



ADVANCES IN NIOSOMAL-BASED DRUG DELIVERY SYSTEMS: DESIGN, APPLICATIONS, AND FUTURE PERSPECTIVES

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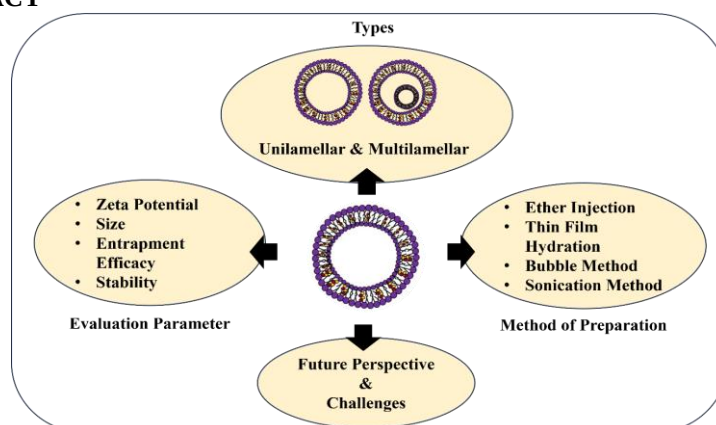
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ABSTRACT

Niosomes, which are vesicular systems made up of non-ionic surfactants and cholesterol, have garnered considerable interest as vehicles for targeted and controlled drug delivery. The versatility of niosomes is particularly appreciated for their capacity to encapsulate both hydrophilic and hydrophobic medications. This review emphasizes their design, methods of preparation, benefits, drawbacks, and future possibilities. Depending on the preparation technique used—such as thin-film hydration, ether injection, ultrasonication, reverse phase evaporation, or microfluidization—niosomes can form either unilamellar or multilamellar vesicles. The components used in the formulation, especially the type of surfactant, cholesterol, and charged substances, significantly influence their stability, efficiency of encapsulation, and drug release patterns. In comparison to traditional systems and even liposomes, niosomes provide improved stability, biocompatibility, low toxicity, cost-effectiveness, and better bioavailability, which enhances patient adherence. Nonetheless, some challenges persist, such as limited shelf stability, drug leakage, and the requirement for specialized equipment and complex processing techniques. Characterizing their physicochemical properties—like particle size, polydispersity index, zeta potential, and encapsulation efficiency—is crucial for forecasting their biological performance. In summary, niosomes offer a versatile and promising strategy for the advancement of drug delivery technologies.

KEYWORDS: Niosomes, Vesicular systems, Targeted drug delivery, Controlled drug delivery, Enhanced bioavailability.

GRAPHICAL ABSTRACT



Advanced Drug Delivery of Niosomes: From Vesicle Design and Preparation to Characterization, Encapsulation, Stability, Applications, and Future Perspectives.

1. INTRODUCTION

Targeted drug delivery systems have emerged as a transformative approach in modern therapeutics by enhancing drug accumulation at the desired site of action while minimizing systemic exposure and adverse effects.^[1] Among the different vesicular carriers studied for this purpose, niosomes have gained significant interest due to their versatile structure, compatibility with biological systems, and economical nature. Niosomes are closed bilayer vesicles mainly composed of non-ionic surfactants, often stabilized with cholesterol and, when necessary, agents that induce charge. When hydrated, these amphiphilic molecules automatically self-assemble into either uni- or multilamellar vesicles that can encapsulate both hydrophilic and lipophilic therapeutic agents. Hydrophilic medications are generally contained in the aqueous core, while lipophilic substances are integrated into the hydrophobic bilayer region.^[2]

When compared to traditional dosage forms, niosomes present various pharmaceutical benefits, such as enhanced drug solubility, increased stability of sensitive molecules, extended circulation duration, controlled release characteristics, and improved bioavailability. Moreover, their formulation offers superior chemical stability and reduced production costs compared to phospholipid-based liposomes, making them appealing options for large-scale production and various clinical applications. Niosomal systems have been widely studied for delivery methods that include oral, parenteral, topical, transdermal, ocular, and targeted routes.^[3]

The physicochemical properties of niosomes, including vesicle size, lamellarity, surface charge, and membrane rigidity, can be modulated through rational selection of surfactant type, cholesterol ratio, preparation technique, and surface functionalization. Such tunability enables optimization of encapsulation efficiency, release kinetics, biodistribution, and therapeutic performance according to the intended application. Consequently, niosomes have been investigated for the delivery of anticancer agents, antimicrobials, peptides, proteins, nucleic acids, vaccines, and central nervous system therapeutics.

Despite these promising attributes, several challenges continue to limit their clinical translation, including storage instability, drug leakage, batch-to-batch variability, and the need for robust large-scale manufacturing processes compliant with regulatory standards. Recent advances in microfluidics, Quality by Design (QbD), and artificial intelligence-assisted formulation optimization are expected to address many of these limitations.^[4] A comparative analysis of niosomes with various nanocarriers beyond liposomes is presented in **Table 1**.

This review provides a comprehensive overview of niosomal drug delivery systems, focusing on their composition, classification, methods of preparation, characterization strategies, therapeutic applications, translational barriers, and future prospects in advanced nanomedicine.

Table 1: Comparative features of niosomes and other nanocarriers.

Feature	Niosomes	Liposomes	Exosomes	Ref.
Composition	Non-ionic surfactants + cholesterol	Phospholipids + cholesterol	Natural extracellular vesicles (lipid bilayer, proteins, nucleic acids)	[5]
Stability	Higher stability; less prone to oxidative degradation than liposomes	Prone to oxidation and hydrolysis of phospholipids	Relatively stable biologically, but storage is challenging	[6]
Cost & Scalability	Low cost, easy to scale-up (simple thin film hydration or microfluidics)	Higher cost due to natural phospholipids and complex preparation	High cost, complex isolation/purification (ultracentrifugation, kits)	[7], [8]
Encapsulation Versatility	Hydrophilic, hydrophobic, amphiphilic drugs; nucleic acids with modifications	Hydrophilic and hydrophobic drugs, peptides, nucleic acids	Endogenous nucleic acids, proteins, drugs (with engineering)	[9]
Targeting Potential	Easily functionalized with ligands, peptides, antibodies	Well-established functionalization protocols	Intrinsic homing ability due to surface proteins; bioengineerable	[10]
Biocompatibility & Safety	Generally biocompatible; surfactant toxicity possible at high doses	High biocompatibility; clinically validated	Natural origin = excellent biocompatibility; risk of heterogeneity, immune effects	[11]
Immunogenicity	Low immunogenicity	Low immunogenicity (depends on composition)	Low to moderate; can modulate immune system	[12]
Drug Release Control	Tunable by surfactant type, cholesterol ratio, stimuli-responsive designs	Tunable; temperature/pH-sensitive liposomes widely explored	Limited control; depends on natural mechanisms unless engineered	[13]

Clinical Translation	Few products in trials; promising for topical, oral, vaccine, cancer therapy	Several approved products (Doxil®, AmBisome®)	No product approved yet; many in early-phase trials	[14]
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2. Niosomes types

Niosomes are typically categorized based on their size and the quantity of bilayer lamellae into Small Unilamellar Vesicles (SUVs), Large Unilamellar Vesicles (LUVs), and Multilamellar Vesicles (MLVs). SUVs usually have a diameter that ranges from 10 to 100 nm and consist of a single lipid bilayer encasing an aqueous core. Due to their smaller size, SUVs are especially advantageous for applications that require improved tissue penetration and cellular absorption, although they may show relatively lower encapsulation efficiency for hydrophilic drugs. LUVs typically range from 100–1000

nm and also possess a single bilayer, but their larger internal aqueous volume enables improved loading of hydrophilic therapeutic agents. MLVs are larger vesicles, usually ranging from 0.5–10 μm , and are composed of multiple concentric bilayers. These vesicles offer greater structural stability and are especially suitable for sustained drug release and encapsulation of lipophilic compounds. The choice of vesicle type significantly influences drug loading capacity, release kinetics, biological distribution, and overall therapeutic performance of the niosomal formulation.^[15]

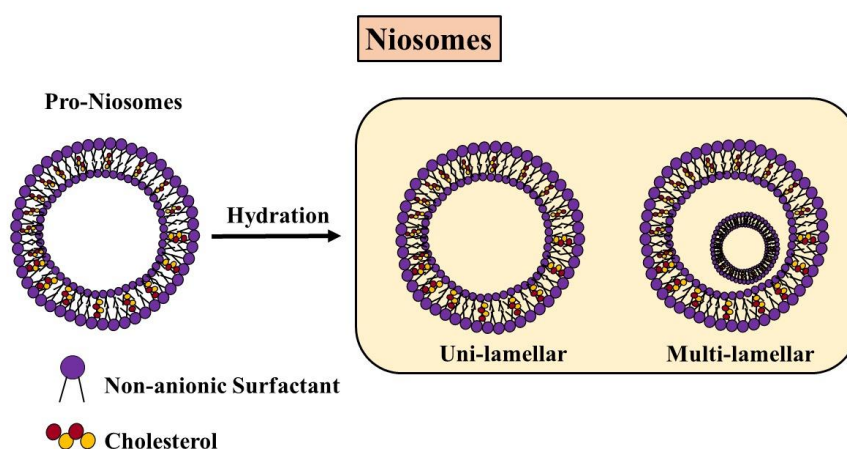


Figure 1 Types of niosomes^[16] (made with PPT)

3. Advantages of Niosomes

Recent studies have confirmed that niosomes offer multiple advantages as vesicular drug delivery systems. They are relatively **stable** and protect entrapped drugs against degradation (e.g. photostability, chemical degradation), improving their lifetime in biological environments. They enhance the **oral bioavailability** of drugs, including poorly water-soluble and high-first-pass-metabolism compounds, by improving absorption, promoting lymphatic uptake, and reducing drug clearance. In topical/transdermal delivery, they increase penetration through the skin by interacting with the stratum corneum, acting as penetration enhancers, improving membrane fluidity, reducing trans-epidermal water loss, and via fusion/adsorption mechanisms.^[17] Their surfactants (e.g., non-ionic surfactants such as Spans and Tweens) are generally **biocompatible, biodegradable, and non-immunogenic**, with lower toxicity than many ionic surfactants or other vesicular systems. Also, they allow versatile administration routes—oral, topical, parenteral—and both hydrophilic and lipophilic drugs can be entrapped in their bilayer/aqueous core. Controlled or sustained release is possible by adjusting surfactant composition, cholesterol content, etc., which helps reduce dosing frequency and

target drug action. Although only a few studies have directly compared patient compliance between niosomal and greasy formulations, existing research on cosmetic and dermal delivery systems indicates that niosomal gels and creams are generally better accepted by users, causing less irritation and providing a more pleasant skin feel than conventional lipid-based or oily formulations.^[18]

4. Limitations and Challenges

Although niosomes are promising carriers, their aqueous dispersions suffer from important stability and manufacturability limitations.^[19] In storage, niosomal vesicles are prone to physical instability (fusion, aggregation and sedimentation), which commonly leads to loss of vesicle integrity, leakage of entrapped drug and increased susceptibility of both the drug and bilayer components to hydrolytic/oxidative degradation — effects that shorten dispersion shelf-life. Moreover, widely used laboratory and pilot preparation methods (thin-film hydration followed by sonication, extrusion or solvent-evaporation/solvent-removal steps) are time-consuming, can be difficult to scale and normally require specialised processing equipment, increasing production complexity and cost. In addition, common sterilization

and storage stresses (e.g., heat/steam, exposure to oxygen) may further compromise bilayer integrity and accelerate chemical degradation of surfactants or encapsulated actives, creating additional hurdles for industrial translation. Although formulation approaches such as proniosomes/proliposomes, lyophilization, incorporation of cholesterol or charged surfactants, and optimization of hydration/processing parameters can mitigate many of these problems, they introduce extra formulation and processing steps and can change release or biocompatibility profiles — so trade-offs remain that must be addressed case-by-case. The physical instability and lengthy preparation processes present significant limitations in the development and application of niosomal formulations.^[20]

5. Structure of niosomes Components

5.1. Non-ionic surfactants

Lipids like cholesterol, hydration mediums, and non-ionic surfactants are utilized to create niosomes. Table 1 presents the ingredients needed for niosome production. Non-ionic surfactants are those surfactants that lack a charge group on their hydrophilic heads. In comparison to their anionic, amphoteric, or cationic counterparts, they exhibit lower toxicity, greater stability, and enhanced biocompatibility. As a result, they are preferred for the creation of stable niosomes intended for both in vitro and in vivo applications. Non-ionic surfactants, which are amphiphilic molecules, consist of two distinct regions: a hydrophilic segment (soluble in water) and a hydrophobic segment (soluble in organic solvents). The main non-ionic surfactants employed in the synthesis of niosomes include fatty acids, alkyl ethers, alkyl esters, and alkyl amides. When selecting a surface molecule for the synthesis of niosomes, it is critical to consider the

Hydrophilic-Lipophilic Balance (HLB) and the Critical Packing Parameter (CPP) values.^[21]

5.2. Cholesterol

Steroids are essential because they alter the bilayer's permeability and fluidity. Usually, non-ionic surfactants are supplemented with cholesterol a waxy steroid metabolite to provide them stiffness and orientational order. It may be assimilated in high molar ratios and does not form the bilayer itself. As an amphiphilic molecule, cholesterol aligns with the hydrocarbon chains of the surfactant and the water phase of the OH group. By limiting the mobility of the hydrocarbon carbons, the stiff steroidal skeleton is alternatively positioned with surfactant molecules in the bilayer to achieve rigidization. It is also known that cholesterol inhibits the conversion from gel to liquid phase.^[22]

5.3. Charged molecules

By incorporating charged groups into the vesicle bilayer, charged molecules make the vesicles more stable. They do this by raising the surface charge density, which stops vesicles from aggregating. They function by offering larger zeta potential values and inhibiting the merging of vesicles caused repelling force between identical charges. In a manner similar to the use of stearylamine and stearyl pyridinium chloride, which are established positively charged compounds in niosomal formulations, diethyl phosphate and phosphatidic acid are the most frequently utilized negatively charged substances for the preparation of niosomes. Typically, 2.5–5 mol% of the charged substance is incorporated into the ribosomal formulation. However, the production of niosomes can be hindered by an increase in the amount of charged molecules used.^[23]

Table 2: Materials required for Niosomes preparation.

Component	Role in niosomes	Examples	References
Non-ionic Surfactants	Form the bilayer membrane of niosomes.	Tweens (20, 40, 60, 80), Spans (20, 40, 60, 80), Brij (30, 35, 52, 58, 72, 76)	[23]
Cholesterol	Increases membrane rigidity and stability.	Cholesterol	[23]
Hydration Medium	Aqueous solution that hydrates the lipid film.	Water, buffered solutions	[24]
Drugs or Active Molecules	Encapsulated within the niosomes.	Various pharmaceuticals, natural products	[25]
Co-surfactants	Enhance niosomes formation and stability.	Phospholipids (e.g., lecithin), diacylglycerols	[25]
Charge-inducing Agents	Modify the surface charge of niosomes.	Phosphatidylglycerol, stearylamine	[26]
Organic Solvents	Used in the preparation process.	Chloroform, ethanol, ether	[27]

6. Technique for Preparation

Numerous techniques for preparing niosomes have been documented in the literature (Table 2); a few of them are briefly covered below.

Table 3: Comparative overview of niosome preparation techniques, their advantages, and drawbacks.

Preparation Technique	Advantages	Drawbacks	Ref.
Thin Film Hydration	Simple, widely used, suitable for hydrophilic and hydrophobic drugs	Poor reproducibility, scale-up challenges	[28]
Reverse Phase Evaporation	High encapsulation efficiency, good for hydrophilic drugs	Use of organic solvents, longer preparation time	[29]
Microfluidization	Uniform size distribution, scalable, reproducible	Requires specialized equipment, higher cost	[30]
Ether Injection	Produces small vesicles, relatively easy	Residual solvent issues, low encapsulation efficiency	[31]
Proniosome Method	Stable dry form, reconstitutes easily, improved shelf life	Additional step for hydration, sometimes incomplete vesicle formation	[32]

6.1. Thin-film hydration method: Niosomes are often prepared using this process. Using this process, niosomes are made by adding cholesterol and a non-ionic surfactant to an organic solvent that is placed in a Round-Bottom Flask. After that, a Rotating Vacuum Evaporator was used to evaporate the organic medium. A thin coating builds on the circular bottom flask's inner surface as it evaporates. The temperature at which the thin layer is hydrated is greater than the surfactant's transition temperature. Phosphate buffer or water are utilized for hydration. Rehydration causes the layer to enlarge and the drug-containing multilamellar vesicles to form film. Film hydration approach is used to formulate the niosomes of *zidovudine*, *benzylpenicillin*, *paclitaxel*, *gallidermin*, *prednisolone*, *tenofovir disoproxil fumarate*, *green tea extract*, and *lornoxicam*.^[33]

6.2. Method of injecting Ether

In this method, cholesterol and a surfactant are dissolved in an organic solvent such as diethyl ether. The resulting mixture is then introduced gradually into a heated aqueous solution containing the drug, where the temperature is maintained at approximately 60°C or above.^[34] As the organic solvent evaporates, the surfactant and drug components organize into

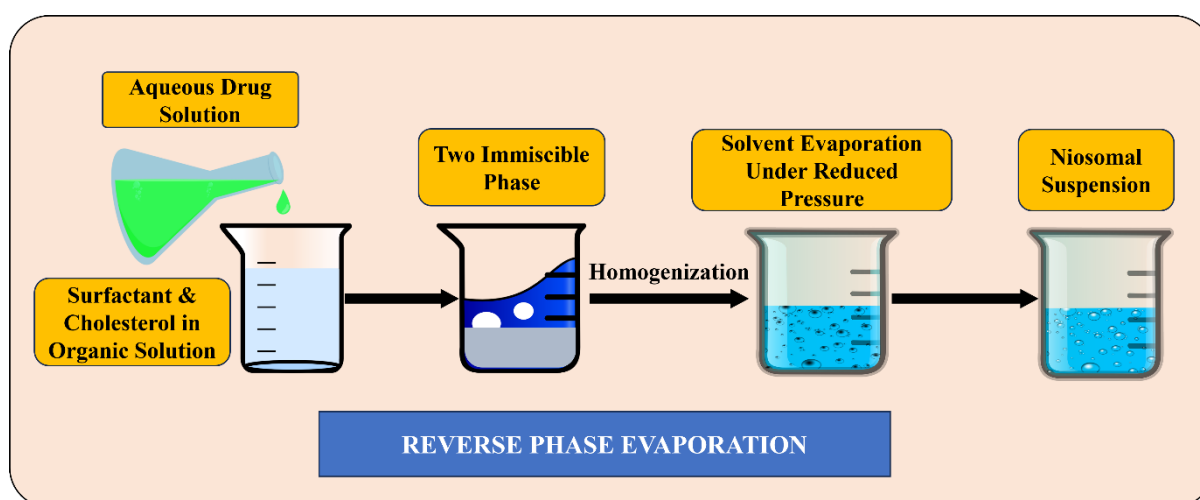
unilamellar vesicles. Niosomes prepared through this technique generally exhibit a diameter in the range of 50–1000 µm.^[35] This method has been employed in the preparation of stavudine-loaded niosomes.^[36]

6.3. Ultrasonication technique

Cefdinir niosomes have been synthesized using sonication technology. They added cholesterol, surfactants, and incorporated drug solution in the buffer (pH 6.8). To form multilamellar vesicles, the resulting mixture was sonicated for 5 minutes at 25°C using a probe sonicator. In order to formulate unilamellar vesicles, further ultrasonication may be performed.^[37]

6.4. Reverse phase evaporation technique

The technique combines cholesterol and surfactants with organic solvents. The water system for the drug is created separately. The organic phase is enhanced by the aqueous phase. A dual-phase system is generated in the mixture. Under negative pressure, the system homogenizes and eliminates the organic phase. During this phase, large unilateral vesicles are produced. This method is used for the production of isoniazid ellagic acid, and bovine serum albumin.^[38] A flow chart is mentioned in the following figure 2.

**Figure 2: Flow chart Process of Reverse Phase Evaporation^[39] (made with PPT).**

6.5. Hand Shaking Method

Among the conventional approaches for niosome preparation, the hand-shaking method remains a straightforward and frequently adopted technique for producing multilamellar vesicles. In this process, cholesterol and a suitable surfactant, such as Span 60, are first dissolved in an appropriate organic solvent. The solvent is subsequently removed under reduced pressure, resulting in the deposition of a thin lipid film on the inner surface of the flask. Hydration of this film is performed using a warm aqueous buffer maintained above the phase transition temperature of the surfactant, and mild mechanical agitation facilitates the formation of multilamellar vesicular structures. The method accommodates both drug types, where lipophilic drugs

are incorporated within the lipid film during preparation, while hydrophilic drugs are dissolved directly into the hydration medium. To achieve a more uniform vesicle population and reduce particle size, additional processing steps such as sonication or membrane extrusion may be applied. Despite being cost-effective and versatile in terms of drug compatibility, the technique presents certain limitations, including batch-to-batch size variability and relatively poor scalability for large-scale production. Vesicle stability and size homogeneity can be further enhanced through the incorporation of charge-inducing agents or by subjecting the preparation to controlled extrusion.^[40] Following figure 3 shows the flow chart process of the Hand Shaking method of preparation of niosomes.

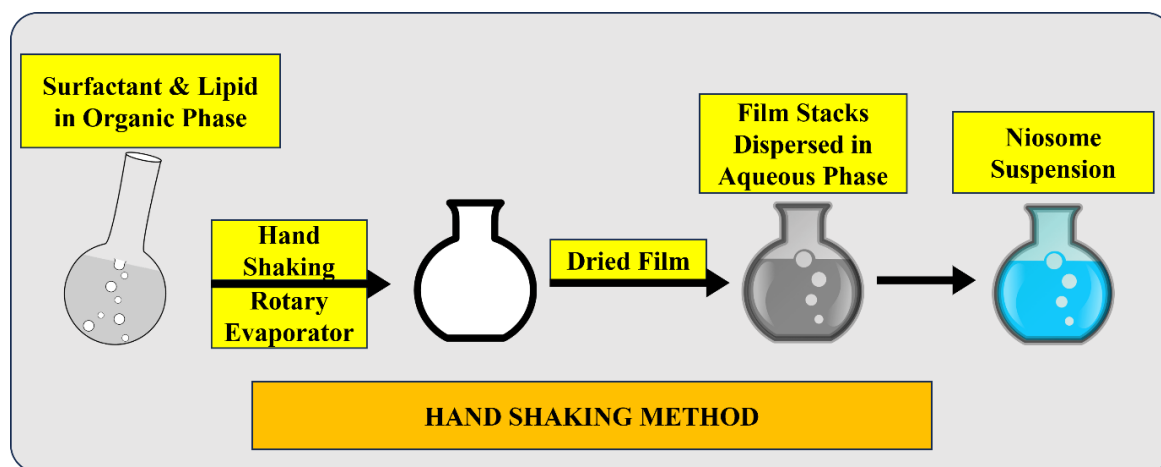


Figure 3: Hand Shaking Method^[41] (made with PPT).

7. Evolution parameter of niosomes

The physicochemical stability and biological behavior of niosomes can be evaluated by measuring certain characteristics. Commonly used parameters for characterizing niosomes include zeta potential (ZP), polydispersity index (PDI), drug release, particle shape, surface morphology, lamellarity, encapsulation efficiency, phase behavior/polymorphism, and in vitro performance.

7.1. Particle Size (PS) and Polydispersity Index (PDI)

The mean diameter of niosomes, which are generally assumed to adopt a spherical morphology, can be determined using several analytical techniques. Laser light scattering and transmission electron microscopy (TEM) are among the most frequently employed methods for this purpose. Additional techniques, including optical microscopy, photon correlation microscopy, ultracentrifugation, and molecular sieve chromatography, have also been reported for niosomal size characterization.

Particle size is a critical parameter as it governs the ability of niosomes to traverse biological barriers, particularly the blood-brain barrier (BBB). Smaller particles are more capable of crossing the BBB, making them especially valuable for brain-targeted drug delivery

and for limiting macrophage-mediated dissemination of pathogens in conditions such as HIV/AIDS and tuberculosis.

The polydispersity index (PDI) reflects the distribution of particle sizes within a niosomal formulation and serves as an indicator of preparation homogeneity. A low PDI value is generally preferred to ensure consistent and predictable particle behaviour. Dynamic light scattering (DLS), also referred to as quasi-elastic light scattering or photon correlation spectroscopy (PCS), represents the most widely used approach for simultaneously assessing particle size and PDI.

DLS operates by monitoring the Brownian motion of dispersed particles resulting from continuous bombardment by solvent molecules, which causes scattering of incident light. The instrument records the intensity, rate, and time-dependent fluctuations of scattered light, all of which correlate with the diffusivity of the particles.^[42] The extent of light scattering depends on the difference in refractive indices between the dispersing medium and the particles, with smaller particles diffusing at a faster rate than larger ones. Based on the quantity of scattered light detected, the mean particle size of a dispersion can be determined rapidly and non-invasively. This technique is valued for its

simplicity, speed, and reproducibility under routine laboratory conditions. A notable advantage of DLS in niosomal characterization is its broad dynamic range, capable of measuring particles spanning from a few nanometres to several micrometres.

Nevertheless, DLS carries inherent limitations. It cannot differentiate between individual particles and aggregated clusters, and the influence of particle solvation on measured values cannot be entirely excluded. Furthermore, the technique is highly sensitive to particulate contamination, and the size obtained represents the hydrodynamic diameter rather than the true geometric dimension of the particle.^[43]

7.2. Zeta Potential (ZP)

The Zeta Potential (ZP) of niosomal dispersions corresponds to the surface charges, depending on the formulation ingredients. To assess the long-term reliability of this technology, along with the in-vivo effectiveness and biological fate of the carriers, it is crucial to analyze the surface charge of the niosomes. Niosomes with high positive or negative charges tend to accumulate very little in a dispersion, unlike those that are mildly or neutrally charged. This phenomenon is due to the lack of electrostatic repulsion in neutral dispersions. When measuring Zeta Potential, Dynamic Light Scattering (DLS) is utilized to gauge the changes in scattered light intensity caused by the movement of niosomes, which results from the influence of an applied electric field on particle charges. The surface charge of niosomes governs their mobility, which in turn affects the intensity of the scattered light.^[44]

7.3. Encapsulation Efficiency (EE)

The degree to which a consignment has been effectively enclosed by the niosomes is gauged by EE. Quantifying the EE is essential since it determines the final dosage of the formulation to be given and affects the consignment release rate. Centrifugation of dialysis is used to remove any API that has not been encapsulated after a niosomal dispersion has been made. After breaking the vesicle with 50% v/v n-propanol or 0.1% w/v Triton X-100 solution, the niosomes consignment are calculated. An approved test approach for the consignment is used to analyse the resulting. Equation (1) is then used to compute the entrapment efficiency.^[45]

$$\%EE = \frac{\text{Amount of API entrapped}}{\text{Total amount of API}} \times 100$$

7.4. Concentration of Drug

Several formulation-related parameters influence the in vitro drug release profile of niosomes, including hydration volume, membrane rigidity, and the physical state of the bilayer. Understanding these variables is essential for optimizing niosomal drug delivery systems.

The dialysis membrane technique represents one of the most commonly adopted approaches for evaluating drug release from niosomal formulations. In this method, a

purified niosomal suspension is introduced into a dialysis bag, which is subsequently sealed at both ends. The sealed bag is then immersed in a beaker containing a physiologically relevant release medium, such as phosphate-buffered saline or simulated body fluid, and maintained at 37°C under continuous stirring to replicate physiological conditions. At predetermined time intervals, aliquots are withdrawn from the external medium and replaced with an equivalent volume of fresh release medium to maintain sink conditions. The collected samples are subsequently analyzed using appropriate quantitative analytical methods to determine the cumulative amount of drug released over time.

In addition to the dialysis bag technique, alternative approaches have also been documented in the literature. Franz diffusion cells, for instance, follow a comparable experimental principle and have been employed as an effective substitute for assessing drug permeation and release from niosomal preparations.^[46]

8. Applications of niosomes

8.1. Protein and Peptide Drug Delivery

Proteins and peptides are sensitive molecules that are often degraded by enzymes in the gastrointestinal tract or bloodstream, making their delivery challenging. Niosomes provide a protective environment for these macromolecules, shielding them from enzymatic degradation and harsh biological conditions. By encapsulating proteins and peptides within their bilayer structure, niosomes enhance their stability and facilitate their transport across biological membranes. This makes niosomes valuable carriers for delivering therapeutic proteins, hormones, vaccines, and enzymes, which would otherwise have limited bioavailability or require frequent dosing.^[47]

A novel amphiphilic peptide was designed and synthesized by Karim et al. with the aim of functioning as a structural component within niosomal drug delivery systems developed for curcumin encapsulation. The peptide was characterized by distinct hydrophilic and hydrophobic regions, which conferred upon it the capacity to undergo spontaneous self-assembly and integrate efficiently into niosomal bilayer membranes. Upon incorporation into vesicles formulated with non-ionic surfactants, the presence of the amphiphilic peptide contributed to improved formulation stability and enhanced biocompatibility. These properties collectively facilitated more effective delivery of curcumin, a naturally derived hydrophobic compound that, despite possessing considerable therapeutic promise, has faced significant barriers to clinical application owing to its inherently poor aqueous solubility and susceptibility to chemical degradation.^[48]

The study involved detailed physicochemical characterization of the peptide and the resulting niosomal formulation, including assessments of particle size, morphology, and encapsulation efficiency. The niosomal

system demonstrated high entrapment efficiency for curcumin and provided a controlled release profile, addressing the challenges of rapid degradation and low solubility associated with free curcumin. The amphiphilic peptide-based niosomes also showed promise for enhancing curcumin's therapeutic efficacy by improving its stability and delivery to target sites. Overall, the research highlights the potential of novel amphiphilic peptide-modified niosomes as effective carriers for hydrophobic drugs like curcumin, offering improved drug delivery, protection from degradation, and sustained release properties.^[49]

8.2. Ophthalmic Drug Delivery

Ocular drug delivery presents inherent challenges, primarily due to rapid lacrimal drainage and the short residence time of conventional formulations on the ocular surface. Niosomes have emerged as a promising strategy to address these limitations by prolonging drug retention, thereby enhancing corneal absorption and overall bioavailability. Their ability to encapsulate both hydrophilic and lipophilic agents within a stable vesicular system offers protection against enzymatic and chemical degradation, resulting in a more sustained therapeutic response. Such attributes make niosomal formulations particularly well-suited for the management of chronic ocular conditions, including glaucoma, conjunctivitis, and dry eye syndrome, where consistent drug action and reduced dosing frequency are clinically desirable.

In a recently conducted study, Aldawsari et al. developed a bimatoprost-loaded niosomal in situ gel system (BMT-ISG) with the objective of optimizing ocular drug delivery for glaucoma management. Niosomes were prepared using Span-60 and cholesterol in a 1:2 molar ratio via the thin-film hydration technique. The optimized formulation demonstrated an entrapment efficiency of $81.2 \pm 1.2\%$ and a mean particle size of 167.3 ± 9.1 nm, dimensions considered conducive to effective corneal penetration. The prepared vesicles were subsequently incorporated into a thermosensitive gel matrix comprising Pluronic F127 and F68, which exhibited a sol-to-gel transition within the temperature range of 28.1–40.5°C, allowing gelation to occur upon contact with the ocular surface. In vitro release studies revealed a prolonged and controlled release of bimatoprost over a 24-hour period, in contrast to the rapid drug release observed with a plain drug solution. In vivo assessment conducted in rabbit models further demonstrated a markedly greater reduction in intraocular pressure (IOP) with the BMT-ISG formulation, recording a decrease of 9.7 ± 0.6 mmHg compared to 5.8 ± 0.6 mmHg for the conventional topical solution, with no evidence of ocular irritation. Collectively, these findings indicate that the BMT-ISG approach holds considerable potential for improving both therapeutic outcomes and patient tolerability relative to standard ophthalmic treatments.^[50]

8.3. Oral Drug Delivery

The oral route is the most favored method for delivering drugs; however, many medications, especially proteins and peptides, have low absorption rates or are degraded in the gastrointestinal tract. Niosomes can enclose these drugs, shielding them from the stomach's acidic environment and the enzymatic breakdown in the intestines. This protective effect improves the oral bioavailability of sensitive medications, enabling more effective treatment with smaller doses. Additionally, niosomal formulations can enhance the solubility and absorption of drugs that poorly dissolve in water, thus broadening the variety of medications that can be taken orally.

Fayed et al. explored the potential of chitosan-encapsulated niosomes as an advanced oral delivery system for atorvastatin, which is a lipid-lowering agent known for its severely low bioavailability due to its limited solubility and significant first-pass metabolism. Conventional niosomes, which were made from Span 60, cholesterol, and dicetyl-phosphate, were processed and then coated with chitosan that was crosslinked with tripolyphosphate, resulting in stable chitosan-encapsulated vesicles. While both systems displayed nanoscale sizes and a spherical shape, the chitosan-encapsulated version resulted in smaller vesicles (96.9 nm) compared to the uncoated niosomes (143.2 nm) and slightly improved entrapment efficiency (57% versus 55.5%). Although the patterns of drug release were similar, in vivo experiments in hyperlipidemic mice demonstrated that chitosan-coated niosomes led to greater cholesterol reductions compared to standard niosomes, with both formulations significantly outperforming plain drug suspension. These results indicate that chitosan encapsulation can enhance the stability and therapeutic effectiveness of atorvastatin-loaded niosomes, positioning this method as a promising strategy for oral lipid-lowering treatment.^[51]

8.4. Gene and Nucleic Acid Delivery

Gene therapy requires efficient delivery of genetic material, such as DNA, siRNA, or antisense oligonucleotides, into target cells. Niosomes, especially those with cationic (positively charged) surfaces, can bind to negatively charged nucleic acids and facilitate their entry into cells. This non-viral delivery system is considered safer and less immunogenic than viral vectors. Niosomes protect nucleic acids from degradation and promote their uptake by cells, making them promising carriers for gene therapy applications, including the treatment of genetic disorders, cancer, and viral infections.

The research by Vado et al. focused on developing and validating a gene delivery method using cationic niosomes for novel urine-derived mesenchymal stem cells (hUSCs). These stem cells, which can be collected noninvasively from urine, offer significant advantages for regenerative medicine and gene therapy. The study

involved isolating and characterizing hUSCs, then formulating various cationic niosomes via reverse-phase evaporation. The niosomes were evaluated for their ability to deliver genetic material into hUSCs, with the GPxT-CQ formulation at a lipid/DNA ratio of 5:1 showing the highest transfection efficiency. Further analysis revealed that these nioplexes primarily entered the cells through caveolae-mediated endocytosis. The authors concluded that their protocol enables efficient gene delivery into hUSCs, opening new possibilities for clinical applications such as gene therapy, disease modeling, and functional genetic studies. This work also enhances understanding of how cationic niosomes interact with these unique stem cells, providing a foundation for future research and therapeutic strategies.^[52]

8.5. Anticancer, Antimicrobial, and Anti-inflammatory Drug Delivery

Niosomes have been widely investigated for their ability to deliver anticancer, antimicrobial, and anti-inflammatory medications. By encapsulating these compounds, niosomes can improve their concentration at the infection, inflammation, or tumor site, while minimizing exposure to surrounding healthy tissues. This focused method enhances the effectiveness of the medications and reduces the likelihood of side effects. For instance, niosomal formulations of antibiotics can effectively target and treat resistant bacterial infections, whereas niosomal anti-inflammatory drugs can offer extended relief for chronic inflammatory conditions.

A study conducted by Parvathi K et al. explored the design, synthesis, and assessment of a novel nanocarrier system aimed at targeted anticancer drug delivery. The researchers created nano-niosomes, which are vesicular structures made from non-ionic surfactants, incorporating iron oxide nanoparticles and further functionalized with folic acid and chitosan. The inclusion of iron oxide nanoparticles provided magnetic properties, which can be utilized for both magnetic targeting and imaging, while chitosan, a biocompatible polymer, enhanced the stability and compatibility of the niosomes. Importantly, folic acid was attached to the surface of the nano-niosomes to specifically target cancer cells that show an abundance of folate receptors, thereby improving the selectivity of drug delivery and reducing effects on healthy cells. The researchers characterized the synthesized nano-niosomes through various physicochemical techniques to verify their size, shape, surface charge, and encapsulation efficiency. In vitro experiments were carried out to evaluate the drug release profile and anticancer effectiveness of the system. Findings indicated that the nano-niosomes displayed a controlled and sustained drug release, particularly in acidic conditions that simulate the tumor microenvironment. Cytotoxicity tests against cancer cell lines showed heightened anticancer activity for the targeted nano-niosomes compared to non-targeted counterparts, suggesting effective cellular uptake and

drug delivery. Overall, this research underscores the potential of iron oxide@folic acid/chitosan-based nano-niosomes as a promising platform for targeted drug delivery in cancer treatment, integrating the advantages of magnetic targeting, receptor-mediated uptake, and controlled release to enhance therapeutic outcomes.^[53]

8.6. Vaccine Delivery

Niosomes have the potential to act as carriers and adjuvants for vaccines, improving the immune response to the antigen they deliver. By encapsulating antigens within their vesicular form, niosomes safeguard them from degradation and facilitate their controlled release to immune cells. Niosomal vaccines can be administered through various methods, including intramuscular, subcutaneous, and even topical applications. The adjuvant properties of niosomes aid in promoting both humoral and cellular immunity, making them important in the advancement of new and more effective vaccines.

Zhang et al. conducted a comparative study to evaluate the effectiveness of niosomal and elastic niosomal carbomer hydrogels for transcutaneous vaccine delivery. The research focused on formulating two types of hydrogels: one containing conventional niosomes and the other containing elastic niosomes, both embedded in a carbomer-based hydrogel matrix. The primary aim was to enhance the transdermal delivery of vaccines by overcoming the barrier function of the skin, thereby improving antigen penetration and immune response. Their findings demonstrated that elastic niosomal hydrogels exhibited superior skin permeation and vaccine delivery efficiency compared to conventional niosomal hydrogels. This enhanced performance was attributed to the greater flexibility and deformability of elastic niosomes, which allowed them to better traverse the stratum corneum. The study concluded that elastic niosomal carbomer hydrogels represent a promising strategy for non-invasive, effective transcutaneous immunization, offering advantages in both antigen stability and immune activation.^[54]

8.7. Brain Targeting with niosomes

Niosomes have demonstrated considerable potential in transporting drugs across the blood-brain barrier (BBB), which is a significant obstacle in neuropharmacology. Their configuration enables both passive and active targeting methods. Passive targeting is facilitated as niosomes can block P-glycoprotein (P-gp) on capillary endothelial cells, aiding drugs in penetrating the BBB and accumulating within brain tissues. Active targeting is achieved by modifying the surface of niosomes with ligands such as transferrin (TF) or glucose moieties, which attach to overexpressed receptors (like transferrin receptors or GLUT-1) on the BBB as well as on brain tumor cells. For example, TF-modified niosomes have been utilized to deliver curcumin for glioma treatment, significantly increasing drug levels in the brain and enhancing therapeutic results while reducing systemic side effects. In a similar manner, glucose-decorated

niosomes have enabled the transport of peptides such as vasoactive intestinal peptide (VIP) to the central nervous system, displaying superior brain delivery efficacy compared to non-targeted systems. The capability to modify niosomes for receptor-mediated endocytosis or transporter-mediated uptake renders them highly effective for targeted drug delivery to the brain, encompassing anti-cancer, neuroprotective, and peptide-based therapies.^{[55], [56]}

A study conducted by Qian, H., Lv, J., and Hu, X (2025) outlines the creation and assessment of transferrin-modified curcumin nano-niosomes (TF-Cur-Nio) for targeted therapy of gliomas. Glioma, a highly aggressive type of brain tumor, presents significant treatment obstacles due to the blood-brain barrier (BBB) and inefficient drug delivery. In this research, curcumin—a natural anticancer compound with poor bioavailability—was encapsulated in niosomes made from non-ionic surfactants and cholesterol, and further enhanced with transferrin to take advantage of receptor-mediated transport across the BBB. The TF-Cur-Nio system exhibited improved targeting of brain tumors, better cellular uptake, and greater anti-glioma effectiveness when compared to formulations without modification. In vivo experiments conducted on a glioma mouse model revealed that TF-Cur-Nio effectively slowed tumor growth, triggered apoptosis, and increased survival rates, all while showing a favorable safety profile with no significant toxicity to key organs. These results underscore the potential of TF-Cur-Nio as a promising and safe approach to glioma treatment, paving the way for further preclinical and clinical exploration.^[57]

9. Obstacles and Prospects for the Future

Although niosomes are generally regarded as safe, concerns about potential cytotoxicity, immunogenicity, and long-term effects on biological systems must be addressed. Ensuring biocompatibility and minimizing toxicity risks associated with niosomes formulations is one of the major challenges in niosomes-based drug delivery. To ensure certain safety of niosomes-based drug delivery systems for clinical applications, future research efforts should concentrate on refining niosomes composition, surface modification techniques, and formulation parameters to improve biocompatibility and decrease toxicity.

Recent advancements in niosome-based drug delivery systems have significantly expanded their clinical and translational potential, with several trials now evaluating their efficacy and safety across therapeutic domains. For instance, a 2024 study demonstrated the promise of brain-targeted niosomes in enhancing central nervous system drug delivery, while other investigations have validated their application in transdermal formulations, showcasing their adaptability across multiple administration routes.^[58]

From a regulatory perspective, both the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) have taken active steps toward establishing comprehensive frameworks for nanotechnology-based drug products. The FDA's 2024 guidance emphasizes the necessity of in-depth physicochemical characterization of nanocarriers, ensuring product quality, bioequivalence, and safety parallel to conventional dosage forms. The guidance also encourages the use of risk-based approaches and advanced analytical methods for nanomaterial assessment. Similarly, the EMA's recent report on nanomedicine regulation highlights the need for harmonized evaluation protocols across the European Union, particularly focusing on nanoscale pharmacokinetics, biodistribution, and toxicity assessment.^[59] Emerging regulatory initiatives are now also promoting adaptive pathways and platform-based approvals, which may accelerate the translation of niosomal formulations from research to clinical use.

Looking forward, Artificial Intelligence (AI), Quality by Design (QbD), and microfluidic technologies are expected to revolutionize niosome design and optimization. AI-driven predictive modeling can accelerate formulation development by correlating formulation parameters (such as surfactant type, cholesterol ratio, and hydration method) with critical quality attributes (e.g., vesicle size, drug entrapment efficiency, and stability). Coupled with QbD principles, researchers can systematically identify critical process parameters, ensuring robust and reproducible niosome formulations that meet predefined quality specifications. Moreover, microfluidic-based fabrication platforms offer precise control over vesicle size, lamellarity, and composition, while enabling continuous, scalable, and solvent-free production.^[60] These technologies not only enhance formulation reproducibility but also support regulatory compliance by ensuring consistent batch quality.

However, despite these technological and regulatory advancements, challenges persist in industrial scalability and Good Manufacturing Practice (GMP) compliance. Niosomal formulations often suffer from batch-to-batch variability, limited long-term stability, and the need for specialized equipment and storage conditions. Large-scale production is further complicated by the sensitivity of niosomes to environmental factors such as temperature and shear stress during manufacturing. The establishment of GMP-compliant, automated, and continuous manufacturing systems remains a major research focus. Innovative processes, such as the SuperSomes technique, have emerged as potential solutions, offering solvent-free, continuous-mode production of nanovesicles with improved uniformity and stability.^[61] In the near future, integrating AI-assisted process monitoring, microfluidic scalability, and QbD-driven manufacturing control could bridge the gap

between laboratory-scale innovation and commercial realization of niosome-based therapeutics.

10. Integration of Clinical Trial Progress and Translational Barriers

Although preclinical studies have established the versatility of niosomes in delivering chemotherapeutics, nucleic acids, vaccines, and diagnostic agents, their translation into clinical practice remains limited compared to liposomes or polymeric nanoparticles. Only a handful of niosome-based formulations have reached early-phase clinical trials, mainly for topical and transdermal applications, owing to their stability, low cost, and relatively simple manufacturing. However, for systemic applications, significant barriers persist. Key challenges include the lack of standardized large-scale manufacturing protocols, batch-to-batch variability in vesicle size and encapsulation efficiency, incomplete understanding of long-term biodistribution and toxicity, and limited regulatory guidance specifically tailored for niosome formulations. Moreover, while niosomes are generally regarded as more stable than liposomes, their surfactant-based composition raises concerns about surfactant toxicity, immunogenicity, and clearance pathways *in vivo*. From a translational perspective, the absence of harmonized regulatory frameworks and comparative clinical data against established carriers makes it difficult to advance niosome candidates through the clinical pipeline.^[62] Therefore, integrating current clinical trial progress with a critical evaluation of these translational hurdles is essential to identify strategies such as advanced manufacturing techniques (microfluidics, spray drying), incorporation of biocompatible surfactants, and early regulatory engagement, which can accelerate the clinical adoption of niosomes as mainstream nanocarriers.

11. Prospects for niosomal drug delivery in the future

Multifunctional Niosomes: Because they can encapsulate a broad variety of medical drugs and deliver them to particular areas within the body, lipid-based vesicular carriers known as niosomes have emerged as potential drug delivery vehicles. Through the integration of multiple functionalities into a single carrier system, multifunctional niosomes—a novel advancement in drug delivery technology—offer special opportunities to improve therapeutic efficacy and drug delivery efficiency. In this thorough examination, we delve into the multifaceted aspects of multifunctional niosomes, including their design principles, applications, challenges, and future prospects. Targeted drug delivery, imaging, diagnostics, and therapeutic monitoring are just a few of the tasks that multifunctional niosomes can accomplish simultaneously. This adaptability is made possible by the integration of multiple functional elements within the niosomes structure, such as targeting ligands, imaging agents, stimuli-responsive materials, and therapeutic payloads. When these functionalities are combined, multifunctional niosomes provide synergistic effects that can greatly improve therapeutic outcomes

and drug delivery efficiency. The design of multifunctional niosomes entails a number of critical considerations, such as the incorporation of functional moieties, the careful selection of suitable lipid components, and the optimization of formulation parameters.^[63] The consistency, biocompatibility, as well as drug-carrying capacity from multifunctional niosomes are all significantly influenced by the lipid composition. Furthermore, options for surface modification, including conjugation with targeting ligands or surface engineering with stimuli-responsive polymers, allow for the regulated release of therapeutic medicines and the selective targeting of sick regions. Multifunctional niosomes are useful in a wide range of therapeutic contexts, including as cancer treatment, viral illnesses, abnormalities of the central nervous system, and cardiovascular conditions. Multifunctional niosomes have the potential to deliver chemotherapeutic medications to tumor locations while also visualizing the tumor microenvironment with contrast chemicals or tracking treatment response using theranostic techniques in cancer therapy. Similar to this, multifunctional niosomes in infectious diseases allow real-time monitoring of drug resistance or microbial load by targeting specific pathogens with antimicrobial peptides or antibodies.^[64] Despite their promising potential, multifunctional niosomes face a number of obstacles that need to be overcome before they are widely used in clinical practice. Personalized medicine is a specialized medicine, an innovative approach to medical care that tailors treatments and treatments to patients based on genetic characteristics, physiological characteristics, and environmental factors. Personalization has received a lot of attention in recent years as a promising strategy to improve patient outcomes, optimizing therapeutic efficacy, and minimizing adverse effects. These challenges include the complexity of formulation design, potential toxicity concerns associated with multifunctional components, and regulatory hurdles related to approval pathways for combination products. Overcoming these challenges requires interdisciplinary collaboration, creative research approaches, and robust preclinical and clinical evaluations to ensure the safety, efficacy, and quality of multifunctional niosome-based drug products. Personalized medicine techniques provide chances to create customized treatment plans that cater to the unique requirements and features of each patient in the context of medication administration.^[65] Because of their adaptability, biocompatibility, and customizable characteristics, niosomal drug delivery systems are well-positioned to promote personalized medicine efforts and spur advancements in drug delivery technology.^[66] With regard to niosomal medication delivery, customized medicine has enormous potential to change healthcare delivery and enhance patient outcomes in the future. Researchers and healthcare professionals can continue to innovate and optimize drug delivery strategies that are tailored to the unique needs and characteristics of individual patients by utilizing the versatility and tunability of niosomal drug delivery systems. This will

mark the beginning of a new era in precision medicine by advancing our understanding of disease mechanisms, drug responses, and patient variability. Future developments in genomics, proteomics, and data analytics are expected to further advance this understanding. In order to improve the functioning, performance, and therapeutic effectiveness of niosomal drug delivery systems, nanotechnology integration entails introducing nanoscale materials and structures into these systems. In the context of niosomal drug delivery, nanotechnology integration encompasses a variety of approaches, including the incorporation of nanomaterials such as nanoparticles, liposomes, polymeric micelles, and quantum dots, as well as the utilization of nanoscale fabrication techniques and surface modification strategies. One important component of nanotechnology integration in niosomal drug delivery is the use of nanomaterials as functional capabilities. These hybrid Nanosystems offer synergistic advantages, combining the distinctive qualities of multiple nanomaterials to achieve superior drug delivery performance. Utilizing nanoscale fabrication techniques to engineer niosomes with precise control over size, shape, and structure is another way to integrate nanotechnology into niosomal drug delivery.^[67] Methods like nanoprecipitation, microfluidics, and electro spraying allow for the fabrication of uniform niosomes with tailored physicochemical properties and improved drug encapsulation efficiency. Furthermore, the integration of nanotechnology in niosomal drug delivery extends to the development of advanced characterization techniques and analytical methods for assessing niosomes properties and behaviour at the nanoscale. Methods like Atomic Force Microscopy (AFM), Dynamic Light Scattering (DLS), Transmission Electron Microscopy (TEM), and Nanoparticle Tracking Analysis (NTA) allow researchers to visualize and characterize niosomes with high resolution and sensitivity. Strategies for surface modification include PEGylation, coating with targeting ligands, or functionalization with stimuli responsive polymers. These strategies can further optimize niosomes interactions with biological systems and improve drug delivery specificity. The design, optimization, and quality control of niosomal drug delivery systems are made easier by these technologies, which provide insights into niosomes shape, size distribution, surface charge, and drug encapsulation efficiency.^[68] additives to improve the attributes of niosomes formulations. Future research on niosomes should move beyond general applications toward specific, translational strategies that can accelerate clinical utility.

11.1 Stimuli-Responsive niosomes

Developing smart niosomes that respond to internal triggers (pH, enzymes, redox gradients) or external stimuli (temperature, light, ultrasound, magnetic fields) could allow precise, on-demand drug release. Such systems are particularly promising for cancer therapy,

where site-specific activation minimizes systemic toxicity.

11.2 Hybrid and Biomimetic Carriers

Combining niosomes with other nanomaterials—such as lipids, polymers, inorganic nanoparticles, or cell-membrane coatings—may enhance stability, targeting, and multifunctionality. Hybrid and biomimetic niosomes could integrate drug delivery with imaging or theranostic functions, paving the way for personalized medicine.

11.3 Advances in Scalable Manufacturing

A major limitation for clinical translation is the lack of reproducible, large-scale production methods. Future work should focus on microfluidics, 3D-printing-assisted fabrication, and continuous manufacturing approaches to produce uniform niosomes with high encapsulation efficiency at industrial scale.

11.4 Regulatory and Clinical Translation Studies

To bridge the bench-to-bedside gap, future studies should incorporate standardized characterization protocols, in vivo biodistribution models, and toxicity evaluations aligned with regulatory expectations. Collaboration between academia, industry, and regulatory agencies is essential to streamline approval pathways.

11.5 Integration with Emerging Technologies

Niosomes should be explored as carriers in advanced biomedical contexts, such as gene delivery (mRNA, siRNA), vaccine platforms, and implantable biomaterials. Their adaptability makes them attractive candid.

12. Novelty and Scope of This Review

Although several reviews on niosomes have been published in recent years, most of them primarily focus on conventional formulation strategies, physicochemical characterization, and general applications. In contrast, the present review emphasizes the emerging landscape of multifunctional and next-generation niosomes, including ligand-targeted, stimuli-responsive, and hybrid systems designed to overcome specific delivery challenges. Furthermore, we extend the discussion to clinical translation, regulatory considerations, and commercialization prospects, which are often underrepresented in earlier reviews. Another distinctive aspect of this work is the integration of niosomes with advanced nanotechnology platforms such as nanofibers, hydrogels, and hybrid nanocarriers, highlighting interdisciplinary approaches for future drug delivery. By combining these perspectives, this review not only consolidates existing knowledge but also provides forward-looking insights into translational potential and future research directions, thereby distinguishing it from previously published reviews.

13. CONCLUSION

Niosomes have established their role as a highly versatile and promising platform for drug delivery, moving

beyond being simple, cost-effective alternatives to liposomes. Their unique ability to encapsulate a wide spectrum of therapeutic agents, from small molecules to large peptides and genes, combined with their enhanced stability and biocompatibility, underscores their significant potential. However, the translation of this potential from the laboratory to clinical practice is contingent upon overcoming several critical challenges. The primary hurdles to widespread clinical adoption are rooted in physicochemical instability and manufacturing scalability. Issues such as vesicle aggregation, fusion, and drug leakage during storage limit shelf-life and compromise therapeutic consistency. Furthermore, traditional preparation methods are often time-consuming and difficult to scale up for commercial production while maintaining uniform particle size and high encapsulation efficiency, which are critical for predictable *in vivo* performance. Overcoming these obstacles requires a concerted focus on developing robust formulations with improved long-term stability and pioneering scalable, reproducible manufacturing technologies. Additionally, navigating the complex regulatory pathways for nanomedicines demands comprehensive preclinical data on long-term safety, biocompatibility, and immunogenicity to ensure these formulations are safe and effective for human use. The future of niosomal research is shifting from simple encapsulation to the design of intelligent, multifunctional delivery systems. The next generation of niosomes will likely serve as theranostic platforms, integrating imaging agents for real-time diagnostics with targeted drug payloads. Innovations in surface modification will enable precise targeting to diseased tissues through ligand conjugation and stimuli-responsive release mechanisms, triggered by local environmental cues like pH or temperature changes. This capacity for customization positions niosomes as a key enabler for personalized medicine, where formulations can be tailored to a patient's specific genetic and pathological profile. By integrating nanotechnology, such as by creating hybrid systems with metallic nanoparticles or polymeric micelles, researchers can unlock synergistic effects and overcome existing limitations. In summary, while the foundational advantages of niosomes are well-documented, the next phase of development must prioritize solving the practical challenges of stability, scalability, and regulatory approval. Future innovation lies in creating sophisticated, multifunctional systems that advance personalized medicine. Focused, interdisciplinary collaboration between academia, industry, and regulatory bodies will be essential to translate the immense promise of niosomes into tangible clinical therapies that are safer and more effective for patients.

Despite remarkable progress in the field of niosomal drug delivery, it is evident that not all formulation strategies or preparation techniques offer equivalent advantages. Thin-film hydration, while simple and widely used, often yields heterogeneous vesicles with

limited scalability, whereas microfluidic and ethanol injection methods enable precise control over particle size and reproducibility, making them more suitable for industrial translation. Similarly, the choice of surfactant critically determines vesicle stability and drug encapsulation efficiency—non-ionic surfactants such as Span 60 and Tween 80 exhibit superior bilayer rigidity and sustained release compared to less stable counterparts. The incorporation of charge-inducing agents or polymer coatings further enhances circulation time and targeting capability, setting advanced hybrid and stimuli-responsive niosomes apart from conventional systems. Collectively, these insights highlight that rational selection of formulation components, guided by Quality by Design (QbD) principles and mechanistic understanding, is essential for achieving optimal therapeutic outcomes and translational viability of niosomal systems.

Furthermore, to make niosomes therapeutically useful, more study is necessary on a few associated difficulties, such as drug hydrolysis in an aquatic niosomes solution that may lead to drug leakage or niosomes aggregation. Additionally, there are a number of problems with niosomal encapsulated medications that need to be resolved. For example, a significant portion of the pharmaceuticals remains unencapsulated during synthesis, which calls for the simplification of certain preparation procedures like filtrations and dialysis.

Furthermore, cholesterol, a crucial ingredient in niosomal formulations that provide greater stability, may have an impact on the biological characteristics of niosomes membranes, such as decreasing their flexibility and lowering drug penetration inside them. Therefore, it is anticipated that further research will enhance the features of niosomes to uncover new potentials and enhance their translation.

Conflict of interest

None.

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