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Advances in Niosome-Based Drug Delivery Systems for Targeted Dermatological Applications

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Abstract:

Dermatological drug delivery remains a major challenge due to the complex structure and barrier properties of the skin, particularly the stratum corneum, which limits the penetration of therapeutic agents. In recent years, niosomes, non-ionic surfactant-based vesicular systems, have emerged as a promising approach to overcome these limitations. Niosomes possess a unique bilayer structure that allows encapsulation of both hydrophilic and lipophilic drugs, enabling enhanced stability, controlled release, and targeted drug delivery to specific skin layers. Their biocompatibility, cost-effectiveness, and ability to improve drug retention make them superior to conventional systems such as creams, gels, and liposomes. Recent advancements in niosomal technology, including elastic niosomes, proniosomes, and surface-modified formulations, have further improved their performance in dermatological applications such as acne, psoriasis, fungal infections, and inflammatory conditions. Moreover, the integration of nanotechnology and development of hybrid niosome–hydrogel systems have expanded their potential for both therapeutic and cosmetic use. This review highlights the structural characteristics, formulation strategies, mechanisms of skin targeting, and current research trends in niosome-based drug delivery systems, emphasizing their potential to revolutionize topical and transdermal therapies.

Keywords:

Niosomes, Dermatological drug delivery, Vesicular systems, Controlled release, Skin targeting, Nanotechnology, Proniosomes, Lipid-based carriers

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1. INTRODUCTION

The skin, being the largest organ of the human body, acts as a vital protective barrier that regulates the exchange of substances and shields internal tissues from external aggressors. However, this same protective function poses a major challenge for effective dermatological drug delivery [1] . The outermost layer of the skin, the stratum corneum, is particularly resistant to drug permeation, which limits the penetration of therapeutic molecules into deeper skin layers. Many topical formulations fail to deliver sufficient drug concentrations at the target site, leading to suboptimal therapeutic effects. Additionally, the physicochemical properties of drugs such as molecular size, lipophilicity, and solubility—further influence their ability to penetrate the skin barrier, complicating the design of effective transdermal and dermal delivery systems [2].

Traditional topical and transdermal delivery methods, including creams, ointments, and gels, have been widely used in dermatology but often suffer from limitations such as poor skin retention, instability, and inconsistent drug absorption. These conventional formulations typically provide only temporary relief and may require frequent application, resulting in reduced patient compliance. Furthermore, they often lead to systemic absorption and side effects due to the lack of site-specific targeting [3].

To overcome these challenges, vesicular drug delivery systems have emerged as a promising approach. Among these, liposomes phospholipid-based vesicles were the first to be explored for skin delivery, owing to their biocompatibility and ability to encapsulate both hydrophilic and lipophilic drugs. However, liposomes are limited by their high production cost, chemical instability, and tendency to undergo oxidation or hydrolysis. This led to the development of niosomes, which are non-ionic surfactant-based vesicles that offer several advantages over liposomes, including higher chemical stability, cost-effectiveness, easier storage, and the potential for large-scale production. Niosomes enhance drug permeation through the skin by improving hydration of the stratum corneum, facilitating controlled drug release, and increasing drug retention at the target site, making them a superior alternative for dermatological applications [4-5].

The present review focuses on the recent advances in niosome-based drug delivery systems for targeted dermatological applications. It aims to discuss the fundamental principles, formulation strategies, characterization methods, and mechanisms by which niosomes improve skin targeting. Furthermore, this review highlights current research trends, therapeutic applications, and future perspectives in the field, emphasizing the potential of niosomes to revolutionize dermatological therapy through enhanced efficacy, safety, and patient compliance [6-7]. *Figure 1*

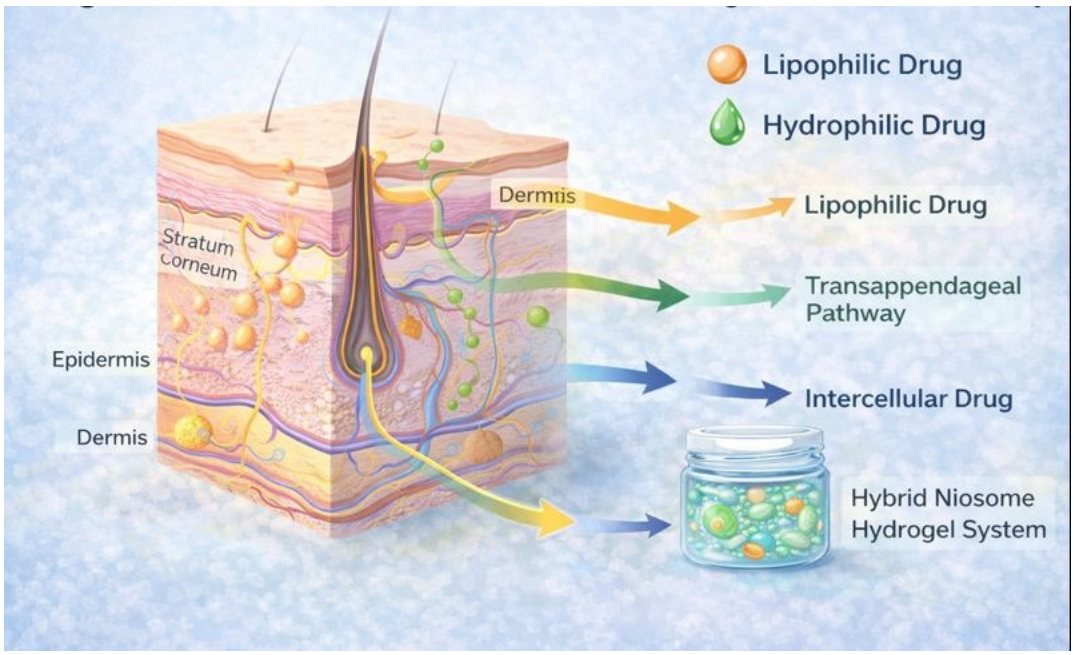

Figure 1: **Schematic of Skin Structure and Drug Penetration Pathways**

2. Niosomes: Structure, Composition, and Preparation

Niosomes are non-ionic surfactant-based vesicular systems that have gained significant attention as efficient carriers for drug delivery, particularly in dermatological applications. Structurally, they are microscopic or nanometric bilayer vesicles formed by the self-assembly of non-ionic surfactants in an aqueous medium, often stabilized by cholesterol or other additives. These vesicles possess both hydrophilic and lipophilic regions, enabling the encapsulation of a wide range of therapeutic agents hydrophilic drugs in the aqueous core and lipophilic drugs within the bilayer membrane. Due to their amphiphilic nature, niosomes enhance drug solubility, stability, and bioavailability, while also facilitating controlled and targeted drug release at the desired site of action [8-9].

The composition of niosomes typically includes three main components: a non-ionic surfactant, cholesterol, and additives. The surfactant is the key building block responsible for vesicle formation and stability; common examples include Span (Span 20, 40, 60, 80) and Tween (Tween 20, 60, 80) series. The hydrophilic-lipophilic balance (HLB) value of the surfactant influences the size, shape, and entrapment efficiency of the niosomes. Cholesterol is added to modulate the fluidity and permeability of the bilayer, enhancing the rigidity and reducing the leakage of encapsulated drugs. Additionally, various additives, such as charge-inducing agents (e.g., dicetyl phosphate or stearylamine), can be incorporated to alter the surface charge, prevent vesicle aggregation, and improve stability during storage [10-11].

Based on their structure and lamellarity, niosomes can be classified into several types. Multilamellar vesicles (MLVs) consist of multiple concentric bilayers, resembling an onion-like structure, and are generally larger in size, making them suitable for the encapsulation of hydrophobic drugs. Small unilamellar vesicles (SUVs) contain a single bilayer membrane and are typically in the nanometer size range, offering advantages in terms of controlled release and deeper skin penetration. Large unilamellar vesicles (LUVs) have larger diameters

and higher aqueous phase volumes, which are beneficial for encapsulating hydrophilic drugs. Proniosomes, on the other hand, are dry, free-flowing formulations that form niosomes upon hydration; they exhibit superior physical stability and ease of handling compared to conventional niosomes [12-13].

Several techniques have been developed for the preparation of niosomes, each with distinct advantages and limitations. The thin-film hydration method is the most commonly used technique, involving the dissolution of surfactant and cholesterol in an organic solvent, followed by solvent evaporation to form a thin lipid film that is later hydrated with an aqueous phase to produce niosomes. The ether injection method involves the slow injection of a surfactant solution in diethyl ether into a heated aqueous phase, leading to the formation of vesicles as the solvent evaporates. In the reverse-phase evaporation method, surfactants and cholesterol are dissolved in an organic solvent and emulsified with an aqueous drug solution, followed by solvent removal under reduced pressure to form stable niosomal vesicles with high encapsulation efficiency. The microfluidization technique uses high shear forces and microchannels to produce uniform and nanosized niosomes, making it suitable for scalable and reproducible production. Each of these methods can be optimized depending on the desired vesicle size, drug type, and application requirements [14-15].

Overall, the versatility of niosomes in terms of composition, structure, and preparation techniques allows researchers to tailor their physicochemical properties for specific dermatological purposes. Their stability, biocompatibility, and capability to enhance skin permeation make them a promising alternative to traditional delivery systems for topical and transdermal therapeutics [16].

Table 1: Common Methods for Niosome Preparation and Their Features

Method	Principle	Advantages	Limitations	Reference
Thin Film Hydration	Lipid film hydration	Simple, scalable	Larger vesicle size	17
Reverse Phase Evaporation	Solvent evaporation	High encapsulation	Uses organic solvent	18
Microfluidization	High shear mixing	Uniform size	Equipment cost	19

3. Mechanism of Skin Targeting and Drug Release

The efficiency of a dermatological drug delivery system largely depends on its ability to overcome the skin's natural barrier, primarily the stratum corneum, which restricts the penetration of most therapeutic agents. Niosomes play a vital role in enhancing skin permeation by interacting with the stratum corneum and facilitating both the transport and retention of drugs in deeper skin layers. Their unique vesicular structure allows them to encapsulate drugs and

deliver them in a controlled and targeted manner, improving local therapeutic concentration while minimizing systemic exposure and adverse effect [20].

The mechanisms through which niosomes enhance skin penetration are multifaceted. One of the major mechanisms involves fusion and adsorption of niosomal vesicles onto the surface of the stratum corneum. Due to their amphiphilic nature, niosomes can merge with the lipid domains of the skin barrier, allowing the encapsulated drug to diffuse through intercellular lipid channels. This fusion process facilitates the direct transfer of the drug from the vesicle to the skin layers, improving deposition and retention at the target site. Additionally, adsorption of niosomes onto the stratum corneum surface increases the local drug concentration gradient, thereby enhancing passive diffusion through the skin [21].

Another important mechanism is the hydration of the stratum corneum caused by niosomes. When applied topically, niosomal formulations create an occlusive film over the skin, reducing transepidermal water loss and increasing the hydration level of the outer skin layer. This hydration effect disrupts the tightly packed lipid structure of the stratum corneum, resulting in increased fluidity and permeability of the barrier. Consequently, the drug can more easily penetrate through the intercellular spaces and reach the deeper epidermal and dermal layers where it exerts its therapeutic action [22.]

Niosomes also facilitate controlled and sustained drug release, which is crucial for maintaining effective drug levels over an extended period. The bilayer structure of niosomes acts as a reservoir, enabling the gradual diffusion of the encapsulated drug into the skin. Factors such as vesicle size, surfactant composition, cholesterol content, and drug–vesicle interactions influence the rate and mechanism of drug release. Smaller vesicles tend to penetrate deeper into the skin, while larger vesicles primarily act as drug depots, releasing the drug slowly at the surface. This controlled release not only prolongs the therapeutic effect but also minimizes the need for frequent application, enhancing patient compliance [23.]

Moreover, niosomes contribute to site-specific drug retention within the skin layers. By modulating their physicochemical properties, such as charge and elasticity, niosomes can be tailored to localize the drug within specific layers epidermis, dermis, or pilosebaceous units depending on the therapeutic requirement. This targeted localization maximizes drug action at the diseased site and minimizes systemic absorption, making niosomal systems particularly advantageous for treating localized dermatological disorders such as acne, psoriasis, eczema, and fungal infections [24.]

In summary, niosomes enhance dermatological drug delivery through a combination of fusion, adsorption, hydration, and controlled release mechanisms. Their ability to improve drug permeation, retention, and controlled delivery makes them a highly promising platform for achieving effective and sustained treatment of various skin conditions. *Figure 2*

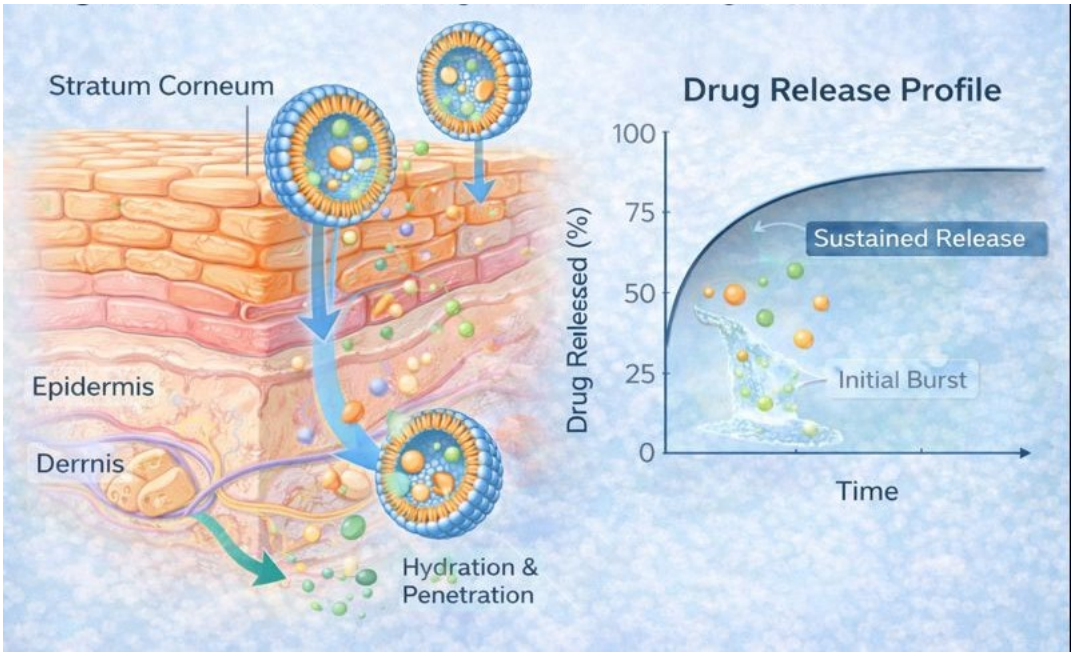

Figure 2: **Mechanism of Drug Penetration Using Niosomes**

4. Types of Niosomes for Dermatological Application

Over the years, various types of niosomal systems have been developed and optimized to enhance drug delivery efficiency, stability, and skin penetration. Depending on their composition, flexibility, and method of preparation, niosomes can be broadly categorized into conventional niosomes, elastic or deformable niosomes, proniosomes, and surface-modified (PEGylated) niosomes. Each type possesses unique structural and functional characteristics that make it suitable for specific dermatological applications [25].

Conventional niosomes are the most basic and widely studied form of niosomal vesicles. They are composed of non-ionic surfactants and cholesterol, forming a bilayer structure capable of encapsulating both hydrophilic and lipophilic drugs. These vesicles are relatively stable and biocompatible, offering controlled and localized drug release at the site of application. Conventional niosomes are effective in improving the solubility and bioavailability of poorly soluble drugs and reducing systemic side effects. However, due to their relatively rigid bilayer structure, they may have limited deformability, which restricts their penetration through the skin's deeper layers. Despite this limitation, they have shown significant success in treating superficial dermatological conditions such as fungal infections and inflammation.

To overcome the limitation of poor skin penetration, elastic or deformable niosomes also known as transfersomes or niosomal gels were developed. These vesicles incorporate "edge activators" such as sodium cholate, Tween 80, or Span 60, which impart flexibility and deformability to the vesicular membrane. This property allows the vesicles to squeeze through the narrow intercellular pores of the stratum corneum without disrupting their structural integrity. The enhanced elasticity not only improves drug permeation into deeper skin layers but also ensures prolonged drug retention at the target site. Elastic niosomes have been particularly useful for the

transdermal delivery of anti-inflammatory and analgesic drugs, offering sustained therapeutic effects with minimal irritation [26-27].

Proniosomes represent another advancement in niosomal technology. They are dry, free-flowing formulations consisting of surfactants, cholesterol, and carriers such as maltodextrin or sorbitol. Upon hydration with water or biological fluids, proniosomes are converted into niosomal suspensions. This approach offers several advantages, including improved stability, ease of storage, transportation, and longer shelf life compared to conventional niosomes. Proniosomes also overcome issues related to aggregation, fusion, and leakage commonly observed in aqueous niosomal dispersions. Due to their reconstitution ability and enhanced stability, proniosomes are increasingly explored for the topical and transdermal delivery of drugs such as tretinoin, ketoconazole, and diclofenac.

In addition to these, PEGylated or surface-modified niosomes have gained attention for their ability to improve the pharmacokinetic and targeting properties of vesicular systems. The modification involves coating or grafting hydrophilic polymers such as polyethylene glycol (PEG) or other biocompatible materials onto the niosomal surface. PEGylation enhances the steric stabilization of niosomes, preventing aggregation and prolonging circulation time when applied systemically. In dermatological applications, surface modification also improves vesicle adhesion to the skin surface, enhances drug retention, and reduces degradation of labile compounds. Furthermore, targeted surface modification with ligands or antibodies can enable site-specific drug delivery to particular skin structures or receptors, making these systems promising for advanced therapeutic interventions [28-29].

When compared collectively, each niosomal type offers distinct advantages. Conventional niosomes provide a simple and effective means for controlled topical delivery, while elastic niosomes enhance penetration through deeper layers of the skin. Proniosomes offer superior physical stability and convenience of handling, whereas PEGylated or surface-modified niosomes enhance targeting efficiency, stability, and biocompatibility. The choice of niosome type depends on the physicochemical nature of the drug, the therapeutic target within the skin, and the desired release profile. Collectively, these diverse niosomal systems provide a versatile platform for improving the safety, efficacy, and patient compliance of dermatological treatments [30-31]. *Table 2*

***Table 2:*Comparison of Different Types of Niosomes in Dermatological Use**

Type	Composition	Features	Example Drugs	Advantages	Reference
Conventional	Surfactant + Cholesterol	Stable vesicles	Ketoconazole	Good stability	32
Elastic	Edge activators	High deformability	Diclofenac	Better skin penetration	33
Proniosomes	Dry, hydrated on use	Long shelf life	Tretinoin	Easy handling	34

5. Applications in Dermatological Disorders

Niosome-based drug delivery systems have shown remarkable potential in the treatment of various dermatological disorders due to their ability to enhance drug penetration, improve localization within skin layers, and provide sustained release of therapeutic agents. Their biocompatibility, structural versatility, and ability to encapsulate both hydrophilic and lipophilic drugs make them a suitable alternative to conventional topical formulations. Over the past decade, extensive research has demonstrated the effectiveness of niosomal formulations in managing several skin conditions such as acne, psoriasis, fungal infections, inflammation, and cosmetic or anti-aging concerns [35].

Acne vulgaris, a chronic inflammatory condition of the pilosebaceous unit, is one of the most common dermatological disorders targeted using niosomal formulations. Conventional topical treatments often suffer from limited drug penetration and cause skin irritation due to the use of harsh solvents. Niosomal formulations of anti-acne agents such as clindamycin and tretinoin have been shown to significantly enhance drug retention within the skin while minimizing systemic absorption and irritation. Niosomal clindamycin gels provide improved antimicrobial activity against *Propionibacterium acnes*, leading to better clinical outcomes and reduced side effects compared to conventional gels. Similarly, niosomal tretinoin formulations offer controlled drug release and reduced skin irritation, addressing a major limitation of conventional tretinoin creams [36].

In the management of psoriasis, a chronic autoimmune skin disorder characterized by hyperproliferation of keratinocytes, niosomal drug delivery systems have demonstrated notable therapeutic advantages. Drugs such as methotrexate and acitretin encapsulated in niosomes exhibit enhanced skin penetration and localized accumulation within psoriatic lesions, thereby improving efficacy while minimizing systemic toxicity. Methotrexate-loaded elastic niosomes, for example, have been shown to provide higher drug deposition in the epidermal and dermal layers, leading to better control of inflammation and scaling. The sustained release profile of these vesicles ensures prolonged therapeutic action with reduced dosing frequency [37].

Niosomes have also proven effective in treating fungal infections of the skin caused by dermatophytes and yeasts. Antifungal agents such as ketoconazole, miconazole, and fluconazole formulated in niosomal gels or creams have demonstrated improved solubility, enhanced drug retention, and superior antifungal efficacy compared to conventional formulations. Ketoconazole-loaded niosomes, for instance, exhibit prolonged release and increased accumulation in the infected site, leading to faster eradication of fungal colonies and lower recurrence rates. Moreover, the controlled release property of niosomes minimizes the irritation and burning sensations commonly associated with topical antifungal treatments [38].

In addition, niosomes have been successfully utilized for the topical delivery of anti-inflammatory drugs such as diclofenac and ibuprofen for the management of local pain, inflammation, and arthritis-associated skin conditions. These formulations improve drug permeation through the skin barrier, leading to enhanced therapeutic efficacy at lower doses. Niosomal diclofenac gels, in particular, provide sustained anti-inflammatory effects and reduce gastrointestinal side effects associated with oral administration. The localized drug delivery

offered by niosomes also contributes to faster onset of action and prolonged relief at the site of application [39].

Beyond therapeutic use, niosomes are increasingly being explored in the cosmetic and anti-aging sector. Active compounds such as vitamin E, coenzyme Q10, retinol, and antioxidants have been successfully encapsulated in niosomal carriers to enhance their stability and facilitate controlled delivery to the deeper skin layers. These formulations improve skin hydration, elasticity, and repair processes while protecting against oxidative stress and photoaging. Niosomal systems also offer a promising approach for the delivery of skin-whitening agents, sunscreens, and moisturizing formulations, providing enhanced cosmetic performance with reduced irritation and improved skin compatibility [40].

In summary, niosomes have emerged as a versatile and effective platform for the targeted and sustained delivery of drugs in a variety of dermatological conditions. Their ability to overcome the skin's barrier, improve drug localization, and minimize systemic exposure positions them as a next-generation solution for both therapeutic and cosmetic dermatological applications. Table 3

Table 3: **Recent Studies on Niosomal Formulations for Dermatological Applications**

Drug	Target Condition	Formulation Type	Findings	Reference
Clindamycin	Acne	Niosomal gel	Improved retention, reduced irritation	41
Methotrexate	Psoriasis	Elastic niosomes	Enhanced skin penetration	42

6. Characterization of Niosomes

Comprehensive characterization of niosomal formulations is essential to ensure their quality, stability, and effectiveness in dermatological drug delivery. The physicochemical properties of niosomes, such as particle size, polydispersity index (PDI), zeta potential, entrapment efficiency, drug release profile, and stability, play crucial roles in determining their performance, including drug penetration, retention, and therapeutic efficacy [43.]

Particle size is one of the most critical parameters influencing the skin penetration ability and stability of niosomes. Smaller vesicles (typically in the nanometer range) can penetrate deeper skin layers, whereas larger vesicles tend to remain on the skin surface, providing localized action. The particle size of niosomes is usually measured using techniques such as dynamic light scattering (DLS), laser diffraction, or electron microscopy (SEM or TEM). Along with size, the polydispersity index (PDI) provides information on the size distribution and uniformity of vesicles. A lower PDI value (generally below 0.3) indicates a more homogeneous and stable formulation, which is desirable for reproducible performance [44.]

The zeta potential reflects the surface charge of niosomal vesicles and serves as an indicator of colloidal stability. High absolute zeta potential values (positive or negative) generate electrostatic repulsion between vesicles, preventing aggregation and improving dispersion stability. Zeta potential measurements are typically performed using a zeta sizer or

electrophoretic light scattering technique. Incorporating charge-inducing agents such as dicetyl phosphate or stearylamine can help maintain optimal zeta potential and enhance the shelf life of the formulation [45].

Entrapment efficiency (EE%) is another vital parameter that determines the proportion of the drug successfully encapsulated within the niosomal vesicles relative to the total amount used in the formulation. High entrapment efficiency ensures improved drug loading and therapeutic efficacy. EE% depends on various factors, including the type of surfactant, cholesterol content, hydration medium, and method of preparation. It is commonly determined by separating the unentrapped drug from the vesicles through centrifugation or dialysis, followed by quantitative analysis using UV–visible spectrophotometry or high-performance liquid chromatography (HPLC) [46].

To evaluate the release behavior of drugs from niosomal formulations, in-vitro release and ex-vivo skin permeation studies are performed. In-vitro release studies are typically conducted using dialysis bags, Franz diffusion cells, or USP dissolution apparatus to simulate drug diffusion over time in physiological conditions. These studies provide insight into the rate and mechanism of drug release, helping to predict in-vivo performance. Ex-vivo skin permeation studies, on the other hand, are carried out using excised animal or human skin to assess the ability of niosomes to penetrate the stratum corneum and deposit drugs into different skin layers. Parameters such as flux, permeability coefficient, and drug deposition are calculated to determine the formulation's efficiency in delivering drugs topically or transdermally [47].

Finally, stability testing is a crucial aspect of niosomal characterization to ensure that the formulation maintains its integrity and performance during storage. Factors such as temperature, humidity, and light exposure can influence vesicle size, zeta potential, and drug leakage. Stability studies are usually performed under accelerated and real-time conditions following ICH guidelines. Monitoring changes in particle size, PDI, and entrapment efficiency over time helps assess the physical and chemical stability of the formulation. To enhance stability, lyophilization, addition of antioxidants, or conversion of niosomal suspensions into proniosomes may be employed [48].

Overall, the systematic characterization of niosomes provides a comprehensive understanding of their physicochemical behavior, ensuring consistency, reliability, and optimal performance in dermatological drug delivery. Well-characterized niosomal formulations offer predictable release kinetics, enhanced skin penetration, and improved therapeutic outcomes.*Figure 3*

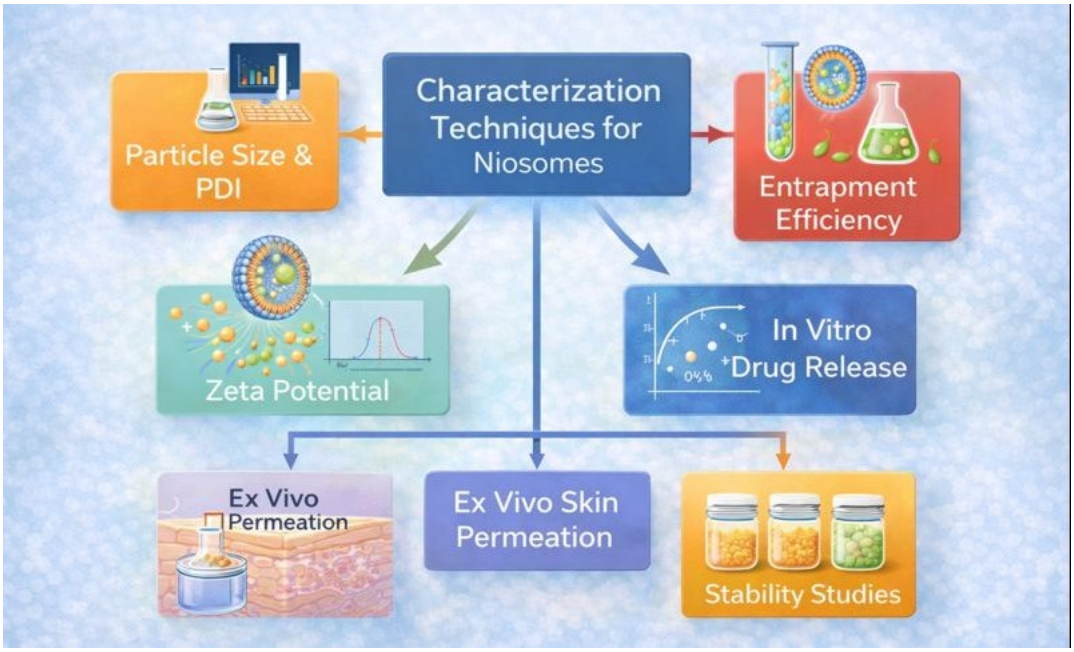

Figure 3: **Flowchart: Characterization Techniques for Niosomes**

7. Challenges and Limitations

Despite the significant advancements and promising results achieved with niosome-based drug delivery systems, several challenges and limitations still hinder their large-scale application and clinical translation in dermatological therapy. Issues related to stability, scale-up, reproducibility, potential skin irritation, and regulatory barriers must be carefully addressed before these systems can be widely adopted in commercial formulations [49].

One of the primary concerns associated with niosomal formulations is their stability during storage and use. Niosomes, being vesicular systems composed of surfactants and cholesterol, are susceptible to aggregation, fusion, and drug leakage over time. These phenomena can lead to changes in vesicle size distribution, reduced entrapment efficiency, and loss of therapeutic activity. Factors such as temperature fluctuations, light exposure, and pH variations can further compromise the integrity of the vesicles. Although the incorporation of cholesterol and charge-inducing agents can improve physical stability, achieving long-term chemical stability remains a challenge. To mitigate these issues, researchers often explore approaches such as lyophilization (freeze-drying) and conversion of niosomes into proniosomes, which are more stable during storage and can be reconstituted upon use [50].

Another major limitation is related to scale-up and reproducibility of niosomal formulations. While many preparation techniques such as thin-film hydration and reverse-phase evaporation are suitable for laboratory-scale production, their translation to industrial-scale manufacturing is often difficult due to process variability and batch inconsistency. Maintaining uniform vesicle size, high encapsulation efficiency, and reproducible physicochemical properties during large-scale production requires precise control over parameters like temperature, mixing speed, and solvent evaporation rate. Advanced technologies such as microfluidization and high-pressure homogenization have shown promise for large-scale production, but they also increase

production costs and require specialized equipment, limiting their feasibility in commercial applications [51].

The potential for skin irritation caused by certain surfactants used in niosomal formulations is another area of concern. Non-ionic surfactants, though generally considered less toxic than ionic ones, can still induce irritation, redness, or allergic reactions when used in high concentrations or with sensitive skin types. This issue becomes particularly critical for formulations intended for chronic or repeated topical application. Careful selection of biocompatible surfactants, optimization of concentration, and incorporation of soothing excipients such as aloe vera or hyaluronic acid can help minimize irritation while maintaining vesicle stability and performance [52].

In addition to formulation-related issues, regulatory and clinical translation barriers significantly limit the commercialization of niosomal drug delivery systems. Despite extensive preclinical research demonstrating their safety and efficacy, very few niosome-based dermatological products have reached the market. This gap is primarily due to the lack of standardized manufacturing protocols, insufficient long-term toxicity data, and challenges in meeting the stringent quality control requirements of regulatory agencies. Furthermore, the complex physicochemical nature of niosomal formulations poses difficulties in defining critical quality attributes (CQAs) for approval. Large-scale clinical studies assessing pharmacokinetics, skin retention, and patient safety are essential to establish their therapeutic reliability and gain regulatory acceptance [53].

In summary, while niosomes hold great potential as an advanced drug delivery platform for dermatological applications, challenges such as stability issues, production scalability, surfactant-related toxicity, and regulatory hurdles must be systematically addressed. Future research should focus on developing robust, reproducible manufacturing techniques, exploring novel biocompatible surfactants, and conducting well-designed clinical trials to bridge the gap between laboratory success and commercial realization [54].

8. Future Perspectives

The field of niosome-based drug delivery is rapidly evolving, with ongoing research focusing on enhancing the functionality, targeting efficiency, and stability of these vesicular systems. Although significant progress has been made, the future of niosomal technology lies in the integration of advanced nanotechnology, smart materials, and personalized medicine approaches to address the current limitations and meet the growing demand for effective dermatological therapies [55].

One of the most promising directions is the development of smart or stimuli-responsive niosomes, which are designed to release their drug payload in response to specific physiological or environmental triggers such as pH, temperature, enzyme activity, or redox conditions. For example, pH-sensitive niosomes can selectively release drugs in inflamed or infected skin regions where the local pH is lower than normal, enhancing therapeutic efficacy while minimizing side effects. Similarly, temperature- and enzyme-responsive systems can be tailored to respond to localized pathological conditions, providing site-specific and controlled drug

delivery. These intelligent delivery systems can significantly improve treatment outcomes for chronic skin disorders like psoriasis, eczema, and acne, where localized and sustained release is crucial [56].

Another emerging trend is the integration of nanotechnology with niosomal systems, resulting in the formation of hybrid niosomal nanoparticles. By combining the structural versatility of niosomes with the unique properties of nanoparticles, such as high surface area and tunable size, researchers can achieve superior drug loading, enhanced stability, and precise skin targeting. Nanostructured niosomes can also be functionalized with ligands, peptides, or antibodies to achieve active targeting of specific skin cells or receptors, thereby increasing the therapeutic precision of dermatological treatments. This approach is particularly relevant in managing complex skin diseases or delivering biomolecules like peptides, growth factors, and nucleic acids that require protection from degradation [57].

The development of hybrid systems, particularly niosome–hydrogel composites, represents another innovative strategy gaining attention in topical and transdermal delivery. In these systems, niosomal vesicles are incorporated within a biocompatible hydrogel matrix, combining the benefits of both carriers—controlled drug release from niosomes and enhanced adherence, hydration, and mechanical stability from the hydrogel. Such hybrid formulations ensure prolonged contact with the skin, improving drug retention and patient comfort. They are also suitable for incorporating multiple active agents, enabling synergistic therapy for conditions such as chronic wounds, burns, and inflammatory skin disorders.

Looking forward, the concept of personalized dermatological care presents a new frontier for niosomal drug delivery. Advances in skin biology, omics technologies, and digital diagnostics have made it possible to tailor treatments according to individual skin types, genetic profiles, and disease states. Niosomes can be customized to deliver specific drug combinations, doses, or release profiles based on patient-specific parameters. The combination of niosomal technology with artificial intelligence (AI)-driven formulation design and 3D-printed skin models could further revolutionize the development of customized skincare and therapeutic products [58].

In conclusion, future research on niosomes is expected to focus on creating multifunctional, responsive, and patient-specific delivery systems that not only enhance therapeutic outcomes but also improve user convenience and compliance. The integration of smart materials, nanotechnology, and personalized medicine will likely transform niosomes from experimental formulations into clinically viable platforms, opening new horizons for targeted and efficient dermatological treatments [59].

9. Conclusion

Niosome-based drug delivery systems have emerged as a promising and versatile platform for improving the therapeutic efficacy of dermatological treatments. Through their unique vesicular architecture composed of non-ionic surfactants and cholesterol, niosomes offer several advantages, including enhanced drug stability, controlled release, biocompatibility, and the ability to encapsulate both hydrophilic and lipophilic compounds. Their capability to overcome the skin's barrier, improve localized drug deposition, and minimize systemic absorption has

made them highly suitable for the treatment of a wide range of skin disorders such as acne, psoriasis, fungal infections, and inflammatory conditions. Moreover, their successful incorporation into cosmetic and anti-aging formulations highlights their broad applicability across both therapeutic and aesthetic dermatology.

Despite these advantages, challenges such as vesicle instability, difficulties in large-scale manufacturing, and limited clinical translation remain significant obstacles. Ongoing research focusing on stabilizing techniques like proniosomal formulations, microfluidization, and lyophilization has shown promise in addressing these limitations. Additionally, the introduction of elastic, surface-modified, and hybrid niosomal systems has further enhanced the efficiency and versatility of this delivery platform. However, the translation of these laboratory-scale successes into clinically approved products requires standardized production methods, long-term stability studies, and comprehensive clinical trials to establish safety and efficacy.

Looking ahead, the integration of advanced technologies such as smart stimuli-responsive materials, nanotechnology, and personalized medicine holds immense potential to revolutionize niosomal drug delivery for dermatological applications. These innovations can lead to the development of intelligent and patient-specific formulations capable of responding to individual physiological conditions and providing precise, sustained therapy. With continued interdisciplinary research, improved formulation techniques, and regulatory support, niosome-based systems are expected to play a pivotal role in the next generation of targeted, effective, and patient-friendly dermatological treatments.

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