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Review

Niosomes: A Versatile Nanocarrier for Drug Delivery Applications

Dr. A. Suresh[1], Kotha Srinivasulu*[2], Amritha. J[3], Suresh Kumar[3], S. Sathya[4]

[1]Principal, [2]Associate Professor, [3]Assistant Professor, [4]Lecturer
The Kaavery Pharmacy College, Mecheri, Affiliated to The Tamilnadu Dr. MGR Medical University, Mecheri, Salem – 636453, Tamilnadu, India.

*Author for Correspondence: Kotha Srinivasulu
Email: srinupharma0@gmail.com

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Abstract

Niosomes are vesicular systems formed primarily from non - ionic surfactants. They have gained attention as multifunctional tools for targeted and controlled drug delivery. These carriers can encapsulate both hydrophilic and lipophilic drugs, offer good stability and biocompatibility, and typically cost less to produce than certain alternatives such as liposomes. By fine tuning their composition, niosomes can provide specialized release profiles that enhance pharmacokinetics while lowering systemic toxicity. In recent decades, multiple studies have explored the structural features, chemical bases, and manufacturing methods of niosomes, illustrating their wide applicability in diverse fields including cancer therapy, vaccine delivery, chronic disease management, and cosmeceutical products. Despite these noteworthy benefits, challenges remain, particularly in terms of formulation stability, drug leakage, and large scale manufacturing. Emerging developments in stimuli responsive and ligand functionalized niosomes open doors for precision medicine, accelerating the transfer of niosome based concepts from bench to clinical settings. This paper delves into niosomes' structure, composition, classification, fabrication processes, release mechanisms, advantages, and therapeutic uses. It also addresses limitations that have restricted widespread adoption, then explores ongoing advances aimed at overcoming these hurdles. The objective is to guide researchers, clinicians, and industry professionals in fully exploiting the capabilities of niosome based systems for contemporary drug delivery solutions.

Keywords: Niosomes

INTRODUCTION

Niosomes, also referred to as non ionic surfactant vesicles, were first described in the late 1970s [1–3]. In concept, they share similarities with liposomes both involve amphiphilic molecules forming closed bilayer vesicles in aqueous environments [4]. The distinguishing feature is that niosomes rely primarily on non ionic

surfactants instead of phospholipids. This unique choice of surfactant often leads to enhanced chemical stability and lower production expenses, making niosomes attractive for encapsulating a variety of therapeutic agents [5].

A key motivator for niosomal research is the pressing need for more sophisticated drug delivery platforms that can increase therapeutic effectiveness while limiting adverse side effects [6]. Many drugs display poor solubility, compromised bioavailability, or a rapid metabolic rate when administered in conventional formats, leading to inconsistent blood levels and suboptimal treatment outcomes [7]. Niosomal vesicles, on the other hand, can envelop drugs, protect them from degradation, and enable more controlled release. This not only lowers how often patients need to dose but also curbs systemic toxicity a key consideration in therapies such as chemotherapy, which have narrow therapeutic windows [8].

Progress in niosome based research aligns closely with developments in materials science and nanotechnology. Investigations have focused on choosing optimal surfactants, adding cholesterol, using charge inducers, and exploring diverse hydration media to develop niosomes with finely tuned properties [9]. In parallel, advancements in characterization methods like dynamic light scattering (DLS), electron microscopy, and differential scanning calorimetry (DSC) have improved how we assess vesicle size, shape, surface charge, and drug encapsulation efficiency [10]. These analytical enhancements help researchers correlate a niosome's physicochemical attributes with its performance in vitro and in vivo, making it possible to design vesicular systems geared toward specific goals.

Niosomes have relevance outside of medicine. For instance, the cosmeceutical sector uses niosomes to deliver skin care actives enhancing hydration, whitening, and anti aging effects [11]. Moreover, niosomes have been tested as vaccine carriers, showing potential for boosting immune responses and potentially reducing booster shots [12]. These applications underscore niosomes' adaptability, straddling both fundamental research and real world uses.

Despite such promise, certain obstacles can hamper clinical success. Foremost among these is stability some niosomal formulations may aggregate, fuse, or leak over time [13]. Additionally, industrial scale production demands consistent control over process variables to ensure uniformity in vesicle size and drug loading [14]. From a regulatory standpoint, niosome based products undergo scrutiny typical for advanced drug delivery systems, requiring extensive safety, effectiveness, and quality assurance data [15].

In this review, we offer a thorough analysis of niosomal systems. The discussion begins with their structural and compositional features, illustrating how these factors influence drug encapsulation and release. We then address classification schemes covering unilamellar, multilamellar, and specialized vesicles and examine both well known and newer fabrication techniques, detailing their strengths and drawbacks. We also explain the mechanics of how niosomes release drugs and behave in biological environments. Further, we survey the numerous advantages that these vesicles provide in both pharmaceutical and cosmeceutical contexts, and we point out the hurdles that still need to be overcome. Finally, we highlight recent technological developments and suggest future directions, especially concerning stimuli responsive or ligand modified formulations.

By weaving together past developments, present findings, and prospective directions, this article aims to serve as a resource for those exploring or using niosomal drug delivery systems. It underscores niosomes' nuanced features and the potential pathways for integrating them more effectively in clinical therapies. In an era increasingly focused on tailored interventions, it is highly likely that niosomes will continue to emerge as vital components of modern drug delivery solutions, improving patient adherence and elevating healthcare overall.

Structure and composition

Niosomes present themselves as spherical vesicles formed by amphiphilic non ionic surfactants mixed with cholesterol and, occasionally, additional ingredients. Their fundamental structure is that of a bilayer: the surfactant molecules align such that hydrophobic tails cluster together and hydrophilic heads interface with water [16]. Although this arrangement appears straightforward, the specific surfactant blend, cholesterol level, and auxiliary additives all critically affect the vesicles' size, surface potential, drug loading efficiency, and release profile.

Cholesterol is a key constituent of many niosomal formulations. It incorporates itself between surfactant molecules and serves to increase membrane rigidity [17]. This rigidity often leads to more stable vesicles, as it reduces membrane permeability and drug leakage. However, if the cholesterol content becomes too high, the membrane might become less fluid and hamper efficient drug release [18]. Some formulations further add charge inducers (like dicetyl phosphate or stearylamine) to discourage vesicle clumping through electrostatic repulsion, thus boosting overall stability [19].

The selection of surfactant is crucial to forming niosomes. Surfactants are commonly classified by their hydrophilic lipophilic balance (HLB), which indicates their preference for aqueous or oily phases [20]. Surfactants with intermediate HLB values (e.g., Tween, Span, Brij) often form stable bilayers. Spans (sorbitan esters) are relatively lipophilic, while Tweens (polysorbates) tend to be more hydrophilic [21]. By altering the ratio of these components, researchers can tailor the resultant vesicle size, encapsulation capacity, and release characteristics. Besides surfactant and cholesterol, the interior aqueous compartment can contain hydrophilic drugs or buffers set

to a specific pH [22]. The external aqueous medium may include additional agents like osmotic stabilizers, antioxidants, or buffering salts that uphold vesicle structure. Freeze drying methods often incorporate cryoprotectants (e.g., trehalose or sucrose) to safeguard the vesicles during storage, especially when they must remain stable over extended periods [23,24].

Recent approaches extend beyond the fundamental surfactant cholesterol setup. Some formulations integrate responsive polymers within the bilayer, leading to niosomes that react to shifts in pH, temperature, or certain enzymes, thus offering triggered release [25]. Meanwhile, targeted niosomes can be produced by coupling proteins, peptides, or aptamers to the vesicle, enabling them to bind specific cell receptors [26]. This approach is particularly relevant in oncology and inflammatory diseases, where localized drug release can limit off target side effects. The cosmeceutical and nutritional sectors frequently use more straightforward niosomal blends aimed at improving topical penetration or preserving micronutrients. For instance, niosomes fortified with essential oils or natural extracts can increase solubility and guard bioactive elements from oxidation [27]. Additionally, non ionic surfactants are often gentler than their ionic counterparts, thereby reducing the risk of skin irritation a valuable trait in dermatological formulations [28]. Methodical characterization of niosomal composition is essential. Techniques such as FTIR, NMR, and XRD help detect possible chemical interactions inside the bilayer, revealing details about surfactant packing, membrane fluidity, and phase separation [29]. Such insights are important when optimizing formulations for specific uses, ensuring that structural changes do not compromise drug release or stability.

To sum up, niosomes' structure and composition can be adjusted in multiple ways, providing a flexible drug delivery vehicle. The synergy of non ionic surfactants, cholesterol, and supplementary additives exerts control over aspects like loading capacity, colloidal stability, and release kinetics. Cutting edge formulations that employ responsiveness or targeted ligands offer new opportunities in precision therapy, while simpler, more conventional configurations still excel in areas such as topical and oral delivery. Going forward, an in depth grasp of composition structure function relationships will be indispensable for developing niosomal systems that live up to their full clinical promise.

Types of niosomes

Unilamellar Niosomes

Unilamellar niosomes consist of one bilayer shell enclosing an aqueous core. They split further into small unilamellar vesicles (SUVs) measuring 20–100 nm and large unilamellar vesicles (LUVs) between roughly 100–400 nm [31]. SUVs may have a smaller interior volume for drug loading but frequently offer better penetration through biological barriers. Conversely, LUVs can encapsulate more water soluble drugs, though their larger size makes them more prone to clearance by the reticuloendothelial system (RES) [32]. Sonication and extrusion methods frequently yield unilamellar vesicles with a narrower size range.

Multilamellar Niosomes

Multilamellar niosomes (MLVs) contain multiple bilayers, resembling onion like layers [3]. Typically exceeding 0.5 μm in diameter, MLVs can entrap larger amounts of both hydrophilic and lipophilic substances as the drug can be localized within multiple lamellar compartments [33]. Nevertheless, MLVs can have more complex release profiles and be more difficult to standardize compared to unilamellar types. They are often explored for sustained release applications aiming to reduce how often patients need dosing.

Vesicle Size Variations

Another way to classify niosomes is by their overall size (small, medium, large), regardless of bilayer quantity [34]. This is particularly valuable in industrial contexts, where formulations need to meet specific dimensional targets to match routes of administration. Sub 200 nm vesicles may be beneficial for tumor targeting or for crossing the blood–brain barrier, whereas larger niosomes may be chosen for topical applications [35]. Achieving a narrow size distribution often involves specialized devices like microfluidizers or high pressure homogenizers [36].

Specialized or "Tailor Made" Niosomes

A number of specialized niosome variants exist. Proniosomes, for example, come in a stable powder or semisolid form that can turn into niosomes upon hydration, which can improve stability and make shipping easier [37]. Polymer coated or polymer hybrid niosomes merge a polymer layer with the surfactant bilayer, improving circulation times or permitting mucoadhesion [38]. Meanwhile, stimuli responsive niosomes can release payloads once triggered by specific pH, temperature, or enzyme levels [39].

Clinical and Cosmetic Implications

The choice among unilamellar, multilamellar, or a specialized design depends on the product's intended use. Smaller unilamellar vesicles often target tumors more effectively through the EPR effect, whereas

multilamellar vesicles in vaccines might provide a gradual release of antigens [12]. For skin applications, polymer hybrid or multilamellar vesicles can extend the release of actives, potentially enhancing topical benefits [40].

Analytical and Regulatory Aspects

No matter the type of niosome, rigorous characterization is necessary. Investigators routinely examine size distribution, polydispersity, zeta potential, drug loading, and release kinetics [41]. More advanced techniques such as DSC or SAXS can reveal details of the bilayer's flexibility or lamellarity. Regulators will typically demand detailed data regarding manufacturing conditions, stability, and reproducibility to confirm product reliability [42]. Overall, categorizing niosomes by bilayer count, diameter, or specialized features isn't merely academic but instead underpins a strategic approach to engineering targeted drug delivery systems. As the technology progresses, we can expect new subtypes to arise, each offering refined benefits for defined therapeutic or cosmetic objectives.

Preparation Methods

Different production techniques impart distinct physical and chemical features to niosomes, influencing everything from size to encapsulation efficiency. Selection of the manufacturing method is therefore guided by drug type, target release characteristics, scale, and economic feasibility [43]. Below are the most common methods, along with newer "green" or eco friendly approaches that are gaining traction.

Thin Film Hydration

Often seen as the traditional approach, thin film hydration involves dissolving surfactants, cholesterol, and any other lipophilic ingredients in an organic solvent before evaporating the solvent under reduced pressure to form a thin film [44]. This film is subsequently hydrated using an aqueous phase containing the drug, causing spontaneous formation of vesicles. Additional steps like sonication or membrane extrusion then tune the vesicle size [45]. Though easy to implement in the lab, scaling up can be complicated due to the complexities around evaporating solvents uniformly.

Reverse Phase Evaporation (RPE)

Reverse phase evaporation is well suited for encapsulating hydrophilic substances more efficiently. Here, a water in oil emulsion is prepared by mixing the drug in an aqueous phase with an organic phase containing the surfactant and cholesterol under stirring or sonication [46]. Removing the organic solvent by evaporation results in large unilamellar vesicles with notably high drug entrapment levels, but the process is more elaborate and demands fine control over emulsification settings [47].

Microfluidization and High Pressure Homogenization

Microfluidization uses a high pressure homogenizer to push fluids through small interaction channels, producing uniform vesicles [48]. The process may follow an initial step that yields multilamellar niosomes, reducing them to more uniform unilamellar particles. High pressure homogenization likewise reduces larger vesicles into smaller ones by repeatedly passing through a homogenizer [49]. Both methods can be advantageous for large scale production, although high shear forces might degrade delicate biomolecules and potentially prompt partial drug leakage.

Ether or Ethanol Injection

In the ether injection method, a solution of surfactant and cholesterol in ether is gradually introduced into a hot aqueous phase; the ether evaporates and forms niosomes [50]. The ethanol injection variant follows a similar rationale but uses ethanol. Both techniques make generating smaller vesicles possible but do require careful management of injection speed, temperature, and agitation [51].

Proniosomes

Proniosomes involve coating surfactants and cholesterol onto a solid carrier like maltodextrin, yielding a stable powder that can turn into niosomes upon hydration [37,52]. This format simplifies storage and handling, as no organic solvent is required during the shelf life. When water or another aqueous medium is added, the surfactant layer hydrates to form niosomes in situ, preserving drug potency and easing shipping logistics.

Sonication and Ultrasonication

Sonication typically complements methods like thin film hydration, breaking larger vesicles into smaller ones [53]. Ultrasound waves disrupt bilayer structures, but excessive sonication can generate localized heat, risking drug breakdown or leakage. Thus, sonication parameters must be optimized [54].

Recent Eco Friendly and Automated Techniques

As environmental and safety concerns grow, researchers seek solvent free or lower solvent methods, sometimes involving supercritical fluids [55]. Microfluidic based processes also enable precise control of flow rates, mixing, and temperature, allowing reproducible large scale production with immediate quality checks [56]. In short, the route chosen to create niosomes has far reaching consequences on their size distribution, stability, and entrapment efficiency. While classical methods like thin film hydration or reverse phase evaporation remain common in small scale research, large scale industrial operations are turning to microfluidization or proniosomes. Moving forward, green techniques and continuous flow systems may well become the norm, bridging bench level science with consistent, regulated production of niosomal medicines.

Mechanism of Action

Niosomes function by encasing active compounds, shielding them from degradation, and orchestrating release profiles in a way that optimizes therapeutic effects. Their mode of action centers on three main themes: drug encapsulation, vesicular transport within the body, and controlled release via bilayer permeation or vesicle breakdown [57].

Encapsulation of Active Agents

Niosomes entrap drugs in their hydrophilic core or within the bilayer, depending on the compound's solubility. Water loving molecules tend to remain in the central aqueous space, while lipophilic or amphiphilic substances reside in the bilayer [58]. The surfactant cholesterol ratio has a major impact on this step; high cholesterol can stiffen the membrane and lower drug leakage but can also dampen drug release by decreasing bilayer permeability [59].

Interaction with Biological Barriers

Depending on how they are administered, niosomes come into contact with various biological barriers, such as intestinal epithelial cells, skin layers, or endothelial cells in the bloodstream [60]. The vesicle size, surface potential, and presence of ligands heavily influence their interaction with such barriers. In transdermal delivery, for instance, smaller vesicles may cross the stratum corneum more effectively, whereas intravenous administration might benefit from sterically stabilized niosomes that evade rapid clearance by the RES [61,62].

Cellular Uptake

Cells often internalize niosomes via endocytosis, particularly when ligands on the vesicle surface target specific receptors [63]. Once inside the cell, niosomes may fuse with endosomes or lysosomes; the acidic environment or enzymatic content can degrade the bilayer, releasing the payload [64]. In cancer therapy, for example, attaching tumor specific ligands to the niosome can boost cellular uptake by malignant cells and reduce nonspecific uptake by healthy tissues [65].

Drug Release Kinetics

Drug release can occur through gradual diffusion across the bilayer or be triggered by destabilizing factors (e.g., acidity, enzymes, or temperature) [59,66]. This controlled release facet is particularly helpful for chronic ailments like arthritis or in chemotherapy strategies requiring sustained or localized drug release to maintain effective concentrations within tumor cells.

In Vivo Biodistribution

Vesicle size, surface charge, and targeting ligands collectively determine how niosomes are distributed within the body [67]. Larger niosomes risk swift uptake by the liver and spleen, whereas sterically stabilized or neutral vesicles can persist longer in circulation [68]. The EPR effect in tumors may also facilitate selective retention of niosomes within malignant tissues [69]. By fine tuning these variables, formulations can be made to distribute effectively while minimizing systemic risks.

Clinical Significance

By taking advantage of encapsulation, targeted uptake, and controlled release, niosomes can elevate therapeutic outcomes for drugs requiring precision. Chemotherapy drugs benefit by localizing cytotoxic effects, and certain antigens in vaccine formulations remain stable while being delivered gradually, maximizing immunogenic response [70,71]. Because each drug and disease condition is unique, scientists can alter niosomal parameters to yield personalized or disease specific delivery profiles. In essence, niosomes act as protective, targeted shuttles for various therapeutic agents. Their success stems from how they unite encapsulation, circulation, and triggered release in a single vehicle a strategy that aligns squarely with efforts to maximize treatment impact while reducing side effects.

Advantages

Niosomes present multiple benefits over conventional dosage forms and other nanocarriers like liposomes. These advantages encompass everything from better drug stability to versatile routes of administration and reduced side effect profiles.

Biocompatibility and Safety

Since non ionic surfactants are generally milder than their ionic counterparts, niosomes often exhibit low toxicity and good biocompatibility [72]. This advantage is vital for treatments needing repeated doses or long term usage. Surfactants from the Tween and Span families, for instance, typically cause minimal irritation, allowing safer formulations in ocular, dermal, or transdermal therapies [73].

Enhanced Drug Stability

Many active agents degrade or lose potency if they encounter enzymes or harsh environments before reaching their target [74]. By encapsulating such agents in niosomes, the drug remains shielded in the core or bilayer, thus boosting overall stability and bioavailability [75]. This enhanced protection is crucial for temperature or enzyme sensitive treatments, such as certain vaccines or protein based drugs.

Dual Encapsulation Potential

Unlike some carriers that favor either water soluble or lipid soluble drugs, niosomes can handle both, thanks to an aqueous core combined with a hydrophobic membrane [76]. This flexibility is especially helpful for combination treatments where two or more active compounds with dissimilar solubilities must be co delivered [77].

Targeted and Controlled Release

Manipulating the niosomal membrane's fluidity or adding targeting ligands can direct niosomes to specific cells or tissues, mitigating non specific distribution [65]. Moreover, the niosome's bilayer composition can be tweaked to yield different release rates, from slow, extended release to more abrupt bursts triggered by pH or temperature changes [78].

Reduced Toxicity and Side Effects

By confining the active agent to the diseased area, lower overall doses are needed, which cuts down on systemic side effects [79]. This approach is especially relevant in chemotherapy, where non target toxicity is a major concern. Another edge niosomes may hold over traditional liposomes is chemical stability in physiological conditions, resulting in more efficient retention of their payload [80].

Cost Effectiveness and Ease of Fabrication

Surfactants and cholesterol are generally cheaper and more resistant to oxidation than many phospholipids, potentially curbing production costs [16]. A variety of fabrication methods (thin film hydration, reverse phase evaporation, microfluidization) can be chosen based on resources and desired product attributes [81]. This adaptability can facilitate the transition from proof of concept experiments to industrial scale production.

Beyond Pharmaceuticals

In addition to drug delivery, niosomes are gaining popularity in cosmetics and nutraceuticals. They can stabilize sensitive molecules like antioxidants or vitamins and deliver them through the skin or GI tract more effectively [11,82]. Their mild nature and capacity to modify release profiles have also appealed to the skincare industry for extended hydration and anti aging benefits.

Multiple Routes of Administration

Because of their structural integrity and compositional adaptability, niosomes can be administered via various routes oral, transdermal, nasal, ocular, or intravenous [83]. For example, flexible niosomes with added "edge activators" can better penetrate the stratum corneum, while ocular formulations can prolong drug residence time on the eye surface [61,84]. This diversity dovetails neatly with individualized medical strategies aiming to optimize each route of administration. All told, niosomes combine design flexibility with robust drug protection and controlled release capabilities. Their ability to increase therapeutic efficacy while limiting toxicity underpins their rising profile in the spheres of pharmaceuticals, cosmeceuticals, and beyond, making them promising tools for next generation, patient centered care.

Applications

Pharmaceuticals

The pharmaceutical sphere has widely embraced niosomes as a means to improve drug effectiveness and lessen adverse effects. In oncology, niosomes loaded with agents like doxorubicin or paclitaxel can boost tumor localization and curb systemic toxicity [85]. Chronic conditions ranging from arthritis to diabetes also benefit from niosomal formulations designed for sustained release, thereby streamlining dosing routines and improving compliance. Additionally, encapsulated anti infectives can target localized infections or bypass resistance mechanisms [86]. Niosome based inhalation treatments are evolving to carry bronchodilators or antimicrobials straight to the lungs, reducing systemic side effects [87].

Cosmetics

Niosomes have also found a niche in the cosmetics industry for delivering vitamins, antioxidants, peptides, and other active ingredients that protect and nourish the skin [88]. Flexible or elastic forms of niosomes can cross the otherwise challenging barrier posed by the stratum corneum [89]. Encapsulating sensitive substances like retinol can lessen skin irritation and oxidation while delivering a slow release that maximizes the product's effectiveness [90]. The extended release capacity makes niosomes ideal for skincare items seeking longer lasting effects.

Vaccines

There is growing momentum in leveraging niosomes for vaccines. Traditional vaccine methods often rely on adjuvants such as aluminum salts, which can provoke side effects. Niosomes, by contrast, may present antigens in a way that bolsters immune processing while also shielding them from enzymatic degradation [91,92]. Efforts to decorate the niosomal surface with specific ligands, like mannose residues, aim to enhance uptake by antigen presenting cells [93]. Non ionic surfactants often show good safety profiles, making them compelling for needle free vaccine formulations, including intranasal or oral delivery routes [94].

Case Studies and Real World Examples

One noted application is the attempt to administer insulin orally by encapsulating it within niosomes potentially circumventing the need for regular injections in diabetic care [95]. There are also documented trials where niosome based antibiotics are used to speed wound healing while regulating infection [96]. In the cosmetic market, certain commercial products now feature niosome encapsulated ingredients to promote anti aging or hydration benefits, showing that the approach resonates with consumers [97]. Early stage clinical studies are exploring whether niosomal vaccines could provide broad coverage against influenza and other emerging pathogens [98].

Comparison with Other Nanocarriers

Liposomes, polymeric nanoparticles, and solid lipid nanoparticles each have their place, but niosomes stand out for their relatively straightforward scale up, chemical stability, and compatibility with both water soluble and lipid soluble agents [99,100]. This dual compatibility and design flexibility often give niosomes an edge in select scenarios though each system has unique strengths and limitations.

Future Directions in Application

Beyond established roles, niosomes show promise in gene therapy, where siRNA, mRNA, or DNA plasmids must be carefully delivered, and in photodynamic therapy, where photosensitizers need precise targeting [101]. They could also integrate with inorganic components like gold nanoparticles for simultaneous diagnosis and treatment (theranostics). In food technology, niosomes may increase the bioavailability and stability of nutrients in functional foods [102]. This broad scope highlights the technology's adaptability and continued evolution. Altogether, the uses for niosomes from pharmaceuticals and vaccines to cosmetics illustrate their capacity for versatile and specialized delivery. Real world examples underscore their growing footprint and underline an expanding frontier for this advanced vesicular system.

Challenges

Despite their broad potential, niosomes face hurdles that can impede widespread clinical adoption. These challenges range from short term stability issues to complex regulatory requirements.

Stability and Shelf Life

Maintaining niosomes' integrity over time is difficult. Temperature swings, pH shifts, and mechanical agitation can cause aggregation, fusion, or drug leakage [103]. Strategies like adding sugars (trehalose, sucrose, mannitol) or lyophilizing the formulation can help, but each solution must be tailored to the specific drug and

surfactant mixture [104]. Freeze drying itself, for instance, can stress the bilayer structure and needs careful optimization.

Encapsulation Efficiency and Leakage

High encapsulation efficiency is critical for maximizing therapeutic output and commercial feasibility. Nonetheless, highly hydrophilic or highly lipophilic molecules may be tricky to encapsulate, leading to subpar loading [105]. Over time, some niosomes can also experience partial drug leakage. Adjusting surfactant type, cholesterol ratio, and other formulation parameters can mitigate these problems, but there is no universal recipe; extensive formulation trials are frequently necessary [106].

Scalability and Reproducibility

Methods like thin film hydration or reverse phase evaporation can be problematic to scale. Uniformly evaporating solvents or forming thin layers might be straightforward in a lab, but is far more complex in industrial sized batches [14]. While continuous flow systems and homogenization based methods may streamline production, differences in hardware and operating conditions can still affect consistency. Further, contamination and compliance with GMP add layers of complexity [107].

Regulatory Hurdles

Because niosomes are relatively modern in drug delivery, they can face extra regulatory examination [108]. Authorities demand rigorous data on toxicity, immunogenicity, biodistribution, and pharmacokinetics. Detailed stability and batch to batch reproducibility studies are also mandatory [109]. Where specialized features like ligand based targeting or stimuli sensitivity are present, even more scrutiny is involved, extending the approval timeline.

High Production Costs and Resource Intensity

While non ionic surfactants might be less expensive than phospholipids, the entire manufacturing pipeline can still be resource heavy. Specialized gear, freeze dryers, and sterile environments all add expense, which can pose challenges for commercial rollout particularly in regions lacking advanced manufacturing infrastructure [16].

Limited Long Term In Vivo Data

Many promising results rest on in vitro or short term in vivo studies [110]. Translating these findings to humans can be complicated by physiological differences across species. Variations in niosome size, composition, and surface modifications can likewise yield inconsistent in vivo outcomes, complicating standardization [111].

Handling and Storage

Certain niosomal preparations need cold chain logistics to retain stability. Inconsistent or repeated freeze thaw cycles in transit can degrade vesicles [112]. Such practical constraints can limit global distribution, particularly in remote regions without reliable refrigeration. In summary, while niosomes offer a compelling route for drug delivery, these obstacles underscore the importance of rigorous formulation research, stable scale up methods, and collaborations among academia, industry, and regulators. Continued innovation in materials science, process optimization, and regulatory science will be crucial in fully leveraging niosomes as mainstream therapeutic options.

Recent Advances

Research around niosomes continues to advance at a fast pace, with a focus on refining targeting capabilities, optimizing release patterns, and ensuring manufacturing consistency. Below are notable developments propelling niosomes closer to clinical practice.

Stimuli Responsive Niosomes

A trend of great interest is creating niosomes that respond to triggers like pH, temperature, or enzymes [25,113]. For example, incorporating pH sensitive polymers allows for drug release predominantly in acidic tumor environments [114]. Temperature sensitive niosomes, for instance, can break down when subjected to mild hyperthermia in cancer treatments [115]. These refinements aim to elevate local concentrations of the drug and reduce systemic damage.

Ligand Modified and Targeted Systems

Attaching peptides, antibodies, or small molecules (e.g., folic acid) to the niosomal surface has enabled precise receptor mediated uptake by specific cells [116]. Some research highlights aptamers short nucleic acid sequences with high affinity for distinct proteins as an emerging strategy for tuning targeting specificity [117].

Coupling diagnostic and therapeutic agents (theranostics) in a single niosome also allows clinicians to track vesicle localization and simultaneously administer treatment [118].

Hybrid Niosomal Constructs

Researchers are experimenting with blends that combine features of niosomes and other nanocarriers. Hybrids of liposomes and niosomes may fuse the structural stability of niosomes with the fluidity and biocompatibility of liposomes [119]. Alternatively, embedding polymers or dendrimers in niosomes can enhance mechanical robustness or modulate release kinetics [120]. These hybrids can handle complex therapeutic goals, such as delivering multiple drug types.

Green and Sustainable Methods

Given environmental concerns, interest is rising in solvent free or low solvent niosome production, such as using supercritical CO2 or microfluidic setups that cut down waste [56,121]. Proniosome based approaches also see renewed focus, as they negate the need for organic solvents in storage. Such eco friendly methods could reduce both cost and environmental impact while meeting regulatory expectations for "greener" pharmaceuticals.

Advanced Characterization Tools

Use of cryo TEM, AFM, and nanoparticle tracking analysis (NTA) has grown, allowing scientists to view real time structural changes and measure size distribution with great precision [122]. These insights refine formulation strategies, bridging the gap between lab tests and consistent in vivo performance.

Clinical Translation

While many niosomal therapeutics are still in preliminary or early clinical evaluation, progress is being made. Trials examining niosome encapsulated cancer drugs or niosome based vaccines against influenza illustrate the growing confidence in these systems' safety and functionality [98,123]. Partnerships among universities, pharmaceutical firms, and CROs will likely accelerate the path from lab benchtop to patient bedside. Collectively, the recent progress in stimuli responsive, targeted, and hybrid niosomes highlights the continuous movement toward more personalized, efficient, and environmentally mindful drug delivery technologies. As these innovations are refined, they aim to address key stumbling blocks like stability and scalability making niosomes a promising force in future medical and related fields.

Future Prospects

Niosomes hold ample promise for reshaping drug delivery and, by extension, treatment outcomes. Here are some overarching themes that might guide future work in this area.

Personalized Medicine and Tailored Formulations

Personalized medicine focuses on customizing treatment based on an individual's genetic and clinical profile [124]. Niosomes, through their adaptable makeup and ability to be functionalized, appear well suited for this paradigm [125]. Tailored formulations might include drug mixtures specified for a patient's tumor biomarkers or ligands matched to overexpressed receptors on diseased cells.

Integration with Emerging Technologies

Artificial intelligence (AI) and machine learning can speed up the process of refining niosomal formulations, predicting how changes in surfactant concentration or process parameters influence size, stability, or drug loading [126]. Microfluidic and 3D printing techniques may enable on demand creation of niosomal therapies within hospital pharmacies, matching dosage and release profiles to individual patient needs [127]. Biosensors and wearable devices could eventually inform real time adjustments to "smart" niosomes, which modulate drug output in response to physiological signals like blood glucose [128].

Overcoming Large Scale Production and Regulation

Expanding to commercial scale manufacturing remains a top priority. Continuous flow reactors and automated quality monitoring systems can produce uniform, large batches of niosomes while minimizing human error [129]. Clearer guidelines and standardization covering nomenclature, quality assessments, and stability testing would facilitate smoother regulatory approvals [130]. This is an area where collaborative frameworks bridging academia, industry, and government bodies could prove highly impactful.

New Therapeutic Horizons

Gene therapy, immuno oncology, and treatments for chronic inflammation or neurological diseases might all benefit from niosomal carriers [131,132]. Since certain gene editing tools or immunological agents demand precise delivery to specific cells, the tailored, targeting potential of niosomes could be pivotal. Likewise, future

cosmeceutical and nutraceutical formulations may incorporate advanced functionalities, including environmental triggers to protect active components or release them precisely when needed [133,134].

Ethical and Sustainability Issues

With any novel technology comes ethical considerations such as equitable distribution, potential misuse, and long term environmental impact. Emphasizing green chemistry, opting for biodegradable materials, and implementing responsible disposal practices for niosome production can address growing sustainability demands [121,135]. Policies must also ensure fair access to advanced treatments, preventing a "technology gap" between resource rich and limited resource regions.

All in all, niosomes occupy a unique position as adaptable drug carriers, primed for synergy with cutting edge technologies and a future leaning strongly toward customization. Continued efforts in scaling up manufacturing, clarifying regulatory pathways, and embracing sustainability can help niosomes realize their full potential across the health, cosmetic, and wellness sectors.

CONCLUSION

Niosomes exemplify the intersection of chemistry, nanotechnology, and pharmaceutical sciences, providing a multifaceted platform for delivering a wide range of therapeutic agents. Originating as non ionic surfactant vesicles, niosomes now encompass sophisticated, adaptable systems that encapsulate diverse substances, from small drugs to larger biomolecules like proteins, vaccines, and nucleic acids. Their customizability, biocompatibility, targeted release capabilities, and relative cost effectiveness have spurred intense interest among researchers and industry developers.

In this article, we examined how niosomes are structured, how they are formulated, and how they achieve their characteristic drug delivery effects. We also explored their distinct benefits enhanced stability, lower side effects, adaptability to varied drug types and highlighted practical examples of their success in treating cancer, facilitating vaccines, and advancing cosmetic and nutraceutical applications. Meanwhile, we recognized the technical, regulatory, and economic challenges, underscoring that bridging the gap from lab prototypes to routine clinical use requires meticulous optimization and extensive collaboration.

Promising avenues for further innovation include developing stimuli responsive designs, integrating ligand based targeting, and adopting green manufacturing processes. Emerging technologies such as AI assisted formulation and continuous flow reactors may help refine niosomes for large scale production. As these methods mature, it seems increasingly likely that niosomes will play a prominent role in advancing disease targeting strategies, from conventional therapies to more experimental areas like gene editing and immunotherapy.

In summary, niosomes stand at the forefront of next generation delivery systems, enabling a more targeted, efficient, and potentially safer therapy regimen. By pushing forward on key fronts stability, scalability, regulatory clarity, and personalization these versatile vesicles could dramatically shape the evolution of pharmaceuticals, cosmetics, and other related fields, moving healthcare closer to the ideal of personalized, optimized treatment for every patient.

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