Revolutionizing Psoriasis Management: Advanced Insights into Niosomal Drug Delivery Systems

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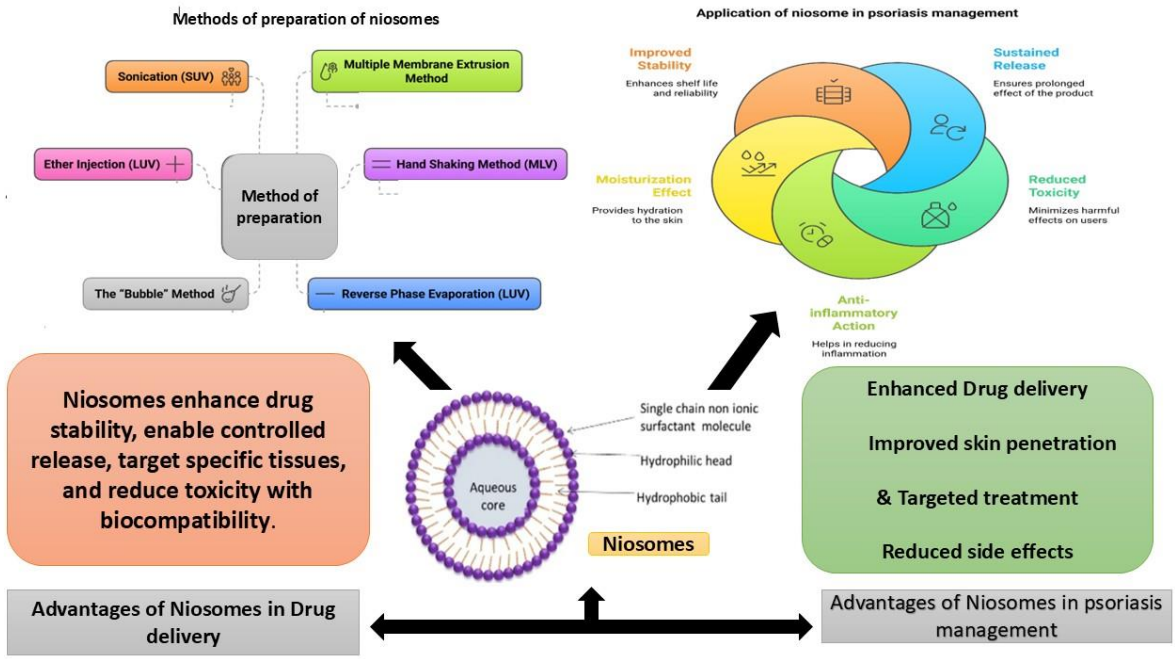
Abstract

Psoriasis is a persistent inflammatory dermatosis distinguished by the excessive proliferation of keratinocytes and alterations in immune function. Notwithstanding the progress in therapeutic interventions, traditional modalities such as corticosteroids and biologics are constrained by limitations, which encompass systemic adverse effects and variable efficacy. Niosomal drug delivery systems have surfaced as a viable alternative, presenting improved transdermal penetration, regulated drug release, and precise delivery to psoriatic plaques. This review investigates the pathophysiological mechanisms underlying psoriasis, critical therapeutic targets, and the methodologies by which niosomes enhance drug bioavailability and modulate immune responses. Furthermore, it examines formulation methodologies, encompassing surfactant selection, encapsulation methodologies, and considerations for stability. The utilization of niosomes in the management of psoriasis, particularly for the administration of corticosteroids, biologics, and combination therapies, is scrutinized. Recent innovations in nano-niosomes, systems responsive to stimuli, and formulations designed through artificial intelligence are also accentuated. In conclusion, future outlooks on clinical application and personalized medicine highlight the prospective impact of niosomal technology in transforming the treatment landscape for psoriasis.

Keywords: Niosomes, Surfactants, Encapsulation, Psoriasis, Drug delivery

Graphical abstract



1. Introduction

1.1 Overview of Psoriasis

Psoriasis is a chronic, immune-mediated skin disorder characterized by erythematous, scaly plaques resulting from hyperproliferation of keratinocytes and persistent inflammation(1, 2). It affects approximately 2–3% of the global population and has significant physical and psychological burdens. The disease is driven by dysregulated immune responses, particularly involving T cells, dendritic cells, and cytokines like TNF-α, IL-17, and IL-23(3, 4). Psoriasis manifests in various forms, including plaque, guttate, pustular, and erythrodermic psoriasis. While genetic predisposition and environmental triggers contribute to its onset, factors like stress, infections, and lifestyle can exacerbate symptoms. Effective management requires a combination of topical, systemic, and biologic therapies (5, 6).

The psychological impact of psoriasis cannot be understated, as individuals often grapple with feelings of embarrassment and social stigma due to visible skin lesions.(7) This emotional burden can lead to significant mental health issues, including anxiety and depression, which are prevalent among those affected by this chronic condition. Furthermore, the association between psoriasis and comorbidities such as cardiovascular disease highlights the need for a comprehensive treatment approach that addresses both physical and mental health aspects. As research continues to uncover the complex interplay of genetic and environmental factors in psoriasis development, it becomes increasingly clear that tailored therapeutic strategies ranging from lifestyle modifications to advanced biologic treatments are essential for improving patient outcomes and quality of life(8). Collaborative care models that involve dermatologists, psychologists, and primary care providers may enhance the overall management of psoriasis, ensuring that patients receive holistic support tailored to their unique needs. This multidisciplinary approach not only fosters better communication among healthcare providers but also empowers patients to take an active role in their treatment journey, ultimately leading to more effective management of their condition. As research progresses, integrating patient education and self-management techniques into treatment plans will further empower individuals to navigate their psoriasis effectively, fostering a sense of control over their health and well-being. Incorporating technology, such as telemedicine and mobile health applications, can also play a crucial role in enhancing access to care and enabling continuous monitoring of patients' conditions(9).

1.2 Current Treatment Approaches and Challenges

Psoriasis management involves a combination of topical, systemic, and biologic therapies, depending on disease severity and patient response. Topical treatments, including corticosteroids, vitamin D analogs (calcipotriol), and calcineurin inhibitors, are the first-line options for mild to moderate psoriasis. They help reduce inflammation and keratinocyte proliferation but often require long-term use, leading to skin thinning and tachyphylaxis(10).
For moderate to severe cases, systemic treatments such as methotrexate, cyclosporine, and acitretin are commonly prescribed. These agents modulate immune responses but come with

significant side effects, including hepatotoxicity, nephrotoxicity, and teratogenicity. Biologic therapies targeting TNF-α (infliximab, etanercept), IL-17 (secukinumab), and IL-23 (guselkumab) have revolutionized psoriasis treatment by providing more targeted immune modulation with improved efficacy and safety. However, they are expensive, require long-term administration, and may increase the risk of infections and malignancies(11).

Challenges in psoriasis treatment include variability in patient response, limited long-term efficacy, and potential adverse effects. Poor adherence to treatment regimens, especially with topical therapies, also hinders effective disease management. Additionally, drug resistance and disease recurrence remain concerns. Innovative drug delivery systems, such as niosomes, offer a promising approach to enhancing therapeutic outcomes while minimizing systemic side effects and improving patient compliance(12).

2. Pathophysiology of Psoriasis and Therapeutic Targets

2.1 Key Molecular and Cellular Mechanisms

Psoriasis is driven by complex interactions between the immune system, keratinocytes, and inflammatory mediators. It is primarily mediated by dysregulated activation of innate and adaptive immune responses, leading to chronic inflammation and epidermal hyperproliferation. The disease process begins with an environmental or genetic trigger that activates antigen-presenting cells, particularly dendritic cells, which in turn secrete pro-inflammatory cytokines such as IL-12 and IL-23. These cytokines promote the differentiation of naïve T cells into Th1 and Th17 cells. Th1 cells produce IFN-γ and TNF-α, which sustain inflammation, while Th17 cells release IL-17 and IL-22, stimulating keratinocyte proliferation and neutrophil recruitment. Keratinocytes, in response to these cytokines, undergo hyperproliferation and produce antimicrobial peptides (AMPs) like LL-37, further amplifying immune activation. This results in the characteristic thickened, scaly plaques seen in psoriasis. Additionally, dysregulation of regulatory T cells (Tregs) contributes to sustained inflammation by failing to suppress excessive immune responses. Angiogenesis also plays a crucial role, with vascular endothelial growth factor (VEGF) promoting increased blood vessel formation, enhancing immune cell infiltration. The interplay of these molecular and cellular mechanisms creates a self-perpetuating inflammatory loop, making psoriasis a chronic, relapsing disease requiring targeted therapeutic interventions(13).

Understanding the intricate interplay of immune cells in psoriasis is crucial for developing targeted therapies. Recent research has illuminated the pivotal role of Th17 cells and their associated cytokines, particularly IL-23, which are central to the inflammatory cascade that characterizes this condition (14). Moreover, the identification of genetic risk loci linked to psoriasis not only enhances our comprehension of its pathogenesis but also opens avenues for personalized medicine approaches tailored to individual genetic profiles. Additionally, emerging evidence suggests that epigenetic modifications may serve as a bridge between genetic predispositions and environmental triggers, further complicating the disease's etiology while offering potential biomarkers for predicting treatment responses Such insights

underscore the necessity for continued exploration into both cellular mechanisms and novel therapeutic targets, aiming to alleviate the burden of this chronic inflammatory disorder(15).

2.2 Drug Targets for Psoriasis Management

Psoriasis treatment aims to disrupt key molecular pathways involved in inflammation, immune dysregulation, and keratinocyte hyperproliferation. Several drug targets have been identified to control disease progression and reduce symptoms effectively.

2.2.1 Tumor Necrosis Factor-alpha (TNF-α) Inhibitors

TNF-α is a pro-inflammatory cytokine that plays a central role in psoriasis pathogenesis by activating dendritic cells and promoting T-cell differentiation. TNF-α inhibitors, such as infliximab, etanercept, and adalimumab, have been highly effective in reducing inflammation and skin lesions. However, long-term use increases the risk of infections and autoimmune complications(15).

2.2.2 Interleukin (IL)-17 and IL-23 Pathway

The IL-17/IL-23 axis is a key driver of psoriatic inflammation. IL-23 promotes Th17 cell differentiation, which secretes IL-17 and IL-22, leading to keratinocyte proliferation and neutrophil infiltration. Targeting IL-17 (secukinumab, ixekizumab) or IL-23 (guselkumab, risankizumab) has demonstrated high efficacy with fewer systemic side effects than TNF inhibitors(16).

2.2.3 JAK-STAT Signaling Pathway

Janus kinase (JAK) inhibitors modulate intracellular signaling pathways that regulate cytokine production and immune cell activation. Tofacitinib and baricitinib are oral JAK inhibitors being explored for psoriasis treatment, offering an alternative to biologics with convenient oral administration(17).

2.2.4 PDE4 Inhibitors

Phosphodiesterase-4 (PDE4) is an enzyme that degrades cyclic AMP, leading to increased pro-inflammatory cytokine production. Apremilast, a PDE4 inhibitor, reduces TNF-α, IL-17, and IL-23 levels, providing a systemic treatment option for moderate psoriasis with a favorable safety profile(18).

2.2.5 Keratinocyte and Immune Cell Modulation

Retinoids like acitretin and calcineurin inhibitors (tacrolimus, pimecrolimus) target keratinocyte differentiation and immune activation, making them effective for localized or systemic psoriasis treatment.

These targeted therapies have transformed psoriasis management, offering precise interventions with improved efficacy and safety compared to traditional treatments(19).

2.3 Role of Topical and Systemic Therapies

Psoriasis treatment is tailored to disease severity, with topical therapies preferred for mild to moderate cases and systemic therapies used for moderate to severe cases. Both approaches aim to reduce inflammation, normalize keratinocyte proliferation, and improve skin barrier function. Topical treatments are the first-line approach for mild to moderate psoriasis. Corticosteroids, the most commonly used agents, provide anti-inflammatory and immunosuppressive effects, reducing erythema and scaling. However, long-term use can lead to skin atrophy, tachyphylaxis, and systemic absorption risks. Vitamin D analogs, such as calcipotriol, regulate keratinocyte proliferation and differentiation, offering an effective steroid-sparing alternative. Calcineurin inhibitors (tacrolimus, pimecrolimus) are used for sensitive areas like the face and intertriginous regions, as they suppress T-cell activation without causing skin thinning. Other topical agents include coal tar, salicylic acid (for scaling reduction), and dithranol, though their use is limited due to irritation and staining(20).

For moderate to severe psoriasis or cases unresponsive to topical treatment, systemic therapies are necessary. Traditional systemic agents include methotrexate, an immunosuppressant that inhibits T-cell activation, and cyclosporine, which blocks T-cell signalling. Both are effective but have significant risks, such as hepatotoxicity, nephrotoxicity, and hypertension. Acitretin, an oral retinoid, regulates epidermal proliferation but is teratogenic and can cause mucocutaneous side effects (21).

Biologic therapies have transformed psoriasis management by specifically targeting immune pathways. TNF-α inhibitors (infliximab, etanercept, adalimumab) reduce systemic inflammation, while IL-17 inhibitors (secukinumab, ixekizumab) and IL-23 inhibitors (guselkumab, risankizumab) directly interfere with psoriatic inflammation pathways. Despite their efficacy, biologics are expensive, require injections, and may increase infection risk. Overall, while topical and systemic therapies provide effective disease control, challenges such as side effects, patient adherence, and treatment resistance highlight the need for advanced drug delivery systems like niosomes to improve therapeutic outcomes (22).

3. Mechanisms of Niosomal Drug Delivery in Psoriasis

3.1 Skin penetration and drug release kinetics

Niosomes represent a promising advancement in drug delivery systems for psoriasis treatment, particularly due to their ability to enhance skin penetration and control drug release kinetics. Ghazwani et al., prepared carvacrol oil (CVC) niosomal gel by thin film hydration method to improve its penetration into the skin for anti-inflammatory actions. The optimized niosomes encapsulating CVC exhibited a vesicle diameter of 180.23 nm, a polydispersity index (PDI) of 0.265, a zeta potential of -31.70 mV, and an entrapment efficiency quantified at 90.61%. In

vitro drug release assessments indicated that CVC-loaded niosomes released 70.24% of the encapsulated drug, a markedly higher percentage in comparison to the CVC suspension, which released only 32.87%. The release kinetics adhered to the Higuchi model and exhibited characteristics of non-Fickian diffusion. A dermatokinetic investigation demonstrated that the niosomal gel formulation significantly enhanced the penetration of CVC into dermal layers in contrast to a conventional formulation. The confocal laser scanning microscopy (CLSM) analysis also revealed that rhodamine B-loaded niosomes achieved greater penetration depth (25.0 µm) when compared to the hydroalcoholic solution (5.0 µm). The study results concluded that the deployment of niosomal gel formulations constitute a viable approach for the localized administration of CVC in the management of inflammatory disorders(23). Thatikonda et al., suggested that encapsulation of drug like nimbolide in to niosomes allows for a controlled release profile. The administration of nimbolide in to niosomes substantially diminishes the severity of psoriasis, encompassing symptoms such as erythema, desquamation, and dermal thickness, while concurrently alleviating splenomegaly, in addition to inhibiting the phosphorylation of pro-inflammatory mediators including NF-κB, MAPKs, and STAT3, which are activated by EGF and IMQ(24). Fen Qiu et al prepared Celastrol Noisome hydrogel (Cel Nio gel) for psoriasis treatment and tested in an IMQ-induced psoriasis mouse model. The study demonstrated that Cel Nio (133 nm, 83.2% EE) were primarily accumulated in the skin, minimizing systemic exposure while significantly reducing inflammatory cytokines in blood. It also showed that the Nio enhanced HaCaT cell uptake, and Cel reduced inflammatory cytokine mRNA levels. Immunofluorescence showed decreased inflammatory factor and Ki-67 expression in skin. The study concluded that Cel Nio gel effectively inhibited keratinocyte inflammation and hyperproliferation, providing both local and systemic anti-psoriatic effects, making it a promising topical therapy(25).

3.2 Targeting Psoriatic Lesions

Targeting psoriatic lesions effectively involves advanced therapeutic strategies, particularly through the use of artificial intelligence and biologic therapies. Recent studies highlight the potential of AI in enhancing phototherapy precision, while biologic treatments significantly improve patient outcomes in psoriatic arthritis.

3.2.1 AI-Mediated Targeted Phototherapy

Praeger et al., reported in their study that an artificial neural network was trained to distinguish psoriatic lesions from unaffected skin with a remarkable accuracy of 96.73%. This technology allows for targeted delivery of narrowband ultraviolet B therapy, minimizing exposure to healthy skin and enabling higher doses for affected areas, thus improving treatment efficacy and reducing side effects. The study also demonstrated that AI-mediated targeted phototherapy using a digital micromirror device is feasible(26).

3.2.2 Biologic and Targeted Therapies

Biologic therapies, including TNF inhibitors and IL-17 inhibitors, have shown to reduce the need for symptomatic treatments and hospitalizations in psoriatic arthritis patients. Vegas et al., performed the nationwide cohort study of 9793 PsA patients assessed the impact of targeted therapies on medication use, hospitalizations, and sick leaves. Initiating targeted therapies significantly reduced the use of NSAIDs (-15%), opioids (-9%), prednisone (-9%), methotrexate (-15%), and mood disorder treatments (-2%), along with decreases in hospitalizations (-12%) and sick leaves (-4%). TNFi showed a greater reduction in NSAID and prednisone use compared to IL17i and IL12/23i, though TNFi was less effective at reducing methotrexate use. Overall, targeted therapies improved treatment outcomes, with TNFi demonstrating a slightly superior effect (27, 28).

3.2.3. Target to treat approach

A treat-to-target approach in managing psoriatic arthritis has been recommended, emphasizing early intervention and tailored treatment plans to achieve optimal outcomes (3). Din et al., evaluated the real-life implementation of the treat-to-target (T2T) strategy in managing psoriatic arthritis. The retrospective review included 89 patients seen between January 2020 and February 2023. The study assessed the use of validated tools like DAPSA28 and PGA to monitor disease activity. Their key findings include 56.2% were males, with a mean age of 43.5 years and mean disease duration of 6.6 years. Common clinical features included axial involvement (43.8%), dactylitis (23.6%), and enthesitis (12.4%). Most patients (97.7%) were on csDMARDs, predominantly methotrexate (77%), while 34.8% were on bDMARDs, commonly tofacitinib, infliximab, or secukinumab. Adverse events occurred in 21.1% of csDMARD users and 3.2% of bDMARD users.Disease activity monitoring tools were inconsistently used (DAPSA28 in 44.9%, PGA in 100%).The target of low disease activity or remission was achieved in 50.6% of patients, with higher success rates in those on bDMARDs (74.2%) compared to csDMARDs (51.2%).The study underscores the importance of T2T in improving disease control and quality of life, while highlighting its limited adoption in routine practice(29).

3.3 Immune Modulation and Anti-Inflammatory Effects

Recent advancements in immunomodulation have shown promise in managing psoriasis by targeting specific cytokines and pathways involved in its pathogenesis. Immunomodulation has emerged as a key therapeutic strategy, with biologics targeting IL-17, IL-23, and IL-12/23 showing significant clinical efficacy. Small molecules like JAK and PDE4 inhibitors have also demonstrated promise. Chen et al., studied the effects of Dexamethasone (DXM) on psoriasis in a murine model, allowing for the evaluation of both clinical and immunological outcomes. The study found that giving DXM orally at a dose of 10 mg/kg significantly reduced the symptoms of psoriasis in mice. It has been also reported that DXM treatment resulted in lower levels of pro-inflammatory cytokines, specifically TNF-α, IL-6, IL-17A, and IL-22, in the skin of the treated mice. This indicates that DXM helps to reduce the inflammatory response

associated with psoriasis. Furthermore, scientist reported that oral administration of DXM was more effective in alleviating psoriasis symptoms than intraperitoneal injection. Mice receiving DXM orally showed greater improvements in skin lesions and overall health. This suggests that DXM could be a helpful treatment for people suffering from this skin condition. Singh et.al., in their review suggested that targeting interleukins such as IL-17 and IL-23 has shown substantial clinical efficacy in reducing psoriasis symptoms(30). Singh et al in their review also reported that Janus kinase (JAK) inhibitors and phosphodiesterase 4 (PDE4) inhibitors are emerging as effective treatments by modulating immune responses. However, challenges such as treatment resistance, safety concerns, and high costs persist. Advancing the understanding of psoriasis pathogenesis is crucial for developing personalized therapies. While immunomodulation has greatly improved patient outcomes, ongoing research is essential to enhance treatment effectiveness, safety, and accessibility (27).

4. Formulation and Development of Niosomes for Psoriasis

The formulation and development of niosomes for psoriasis treatment represent a significant advancement in topical drug delivery systems.

4.1 Key Components: Surfactants, Cholesterol, and Additives

The key components of niosomes include non-ionic surfactants, cholesterol, and various additives, each playing a crucial role in the formation and functionality of these vesicles. Non-ionic surfactants are essential for the self-assembly of niosomes, forming the bilayer structure that encapsulates drugs. They provide the amphiphilic nature necessary for the vesicle formation, allowing the entrapment of both hydrophilic and lipophilic substances. Fatemeh Nowroozi et al found that the type of surfactant used significantly affects the particle size of niosomes. Specifically, niosomes made with Tween 60 had a larger particle size compared to those made with Span 60 and Brij 72. This suggests that surfactants with higher HLB (Hydrophilic-Lipophilic Balance) values lead to larger niosomes sizes at the same cholesterol content (31). Matlapudi MS et al aimed to enhance the topical delivery of Desonide for effective psoriasis treatment. The niosomes were prepared by film hydration method using Cholesterol, Span 80 and Carbopol 940 (gelling agent). A Box-Behnken (BB) design, using Design-Expert® software, was employed to statistically optimize formulation variables. Three independent variables were evaluated: Span 80 (X1), Cholesterol (X2) and Sonication Time (X3). The Vesicle size (Y1: PS nm) and Entrapment Efficiency (Y2: EE %) were selected as dependent variables. The Vesicle size was obtained in a range between 114 nm to 216 nm, EE% was found in a range between 72% to 88%, PDI value is found between 0.31 to 0.45. The study concluded that higher cholesterol concentrations have been shown to increase vesicle size and improve drug entrapment efficiency, which is essential for delivering therapeutic agent(32). The incorporation of various additives in niosomal formulations can significantly improve their therapeutic efficacy against psoriasis. Bhaskaran & Reddy et al.; prepared niosomal urea gel using chitosan polymer, to test the same on healthy human volunteers to check the irritation on the skin and to study its clinical effectives on psoriasis patients. The urea niosomes were prepared by both lipid layer hydration and trans membrane pH gradient method.

Surfactants such as spans were used with cholesterol in 1:1 molar ratio with 5% dicetyl phosphate. They observed that niosomes prepared using span 60 showed a better entrapment than span 40 and span 80 and chitosan enhanced stability and drug retention of niosomal formulation, leading to improved skin deposition and reduced irritation compared to plain gels(33).

4.2 Preparation Techniques of niosomes

The preparation techniques of niosomes significantly influence their characteristics, stability, and efficacy as drug delivery systems. Various preparation methods, including film hydration, sonication method, ether injection method and novel techniques like ball milling, have been explored to optimize niosomes properties. Matlapudi MS and other researchers utilized the film hydration technique to create Desonide-loaded niosomes, resulting in vesicle sizes ranging from 114 nm to 216 nm and an entrapment efficiency (EE) of 72% to 88%. The study demonstrated enhanced skin permeation compared to conventional gels(32). Qiu and other scientist prepared Celastrol niosomes using thin-film hydration and Sonication method, achieving a particle size of 133 nm and an EE of 83.2%. This formulation effectively targeted skin keratinocytes, reducing inflammatory cytokines. Curcumin, a bioactive compound with significant therapeutic potential, faces challenges such as poor bioavailability and rapid degradation. The ether injection method for preparing curcumin-loaded niosomes presents a promising solution to enhance its delivery and stability. This technique utilizes non-ionic surfactants to form vesicles that encapsulate curcumin, improving its solubility and controlled release In this study drug content was found to be 8.04mg/ml, Entrapment efficiency was found to be 95.2% and the percentage of drug release was 34.5% at 4th hour (34). The novel technique for the one-step preparation of liposomes and non-ionic surfactant vesicles without organic solvents leverages innovative methods that utilize gas-liquid interfaces. This approach, particularly the 'Bubble' method, facilitates the formation of lipid bubbles and liposomes through mild processes that minimize energy consumption. This method involves mixing gas-dissolved water with lipid materials, allowing amphiphilic lipid molecules to adsorb and assemble at the gas-liquid interface, forming lipid bubbles This method contrasts with traditional techniques like ultrasonic cavitation, offering a gentler and more energy-efficient alternative for bubble preparation(35). Kanpipit N and other scientists evaluated the effects of various niosomes formulations containing lycopene-rich extracts from tomatoes, carrots, and mixed red vegetables, and compared the niosomes preparation methods between the conventional thin-film hydration method and microfluidic method. Noisome formulations produced using the microfluidic method method generally resulted in significantly smaller particle sizes (237.97–281.73nm) compared to those produced with the thin-film hydration method (245.17–457.47nm) The results showed that the microfluidic method was more efficient than the thin-film hydration method for large-scale production, as it requires fewer steps and offers greater uniformity, homogeneity and better control over smaller niosomes sizes(36). Temprom L et.al; focused on developing an optimized niosome formulation for encapsulating melatonin using the ball milling (BM) method. Niosomes were prepared with Span 60 and cholesterol in different molar ratios (2:1, 1:1, and 1:2) and characterized for their physical properties and stability using FTIR, TEM, and dynamic light scattering. The BM

method effectively produced smaller, stable niosomes with diameters ranging from 250 to 600 nm and low polydispersity index values. The 1:1 Span 60 to cholesterol ratio showed the highest stability, ideal for further drug release studies. Melatonin entrapment efficiency ranged from 85.09% to 86.69%. The in vitro release study showed a prolonged release profile, reaching 21% after 48 hours, following Higuchi's diffusion model. The BM technique demonstrated potential for enhancing the delivery of poorly soluble drugs with improved release characteristics(37). These methods are crucial for optimizing the properties of niosomes, which can significantly impact their stability, bioavailability, and effectiveness in drug delivery applications.

4.3 Encapsulation of Anti-Psoriatic Agents

Niosomes structure allows for the encapsulation of both hydrophilic and lipophilic drugs, enhancing drug stability, solubility, and bioavailability. The encapsulation of anti-psoriatic agents in niosomes for topical application offers several advantages, including improved penetration, targeted delivery, and sustained release, which are crucial for effective psoriasis management. Desonide, a topical corticosteroid, has been encapsulated in niosomes using the film hydration technique. This formulation, optimized using a Box-Behnken design, demonstrated improved skin permeation and retention compared to conventional gels. The niosomes were prepared with cholesterol, Span 80, and Carbopol 940, achieving vesicle sizes between 114 nm to 216 nm and entrapment efficiencies ranging from 72% to 88% (38). Encapsulation of drug which is having the poor bioavailability and sensitive to environment in niosomal formulation can protect drugs from degradation, thereby enhancing their stability(39).

5. Applications of Niosomes in Psoriasis Management

Niosomal drug delivery systems offer a multifaceted approach to psoriasis management by enhancing drug penetration, reducing systemic exposure, improving stability, and enabling combination therapies. These advantages position niosomes as a valuable tool in developing more effective and patient-friendly psoriasis treatments**.**

Table 1: Applications of Niosomes in Psoriasis Management

Application	Study Details	Results	Citation
Cyclosporine and Pentoxifylline Co-Delivery via Niosomes	Researchers developed niosomes encapsulating both Cyclosporine (a hydrophobic drug) and Pentoxifylline (a hydrophilic drug) aimed at effective psoriasis	The co-delivery system demonstrated enhanced skin penetration and retention of both drugs. In animal	

	management. The study involved in-vitro optimization, ex-vivo permeation studies, and in-vivo evaluations using animal models.	studies, the niosomal formulation significantly reduced psoriasis severity compared to controls, suggesting a promising approach for topical psoriasis treatment.	
Capsaicin-Loaded Niosomes	Investigation of capsaicin-loaded niosomes for controlled local delivery in psoriasis treatment. In vitro and in vivo studies evaluated skin retention and therapeutic efficacy.	Emulgel formulation showed enhanced skin retention of capsaicin, suggesting effective localized treatment for psoriasis.	
Methotrexate (MTX)	Phase I and II Clinical Trials: Developed niosomal MTX incorporated into chitosan gel; assessed for irritation on 10 healthy volunteers; evaluated efficacy in a double-blind, placebo-controlled study on 10 psoriasis patients over 12 weeks.	No significant irritation observed; significant reduction in Psoriasis Area and Severity Index (PASI) scores from 6.2378±1.4857 to 2.0023±0.1371 after 12 weeks.	(42)
Nimbolide (NIM)	Preclinical Study: Formulated NIM-loaded niosomes; characterized using Zeta sizer, TEM, and HPLC; evaluated anti-psoriatic potential in a psoriasis mouse model.	Enhanced skin penetration; reductions in keratinocyte hyperproliferation, oxidative stress, splenomegaly, inflammatory cytokines, PASI scores, and rete ridges compared to NIM alone.	(43)
Diacerein	Preclinical Study: Developed diacerein-entrapped niosomes with cholesterol; assessed penetration in rat skin using confocal laser scanning microscopy.	Enhanced penetration into epidermal and dermal layers; potential for targeted	(44)

		delivery reducing systemic side effects.	
Tazarotene	Preclinical Study: Formulated tazarotene-loaded niosomal gel; evaluated skin retention and local accumulation efficiency (LAE) in comparison to conventional gel.	Increased skin retention and LAE; reduced side effects and improved bioavailability over conventional formulations.	(45)
Ammonium Glycyrrhizinate	Preclinical Study: Formulated ammonium glycyrrhizinate niosomes; evaluated in murine models for psoriasis treatment.	Reduced edema and nociception compared to placebo and drug alone; potential nano-vesicular system for psoriasis treatment.	(46)

These studies demonstrate the potential of niosomal formulations to enhance the efficacy and safety of topical treatments for psoriasis by improving drug penetration, retention, and targeted delivery while minimizing systemic side effects.

5.1 Stability and Scalability Considerations

The stability and scalability of niosomes in the treatment of psoriasis present significant advantages over traditional drug delivery systems. Niosomes exhibit greater stability compared to liposomes, particularly during formulation and storage, due to their non-ionic surfactant composition(47, 48). The scalability of niosomes for commercial production remains a critical consideration as researchers strive to translate laboratory successes into clinically viable solutions. The complexity involved in formulating niosomes, including the precise selection of surfactants and their concentrations, can significantly impact both stability and drug release profiles, necessitating rigorous optimization processes (49). Rane et al., developed an MF-loaded niosomal gel using Span 60 and Cholesterol (2:1) via the thin film hydration method, incorporating Carbopol as the gelling agent. The optimized niosomal gel formulation (with 2% Carbopol) demonstrated improved drug diffusion over 7 hours and a higher flux rate than plain MF. The niosomes had a stable zeta potential of -24 mV, a polydispersity index (PDI) of 0.409, and an average size of 252.7 nm. The niosomes exhibited a zeta potential of -24 mV, which suggests that the formulation is stable. A stable formulation is crucial for ensuring consistent drug delivery and efficacy. The study concluded that niosomal gel is an effective carrier for enhancing MF delivery through the transdermal route(50). Zhe Sun developed a clobetasol propionate-loaded niosomal gel to enhance drug delivery and deposition in psoriatic skin. Using a Box-Behnken design, the formulation was optimized with Span 60, cholesterol, and sonication to achieve a particle size of 188 nm and 78% drug entrapment. The optimized gel showed improved permeability (61.12% vs. 8.56% for marketed cream) and a 5.1-fold increase

in drug deposition. Fluorescence studies confirmed better skin localization, and the gel significantly reduced PASI scores in a psoriatic model. This study indicated that niosomal formulations significantly outperform traditional creams in terms of drug deposition and therapeutic efficacy, as evidenced by reductions in the Psoriasis Area Severity Index scores in clinical models(51).

6. Use of Natural Bioactive in Niosomal Formulations

Niosomal formulations have been explored to enhance the delivery and efficacy of natural bioactive compounds in psoriasis treatment. The **Table 2** below summarizes studies investigating the use of natural bioactive in niosomal formulations for psoriasis management.

Table 2: Use of Natural Bioactive Compounds in Niosomal Formulations for Psoriasis Management

Natural Bioactive	Niosomal Composition	Key Findings	Citation
Celastrol	Span 20, Span 60, and cholesterol (3:1:1)	Niosomal hydrogel exhibited a 13-fold increase in skin deposition compared to non-niosomal formulations; significant reduction in psoriasis severity in mouse models.	(52)
Curcumin	Non-ionic surfactant-based niosomes	Niosomal curcumin suppressed IL-17/IL-23 axis in psoriatic skin lesions; demonstrated potential as a topical treatment in a pilot randomized controlled trial.	(53)
Capsaicin	Span 80 and cholesterol	Niosomal capsaicin showed enhanced skin retention and controlled local delivery; potential for improved patient compliance in psoriasis management.	(54)

7. Future Perspectives

7.1 Integration of AI and Machine Learning in Formulation Design

The incorporation of Artificial Intelligence (AI) and Machine Learning (ML) in drug delivery systems has significantly transformed pharmaceutical research and development. In the context of psoriasis treatment, AI-driven approaches are being explored for optimizing niosomal formulation design. Niosomes, as non-ionic surfactant-based vesicles, offer enhanced drug penetration and stability, making them a promising delivery system for anti-psoriatic drugs. By leveraging AI and ML, researchers aim to improve formulation efficiency, predict drug release profiles, and personalize treatments based on patient-specific responses (55, 56). ML models can predict the optimal surfactant-to-cholesterol ratio, hydration time, and sonication conditions to ensure desirable particle size and high drug entrapment efficiency. Despite the

promising advancements, challenges such as data scarcity and regulatory hurdles remain. Continuous research and collaboration are essential to fully harness AI and ML's potential in pharmaceutical formulation design, particularly for complex conditions like psoriasis(52).

7.2 Clinical Translation and Potential for Personalized Medicine

The integration of clinical translation and personalized medicine in psoriasis represents a significant advancement in treatment strategies, focusing on tailoring therapies to individual patient profiles. This approach leverages insights from genetic, environmental, and immunological factors to optimize treatment efficacy and minimize adverse effects.

Table 3: Clinical Translation and Potential for Personalized Medicine Using Niosomal Formulations in Psoriasis Management

Clinical Translation Insights	Personalized Medicine Potential	Therapeutic Agent	Mechanism of Action	Citation
Lakshmi et al., (2007) Conducted a double-blind, placebo-controlled study demonstrating that methotrexate-loaded niosomal gel significantly reduced Psoriasis Area and Severity Index (PASI) scores, indicating enhanced therapeutic efficacy.	Highlights the potential for tailoring methotrexate delivery to individual patient needs, minimizing systemic exposure and associated side effects.	Methotrexate	Inhibits dihydrofolate reductase, leading to suppression of DNA synthesis in rapidly proliferating cells.	**(57)**
Moghddam et al., (2022) Developed diacerein-entrapped niosomes that showed enhanced penetration into epidermal and dermal layers in rat models, suggesting improved localized treatment.	Indicates the possibility of customizing anti-inflammatory therapy based on patient-specific inflammatory profiles.	Diacerein	Inhibits interleukin-1β (IL-1β) activity, reducing inflammation and cartilage degradation.	**(45)**
Aggarwal et al., Formulated	Supports personalized	Tazarotene	Modulates gene expression to	**(58)**

tazarotene-loaded niosomal gel with increased skin retention and local accumulation, potentially reducing systemic side effects.	dosing strategies to optimize efficacy while minimizing adverse effects.		normalize keratinocyte differentiation and reduce inflammation.	
Gupta et al., Investigated capsaicin-loaded niosomes, demonstrating significant enhancement in skin retention and controlled local delivery, which may improve patient compliance.	Suggests the ability to personalize pain management in psoriasis by adjusting capsaicin delivery.	Capsaicin	Activates transient receptor potential vanilloid 1 (TRPV1) channel, leading to desensitization of nociceptive neurons.	**(59)**
Pandey et al., Developed cyclosporine and pentoxifylline co-loaded niosomes, showing effective management of psoriasis with reduced systemic toxicity in animal studies.	Opens avenues for combination therapies tailored to individual patient responses and disease severity.	Cyclosporine and Pentoxifylline	Cyclosporine inhibits calcineurin, reducing T-cell activation; Pentoxifylline inhibits phosphodiesterase, leading to anti-inflammatory effects.	**(60)**

These studies collectively underscore the potential of niosomal formulations to enhance the clinical management of psoriasis. By improving drug delivery and minimizing systemic exposure, niosomes offer opportunities for personalized treatment strategies tailored to individual patient profiles and disease characteristics.

8. Conclusion

In recent decades, niosomes drug delivery systems have attracted researchers' attention. Most studies concluded that niosomes systems could increase the stability of drugs that are sensitive to environmental conditions or particularly could protect them in harsh conditions of the GI tract for oral drug delivery. Furthermore, niosomes systems could increase the absorption of drug molecules with low absorption properties. Niosomes, a type of vesicular delivery system

made of a non-ionic surfactant, were first developed for cosmetic and industrial use. They showed good stability compared to lipid bilayers and didn't need special conditions for manufacturing as needed in producing liposomes (for example, vacuum condition or nitrogen gas). Therefore, these niosomes systems are attractive to many researchers. However, in the case of anti-inflammatory agents, which include chemical and natural compounds, they mostly have absorption challenges and also have serious adverse effects. In the future, these formulations will have many applications in the field of targeted drug delivery, especially in the area of skin disease, due to their physicochemical properties and biological effects. Polymers can be placed on the surface of niosomes to prepare targeted carriers. Their use, however, has limitations, such as high production costs. In conclusion, this literature indicates that niosomes revolutionizing effective in psoriasis management.

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