitations include:

- Risk of premature skin aging and carcinogenesis due to cumulative UV exposure.
- Inconvenience of frequent hospital visits.
- Reduced efficacy in dark skin types or thick plaques.[25]

2.3.4. Biological Therapies: Advances with Limitations

Biologics have revolutionized psoriasis treatment by specifically targeting cytokines such as TNF-α, IL-17, and IL-23. Though highly effective in severe cases, biologics are:

- Cost-prohibitive for many patients.
- Administered parenterally, reducing convenience.
- Associated with risk of infection and immunosuppression.[26]

3. Microsponge Technology: An overview

3.1 Definition and Structure of Microsponge

Definition: Microsponge systems are defined as highly cross-linked, porous polymeric particles—typically ranging from 5 to 300 μm in diameter—that can encapsulate both hydrophilic and lipophilic drugs. These particles act like microscopic reservoirs that gradually release the drug over time in response to physiological conditions such as pH, temperature, or moisture. Their ability to retain and protect drugs while minimizing side effects makes them suitable for long-term topical applications [27,28]

Structure - Structurally, a microsponge is made up of an interconnected network of pores forming a sponge-like architecture. This internal structure provides a large surface area, which allows a high payload of drug to be incorporated. The outer shell is formed by a biocompatible polymer, most commonly polymethyl methacrylate (PMMA), ethyl cellulose, or polyvinyl alcohol, depending on the formulation's desired properties.

Key features of microsponge structure include:
Porosity: The internal cavity contains multiple micropores that allow drug loading and slow diffusion.

Cross-linked polymer matrix: Ensures mechanical stability and controlled release.

Surface modification: Some systems include surface coatings to improve adhesion to the skin or to modify release kinetics.
These characteristics enable microsponge systems to localize drug delivery within the skin layers without systemic absorption, minimizing irritation and increasing residence time at the site of inflammation critical in managing conditions like psoriasis.[29,30]

3.2 Historical Background

Microsponge technology was developed in the late 1980s as an innovative approach to address the limitations of conventional drug delivery systems, especially for topical formulations. The primary objective behind this development was to create a carrier system that could entrap active pharmaceutical ingredients within a porous structure and gradually release them in a controlled manner over time.

The concept was initially applied in the cosmetic industry, where microsponges were used to deliver ingredients like benzoyl peroxide and retinoids. These early applications aimed to reduce local irritation and enhance the therapeutic benefits of the active compounds by allowing sustained release and minimizing direct contact with the skin surface. The success in

cosmetic formulations led to growing interest in adapting the technology for pharmaceutical use.

Microsponge systems are composed of porous, polymeric microspheres that can incorporate a wide range of drugs, including hydrophilic and lipophilic molecules. Their sponge-like structure provides a large surface area, which helps in efficient drug loading and regulated release. Over time, microsponge technology gained popularity in the field of dermatology due to its ability to deliver drugs locally, reduce systemic side effects, and improve patient compliance.

In the context of psoriasis treatment, microsponges are particularly beneficial because they can deliver anti-psoriatic agents directly to the affected skin in a sustained and controlled manner. This localized delivery helps reduce inflammation, minimize dosing frequency, and avoid unwanted drug absorption into systemic circulation. With advancements in polymer science and formulation techniques, microsponges are now widely integrated into topical gels and other semisolid preparations, offering promising outcomes in treating chronic skin conditions like psoriasis. [31]

3.3 Advantages of microsponges in Topical Delivery

3.3.1 Controlled and Sustained Drug Release

Microsponges allow gradual release of the drug at the application site, maintaining consistent levels over time. This reduces the need for frequent application and enhances patient compliance in chronic therapies like psoriasis.

3.3.2 Improved Stability of Sensitive Drugs

Drugs that degrade upon exposure to light, oxygen, or moisture are better protected inside the microsponge matrix. This ensures greater chemical stability and a longer shelf life.[32]

3.3.3 Reduced Side Effects and Irritation

Localized drug action minimizes systemic absorption and avoids sudden drug concentration spikes, which are common causes of skin irritation. This is especially beneficial for inflamed or sensitive psoriatic skin.

3.3.4. Enhanced Cosmetic Properties

Microsponge-based gels are typically non-oily, smooth, and more pleasant to use compared to traditional ointments. Their light texture supports better acceptance and ease of application.[33]

3.3.5 Versatility with Different Drug Types

Microsponge systems are compatible with a wide range of drug types—both lipophilic and hydrophilic—making them suitable for various formulations including herbal, synthetic, and combination therapies.[32]

3.4 Limitation and Challenges

Although microsponge systems offer significant benefits in controlled and localized topical drug delivery, several formulation and practical challenges limit their broader application in clinical and industrial settings.

3.4.1 Limited Drug Loading Capacity

Microsponges can encapsulate only a limited amount of active pharmaceutical ingredients. For drugs that require higher concentrations, especially in the treatment of severe psoriasis, this may reduce therapeutic effectiveness or lead to formulation instability if overloaded.[34]

3.4.2 Particle Size Control Issues

Uniform particle size is crucial for consistent drug release and skin penetration. However, maintaining uniformity during production remains difficult, which can result in batch variations and unpredictable release behavior.

3.4.3 Low Entrapment Efficiency for Some Drugs

Hydrophilic drugs often exhibit poor entrapment in the microsponge matrix due to low compatibility with hydrophobic polymers, reducing formulation efficiency and requiring additional processing or stabilizers.[35]

3.4.4 Polymer Compatibility and Irritation Risk

Microsponge formation relies on specific polymers like ethyl cellulose. Not all drugs are compatible with these materials, and some patients may experience irritation or hypersensitivity reactions.[34]

3.4.5 Manufacturing and Scale-Up Difficulties

While microsponge systems are easy to prepare in laboratories, large-scale manufacturing demands precise equipment and strict process control, which can increase production costs and limit accessibility in resource-limited settings.[35]

3.4.6 Regulatory and Safety Uncertainties

Despite their potential, microsponge formulations still lack well-defined regulatory guidelines. Moreover, long-term safety data, especially regarding polymer toxicity and biodegradability, is limited, delaying broader clinical adoption.[34]

4. Preparation Techniques of Microsponges

4.1 Liquid–Liquid Suspension Polymerization

This is the most common method used for drugs that are thermally stable.
The drug and monomers (like styrene or methyl methacrylate) are dissolved in an organic solvent to form the internal phase.

This is added to an aqueous phase containing a stabilizer such as polyvinyl alcohol (PVA).
A polymerization initiator like benzoyl peroxide is used to start the reaction.

Microsponge particles form as the monomers polymerize, and are then filtered, washed, and dried.

Advantage: Suitable for large-scale production and results in highly porous microsponges.[36]

4.2 Quasi-Emulsion Solvent Diffusion Best suited for heat-sensitive drugs.
The drug and polymer (e.g., ethyl cellulose) are dissolved in a volatile organic solvent like dichloromethane to form the internal phase.
This is emulsified into an external aqueous phase containing a surfactant (e.g., PVA).
The solvent diffuses out and evaporates, forming solid porous microsponges.
The microsponges are then filtered and dried.

Advantage: Offers controlled drug release and better particle size control.[37]

4.3 Spray Drying
A rapid and industrially scalable method used for thermally stable compounds.
A solution of drug and polymer is prepared in a volatile solvent.
This is sprayed through a nozzle into a hot air chamber, where the solvent evaporates rapidly.
Fine, dry microsponge particles are formed and collected.

Advantage: High reproducibility, easy scale-up, and controlled release characteristics.[38]

4.4 Ultrasound-Assisted Emulsion Polymerization
A newer approach involving ultrasonic waves to aid emulsification and polymerization.
The monomer and drug mixture is subjected to ultrasound during emulsification.
This improves droplet dispersion, leading to better entrapment and smaller microsponge particles.

Advantage: Enhanced particle uniformity and drug loading.[39]

5. Characterization of Microsponges

5.1. Particle Size and Distribution
The particle size of microsponges plays a key role in determining their drug delivery efficiency, especially in topical formulations for skin conditions like psoriasis. The ideal size range for microsponges used in dermal delivery is typically between 5 to 300 micrometers (μm).
Smaller particles (closer to 5 μm) may penetrate deeper into the skin layers but must be carefully controlled to avoid systemic absorption.
Larger particles (closer to 300 μm) generally stay on the skin surface, ensuring localized action, which is ideal for psoriasis treatment.

Uniform particle distribution ensures:
- Consistent drug release rate from each microsponge.
- Homogeneous spread in the gel, giving better texture and feel.

- Reduced risk of irritation or clogging of skin pores.

Measurement Techniques:

- **Dynamic Light Scattering (DLS):** Commonly used to measure nanoparticles and microparticles in suspension.
- **Laser Diffraction (LD):** Used for bulk particle size analysis in powders and emulsions. These methods help ensure that the microsponge formulation maintains the desired release kinetics and patient acceptability.[40]

5.2 Surface Morphology (SEM Analysis)

Scanning Electron Microscopy (SEM) is used to observe the shape, surface texture, and porosity of microsponges.

Microscopically, ideal microsponges appear as spherical, porous particles, which support high drug-loading capacity and extended release.[41]

5.3 Drug Loading and Entrapment Efficiency

Drug loading refers to the total amount of drug present within the microsponge relative to the total weight of the microsponge formulation.

Entrapment efficiency shows how efficiently the microsponge system has captured and retained the drug during the preparation process.

These parameters are essential in psoriasis treatment because they:

- Help ensure accurate dosing of the drug,
- Prevent wastage of costly therapeutic agents
- Support controlled release over a long duration, reducing the need for frequent application.

Calculation Formulas:

- Drug Loading (%) = (Weight of drug in microsponge / Total weight of microsponge) × 100
- Entrapment Efficiency (%) = (Amount of drug entrapped / Initial drug used) × 100 [42]

5.4 Porosity and Surface Area Analysis

Brunauer–Emmett–Teller (BET) analysis is employed to determine the specific surface area and porosity.

High porosity supports drug absorption and controlled diffusion, essential for chronic conditions like psoriasis.[43]

5.5 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR helps confirm whether the drug is chemically stable after encapsulation.

It also detects any undesired interactions between the drug and the polymer, which could affect drug release, stability, or therapeutic efficacy.

A successful FTIR analysis will show:

- Characteristic peaks of both the drug and the polymer.
- No major shifts or disappearance of key peaks, which means there is no chemical reaction or degradation during microsponge formation.[44]

5.6 Thermal Analysis (DSC and TGA) -

- Differential Scanning Calorimetry (DSC) determines drug crystallinity and interaction with the polymer.
- Hermogravimetric Analysis (TGA) evaluates thermal stability and moisture content, critical for shelf life.[45]

5.7 In Vitro Drug Release

In Vitro Drug Release studies are typically conducted using Franz diffusion cells, which mimic skin conditions and allow the evaluation of drug release behavior over time. This technique helps predict how the drug will diffuse from the microsponge gel through the skin layers under realtime conditions. It is crucial for ensuring sustained and localized drug delivery, especially in the treatment of chronic conditions like psoriasis, where controlled drug exposure helps reduce side effects and improve therapeutic outcomes.[46]

6. Microsponge-Based Topical Gels

6.1 Gels base selection

Choosing the right gel base is a vital step in developing microsponge-loaded topical formulations, particularly for treating psoriasis. The gel base not only acts as a medium for microsponges but also plays an important role in controlling drug release, enhancing skin penetration, and improving patient acceptability.

Among the various gelling agents, Carbopol polymers such as Carbopol 934 and 940 are widely used due to their favorable properties like high viscosity, clear appearance, ease of application, and compatibility with different drugs. These carbomers also help maintain the structure and stability of the gel, allowing for effective dispersion of microsponges.

In psoriasis care, formulations that are non-irritant, soothing, and non-oily are preferred. For this reason, humectants such as glycerin and propylene glycol are often added to increase skin moisture and softness. Adjusting the pH of the gel to around 5.5–6.5 helps to match the skin's natural environment and reduces the risk of irritation.

An ideal gel base allows even distribution of the microsponge particles, ensures sustained drug delivery, and adheres well to the skin for longer action. Ultimately, the physical characteristics of the gel, like its thickness and stickiness, greatly influence how well the formulation works in managing psoriasis symptoms.[47]

6.2 Integration of Microsponges into Gels

Incorporating microsponges into gel formulations is a crucial step in developing effective topical drug delivery systems, especially for chronic skin disorders like psoriasis. After their preparation, microsponges are carefully filtered, washed, and dried to remove any remaining free drug or unwanted residues.

These purified microsponges are then gently mixed into a gel base using controlled mechanical stirring. Common gelling agents such as Carbopol 934, HPMC, and xanthan gum are often selected due to their skin-friendly texture, appropriate viscosity, and smooth application. To ensure uniformity and stability, factors like polymer concentration, stirring time, and pH of the formulation must be precisely adjusted.

The final gel typically has a pH close to that of normal skin (5.5–6.5), which reduces the risk of irritation and promotes user comfort. The gel base not only serves as a medium for the microsponges but also supports prolonged and localized drug release at the site of application. For psoriasis treatment, this integration technique offers multiple benefits—such as sustained drug action, fewer applications, reduced systemic side effects, and better adherence to therapy— making it a promising approach in dermatological care.[48]

6.3 Rheological Properties and Stability

The flow behavior and mechanical consistency of microsponge-based topical gels play a key role in determining their clinical effectiveness and patient usability. Rheological characteristics such as viscosity, spreadability, and shear-thinning behavior directly impact how easily the gel can be applied and how well it remains on the skin surface during treatment.

Typically, these gels show pseudoplastic or shear-thinning properties—where viscosity decreases with increasing shear stress. This behavior supports better application by allowing the gel to spread smoothly while maintaining adherence once applied. The inclusion of microsponges may slightly alter the gel's viscosity, but using optimized concentrations of gelling agents like Carbopol 934, HPMC, or xanthan gum ensures a balanced consistency suitable for dermatological use.

From a stability perspective, maintaining the physical, chemical, and functional properties of the formulation during storage is essential. Stability assessments generally involve monitoring of pH, drug content, appearance, and viscosity over a set period. A stable microsponge gel should resist phase separation, preserve its homogeneity, and retain drug potency throughout its shelf life.

To predict long-term performance, accelerated stability testing is often performed under stress conditions such as high temperature and humidity. These studies help ensure that the formulation remains effective and safe, especially for chronic skin conditions like psoriasis that require extended use.[49]

6.4 Release Kinetics from Gel Form

Understanding how drugs are released from microsponge-based gels is essential for achieving long-lasting and targeted treatment in chronic skin conditions like psoriasis. In such formulations, microsponges act as miniature carriers that gradually release the drug, avoiding a rapid burst and instead ensuring steady delivery over time.

The release process occurs in several stages—first, the drug diffuses from the internal pores of the microsponge, then it travels through the surrounding gel matrix, and finally penetrates the skin layers. This step-by-step mechanism depends on multiple factors, including the nature of the polymer used, the degree of cross-linking in the microsponge, drug solubility, and the thickness or viscosity of the gel base.

To evaluate how the drug is released, researchers often perform in vitro studies using Franz diffusion cells, which mimic how the drug passes through the skin. The release patterns are analyzed using mathematical models such as zero-order, first-order, Higuchi, and Korsmeyer–Peppas models. These models help determine whether the drug is released steadily, based on concentration, or primarily through diffusion.

Most microsponge gels show a release profile consistent with the Higuchi or Korsmeyer–Peppas model, indicating that diffusion controls the process. This controlled release helps keep the drug localized for a longer time, reduces how often the gel must be applied, and limits side effects— making it highly beneficial for patients managing psoriasis.[50]

7. Herbal Actives in Microsponge Gels for Psoriasis

7.1 Role of Herbal Extracts

Herbal extracts have gained attention in psoriasis treatment due to their natural antiinflammatory, antioxidant, and immune-balancing effects. When incorporated into microspongebased gels, these plant-derived compounds provide a targeted and sustained therapeutic effect, which helps reduce the need for frequent application and lowers the risk of systemic side effects. Phytochemicals such as curcumin (from turmeric), aloe vera, capsaicin, and boswellic acid have shown promise in relieving symptoms like itching, redness, and scaling. These effects are primarily achieved by controlling inflammatory pathways and neutralizing oxidative stress in the affected skin.

The microsponge delivery system improves the performance of these herbal agents by enhancing their stability, reducing degradation, and allowing slow and even release into the skin. This not only increases skin retention time but also reduces the chances of irritation, which is sometimes associated with direct application of herbal extracts in conventional formulations. Overall, combining herbal actives with microsponge technology offers a natural and effective approach to manage psoriasis, supporting safer and more patient-friendly topical therapy.[51]

7.2 Benefits of Glycyrrhiza glabra in Skin Disorders

Glycyrrhiza glabra (licorice) is a medicinal herb widely recognized for its therapeutic benefits in dermatology. Its active compound, glycyrrhizin, exhibits strong anti-inflammatory and antioxidant activities that help in managing inflammatory skin conditions like psoriasis . By regulating cytokine levels and reducing oxidative stress, it contributes to minimizing skin redness, itching, and flaking.

Licorice extract also promotes skin repair and barrier protection, making it useful in soothing irritated or sensitive skin.[52] When incorporated into a microsponge gel formulation, it ensures better skin penetration, protects the phytoconstituents from degradation, and provides a sustained release effect. This enhances local action, reduces the need for frequent application, and lowers the risk of irritation compared to conventional formulations.[53]

7.3 Studies Supporting Herbal Microsponge Gels

Herbal-loaded microsponge gels have shown promising results in treating psoriasis by improving the stability and controlled release of natural actives like curcumin and Glycyrrhiza glabra.[54] These systems reduce skin irritation and enhance patient compliance in long-term therapy .[55] A 2023 study on curcumin microsponges showed better anti-psoriatic effects than conventional gels due to improved retention .[54] Similarly, Glycyrrhiza glabra-based microsponges significantly reduced redness and scaling, confirming their dermatological potential.[55]

8. Evaluation of Microsponge Gels

Proper evaluation of microsponge-based topical gels is essential to confirm their performance, safety, and stability for use in chronic skin disorders like psoriasis. Various parameters are assessed during the formulation process to ensure optimal therapeutic action.

8.1 Physical Characteristics and pH

Initial assessment includes observing the gel's appearance, texture, and uniformity. The pH is adjusted close to skin's natural range (5.5–7.0) to minimize irritation and maintain skin compatibility.[56]

8.2 Rheology and Viscosity

Viscosity is tested using instruments such as the Brookfield viscometer to ensure proper spreadability and retention. Non-Newtonian flow behavior (shear-thinning) is desired, allowing ease of application without dripping.[57]

8.3 Drug Content and Uniformity

To ensure consistent therapeutic efficacy, the drug must be evenly distributed throughout the gel. This is typically confirmed using spectrophotometric or chromatographic techniques.[56]

8.4 In Vitro Drug Diffusion

Franz diffusion cells simulate the drug release across skin or synthetic membranes. These tests reveal the controlled release capabilities of the microsponge system, which is essential for sustained treatment of psoriasis.[58]

8.5 Spreadability and Extrudability

Spreadability influences the ease with which the gel can be applied to the skin, while extrudability reflects its ability to be dispensed from containers. Both are critical for patient adherence.[56]

8.6 Stability Testing

Gels are subjected to stability studies under various conditions (as per ICH guidelines) to check changes in drug content, pH, and physical stability over time.[57]

8.7 Skin Irritation Studies

To assess biocompatibility, gels are tested on animal models or reconstructed human skin. Herbal microsponge formulations often demonstrate low irritation potential, making them safer for chronic use.[58]

9. Recent Advances and Case Studies

9.1 Recent Formulation for Psoriasis Using Microsponges

a) Tazarotene Microsponge Gel (2024)

Objective: To reduce the skin irritation caused by regular tazarotene gels through a controlledrelease microsponge formulation.
Formulation: Tazarotene was loaded into microsponges using emulsion solvent diffusion and then mixed into a Carbopol gel base.
Results: The optimized gel showed 87.6% drug release in 12 hours, better skin absorption, and much less irritation, making it more suitable for long-term use in psoriasis.[59]

b) Botanical-Metal Oxide Nanocomposite Gel (2025)

Objective: To create a gel that uses both herbal extracts and metal oxides for faster healing of psoriatic skin.
Formulation: A hydrogel base made from fish collagen and agar was loaded with CeO_2, ZnO, Ag nanoparticles along with neem, ginger, and bitter melon extracts.
Results: In animal studies, the gel reduced inflammation and completely healed skin lesions within 14 days, showing strong antioxidant and anti-inflammatory effects.[60]

9.2 Comparison with other Nanocarriers

Microsponge-based delivery systems have shown several advantages over conventional nanocarriers used in topical therapy for psoriasis. A comparison is outlined below:

a) Liposomes are known for good drug encapsulation and hydration benefits. However, they often suffer from poor stability and drug leakage. In contrast, microsponges exhibit enhanced shelf-life and provide sustained drug release.
b) Niosomes offer better skin penetration but may cause surfactant-related toxicity and drug loss. Microsponges, on the other hand, ensure improved skin compatibility and greater formulation stability.[61]
c) Solid Lipid Nanoparticles (SLNs) are effective in enhancing delivery of lipophilic drugs but may undergo polymorphic transitions, resulting in drug expulsion. Microsponges maintain chemical stability and are especially useful for photosensitive drugs.
d) Nanoemulsions facilitate quick drug absorption due to their small droplet size. However, high surfactant levels in them may irritate the skin. Microsponges minimize this issue through controlled, localized release.[62]

10. Regulatory and Safety Considerations

10.1 GRAS Status of Excipients

The Generally Recognized as Safe (GRAS) status is a regulatory classification established by the U.S. Food and Drug Administration (FDA) to identify substances—such as pharmaceutical excipients—that are considered safe under their intended conditions of use. This designation is based on either extensive historical usage or robust scientific validation, ensuring the ingredient's safety profile in food and pharmaceutical products.[63]

In microsponge-based topical gels, GRAS-certified excipients are widely employed due to their proven compatibility with skin applications. Key excipients such as ethyl cellulose, Carbopol® (carbomer), polyvinyl alcohol (PVA), and triethanolamine (TEA) are frequently used as matrix formers, thickening agents, stabilizers, or pH modifiers. These substances are known for their non-irritant, biocompatible, and non-sensitizing properties, making them particularly suitable for long-term use in chronic dermal conditions like psoriasis.[64]

10.2 Regulatory Pathways for Herbal and Nano Topicals

The development of herbal and nanotechnology-based topical systems such as microsponge gels has expanded rapidly due to their potential in treating chronic skin conditions like psoriasis. However, these systems face complex regulatory scrutiny because of their multifaceted composition, novel delivery mechanisms, and long-term skin interaction. This has prompted regulatory bodies to refine their frameworks to ensure consistent standards in safety, efficacy, and quality control.[65]

10.2.1 Regulatory Classification

Globally, regulatory classification of herbal or nano-based topical products depends on their intended use, claims made, and formulation type.

In India, herbal products are primarily regulated under the Drugs and Cosmetics Act, 1940, through the AYUSH framework. When these herbal actives are incorporated into advanced carriers like microsponges, the formulations may fall under cosmeceuticals or new drugs, requiring approval from the Central Drugs Standard Control Organization (CDSCO).[66] In

the United States, the FDA regulates products based on claims. If a topical product claims to treat, mitigate, or prevent a disease, such as psoriasis—even if it contains herbal or GRAS ingredients—it is classified as a drug. For nanoformulations, including microsponge-based systems, developers may need to submit either an Investigational New Drug (IND) application or follow the 505(b)(2) approval pathway to meet regulatory standards.[67]

10.2.2 Guidelines for Nanotechnology-Based Formulations

International regulatory bodies, such as the US FDA and the European Medicines Agency (EMA), have introduced specific guidance for nanomaterial-containing drug products. These guidelines emphasize:

- Detailed physicochemical characterization (particle size, surface charge, morphology).
- Toxicological assessment, especially dermal safety for chronic use.
- Reproducibility and stability of nanosystems during manufacturing.[67]

In India, although dedicated regulatory guidelines for nano-topicals are not yet formalized, institutions like the Indian Council of Medical Research (ICMR) and the Department of Biotechnology (DBT) have proposed frameworks focused on the safety, quality, and risk assessment of nanomedicines. Most nanoformulations are currently evaluated on a case-bycase basis.[66]

10.2.3 Challenges and Considerations

a) Standardization of Herbal Extracts: The active ingredients in herbal extracts can vary from batch to batch, making it hard to ensure consistent quality.
b) Reproducibility of Nanoformulations: Microsponge formulations require strict control over particle size, structure, and drug content to ensure batch-to-batch uniformity.
c) Dual Evaluation Requirement: When herbal ingredients are combined with nanocarriers, regulatory bodies may ask for safety and efficacy data for both components.
d) Need for Long-Term Safety Data: Since these products are used for chronic skin conditions like psoriasis, studies on long-term skin safety and absorption are essential for approval.[68]

10.3 Safety and Toxicity concerns

Microsponge-based topical gels are promising for localized drug delivery, but their safety profile requires thorough evaluation. Although the polymers used, such as ethyl cellulose, are generally biocompatible, there is a potential risk of skin irritation or hypersensitivity, especially with prolonged use on psoriatic skin. Particle size is another concern, as very small microsponges might penetrate deeper skin layers, increasing the risk of systemic absorption. Moreover, residual solvents from the manufacturing process can lead to cytotoxicity if not completely removed. Long-term use also warrants assessment of dermal toxicity and immune responses, especially due to the compromised skin barrier in psoriasis patients.[69]

11. Future Perspectives

Microsponge-based topical gels have already demonstrated significant potential in delivering antipsoriatic agents with controlled release and minimal side effects. However, future

developments aim to enhance their therapeutic performance, patient compliance, and commercial translation through innovations in formulation science and nanotechnology.

One key direction is the development of microsponge hybrid systems. Combining microsponges with other delivery technologies such as liposomes, nanoparticles, or hydrogels may allow for multimodal drug release, deeper skin penetration, and enhanced retention time at the target site. These hybrid approaches are expected to provide stage-wise drug delivery, particularly useful for managing both acute flares and chronic phases of psoriasis.

Another promising area is the use of biodegradable and natural polymers in microsponge fabrication, which could further reduce the risk of long-term toxicity and make the systems more environmentally and biologically safe. Also, the integration of herbal bioactives into microsponge systems is gaining interest due to their lower toxicity and synergistic anti-inflammatory properties, aligning with the growing demand for green and patient-friendly therapies.

Advancements in 3D printing, AI-assisted formulation design, and skin-on-chip testing models are expected to revolutionize the screening and development of next-generation microsponge gels. These tools will enhance predictability, personalization, and safety evaluation, ultimately accelerating the pathway from lab to clinic.

In the long term, microsponge-based gels could be engineered not just for drug delivery but also for responsive treatment, where drug release is triggered by specific skin conditions (e.g., pH, enzymes, inflammation), offering precision therapy for psoriatic patients.[70]

12. Conclusion

Psoriasis is a long-standing inflammatory skin disorder that requires continuous and effective topical treatment. Traditional formulations often fall short due to issues like rapid drug degradation, poor penetration through the skin barrier, and frequent need for application. Microsponge-based topical gels have emerged as a promising alternative, providing multiple benefits such as sustained drug release, improved skin retention, reduced irritation, and enhanced patient comfort.

The unique porous structure of microsponges allows them to carry both synthetic drugs and herbal extracts, enabling localized and prolonged therapeutic action. This feature is particularly important for treating psoriasis, where consistent drug levels at the site of inflammation are needed to reduce symptoms and flare-ups. Microsponge systems also help in minimizing systemic exposure, thus lowering the risk of side effects.

Compared to other nanocarriers like liposomes or niosomes, microsponges offer better stability, controlled release profiles, and ease of formulation. These characteristics make them suitable for long-term topical treatment. However, challenges such as optimizing drug loading, maintaining structural integrity, and meeting regulatory requirements still need attention.

Advances in formulation science and improved understanding of skin pharmacokinetics can help overcome these limitations.

In summary, microsponge-based gels represent a modern and efficient platform for delivering drugs in psoriasis therapy. With continued research and clinical validation, these systems have the potential to become a reliable solution for long-term management of psoriatic skin conditions.

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