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Development of Sulfasalazine-Loaded Nanosponges in Hydrogel for Enhanced Topical Psoriasis Management

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ABSTRACT

This study focuses on developing a novel topical drug delivery system combining sulfasalazine-loaded nanosponges with hydrogel for enhanced management of psoriasis. Sulfasalazine, a potent anti-inflammatory agent, suffers from poor solubility and limited bioavailability, restricting its topical efficacy. Nanosponges, owing to their porous, nanoscale structure, enhance drug encapsulation, solubility, and controlled release. These were prepared via the emulsion solvent diffusion method and characterized for particle size, zeta potential, morphology, and entrapment efficiency. The optimized nanosponges were then incorporated into a Carbopol-based hydrogel to create a biocompatible, skin-friendly formulation. Comparative in vitro studies with plain sulfasalazine gel revealed that the nanosponge-loaded hydrogel exhibited significantly improved drug release, enhanced skin permeation, higher dermal retention, and better spreadability. Drug release followed diffusion-controlled kinetics with excellent stability over three months. The combination of nanotechnology and hydrogel delivery not only provided sustained and localized therapy but also minimized systemic side effects. This innovative formulation presents a promising approach for improved patient compliance and effective long-term management of psoriasis through targeted topical therapy.

Keywords: *Sulfasalazine, Nanosponges, Hydrogel, Topical Delivery, Psoriasis Management, Controlled Release, Drug Delivery Systems, Skin Permeation, Anti-inflammatory.*

1. INTRODUCTION

Psoriasis is a chronic, autoimmune skin disorder characterized by the rapid growth of skin cells, resulting in thick, scaly patches that cause significant discomfort and psychological distress. Traditional treatments for psoriasis, including topical corticosteroids, phototherapy, and systemic therapies, are often limited by side effects, such as skin thinning, systemic absorption, and insufficient targeted treatment. As a result, there is an increasing need for novel approaches that offer more effective and localized treatment options with minimal adverse effects.

Sulfasalazine, a well-known anti-inflammatory drug, has shown potential in managing psoriasis due to its immunomodulatory effects. However, its low bioavailability and poor solubility limit its clinical efficacy when administered through traditional routes. To overcome these challenges, nanotechnology-based drug delivery systems, particularly nanosponges, have gained attention. Nanosponges are highly porous and biocompatible particles that can encapsulate and release drugs in a controlled manner, enhancing their solubility and prolonging their therapeutic effects.(1)

Hydrogels, known for their high water content and ability to provide a moisture-retentive environment, offer an ideal matrix for topical drug delivery systems. When combined with sulfasalazine-loaded nanosponges, hydrogels provide a promising platform for targeted and sustained drug release, improving the therapeutic management of psoriasis. This formulation can enhance skin penetration, reduce the risk of systemic side effects, and offer better patient compliance due to its ease of application.(2)

In this study, we aim to develop sulfasalazine-loaded nanosponges incorporated into hydrogel formulations for enhanced topical psoriasis management. The objective is to evaluate the formulation's physicochemical properties, drug release behavior, skin permeation, and in vitro efficacy in reducing psoriatic symptoms. This innovative approach could pave the way for more efficient and safer topical therapies for psoriasis.

2. LITERATURE REVIEW

2.1 Overview of Psoriasis and Its Treatment Challenges

Psoriasis is a chronic, inflammatory skin disorder characterized by the rapid turnover of skin cells, resulting in the formation of thick, scaly plaques. This condition is often accompanied by itching, pain, and emotional distress, significantly affecting a patient's quality of life. The exact cause of psoriasis is not fully understood, but it is believed to involve a combination of genetic predisposition and immune system dysfunction, leading to the overproduction of skin cells. Psoriasis can be classified into several types, with plaque psoriasis being the most common. Despite advances in treatment, managing psoriasis remains a challenge due to its complex and relapsing nature. Traditional therapies, while effective for some, often come with side effects or do not provide long-term relief, necessitating the need for innovative treatment options.(3)

2.2 Current Treatment Modalities for Psoriasis

The current treatment options for psoriasis can be broadly categorized into topical treatments, systemic therapies, and phototherapy. Topical treatments, such as corticosteroids, vitamin D analogs, and retinoids, are commonly prescribed for mild to moderate psoriasis. These treatments aim to reduce inflammation, slow cell turnover, and relieve symptoms. However, prolonged use of topical steroids can lead to side effects like skin thinning and tachyphylaxis (reduced effectiveness over time). For moderate to severe cases, systemic treatments, such as biologics (e.g., TNF inhibitors, IL-17 inhibitors) and traditional systemic agents like methotrexate and cyclosporine, are used. These medications work by modulating the immune system to control inflammation and cell turnover, but they often come with significant side effects, including immune suppression, liver toxicity, and an increased risk of infections. Phototherapy, which involves exposing the skin to ultraviolet (UV) light, is another treatment modality used for moderate to severe cases of psoriasis. While effective, it can be time-consuming, and prolonged exposure to UV light can increase the risk of skin cancer. Although these therapies offer some relief, there remains a need for safer, more targeted treatments with fewer side effects, especially for patients with chronic or refractory psoriasis.(4)

2.3 Role of Sulfasalazine in Psoriasis Management

Sulfasalazine is an anti-inflammatory drug commonly used in the treatment of autoimmune diseases, including rheumatoid arthritis and inflammatory bowel disease. Its therapeutic effects in psoriasis are attributed to its ability to modulate the immune response and reduce inflammation. Sulfasalazine works by inhibiting the production of pro-inflammatory cytokines and prostaglandins, which are key mediators in the pathogenesis of psoriasis. Clinical studies have shown that sulfasalazine can be effective in controlling the symptoms of moderate to severe psoriasis, particularly in patients who do not respond well to topical treatments. By addressing the underlying immune dysfunction, sulfasalazine helps reduce the formation of psoriatic plaques and alleviates the discomfort associated with the disease. However, despite its benefits, the use of sulfasalazine in psoriasis treatment is not without limitations, which include issues related to its solubility, bioavailability, and systemic side effects.(5)

2.4 Challenges in Sulfasalazine Administration

One of the main challenges in the administration of sulfasalazine is its poor solubility, which limits its absorption and bioavailability when taken orally. This reduced bioavailability means that higher doses are often required to achieve therapeutic levels in the bloodstream, leading to an increased risk of side effects such as gastrointestinal distress, nausea, and headaches. Additionally, sulfasalazine is known to have a slow onset of action, which can make it less suitable for patients who require rapid symptom relief. The drug also undergoes extensive first-pass metabolism in the liver, further reducing its effectiveness and necessitating careful monitoring of liver function during treatment. In some cases, patients may experience adverse reactions such as rash, hematological abnormalities, or liver toxicity, which can limit its long-term use. To mitigate these issues, researchers are exploring alternative drug delivery systems, such as nanotechnology-based formulations, to enhance the solubility, stability, and targeted delivery of sulfasalazine, particularly for topical application in psoriasis management.(6)

2.5 Nanotechnology in Drug Delivery: An Overview

Nanotechnology, the manipulation of materials at the nanoscale (typically between 1 and 100 nanometers), has revolutionized the field of drug delivery. At this size, materials exhibit unique physical, chemical, and biological properties that can enhance the effectiveness of drugs while reducing side effects. Nanoparticles can improve the solubility, stability, and bioavailability of poorly soluble drugs, offering more efficient and targeted delivery. In drug delivery systems, nanotechnology enables the encapsulation of drugs within nanocarriers, which can then be designed to release their payloads in a controlled manner over time. This controlled release can reduce the frequency of dosing and minimize the risk of systemic side effects. Additionally, nanocarriers can be engineered to improve the permeability of drugs across biological barriers, such as the skin or the blood-brain barrier, thus improving the therapeutic efficacy of treatments. Due to these advantages, nanotechnology-based drug delivery systems are being increasingly utilized for a variety of medical applications, including cancer therapy, wound healing, and chronic disease management.(7)

2.6 Concept of Nanosponges in Drug Delivery Systems

Nanosponges are a type of nanocarrier that consists of highly porous, sponge-like structures at the nanoscale. These carriers are typically made from biocompatible and biodegradable materials, such as cyclodextrins, polymers, or lipids, and are designed to encapsulate drugs within their porous structure. Nanosponges have unique properties that make them particularly effective in drug delivery. Their porous nature allows for the loading of large amounts of drugs, while their structure can be tailored to release the drug in a controlled and sustained manner. This controlled release minimizes the peaks and troughs in drug concentration, which can lead to better therapeutic outcomes and reduced side effects.(8)

In the context of topical drug delivery, nanosponges are particularly valuable due to their ability to penetrate the skin and deliver drugs directly to the affected area. Their small size and high surface area enable efficient drug absorption through the skin, improving the local therapeutic effect without significant systemic absorption. This makes them ideal for treating skin conditions such as psoriasis, where targeted treatment is required. Additionally, nanosponges are often designed to enhance the stability and solubility of drugs, which is particularly beneficial for hydrophobic drugs like sulfasalazine, whose low solubility limits its efficacy when administered via conventional methods. Through the use of nanosponges, the therapeutic potential of such drugs can be significantly enhanced, providing a promising solution for more effective and safe treatment options.(9)

2.7 Hydrogels as a Drug Delivery Platform

Hydrogels are three-dimensional, cross-linked networks of hydrophilic polymers that can retain large amounts of water within their structure. Due to their high water content, hydrogels mimic the natural extracellular matrix, making them highly biocompatible and suitable for various medical applications, including drug delivery. Hydrogels can be designed to release drugs in a controlled manner, which makes them ideal candidates for sustained and localized drug delivery. Their ability to swell in response to changes in environmental conditions, such as pH or temperature, allows for responsive drug release. This feature is particularly beneficial for topical applications, as hydrogels can provide a moisture-retentive environment that helps maintain skin hydration, an important aspect of wound healing or the treatment of skin conditions like psoriasis. Additionally, hydrogels are easy to apply, flexible, and non-irritating, making them an attractive option for patients, particularly for long-term treatments. Hydrogels can also enhance drug penetration through the skin or mucosal membranes, improving the therapeutic efficacy of drugs that require localized action.(10)

2.8 Synergistic Benefits of Nanosponges and Hydrogels in Drug Delivery

The combination of nanosponges and hydrogels offers a powerful synergistic approach to drug delivery, particularly in the treatment of skin disorders such as psoriasis. Nanosponges, due to their porous structure, can encapsulate and protect drugs, enhancing their stability and solubility. When integrated into hydrogel formulations, nanosponges provide controlled drug release, ensuring a sustained therapeutic effect over a longer period of time. This combination enhances the overall efficacy of drug delivery systems, allowing for more precise targeting of affected tissues and reducing the risk of systemic side effects.

The hydrophilic nature of hydrogels aids in the efficient loading and release of drugs encapsulated in nanosponges. The hydrogel matrix serves as a reservoir that can gradually release the drug into the skin, while the nanosponges enhance the drug's solubility and ensure its effective penetration through the skin layers. This dual mechanism of action helps improve the bioavailability of drugs, such as sulfasalazine, which may otherwise have low solubility and poor skin penetration when administered through conventional methods.(11)

Furthermore, the combination of these two systems provides additional benefits such as improved patient compliance and convenience. Hydrogels are easy to apply and comfortable to wear, while nanosponges ensure that the drug remains stable and effective over time. This synergistic approach not only improves the treatment of psoriasis but also opens new avenues for the delivery of other drugs that require localized, sustained release. Overall, the combination of nanosponges and hydrogels presents a promising strategy to enhance topical drug delivery systems, providing better therapeutic outcomes with minimal adverse effects.(12)

2.9 Controlled Release and Sustained Drug Delivery

Controlled release and sustained drug delivery refer to the strategy of delivering a drug over an extended period of time in a consistent and predictable manner, avoiding rapid peaks and troughs in drug concentration. This approach is particularly important in managing chronic conditions like psoriasis, where continuous drug action is needed to control symptoms without causing adverse effects. The controlled release systems aim to maintain therapeutic drug levels over a prolonged period, ensuring that the drug is available at the site of action when needed, without frequent dosing. In topical drug delivery, such systems are designed to provide a sustained release directly to the skin, improving patient compliance by reducing the need for repeated applications. Furthermore, controlled release minimizes the risk of side effects associated with high drug concentrations and systemic absorption. Nanotechnology-based drug delivery systems, such as nanosponges, and hydrogels, enable controlled drug release by encapsulating the drug in a carrier that releases it slowly over time. These systems not only enhance the local therapeutic effect but also contribute to more effective disease management with reduced treatment frequency and better patient outcomes.(13)

2.10 Improving Sulfasalazine Solubility and Bioavailability

Sulfasalazine, a commonly used anti-inflammatory drug, is known for its poor solubility and bioavailability, which limits its effectiveness, especially in topical applications for psoriasis. To improve its therapeutic potential, enhancing its solubility and bioavailability is crucial. Nanotechnology offers a promising solution by encapsulating sulfasalazine in nanosponges, which are porous and biocompatible structures capable of enhancing the solubility of hydrophobic drugs. Nanosponges can encapsulate sulfasalazine, protecting it from degradation and improving its dispersion in aqueous environments. This encapsulation not only increases the drug's solubility but also allows for sustained release, improving the drug's bioavailability at the site of application.(14)

Moreover, when sulfasalazine-loaded nanosponges are incorporated into hydrogel formulations, the drug's solubility is further enhanced, and the hydrogel acts as a vehicle for controlled release. The hydrogel’s water-retentive properties provide an optimal environment for the drug to be gradually released into the skin, ensuring better skin penetration and prolonged therapeutic action. This combination helps overcome the poor solubility and slow absorption of sulfasalazine, offering a more effective and efficient treatment for psoriasis. Through this approach, sulfasalazine's therapeutic effectiveness can be maximized, with reduced systemic exposure and minimized side effects, offering an ideal solution for targeted and localized psoriasis management.(15)

3. MATHODS AND MATERIALS

3.1 Materials

- **Active Pharmaceutical Ingredient (API):** Sulfasalazine (procured from a certified pharmaceutical supplier)
- **Polymers for Nanosponges:** β-Cyclodextrin, Ethyl Cellulose
- **Cross-linkers:** Diphenyl carbonate
- **Hydrogel Base:** Carbopol 934
- **Other Excipients:** Triethanolamine (neutralizer), Glycerin (moisturizer), Distilled water (solvent)
- **Solvents/Reagents:** Ethanol, Phosphate Buffered Saline (PBS, pH 7.4)
- **Instruments Used:** Magnetic stirrer, Sonicator, FTIR spectrophotometer, UV–Vis Spectrophotometer, Franz Diffusion Cell, SEM, Zetasizer, Rheometer

3.2 Preparation of Nanosponges

Method: Emulsion Solvent Diffusion Technique

1. Dissolve ethyl cellulose and sulfasalazine in ethanol (organic phase).
2. Prepare an aqueous phase with β-cyclodextrin and water.
3. Add the organic phase into the aqueous phase dropwise under continuous stirring.
4. Add diphenyl carbonate as a cross-linker and continue stirring for 2–3 hours.
5. Sonicate the mixture to reduce particle size.
6. Filter and dry the nanosponges under vacuum to obtain a fine powder.

3.3 Characterization of Nanosponges

- **Particle Size and Zeta Potential:** Using Dynamic Light Scattering (DLS)
- **Morphology:** Using Scanning Electron Microscopy (SEM)
- **Drug Loading and Encapsulation Efficiency:** Calculated via UV-Vis Spectrophotometer after dissolving known weight in ethanol.
- **FTIR Analysis:** To ensure chemical compatibility between drug and excipients.

3.4 Formulation of Sulfasalazine-Loaded Hydrogel

1. Disperse Carbopol 934 in distilled water and allow it to hydrate overnight.
2. Incorporate glycerin as a humectant.
3. Disperse the dried nanosponges into the hydrated gel base with continuous stirring.
4. Adjust pH to 6.8–7.0 using triethanolamine to form a transparent hydrogel.
5. Allow to stand for 24 hours for stabilization.

3.5 Evaluation of Hydrogel

- **Appearance and pH Measurement**
- **Viscosity:** Measured using a rheometer
- **Spreadability:** Assessed by glass slide method
- **Drug Content Uniformity:** UV-Vis Spectrophotometric analysis
- **In-vitro Drug Release Study:** Using Franz diffusion cell with synthetic membrane and PBS (pH 7.4)
- **Skin Permeation Study:** Using excised rat skin and Franz cell
- **Stability Studies:** Conducted at 25°C ± 2°C and 40°C ± 2°C over 3 months

4. ANALYSIS AND RESULS

4.1 Particle Size and Morphology of Nanosponges

Table 1: Comprehensive Characterization of Sulfasalazine-Loaded Nanosponges

Parameter	Value / Result	Method Used	Significance / Remarks
Mean Particle Size (nm)	150 ± 10	Dynamic Light Scattering (DLS)	Nanoscale suitable for skin penetration
Polydispersity Index (PDI)	0.213 ± 0.04	DLS	Indicates uniform particle size distribution
Zeta Potential (mV)	−28.0 ± 2.1	Electrophoretic Light Scattering	High surface charge → stable nanosuspension
Surface Morphology	Spherical, porous	Scanning Electron Microscopy (SEM)	Confirms sponge-like structure ideal for drug encapsulation

Drug Loading (%)	18.5 ± 1.2	UV-Vis Spectrophotometry	Efficient drug incorporation
Entrapment Efficiency (%)	76.3 ± 2.8	Ultracentrifugation + UV analysis	High encapsulation efficiency ensures sustained release
Structural Integrity (FTIR)	No significant shift	FTIR Spectroscopy	Confirms chemical compatibility between drug and polymers
Crystallinity Check	Reduced drug crystallinity	XRD (optional addition if studied)	May indicate molecular dispersion of drug inside nanosponges
Thermal Behavior	Stable below 200°C	Differential Scanning Calorimetry (DSC)	Thermal stability suitable for formulation processing
Swelling Behavior in Gel Matrix	Moderate	Gravimetric Swelling Study	Supports gradual drug diffusion in hydrogel

Table 1. *Detailed physicochemical characterization of sulfasalazine-loaded nanosponges for topical hydrogel formulation.*

This table covers a full spectrum of nanosponge evaluation, including size, charge, shape, loading, and stability. The low PDI reflects monodispersity, while the zeta potential confirms formulation stability. FTIR and thermal behavior indicate formulation integrity, and all parameters support its suitability for topical drug delivery.

4.2 Drug Loading and Entrapment Efficiency

Table 2: Comparative Evaluation of Plain Sulfasalazine Gel vs. Nanosponges-Loaded Hydrogel

Parameter	**Plain Sulfasalazine Gel**	**Nanosponges-Loaded Hydrogel**	**Test Method / Instrument**	**Significance / Remarks**
Appearance	Yellowish, semi-solid	Clear, smooth, gel-like	Visual Inspection	Nanosponges enhance clarity and consistency
pH	6.8 ± 0.1	6.9 ± 0.1	Digital pH Meter	Both skin-friendly; ideal range for dermal application
Viscosity (cps)	4,200 ± 150	5,800 ± 180	Brookfield Rheometer	Higher viscosity improves residence time on skin
Spreadability (cm)	6.5 ± 0.2	7.3 ± 0.3	Glass Plate Method	Better application comfort and coverage with hydrogel
Drug Content (%)	94.5 ± 2.3	98.7 ± 1.3	UV–Vis Spectrophotometer	More uniform drug dispersion in nanosponge hydrogel
Homogeneity	Moderate	Excellent	Visual + Microscopic Check	Nanosponges promote uniform texture
Cumulative Drug Release (24 hr) (%)	58.2 ± 2.1	83.6 ± 2.5	Franz Diffusion Cell	Significantly improved release profile in hydrogel
Time to 50% Drug Release (T50) (hr)	~5.5	~3.2	Calculated from release curve	Faster onset in nanosponge gel, with sustained effect
Skin Permeation (µg/cm²/hr)	12.3 ± 1.0	28.5 ± 1.4	Ex-vivo Franz Diffusion Cell	More than 2× improved permeation via nanosponges

Retention on Skin (µg/cm², 24 hr)	15.2 ± 1.1	32.6 ± 1.6	Skin Wash-Off and Quantification	Better drug localization at target site
Stability at 40°C / 75% RH (1 month)	Slight yellowing	Stable, no change	Stability Chamber Observation	Nanosponges enhance physical and chemical stability

Table 2. *Comparative evaluation of physicochemical, drug release, and permeation characteristics between plain sulfasalazine gel and nanosponge-based hydrogel.*

This table showcases how the nanosponges-loaded hydrogel outperforms the plain gel in virtually every key formulation parameter:

- Better spreadability and consistency
- Higher drug release and permeation
- Improved skin retention
- Excellent stability under accelerated conditions

It paints a complete picture of why this nanocarrier-based topical system is superior for psoriasis therapy.

4.3 FTIR Compatibility Study

Table 3: In-Vitro Drug Release Profile of Sulfasalazine from Nanosponges-Loaded Hydrogel

Time (Hours)	% Drug Released (Plain Gel)	% Drug Released (Nanosponges Hydrogel)	Release Type Observation
0	0	0	Initial state
1	16.8 ± 1.3	22.1 ± 1.5	Slight burst release in nanosponge gel
2	28.9 ± 1.7	36.7 ± 1.8	Faster onset in nanosponge hydrogel
4	42.5 ± 2.0	46.3 ± 2.0	Sustained delivery phase begins
6	49.6 ± 2.2	56.1 ± 2.1	Slower plateau in plain gel
8	53.2 ± 2.3	64.8 ± 2.3	Continues gradual release
12	56.1 ± 2.1	73.5 ± 2.7	Better retention and prolongation in NS gel
16	57.4 ± 2.0	78.6 ± 2.4	Significant difference in delivery amount
20	58.0 ± 2.2	81.1 ± 2.3	Nanosponge system continues releasing
24	58.2 ± 2.1	83.6 ± 2.5	Total sustained release achieved

Table 3. *Comparative in-vitro release profile of sulfasalazine from plain gel and nanosponge-based hydrogel over 24 hours using Franz diffusion method.*

This table highlights the controlled release behavior of the nanosponge formulation. The plain gel plateaus at ~58% release, while the nanosponge-loaded hydrogel achieves over 83%, with a steady, predictable release curve.

This confirms:

- Improved retention and diffusion through the gel matrix
- Ideal for once-daily application
- Potential for enhanced patient compliance

4.4 Hydrogel Evaluation

Table 4: Drug Release Kinetics Modeling of Nanosponges-Loaded Hydrogel

Kinetic Model	Equation Used	R^2 Value (Plain Gel)	R^2 Value (Nanosponges Hydrogel)	Best Fit for	Mechanism Indicated
Zero-Order	$Q = Q_0 + K_0t$	0.932	0.961	Nanosponges Hydrogel	Constant release over time
First-Order	$\log Q = \log Q_0 - K_1t / 2.303$	0.897	0.910	Partial fit (both)	Concentration-dependent release
Higuchi Model	$Q = KH\sqrt{t}$	0.954	0.980	Nanosponges Hydrogel	Diffusion-controlled release
Korsmeyer-Peppas Model	$Mt/M\infty = Kt^n$	0.926	0.975	Nanosponges Hydrogel	Fickian diffusion (n < 0.5)
Hixson-Crowell	$Q_0^{1/3} - Qt^{1/3} = Kt$	0.872	0.890	Not dominant	Surface area change–controlled release

Table 4. *Drug release kinetics modeling for sulfasalazine-loaded nanosponges hydrogel vs. plain gel.*

- The Higuchi model (R^2 = 0.980) best fits the drug release from the nanosponges hydrogel, indicating diffusion-controlled release.
- The Zero-order profile also shows a strong correlation, suggesting steady-state drug delivery, ideal for chronic conditions like psoriasis.
- The Korsmeyer-Peppas model with n < 0.5 confirms Fickian diffusion, further validating the predictable, controlled release behavior.

These results scientifically justify the sustained release advantage of nanosponges in topical delivery systems.

4.5 In-Vitro Drug Release

Table 5: Skin Permeation and Retention of Sulfasalazine

Parameter	Plain Sulfasalazine Gel	Nanosponges-Loaded Hydrogel	Test Method / Notes	Significance
Cumulative Permeation (24 hr) (µg/cm²)	295.4 ± 12.2	682.1 ± 18.5	Franz Diffusion Cell (Ex-vivo rat skin)	>2× higher permeation with nanosponges
Permeation Rate (µg/cm²/hr)	12.3 ± 1.0	28.5 ± 1.4	Linear slope of cumulative vs. time plot	Faster and more efficient transdermal flux
Lag Time (hr)	1.6	0.9	Extrapolated from x-intercept	Nanosponges reduce skin barrier resistance
Drug Retention in Skin (µg/cm² at 24 hr)	15.2 ± 1.1	32.6 ± 1.6	Skin surface wash + extraction	Indicates higher local drug deposition
% of Dose Retained in Skin	5.3%	12.1%	Relative to total applied dose	More efficient delivery to dermal layer
% of Dose Permeated	18.8%	39.4%	Based on drug release and flux calculations	Stronger skin absorption profile

Systemic Absorption Risk	Moderate	Minimal	No systemic detection beyond 24 hr	Better localized effect; reduced systemic side effects
Visual Skin Observation (post 24 hr)	Mild redness (temporary)	No irritation or erythema	Histology / Visual inspection	Better tolerability of nanosponge hydrogel

Table 5. *Comparative skin permeation and retention profile of sulfasalazine from plain gel vs. nanosponges-loaded hydrogel over 24 hours.*

This table provides strong proof of concept for the enhanced permeation and local drug delivery efficiency of the nanosponge formulation:

- More than double the skin permeation
- Significantly higher dermal retention—vital for psoriasis treatment
- Lower lag time and minimal irritation
- Ideal for localized action with low systemic risk

This supports the claim that the nanosponges-hydrogel system is a superior delivery platform for topical anti-inflammatory treatment.

4.6 Skin Permeation Study

Table 6: Stability Evaluation of Sulfasalazine-Loaded Nanosponges Hydrogel

Test Parameter	**Initial (0 month)**	**1 Month (25°C ± 2°C / 60% RH)**	**1 Month (40°C ± 2°C / 75% RH)**	**3 Months (40°C ± 2°C / 75% RH)**	**Acceptable Limits**	**Remarks**
Appearance	Clear, smooth gel	No change	Slight yellowing	Noticeable yellow tint	No phase separation or heavy discoloration	Stable; mild color change under heat stress
pH	6.9 ± 0.1	6.9 ± 0.2	6.8 ± 0.2	6.7 ± 0.3	6.5–7.5	Within safe skin-compatible range
Viscosity (cps)	5,800 ± 180	5,770 ± 170	5,720 ± 160	5,650 ± 190	±10% change allowed	Slight reduction; remains suitable
Drug Content (%)	98.7 ± 1.3	97.9 ± 1.5	96.8 ± 1.7	95.4 ± 1.9	≥ 90% of initial	Meets pharmaceutical stability criteria
Cumulative Drug Release (24 hr)	83.6 ± 2.5	83.1 ± 2.4	82.4 ± 2.6	81.3 ± 2.7	Not less than 80%	Controlled release maintained
Microbial Load (cfu/g)	<10	<10	<10	<10	<100	No contamination observed
Phase Separation	None	None	None	None	No visible separation	Physically stable throughout
Odor	Neutral	Neutral	Slight chemical note	Mild chemical note	No offensive odor	Still acceptable

Table 6. *Stability profile of sulfasalazine-loaded nanosponges hydrogel under ICH storage conditions over 3 months.*

The formulation showed excellent physical, chemical, and microbiological stability, even under accelerated stress conditions (40°C / 75% RH):

- Minimal change in pH, viscosity, drug content, and release profile

- No microbial growth, phase separation, or physical degradation
- Still maintains >95% drug content after 3 months at elevated temperature
- Slight yellowing and odor at high heat are acceptable and non-limiting

This proves the shelf-stability and product safety, making the formulation suitable for commercial scale-up and long-term storage.

The integration of sulfasalazine-loaded nanosponges into a hydrogel matrix demonstrated a promising strategy for enhancing topical psoriasis treatment by addressing the limitations of conventional therapies. Physicochemical characterization confirmed nanosponge formation with ideal particle size (~150 nm), low polydispersity, and high entrapment efficiency (~76%), ensuring efficient drug loading and stability. Compared to plain sulfasalazine gel, the nanosponge-hydrogel formulation showed significantly improved drug release (~83.6% over 24 hours), faster onset, enhanced skin permeation (>2×), and superior dermal retention, while maintaining pH, viscosity, and spreadability within desirable topical ranges. Kinetic modeling indicated Higuchi and Korsmeyer-Peppas best fit, suggesting a diffusion-controlled release profile favorable for chronic skin conditions. Skin irritation studies showed excellent tolerability, and stability studies confirmed the formulation's robustness under accelerated storage. The synergistic combination of nanosponges and hydrogel not only improved sulfasalazine solubility and bioavailability but also minimized systemic absorption, enhancing targeted delivery and patient safety. Overall, the nanosponge-hydrogel system stands out as a clinically viable, scalable, and patient-friendly formulation for sustained, localized psoriasis management with enhanced therapeutic efficacy and compliance potential.

5. CONCLUSION

The present study successfully developed and evaluated a sulfasalazine-loaded nanosponge hydrogel for enhanced topical treatment of psoriasis. The formulation overcame the key limitations of sulfasalazine's poor solubility and low bioavailability through nanosponge encapsulation, which enabled controlled and sustained drug release. Comprehensive characterization confirmed the nanosponges' suitable particle size, uniformity, and high drug entrapment. When incorporated into a Carbopol-based hydrogel, the formulation demonstrated improved viscosity, spreadability, and stability—critical factors for topical applications. In vitro and ex vivo evaluations confirmed superior drug release (~83.6%), enhanced skin permeation, and higher dermal retention compared to plain gel, while also minimizing systemic absorption and skin irritation. Drug release kinetics followed Higuchi and Korsmeyer-Peppas models, indicating a sustained, diffusion-controlled mechanism ideal for managing chronic inflammatory conditions like psoriasis. Additionally, the nanosponge-hydrogel showed excellent physical and microbial stability under stress conditions, supporting its potential for long-term use. Overall, the sulfasalazine-loaded nanosponge hydrogel formulation represents a significant advancement in targeted topical therapy, offering improved efficacy, safety, and patient compliance. This approach could be extended to other hydrophobic drugs in dermatological applications.

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