RESEARCH PAPER

Nanosponge-Based Topical Delivery Systems for Psoriasis: Advances, Challenges, and Future Perspectives

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Abstract
Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by abnormal keratinocyte proliferation, epidermal hyperplasia, and persistent inflammation. Although topical therapy remains an important approach for mild-to-moderate psoriasis, conventional formulations are often associated with poor drug solubility, inadequate skin penetration, rapid drug release, limited skin retention, and potential adverse effects. Nanotechnology-based delivery systems have therefore emerged as promising strategies for improving localized and controlled drug delivery. Among these, nanosponges are porous, three-dimensional, cross-linked nanocarriers capable of incorporating active pharmaceutical ingredients and functioning as drug reservoirs. Their unique architecture offers advantages including enhanced solubility, drug protection, controlled release, and improved skin deposition. This review discusses the potential of nanosponge-based topical delivery systems for psoriasis, with emphasis on their pharmaceutical characteristics, types, preparation strategies, drug-loading mechanisms, and physicochemical characterization. Current evidence on nanosponge formulations containing antipsoriatic agents, including clobetasol propionate, curcumin, caffeine, and sulfasalazine, is critically examined with respect to drug release, skin delivery, and preclinical therapeutic outcomes. The incorporation of nanosponges into topical gels and hydrogels is also discussed as an approach to improve residence time, spreadability, and localized drug delivery. Despite encouraging preclinical findings, challenges remain regarding formulation optimization, batch reproducibility, dermal safety, scale-up, regulatory requirements, and clinical validation. Future development may focus on targeted and stimuli-responsive nanosponges, combination therapy, quality-by-design approaches, artificial intelligence-assisted optimization, and scalable manufacturing. Overall, nanosponges represent a promising platform for developing localized, sustained, and patient-friendly topical therapies for psoriasis.

Keywords: Psoriasis; Nanosponges; Topical drug delivery; Controlled release; Nanotechnology
How to cite this article: Sandhya Ravindra Lanke1* Dr Hitesh Kumar Kinger1. Nanosponge-Based Topical Delivery Systems for Psoriasis: Advances, Challenges, and Future Perspectives. Int J Drug Deliv Technol. 2026;16(77s):1114-1126. DOI:

10.25258/ijddt.16.77s.130.

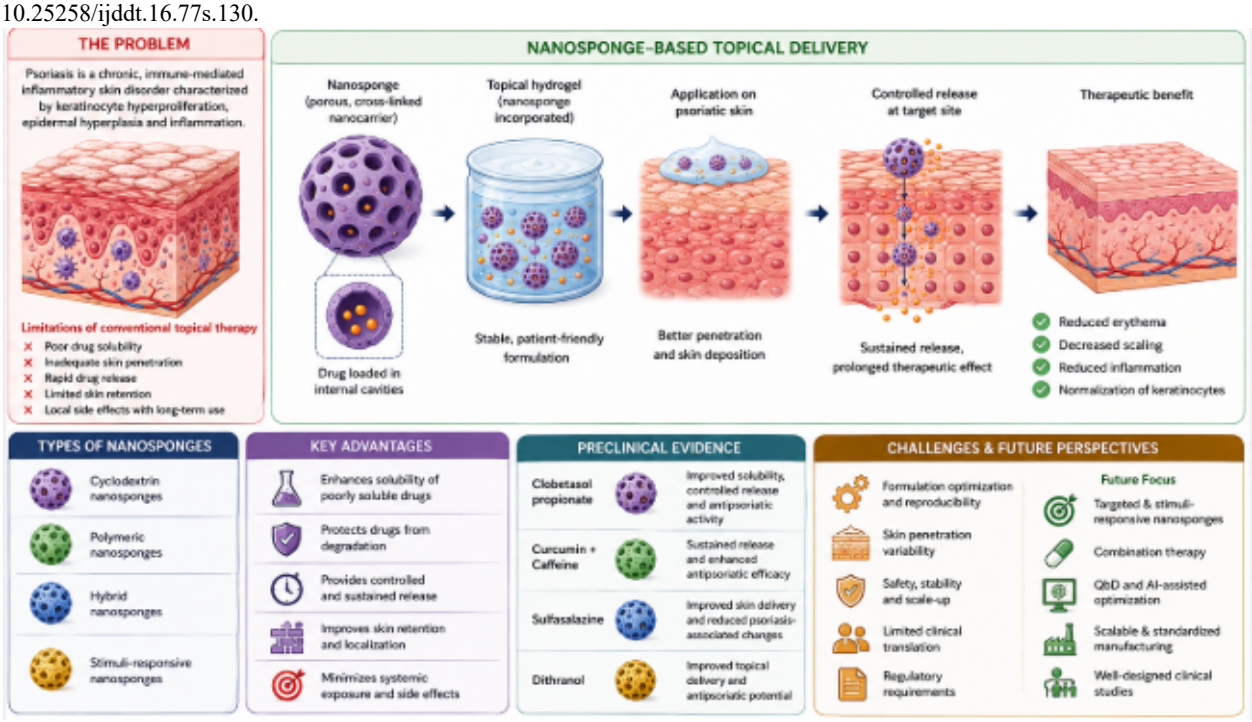

Figure 1: Graphical Abstract

1. Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disorder characterized by excessive keratinocyte proliferation, epidermal hyperplasia, and persistent inflammation. It affects approximately 2–3% of the global population and commonly presents as well-demarcated, erythematous, scaly plaques. The pathogenesis involves complex interactions between genetic, environmental, and immune factors, with the interleukin (IL)-23/IL-17 axis and tumor necrosis factor-α (TNF-α) playing important roles in disease progression. [1,2]

Topical therapy remains an important treatment option for mild-to-moderate psoriasis; however, the stratum corneum represents a major barrier to drug penetration. Conventional creams, ointments, and gels may also exhibit poor drug solubility, limited skin retention, rapid drug release, and inadequate localization at the site of inflammation. These limitations have encouraged the development of nanotechnology-based topical delivery systems, including liposomes, niosomes, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, polymeric nanoparticles, and nanogels. Such systems can improve drug solubilization, skin deposition, stability, and controlled release. [3–5]

Among these approaches, nanosponges have emerged as promising porous, three-dimensional, cross-linked nanocarriers capable of incorporating active pharmaceutical ingredients within their internal cavities. Their ability to improve the apparent solubility of poorly water-soluble drugs, protect incorporated molecules, provide controlled release, and enhance localized drug delivery makes them attractive for topical psoriasis therapy. Recent studies have reported nanosponge-based formulations containing antipsoriatic agents such as clobetasol propionate, curcumin, caffeine, and dithranol, with improvements in drug release characteristics and experimental antipsoriatic activity. [6,7]

However, nanosponge-based antipsoriatic delivery remains an emerging field, with challenges related to formulation optimization, stability, skin penetration, safety, scale-up, and clinical translation. Therefore, this review summarizes recent advances in nanosponge-based topical delivery systems for psoriasis, focusing on formulation strategies, characterization, drug-release behavior, skin delivery, therapeutic evaluation, current challenges, and future perspectives.

2. Psoriasis: Pathophysiology and Therapeutic Challenges

Psoriasis is driven by a complex interaction between keratinocytes, dendritic cells, T lymphocytes, and inflammatory mediators. Activation of dendritic cells promotes differentiation and expansion of Th17 cells through the IL-23 pathway, resulting in increased secretion of IL-17A, IL-17F, TNF-α, and other cytokines. These mediators stimulate keratinocyte proliferation and the release of additional chemokines and inflammatory factors, establishing a persistent

inflammatory feedback loop that contributes to epidermal hyperplasia and plaque formation. [8,9]

Topical corticosteroids, vitamin D analogues, retinoids, calcineurin inhibitors, and keratolytic agents remain important therapeutic options, particularly in mild-to-moderate psoriasis. However, conventional topical formulations may be limited by poor drug solubility, inadequate penetration through the stratum corneum, rapid drug release, and insufficient retention at the target site. Long-term use of potent corticosteroids may additionally cause local adverse effects, including skin atrophy, telangiectasia, and other steroid-associated complications. [10,11]

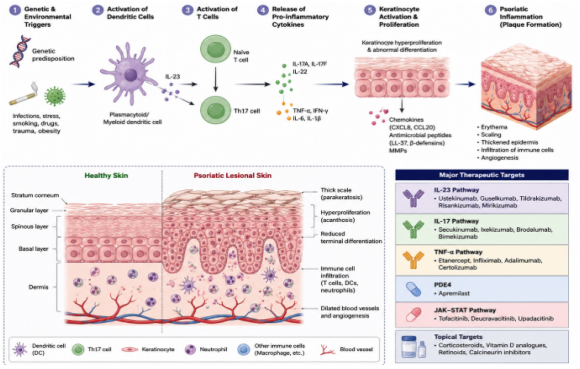

Figure 2: Pathogenesis of Psoriasis and Theraputic Targets

The abnormal architecture and increased thickness of psoriatic epidermis can further influence drug penetration and distribution. Consequently, achieving an appropriate drug concentration within the epidermis while minimizing unnecessary systemic exposure remains an important objective in topical psoriasis therapy. Advanced delivery systems capable of improving drug solubilization, controlling release, increasing skin retention, and enhancing localization at inflamed tissue may therefore provide significant therapeutic advantages. [12]

Table 1. Current Therapeutic Approaches for Psoriasis and Their Limitations

Therapeutic approach	Examples	Major advantages	Major limitations
Topical corticosteroids	Clobetasol, betamethasone	Rapid anti-inflammatory action	Skin atrophy, tachyphylaxis, recurrence
Vitamin D analogues	Calcipotriol, calcitriol	Reduces keratinocyte proliferation	Irritation, slower response
Topical retinoids	Tazarotene	Normalizes keratinocyte differentiation	Irritation, dryness
Calcineurin inhibitors	Tacrolimus, pimecrolimus	Useful for sensitive areas	Burning and irritation
Keratolytics	Salicylic acid, urea	Reduces scaling and facilitates penetration	Irritation at higher concentrations
Systemic therapies	Methotrexate, cyclosporine	Effective in moderate–severe disease	Systemic adverse effects
Biologics	Anti-TNF, anti-IL-17, anti-IL-23	High therapeutic efficacy	Cost, immunological risks
Phototherapy	UVB, PUVA	Effective for extensive disease	Multiple treatment sessions, phototoxicity

3. Nanotechnology in Topical Psoriasis Therapy

Nanotechnology-based delivery systems have emerged as promising approaches for improving the topical treatment of psoriasis. Their nanoscale dimensions and large surface area can enhance drug solubilization, skin interaction, drug retention, and controlled release, while potentially reducing unwanted systemic exposure. Different nanocarriers, including liposomes, niosomes, nanoemulsions, solid lipid nanoparticles, nanostructured lipid carriers, polymeric nanoparticles, nanogels, nanocrystals, and

nanosponges, have been investigated for delivering conventional and natural antipsoriatic agents. [13,14]
Lipid-based nanocarriers can improve skin permeation and provide controlled release of incorporated drugs, whereas polymeric systems offer advantages in structural stability, drug protection, and release modulation. Nanosponges represent a distinct class of porous polymeric carriers in which interconnected cavities provide sites for drug incorporation. Cyclodextrin-based nanosponges are particularly attractive because cross-linking converts individual cyclodextrins into a three-dimensional porous network capable of accommodating drug molecules and modifying their release characteristics. [15,16]
For topical psoriasis therapy, nanocarriers may facilitate drug localization within the epidermis and dermis while improving the physicochemical properties of poorly soluble drugs. However, the therapeutic performance of each nanocarrier depends on particle size, surface properties, composition, drug–carrier interactions, formulation vehicle, and the characteristics of the diseased skin. Therefore, selecting an appropriate nanocarrier requires consideration of both the physicochemical properties of the drug and the therapeutic requirements of psoriasis. [13,17]
Among the available systems, nanosponges are gaining particular interest because their porous architecture can combine drug-loading capacity, solubility enhancement, and controlled release within a single platform. These characteristics provide a rationale for further investigation of nanosponges as specialized topical carriers for antipsoriatic drugs.

Table 2. Nanotechnology-Based Topical Delivery Systems for Psoriasis

Nanocarrier	Main characteristics	Potential benefit in psoriasis	Major limitation
Liposomes	Phospholipid vesicles	Improved skin deposition	Physical instability
Niosomes	Non-ionic surfactant vesicles	Controlled drug delivery	Surfactant-related instability
Transfersomes	Highly deformable vesicles	Enhanced skin penetration	Formulation sensitivity
Ethosomes	Ethanol-rich vesicles	Improved transdermal delivery	Possible irritation
SLN	Solid lipid nanoparticles	Controlled release, drug protection	Limited drug loading
NLC	Solid + liquid lipid matrix	Higher loading and flexibility	Complex optimization
Nanoemulsions	Fine oil/water dispersions	Solubility and penetration enhancement	Relatively rapid drug release
Polymeric nanoparticles	Polymer-based nanocarriers	Controlled and sustained delivery	Manufacturing complexity
Nanogels	Cross-linked nanoscale gels	High water content and skin compatibility	Stability concerns
Nanosponges	Porous cross-linked networks	Drug loading, solubility enhancement, sustained release	Limited clinical evidence

4. Nanosponges: Concept and Pharmaceutical Significance

Nanosponges are porous, three-dimensional, cross-linked polymeric nanocarriers containing

interconnected cavities capable of incorporating active pharmaceutical ingredients. Their internal cavities and large surface area allow interaction with both hydrophilic and hydrophobic molecules, making them useful for improving the solubility, stability, and release characteristics of poorly water-soluble drugs. The physicochemical properties of nanosponges can be modified by changing the type of polymer, cross-linking agent, degree of cross-linking, and preparation conditions. [18,19]

Cyclodextrin-based nanosponges are among the most extensively investigated systems because cyclodextrins provide hydrophobic cavities capable of forming inclusion complexes, while cross-linking produces a stable porous network. This structure can provide higher drug-loading capacity and more prolonged release than conventional cyclodextrin complexes. In addition, nanosponge formulations can be incorporated into topical gels and other semisolid systems, making them particularly relevant for localized skin delivery. [20]

For topical applications, nanosponges can function as drug reservoirs that gradually release the incorporated active at the skin surface or within the target skin layers. Their ability to enhance drug retention, regulate release, and improve the delivery of poorly soluble molecules provides a strong pharmaceutical rationale for their application in psoriasis. However, the final performance depends strongly on particle size, porosity, surface characteristics, drug–polymer interactions, and formulation composition. [21]

5. Types of Nanosponges for Psoriasis

Nanosponges can be broadly classified according to their polymeric composition, cross-linking chemistry, and functional characteristics. Cyclodextrin-based nanosponges are the most extensively investigated systems and are commonly prepared by cross-linking α-, β-, or γ-cyclodextrin with agents such as carbonate-forming, ester-forming, or other multifunctional cross-linkers. The resulting three-dimensional porous network provides internal cavities and interconnected channels suitable for drug incorporation and controlled release. [22,23]

Polymeric nanosponges can also be developed using biodegradable or synthetic polymers to modify particle characteristics, drug-loading capacity, and release behavior. Hybrid nanosponges combine different polymers or functional materials to provide additional control over drug delivery. More recently, stimuli-responsive nanosponges have been investigated in which changes in pH, temperature, redox conditions, or other environmental factors can modify the structure or drug-release behavior of the carrier. [24]

For psoriasis, cyclodextrin-based and polymeric nanosponges are particularly relevant because they can accommodate poorly soluble anti-inflammatory drugs and potentially improve their localization within the skin. Surface modification or incorporation of functional groups may further provide opportunities for enhanced skin interaction or targeted delivery. Selection of the nanosponge type should therefore consider drug physicochemical properties, desired release profile, skin deposition, biocompatibility, and intended therapeutic outcome. [25]

Table 3. Types of Nanosponges and Their Pharmaceutical Characteristics

Nanosponge type	Typical components	Important characteristics	Pharmaceutical relevance
Cyclodextrin nanosponges	α-, β-, or γ-CD + cross-linker	Porous network, inclusion capability	Suitable for poorly soluble drugs
Polymeric nanosponges	Biodegradable/synthetic polymers	Adjustable structure and release	Controlled topical delivery
Hybrid nanosponges	Combination of polymers/materials	Multifunctional properties	Enhanced delivery performance
Stimuli-responsive nanosponges	Functional polymers	Environment-dependent release	Potential targeted delivery
Surface-modified nanosponges	Functionalized polymer surface	Modified interaction with skin	Improved localization

6. Mechanism of Nanosponge-Mediated Topical Delivery

The therapeutic potential of nanosponges in psoriasis is primarily associated with their porous structure, high surface area, and ability to act as drug reservoirs.

After topical application, the nanosponge system can improve the apparent solubility of poorly water-soluble drugs and maintain the drug in a dispersed state within the formulation. The incorporated drug is subsequently released from the nanosponge matrix through diffusion and gradual desorption, providing a more controlled drug-release profile than conventional formulations. [26,27]

Following application to psoriatic skin, nanosponges may increase drug retention within the epidermal and superficial dermal layers while limiting rapid drug loss from the formulation. Their incorporation into hydrogels or other semisolid vehicles can further increase residence time at the application site. This localized delivery may help maintain therapeutic drug concentrations near inflamed tissue while reducing unnecessary systemic exposure. [28]

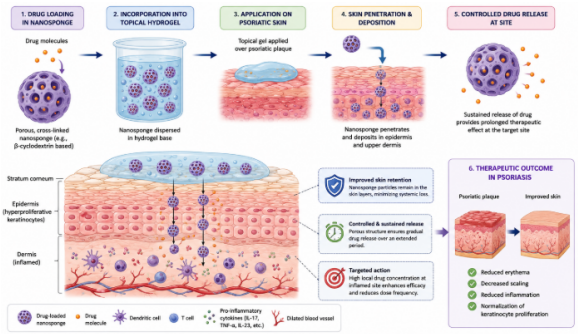

Figure 3: Nanosponges based topical delivery mechanism

The nanosponge architecture can also protect incorporated drugs from environmental degradation, particularly when the active molecule is sensitive to oxidation, hydrolysis, or photodegradation. In addition, the physicochemical characteristics of the nanosponge, including particle size, surface charge, porosity, cross-linking density, and polymer composition, can be modified to regulate drug loading and release. Thus, nanosponge-mediated delivery provides a multifunctional approach involving solubility enhancement, drug protection, controlled release, and localized topical deposition. [26,29]

7. Nanosponge-Based Formulations Investigated for Psoriasis

Although nanosponge-based therapy for psoriasis is still at a preclinical stage, several studies have demonstrated its potential for improving topical antipsoriatic delivery. Iriventi et al. developed a β-cyclodextrin nanosponge containing curcumin and caffeine using dimethyl carbonate as a cross-linker and incorporated the system into a topical gel. The optimized formulation showed nanoscale particle dimensions, sustained drug release for approximately 12 h, and enhanced antipsoriatic activity compared with conventional curcumin treatment in an experimental psoriasis model. [30]

Clobetasol propionate-loaded β-cyclodextrin nanosponges have also been investigated to improve the delivery of this potent corticosteroid while controlling drug release. The nanosponge increased the aqueous solubility of clobetasol propionate approximately 45-fold and demonstrated controlled drug release. Incorporation into Carbopol hydrogel produced a formulation with improved antipsoriatic activity, including a reduction in epidermal thickness and favorable histological changes in a mouse tail model. [31]

Dithranol-loaded nanosponges represent another approach for addressing the poor stability and solubility of this classical antipsoriatic agent. β-Cyclodextrin-based dithranol nanosponges have been incorporated into topical hydrogels and evaluated for antipsoriatic activity, with experimental findings supporting improved drug activity and modulation of oxidative-stress-related parameters. These studies collectively indicate that nanosponge systems can be adapted to both synthetic and natural antipsoriatic agents and may provide controlled topical drug delivery. [32]

Despite these encouraging findings, the available evidence remains limited and is predominantly based on formulation development and animal studies. Comparative studies between nanosponge systems and established topical nanocarriers, together with systematic evaluation of skin deposition, long-term safety, pharmacokinetics, and clinical efficacy, are required to establish their translational potential.

Table 4. Reported Nanosponge-Based Formulations for Psoriasis

Active agent	Nanosponge system	Topical dosage form	Major findings	Experimental model
Curcumin + caffeine	β-Cyclodextrin nanosponge	Topical gel	Sustained release and enhanced antipsoriatic activity	Experimental psoriasis model
Clobetasol	β-Cyclodextrin	Carbopol	Improved solubili	Mouse tail model

propionate	nanosponge	hydrogel	ty, controlled release and antipsoriatic activity	
Sulfasalazine	Cyclodextrin nanosponge	Hydrogel	Improved skin delivery and reduced psoriasis-associated changes	Mouse tail and imiquimod models
Dithranol	β-Cyclodextrin nanosponge	Hydrogel	Improved topical delivery and antipsoriatic potential	Preclinical model

8. Formulation Strategies for Nanosponge-Based Topical Systems

The preparation method plays an important role in determining the particle size, porosity, drug-loading capacity, morphology, and release characteristics of nanosponges. Commonly reported approaches include solvent evaporation, emulsion solvent diffusion, melt-based techniques, and ultrasound-assisted methods. The selection of method depends on the physicochemical properties of the polymer, cross-linking agent, and drug. [33,34]

In cyclodextrin-based nanosponges, cross-linking agents react with cyclodextrin molecules to generate a three-dimensional porous network. The drug may subsequently be incorporated into the nanosponge cavities through physical loading or complexation. Parameters such as polymer-to-cross-linker ratio, reaction conditions, drug concentration, solvent composition, and processing time can significantly influence the final characteristics of the formulation. [35]

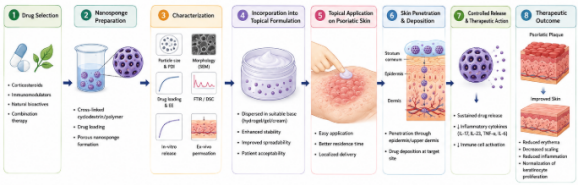

Figure 4: Nanosponge based topical therapy for psoriasis

For topical psoriasis therapy, the optimized nanosponge is generally incorporated into a suitable semisolid vehicle such as a hydrogel. Carbopol-based hydrogels have been investigated for nanosponge delivery because they can provide appropriate viscosity, spreadability, and residence time on the skin. The combination of nanosponge and hydrogel therefore provides both a nanoscale drug reservoir and a patient-friendly topical dosage form. [36]

9. Characterization of Nanosponge-Based Formulations

Comprehensive characterization is essential for establishing the quality, stability, and drug-delivery performance of nanosponge-based topical formulations. Particle size and polydispersity index provide information about the nanoscale dimensions and size distribution, while zeta potential helps assess surface charge and colloidal stability. Morphological characteristics are commonly evaluated using scanning or transmission electron microscopy to confirm particle shape and surface architecture. [37]

Drug-related parameters, including drug loading and entrapment efficiency, are important indicators of the capacity of the nanosponge system to incorporate the therapeutic agent. Fourier-transform infrared spectroscopy, differential scanning calorimetry, and X-ray diffraction can be used to investigate drug–polymer interactions, changes in crystallinity, and possible inclusion or complex formation. Porosity and surface characteristics are particularly relevant because the internal structure influences drug accommodation and release. [38]

For topical psoriasis applications, evaluation should additionally include pH, viscosity, spreadability, skin adhesion, in-vitro drug release, ex-vivo skin permeation, and skin deposition. These studies help determine whether the formulation can remain at the application site while providing controlled delivery to the relevant skin layers. Stability studies and irritation or sensitization assessments are also necessary before considering further preclinical or clinical development. [39]

Table 5. Characterization Parameters of Nanosponge-Based Formulations

Characterization parameter	Technique	Purpose
Particle size	Dynamic light scattering	Determines nanoscale size
PDI	Dynamic light scattering	Determines size distribution
Zeta potential	Electrophoretic mobility	Indicates surface charge and stability
Morphology	SEM/TEM	Determines particle structure
Drug loading	UV/HPLC	Determines incorporated drug
Entrapment efficiency	UV/HPLC	Determines encapsulation efficiency
FTIR	FTIR spectroscopy	Evaluates drug–polymer interactions
Thermal behavior	DSC	Determines thermal transitions
Crystallinity	XRD	Evaluates crystalline/amorphous state
Porosity	Surface analysis	Determines internal pore characteristics
In-vitro release	Dialysis/diffusion method	Determines release profile
Ex-vivo permeation	Franz diffusion cell	Evaluates skin permeation
Skin deposition	Tissue extraction	Determines drug retention
pH	Digital pH meter	Determines topical compatibility
Viscosity	Viscometer	Determines rheological properties
Spreadability	Spreadability test	Evaluates application performance
Stability	ICH-based studies	Determines formulation stability

10. Nanosponge-Loaded Topical Gels and Hydrogels

Nanosponge systems are frequently incorporated into gels or hydrogels to obtain a suitable topical dosage form with improved residence time and application properties. The nanosponge serves as a drug reservoir, while the gel matrix facilitates spreading and maintains the formulation at the application site. This combination can provide controlled drug release and improve drug retention within the skin. [40,41]

Carbopol-based hydrogels have been investigated for nanosponge delivery of antipsoriatic drugs. In a clobetasol propionate formulation, β-cyclodextrin nanosponges were incorporated into Carbopol hydrogel and demonstrated favorable rheological and spreadability characteristics together with improved antipsoriatic activity in an experimental model. [31]

More recently, nanosponge-based hydrogels have also been explored for natural bioactive compounds. A berberine-loaded nanosponge hydrogel was reported to improve skin deposition and reduce psoriasis-associated inflammatory and oxidative-stress markers in an experimental model, highlighting the potential of combining nanosponges with bioactive compounds and functional hydrogel matrices. [42]

The selection of the gel-forming polymer, nanosponge concentration, viscosity, pH, spreadability, adhesion, and drug-release characteristics should therefore be optimized to achieve effective and patient-acceptable topical delivery.

11. Preclinical Evaluation of Nanosponge-Based Antipsoriatic Systems

Preclinical evaluation is essential for determining whether nanosponge-based formulations can improve topical antipsoriatic efficacy while maintaining adequate safety. Commonly investigated models include the mouse tail model and imiquimod-induced psoriasis-like inflammation, which allow assessment of epidermal hyperplasia, keratinization, inflammatory changes, and overall therapeutic response. Histopathological examination, psoriasis severity scoring, and measurement of oxidative and inflammatory biomarkers can provide complementary evidence of treatment efficacy.

Recent studies demonstrate encouraging results with nanosponge-based systems. A 2025 study developed a sulfasalazine-loaded cyclodextrin nanosponge hydrogel and evaluated it using mouse tail and imiquimod-induced psoriasis-like models. The optimized formulation showed sustained drug release, improved skin permeation, favorable safety, and a marked reduction in psoriasis-associated changes, including epidermal thickness and disease severity scores. Histopathological and oxidative-stress assessments further supported its antipsoriatic activity. [43]

Similarly, clobetasol propionate-loaded cyclodextrin nanosponges incorporated into Carbopol hydrogel demonstrated antipsoriatic activity in the mouse tail model, together with favorable changes in biochemical markers associated with oxidative stress. [31] These findings indicate that nanosponge systems may improve the therapeutic performance of both conventional anti-inflammatory drugs and poorly soluble therapeutic agents.

Nevertheless, most available studies remain preclinical, and differences in formulation composition, animal models, treatment duration, and outcome measures make direct comparison difficult. Future investigations should therefore incorporate standardized evaluation protocols, detailed skin-distribution studies, long-term safety assessment, and pharmacokinetic investigations before clinical translation can be considered.

12. Comparison of Nanosponges with Other Nanocarriers

Different nanocarriers have been investigated to overcome the limitations of conventional topical therapy for psoriasis. Liposomes and niosomes can improve drug deposition and skin interaction, while transfersomes and ethosomes are designed to enhance penetration through the skin. Solid lipid nanoparticles and nanostructured lipid carriers provide controlled release and can improve the stability of incorporated drugs. Nanoemulsions are particularly useful for solubilizing poorly water-soluble compounds and enhancing their topical distribution. [44,45]

Nanosponges differ from many of these systems because their highly cross-linked porous network provides internal cavities that can accommodate drug molecules and function as a sustained-release reservoir. They can improve drug solubility while protecting incorporated molecules and can be incorporated into hydrogels or other topical vehicles. However, nanosponges may require more complex preparation and optimization of cross-linking conditions, and their clinical evidence in psoriasis remains considerably less developed than that of some lipid-based nanocarriers. [46]

Thus, nanosponges should not necessarily be considered superior to all other nanocarriers. Their major potential advantage lies in combining solubility enhancement, drug protection, controlled release, and compatibility with topical semisolid formulations within a single platform. Selection of the most appropriate carrier should therefore depend on the physicochemical properties of the drug, desired skin localization, release profile, safety requirements, and intended therapeutic application.

Table 6. Comparison of Nanosponges with Other Nanocarriers

Parameter	Nanosponges	Liposomes	Niosomes	SLN/NLC	Nanoemulsions
Drug solubility enhancement	High	High	Moderate–high	Moderate	High
Drug loading	High	Moderate	Moderate	Moderate–high	Low–moderate
Controlled release	High	Moderate	Moderate	High	Low–moderate
Drug protection	High	High	High	High	Moderate

Skin retention	High	High	High	High	Moderate
Structural stability	Good	Moderate	Good	Good	Moderate
Preparation complexity	Moderate	High	Moderate	Moderate	Moderate
Topical formulation compatibility	High	High	High	High	High
Psoriasis-specific evidence	Emerging	Relatively established	Emerging	Emerging	Emerging
Clinical translation	Limited	More advanced	Limited	Limited	Moderate

13. Advantages of Nanosponge-Based Topical Delivery

Nanosponge-based systems offer several characteristics that are advantageous for topical psoriasis therapy. Their porous structure provides a large internal surface area for drug incorporation and can improve the solubility of poorly water-soluble molecules. The cross-linked network also allows modulation of drug release, providing a sustained drug supply at the application site rather than rapid release from conventional formulations. [47,48]

Another important advantage is the potential to improve drug retention and deposition within the skin. Nanosponge characteristics such as particle size, cross-linking density, porosity, and surface properties can be adjusted to influence drug–carrier interactions and skin delivery. Their incorporation into gels or hydrogels can further improve residence time, spreadability, and patient acceptability. [49]

Nanosponges may also protect incorporated drugs from chemical or environmental degradation and can accommodate both hydrophilic and hydrophobic molecules. These properties are particularly relevant to psoriasis, where localized and sustained delivery may improve therapeutic effectiveness while reducing unnecessary systemic exposure. However, these advantages must be confirmed for individual drug–nanosponge systems because formulation performance depends strongly on nanosponge composition and drug properties. [47,50]

14. Current Challenges and Limitations

Despite their potential, nanosponge-based topical systems face several challenges that may limit their translation into clinical applications. Formulation variables such as polymer type, cross-linker concentration, degree of cross-linking, particle size, porosity, and drug-loading conditions can substantially influence nanosponge performance. Achieving consistent particle characteristics and drug-release profiles between batches remains an important manufacturing challenge. [51,52]

Safety evaluation is another important consideration. Although cyclodextrins generally possess favorable biocompatibility, the safety of a nanosponge depends on its composition, cross-linker chemistry, particle characteristics, drug, and route of administration. Therefore, cytotoxicity, skin irritation, sensitization, dermal penetration, and systemic exposure should be evaluated for each formulation rather than assuming safety based only on the individual components. [53]

Clinical translation is further limited by the relatively small number of psoriasis-specific studies and the predominance of preclinical evidence. Large-scale manufacturing, reproducibility, quality control, regulatory characterization, and cost-effective production require further development. Application of quality-by-design (QbD) principles and standardized characterization protocols may help establish critical material attributes and critical process parameters, thereby improving formulation robustness and facilitating scale-up. [54]

Table 7. Challenges, Possible Solutions, and Future Research Directions

Current challenge	Possible solution	Future direction
Batch-to-batch variability	QbD-based optimization	Robust manufacturing

Variable particle size	Optimization of process parameters	Standardized production
Limited clinical evidence	Well-designed clinical trials	Clinical translation
Skin penetration variability	Surface engineering	Targeted skin delivery
Cross-linker safety concerns	Biocompatible cross-linkers	Safer nanosponge chemistry
Limited long-term safety data	Extended dermal toxicity studies	Long-term safety validation
Scale-up difficulties	Process engineering	Industrial manufacturing
Complex formulation optimization	Design of experiments/AI	AI-assisted formulation
Limited targeting	Surface functionalization	Lesion-specific delivery
Single-drug therapy	Co-loading multiple actives	Combination therapy
Conventional release behavior	Stimuli-responsive systems	Smart nanosponges
Regulatory uncertainty	Standardized characterization	Regulatory frameworks

15. Future Perspectives

Future development of nanosponge-based topical systems for psoriasis should focus on improving lesion-specific drug delivery, formulation reproducibility, and clinical translation. Stimuli-responsive nanosponges capable of modifying drug release in response to pH, temperature, oxidative stress, or other characteristics of the psoriatic microenvironment may provide more precise and sustained treatment. Surface functionalization with targeting ligands may further improve localization within inflamed skin. [55]

Combination therapy represents another promising direction, particularly through co-loading of corticosteroids, immunomodulators, antioxidants, or natural bioactive compounds within a single nanosponge system. Integration with hydrogels, microneedles, or other advanced topical platforms may further enhance skin deposition and therapeutic performance. Artificial intelligence and quality-by-design approaches could also facilitate optimization of formulation variables and prediction of critical quality attributes. [56]

However, successful translation will require standardized characterization methods, long-term dermal safety studies, well-designed comparative animal studies, and adequately powered clinical trials. Scalable and reproducible manufacturing, cost-effective production, and clear regulatory requirements will also be essential. Ultimately, the development of personalized and lesion-targeted nanosponge systems may help establish nanosponges as a clinically relevant platform for localized psoriasis management.

16. Conclusion

Nanosponge-based topical delivery systems represent a promising approach for improving the localized treatment of psoriasis. Their porous and cross-linked structure provides opportunities for enhancing drug solubility, protecting unstable molecules, controlling drug release, and improving drug retention within the skin. Preclinical studies involving agents such as clobetasol propionate, curcumin, caffeine, and sulfasalazine have demonstrated encouraging improvements in formulation performance and antipsoriatic activity. However, the available evidence remains predominantly preclinical, and substantial challenges related to formulation reproducibility, long-term dermal safety, scale-up, regulatory requirements, and clinical validation remain. Future research should therefore focus on standardized evaluation, quality-by-design approaches, targeted and stimuli-responsive systems, combination therapy, and well-designed clinical studies. With continued optimization and translational research, nanosponges may become a valuable platform for more localized, sustained, and patient-friendly psoriasis therapy.

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