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Review Article

Niosomal Nanovesicular Spray Systems for Topical Drug Delivery: Formulation Strategies, Characterization, and Therapeutic Applications

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A B S T R A C T

Topical drug delivery is commonly used for localized therapy, but conventional gels, creams, and ointments often face limitations in skin penetration and consistent therapeutic response. Niosome-based nanosprays provide an advanced alternative by encapsulating both hydrophilic and lipophilic drugs in non-ionic surfactant vesicles with a bilayer structure. Key formulation factors affecting performance include surfactant type, cholesterol content, vesicle size and surface properties, and drying methods. Converting liquid dispersions into dry nanospray powders enhances stability, handling, and storage while preserving vesicle integrity. Preclinical studies show that niosomalnanosprays penetrate deeper skin layers, extend dermal retention, and improve therapeutic outcomes for dermatological and inflammatory conditions compared with traditional topical systems. Despite these advantages, challenges remain in scaling up production, ensuring long-term stability, and validating clinical efficacy. Employing quality-by-design strategies and optimizing formulations are essential for translating niosome-based nanosprays into commercially viable and effective therapeutic products.

Keywords: Niosomes; Nanovesicular spray systems; Topical drug delivery; Transdermal therapy; Nanospray drying technology

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INTRODUCTION

Niosomes are vesicular drug delivery systems composed of non-ionic surfactants and cholesterol that can encapsulate both hydrophilic and lipophilic drugs(1).As shown in Figure 1, the niosomal system exhibits high compatibility with solvents resulting in increased stability, bioavailability and solubility of both hydrophilic and lipophilic agents. In1975,researchers introduced niosomes in order to solve the limitationsof liposomal drug delivery(2). Niosomes are produced by the self-assembly of non-ionic surfactants (such as Span, Tween or their derivatives) with cholesterol, thus creating a bilayer structure that behaves like liposomes, but also contains unique physicochemical properties based on the way the components within the niosome are combined (3). Although numerous studies have explored niosomal vesicles for drug delivery, most reviews primarily focus on conventional liquid dispersions or semisolid formulations. Limited attention has been given to the development of nanospray-dried niosomal systems that combine vesicular carriers with advanced spray drying technology. Such systems may improve storage stability, facilitate controlled drug release, and enable convenient administration through topical or mucosal routes. Therefore, the present review aims to summarize current progress in the formulation of niosomal systems, the principles of nanospray drying, and the potential applications of spray-based vesicular drug delivery platforms.Although numerous studies have reported the development of niosomal drug delivery systems, limited attention has been given to the integration of vesicular carriers with nanospray drying technology. The combination of these two approaches may significantly improve formulation stability, storage properties, and drug delivery efficiency. This review therefore summarizes current advances in niosomal formulation strategies and nanospray drying technology, with particular emphasis on their potential for topical and mucosal drug delivery applications(4-6).

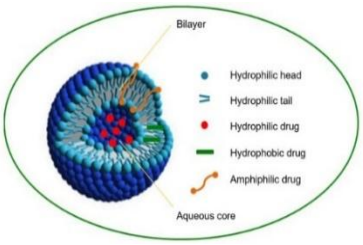

Figure 1: Structure of niosomal vesicle

Table 1. Classification of niosomal systems along with their structural composition and the major functional advantages associated with their use in drug delivery applications.

Aspect	Details
Types of Niosomes	Proniosomes – dry precursor systems forming niosomes upon hydration; Elastic niosomes – deformable vesicles for enhanced transdermal delivery; Polyhedral niosomes – geometrically defined vesicles; Discomes – disc-shaped, structurally stable vesicles; Aspasomes – vesicles containing ascorbyl palmitate with antioxidant potential(7).
Core Components	Non-ionic surfactants (Span, Tween) forming bilayer membrane; Cholesterol for membrane rigidity and reduced leakage; Charge-inducing agents (dicetyl phosphate, stearylamine) to prevent aggregation; Edge activators (Tween 80, PEG) for flexibility and enhanced penetration; Aqueous core for hydrophilic drug entrapment(8).
Formulation Variables	Surfactant:cholesterol ratio (commonly 1:1 or 2:1) influences vesicle stability, entrapment efficiency and release characteristics(9).
Key Advantages	Improved oxidative and hydrolytic stability; cost-effective production; adaptable for oral, topical, parenteral and transdermal routes; protection of labile drugs; capability to encapsulate both hydrophilic and lipophilic drugs; relatively low toxicity due to non-ionic nature(10).

Mechanism of skin permeation of niosomes

Several mechanisms of penetration have been described: Niosomes aggregate, fuse, and adhere to the membranes of the corneocytes, creating high thermodynamic activity of the drug at the interface between vesicles and stratum corneum, thus driving the diffusion of lipid-soluble drugs into and through the barrier.

Niosomes can disrupt and liquefy the lipids in the stratum corneum, helping to make the intercellular barrier more"loose" and permeable, with the non-ionic surfactant acting as a penetration enhancer.Some intact vesicles may penetrate the upper layers of the stratum corneum or through appendageal routes (like hair follicles), and act as local depots of drugs that provide sustained release(11).

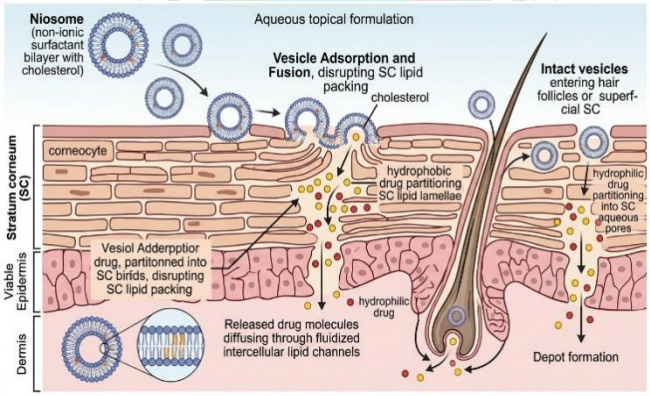

Figure 2: Mechanism of drug transport through skin using niosomes.

Table 2: Comparative overview of different vesicular carriers used in transdermal and topical drug delivery, highlighting differences in composition, flexibility, penetration mechanisms, and stability (12-15).

Feature	Niosomes	Liposomes	Transfersomes	Ethosomes
Main components	Non-ionic surfactants with cholesterol	Phospholipids with cholesterol	Phospholipids with edge activators	Phospholipids with high ethanol content
Flexibility	Moderately flexible	Relatively rigid	Highly deformable	Highly flexible due to ethanol
Penetration mechanism	Surfactants disturb skin lipids and promote vesicle fusion	Mainly act by hydration and occlusion of the skin barrier	Elastic vesicles pass through narrow intercellular spaces	Ethanol fluidizes skin lipids enabling deeper permeation
Depth of delivery	Mainly epidermal	Mostly superficial	Deeper epidermal or dermal delivery	Often deepest penetration

Stability & cost	Stable and relatively inexpensive	Costly with possible phospholipid degradation	Less stable due to edge activators	Ethanol may affect long-term stability
Irritation potential	Usually low	Low and well-established safety	Possible irritation at high surfactant levels	Ethanol may cause dryness or irritation

NIOSOMAL NANOSPRAY

Nanospray drying has become a pivotal manufacturing method for converting water-based niosome dispersions to solid-form, stable and easily handled forms of niosomes (solid-form niosomes).The nanospray dry process enables quick removal of solvents at high speeds in combination with controlled morphology of the particles thus maintaining the integrity of the niosomal formulation while making niosomes dry powders ready to use for pharmaceutical product development[16,17].

Through the combination of using niosomes and nanospray-drying techniques, greater control of particle characteristics such as size/shape and moisture content occurs, all of which are critical to the successful release of drugs from niosomes and, further, to provide drugs with improved bioavailabilityand reproducibility with each batch of niosomes. Compared to traditional spray-drying processes, nanospray-drying creates smaller droplets due to shorter droplet retention time during drying, therefore less thermal damage to temperature-sensitive drugs, and less chemical degradation due to dryness of resulting powders. Due to these characteristics of the nanospray-dried niosomes they are ideally suited for non-invasive delivery methods such as nose, lungs or skin[18-23].

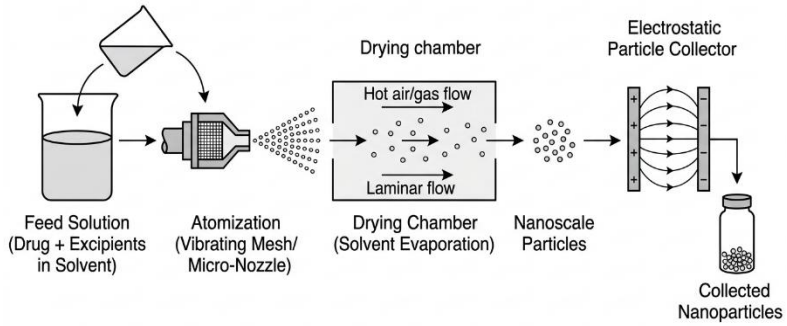

Figure 3: Basic steps involved in the nanospray drying process.

Ideal Characteristics of Niosomal Nanospray

1. Efficient drug entrapment is essential to improve therapeutic performance. A well-designed niosomal system should be able to carry both hydrophilic and lipophilic drugs effectively.
2. Niosomal nanosprays with particle sizes around 100–300 nm and uniform distribution help achieve better drug release and enhance penetration across biological barriers, improving cellular uptake.
3. Stability during storage and use is critical. Maintaining vesicle integrity prevents drug leakage and aggregation, while nanospray drying into powder form improves stability by reducing moisture-related degradation.
4. The formulation should allow controlled and sustained drug release, ideally responding to factors like pH, temperature, or enzymes, to ensure targeted action and minimize side effects.
5. All formulation components, especially surfactants and cholesterol, must be safe and non-irritating, ensuring compatibility with the body for different routes of administration such as nasal, pulmonary, or topical use[24].

Nanospray Performance of Niosomes is affected by a Variety of Factors

1. **Surfactant Concentration or Type :** The selection of non-ionic surfactant (Span, Tween) has an impact on how vesicles will be formed, what size they are, and whether they are stable.
2. **Cholesterol Content :** Cholesterol acts to stabilize the niosome's bilayer, increase its rigidity, and decrease the niosome's permeability.
3. **Manufacturing Method :** Physically manufacturing niosomes by using thin film hydration, reverse phase evaporation, or microfluidization may yield niosomes with different lamellarity, drug loading, or sizes; Drying using nanospray drying needs to control inlet temperature, feed rate, atomization, and other similar parameters in order to produce a particle that has an optimal morphology and moisture content.
4. **Drug Properties :** The molecular weight of the drug being encapsulated, its solubility, and whether or not it is stable will all determine how efficiently and completely the drug is encapsulated and released from a niosome. A hydrophobic drug will typically form part of the bilayer structure of a niosome, while a hydrophilic drug will be found in the niosome's aqueous core
5. **Environmental Conditions :** The stability of a niosome including how well it will release its drug will be affected by environmental conditions, such as pH, ionic strength, and temperature. Stimuli-responsive niosomes are able to

sense their pathological microenvironment and to release their drug quickly once they reach that location.

6. **Route of Administration:** The route of administration (e.g., nasal, pulmonary, or topical) determines the differences in the drug delivery system as indicated by the requirements associated with the formulation for the specific route of administration (e.g., particle size, moisture content, and compatibility of excipients with the drug). The formulation of Niosomal Nanospray Technology utilizes the benefits of modernizing the formulation process and additionally modernizes the drying (i.e., the production of stable nanoparticles) to deliver targeted delivery systems for increased efficacy of drugs[25].

Drug Release Behavior of Nanospray-Dried Niosomes

Nanospray-dried niosomal systems release drugs via either diffusion through their vesicular membranesor matrix degradation, or also by some combination of these processes. The majority of formulation release profiles typically have a very rapid initial phase due to surface-associated drug(s) and a longer-lasting phase dueto drug diffusion from the liposome into the bilayer or aqueous core. Many mathematical models of these systems also agree with diffusion kinetics, indicating the importance of noisome construction in determining the drug transport mechanisms for all these formulations.

Another factor that affects the rate of drug delivery/absorption is the method of administration. In particular, a nanospray-dried niosome product may improve the ability to interact with and remainon the nasal and pulmonary mucosa, thereby increasing inhaled drug absorption. In the case of transdermal drug administration, the niosomestructure can enhanceinteractions with dermal lipids, thus producing localized drug deposition and a prolonged release profile [26,27].

Broader Pharmaceutical Relevance of Nanospray Technology

Beyond particle size control, nanospray drying contributes to improved formulation robustness by enabling the production of dry powders with reduced hygroscopicity and enhanced storage stability. The technology also offers opportunities for surface functionalization and co-processing with stabilizing excipients, allowing the development of multifunctional delivery systems. From a manufacturing perspective, nanospray drying represents a bridge between laboratory-scale formulation development and scalable solid dosage production, although further optimization is required to address throughput and regulatory validation[28-33].

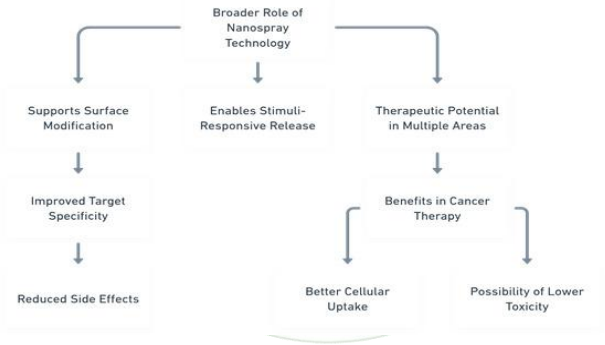

Figure 4: Role of nanospray technology in improving drug delivery performance.

Recent Research on Niosomal and Nano Spray-Dried Vesicular Systems

Table 3: Summary of selected recent studies reporting the development and evaluation of niosomal formulations and nanospray-dried vesicular delivery systems.

Author(s)	Drug / Active Compound	Delivery System / Formulation	Key Findings	References
Glaubitt K., et al. (2019)	Lipid-based formulations	Nano spray-dried solid lipid nanoparticles	Nano spray drying enabled conversion of SLN emulsions into dry powders with good recovery. However, certain lipid compositions showed a tendency toward particle aggregation during drying.	(34)
Makvana C., et al. (2019)	Antihypertensive agent	Niosomal controlled-release formulation	Optimized niosomal vesicles demonstrated high drug entrapment efficiency (79–98%) and vesicle sizes ranging from 2.5–3.4 µm, producing sustained drug release profiles.	(35)
Elbary A.A., et al. (2021)	Chloroquine	Spray-dried niosomes for pulmonary delivery	Spray drying with lactose carriers produced inhalable niosomal powders that prolonged lung retention while minimizing systemic exposure.	(36)
Aldawsari M.F., et al. (2021)	Nanoparticle formulations	Chitosan nanocomposite microparticles prepared by nano spray drying	The nano spray drying process improved aerosol performance and encapsulation efficiency, suggesting suitability for pulmonary drug delivery systems.	(37)

Ghasemiyeh P., et al. (2024)	Lipid-based drugs	Spray-dried solid lipid and nanostructured lipid carriers	Spray drying provided scalable production of stable lipid nanoparticle powders with enhanced drug stability and improved potential for inhalation therapies.	(38)
Patel R., et al. (2023)	Various therapeutic agents	Spray-dried nanoparticle agglomerates	Controlled agglomeration of nanoparticles into respirable microparticles improved lung deposition and enhanced therapeutic performance in respiratory applications.	(39)
Alshehri S., et al. (2020)	Repaglinide	Surface-modified niosomes	Modification of surfactant composition and vesicle charge significantly enhanced oral bioavailability of the poorly soluble antidiabetic drug.	(40)
Makwana C., et al. (2024)	Nisin	Niosomes incorporated into fast-disintegrating films	Microfluidic-prepared niosomes provided sustained drug release and demonstrated antimicrobial activity against Gram-positive bacteria when delivered via oral mucosal films.	(41)
Demir S., Degim I.T. (2020)	Chitosan (model polymer)	Chitosan nanoparticles via nano spray drying	Particle size could be controlled by adjusting spray dryer nozzle size; increased polymer concentration improved yield and surface charge stability.	(42)
Arpagaus C., et al. (2022)	Peptides and proteins	Nano spray-dried vesicular formulations	The technique allowed gentle drying of thermosensitive biomolecules producing particles as small as ~300 nm with high production efficiency.	(43)

MAJOR ADVANCEMENTS: Three major advancements that have contributed to the development of niosomal nanospray formulations as successful drug delivery vehicles can be categorized as follows: Surfactant compositions, surface modifications and stimuli responsive niosomal formulations.

1. **Optimized surfactant compositions:** The use of specific non-ionic surfactants in combination is vital for the formulation of niosomalnanosprays, as they each affect the size, stability and drug loading ability of the niosome vesicle. Surfactants with a different Hydrophilic-Lipophilic Balance (HLB) Value can therefore be selected to provide a variety of vesicle characteristics.By selecting surfactants that have appropriate HLB values, the manufacturers can create a stable and uniform niosome. Manufacturers may use a combination of surfactants with different HLB values to generate vesicles that possess a higher degree of structural integrity, and to retain the drug for longer periods of time during storage[29].Novel amphiphilic surfactants based upon natural sources, such as sugars and amino acids, are being investigated as a means of providing niosomes with an improved safety profile. These surfactants enhance the biocompatibility of niosomes while also reducing irritancy and/or toxicity. Overall, the advancements noted above will enable improvements in formulation performance through the determination of greater physicochemical stability, increased entrapment efficiency, and improved controlled release of drug in vivo[(44,45)].

2. **Surface Modification:** Another significant improvement in niosomal nanospray formulations is the incorporation of surface-modified niosomes for targeted delivery. Researchers have created new targeted drug delivery systems by using specific ligands and/or molecules to modify the surface of the niosomes.These targeted drug delivery systems can selectively accumulate within desired tissues/organs, and they are particularly promising in the field of Cancer Therapy because niosomes that have been modified with tumor-specific antibodies/peptides increase drug accumulation within Tumor tissues and decrease off-target effects.The incorporation of cell-penetrating peptides onto the surface of niosomes has allowed drugs to be delivered intracellularly by providing them access to the intracellular milieu bypassing cellular barriers that typically impede their effectiveness.The surface modification of niosomes using polyethylene glycol (PEG), has also been widely used to generate "Stealth" Niosomes, increasing circulation times and decreasing the clearance of niosomes via the reticuloendothelial system. Mucosal Penetration and Bioavailability: The introduction of nanospray formulations significantly improves mucosal penetration and bioavailability of niosomes. By enabling niosomes to penetrate mucosal barriers more efficiently than previously possible, nanosprays facilitate the cellular absorption of niosome formulation drugs, resulting in increased drug bioavailability for poorly soluble or poorly absorbed drugs.The improvements made in mucosal penetration and bioavailability through nanospray formulations expand the number of drugs eligible for noninvasive delivery options as well as improving therapeutic outcomes[(45-47)].

3. **Stimuli-responsive niosome systems**: It is an advanced application of niosome technology which offer the ability to control drug delivery at the target site through the use of chemical/physical changes induced by internal or external stimuli. An example of this type of niosome system is the pH-dependent niosome system. These niosome systems utilize the acidic microenvironment associated with tumor tissue and/or intracellular compartments to enable drug release at a defined pH. The formulation typically includes lipid/polymers that exhibit a pH-dependent structure change (e.g., conformation or degradation) under acidic conditions which results in the

destabilization of the niosome vesicle and drug release.Thermoresponsiveniosome systems have also been researched; this system utilizes the temperature-dependent phase transitions of the thermosensitive component which trigger drug release when they reach their target temperature. These systems have been found to be effective when combined with localized heating (e.g., hyperthermia) for treating cancers. Additionally, redox-responsive niosomesystems release their contents in response to elevated levels of glutathione in tumor cells, providing an alternative approach to intratumoral drug delivery. Light-responsive or ultrasound-responsive niosome systems can be employed as methods to locally trigger the release of the therapeutic agent(s) in a precise time frame and location, leading to potentially better therapeutic effects with minimal side effects[48-50].

4. **Nanospray Drying Technologies:** The development of nanospray dry technology has made it possible to manufacture dry powder niosomes that have uniform size and shape. These dry powders are more stable than other methods of producing niosomes and are ideal for administration through the lungs (pulmonary route) or nose (nasal route). Administering drugs through these routes provides new opportunities to treat both respiratory illnesses and systemic conditions without requiring injections, increasing comfort and compliance for patients[51,52].

5. **Pulmonary drug delivery applications:** Niosome formulations are being examined for their ability to deliver drugs through the pulmonary route. Niosome formulations have the ability to deposit drug deep within the lung, therefore improving lung delivery of the drug to the alveoli. Additionally, niosome formulations protect the drug from degradation by enzymes located within the lung and thus allow for sustained release of drugs over time, reducing dosing frequency.The administration of medication through the lungs using niosome-based products for people who suffer from conditions such as asthma, COPD, and lung cancer has many advantages over existing treatment options[53,54].

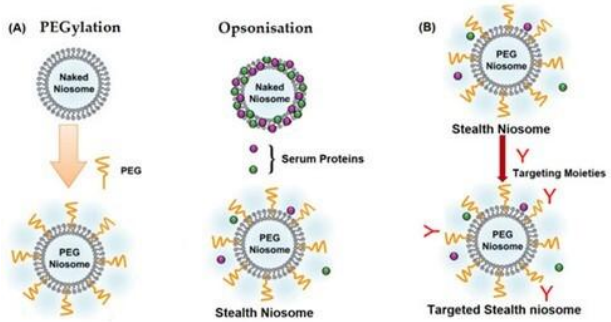

Figure 5: Surface modification of niosomes for improved circulation and targeting.

The advantages of Niosomal Nanospray are summarized in table 3(55-57).

Table 4: Advantages of Niosomal Nanospray

Advantage	Description
A. Improved stability	Niosomal nanosprays offer better protection for drugs against light, heat, and pH variations. Their bilayer structure shields active compounds from degradation, resulting in longer shelf life and improved therapeutic reliability.
B. Lower cost	The use of non-ionic surfactants and a simpler production method makes these systems more economical than many other nanocarriers. Lower material cost and straightforward scale-up reduce overall manufacturing expenses.
C. **Easier large-scale production**	The preparation method can be readily transferred to industrial equipment, allowing smooth scale-up from lab batches to commercial quantities. This supports their feasibility for mass production.
D. **Better control over particle size**	Nanospray technology provides precise control over particle size and uniformity. Consistent particle distribution helps achieve predictable drug release and effective targeting.
E.Higher drug encapsulation efficiency	The vesicular structure accommodates both water-soluble and lipid-soluble drugs, allowing more of the drug to be trapped within the niosomes. This can reduce the required dose and limit wastage.
F.Enhanced cellular uptake	Their nanoscale size and favorable surface characteristics promote better interaction with cell membranes. This leads to improved internalization and stronger therapeutic activity, especially for drugs with limited cellular penetration.

Table 5: Comparative evaluation of nanospray drying and commonly used particle fabrication techniques in pharmaceutical drug delivery(58-60).

Attribute	Nanospray Drying	Conventional Spray Drying	Freeze Drying (Lyophilization)	Vesicle Preparation without Drying
Typical particle size	100–300 nm	0.5–5 µm	Micron-scale aggregates	200–1000 nm
Particle size uniformity	High	Moderate to low	Low	Low
Encapsulation efficiency	High	Moderate	Variable	Moderate
Exposure to thermal stress	Moderate (short exposure)	High	Minimal	None
Moisture content of final product	Low	Moderate	Very low	High
Physical stability during storage	High	Moderate	High	Low

Powder flow and dispersibility	Good	Moderate	Poor (requires post-processing)	Not applicable
Process duration	Short	Short	Long	Short
Scalability	Moderate (emerging industrial adoption)	High	Limited	Limited
Suitability for inhalation or nasal delivery	High	Limited	Limited	Poor
Regulatory familiarity	Emerging	Established	Established	Limited

These characterization techniques provide essential information regarding vesicle stability and drug loading capacity. Particle size and zeta potential measurements are particularly important because they influence vesicle aggregation, storage stability, and interaction with biological membranes.

QUALITY BY DESIGN (QBD) OF NIOSOMAL NANOSPRAY: By first defining what "quality" means to the patient and then methodically determining which materials, production stages, and qualities need to be regulated, Quality by Design provides an organized approach to creating a niosomal nanospray. QbD is particularly helpful for connecting formulation parameters to particle size, stability, and performance in nanosystems such as niosomes/nanocrystals.

1. **Essential QbD Components**: CMA, CPP, and CQA the Quality Target Product Profile (QTPP) is the first step in QbD for pharmaceuticals. Next, Critical Quality Attributes (CQAs), Critical Material Attributes (CMAs), and Critical Process Parameters (CPPs) are identified, and they are connected by risk assessment and Doe.

a) **CQAs** are characteristics that must not exceed certain thresholds in order to guarantee quality; in nano, semi-solid, and topical systems, these characteristics include drug concentration, particle size and distribution, pH, rheology/viscosity, penetration rate, and chemical, physical, and microbiological stability.
b) **CMAs:** important characteristics of drugs and excipients that influence CQAs, such as API solubility, polymorph, lipophilicity, particle shape, surfactant type/HLB, and stabilizer level.
c) **CPPs:** Process variables such as mixing speed, temperature, milling speed/time, addition order, and heating/cooling rates are examples of CPPs whose variability affects CQAs[61-64].

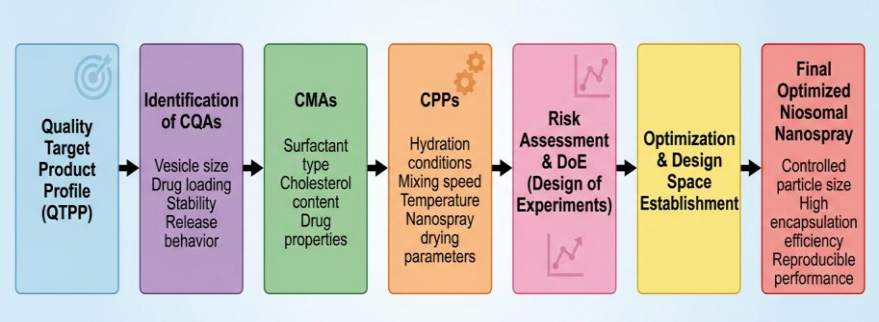

Figure 6: Quality by Design (QbD) approach for optimization of niosomal formulations.

Recent Patents on Niosomal Spray Systems

Recent patent filings demonstrate increasing interest in vesicular systems for dermal drug delivery. Several innovations describe the use of niosomal carriers to improve drug stability, enhance penetration through the skin barrier, and optimize therapeutic performance

Table 6: Representative patents describing recent innovations related to niosomal formulations and nanovesicular spray systems for dermal and topical therapeutic applications.

Patent Title	Patent Number	Year	Country / Office	Key Innovation	References
Topical composition containing cannabidiol-loaded niosomes	US20230081357A1	2023	United States (USPTO)	Describes a dermal formulation in which cannabidiol is encapsulated in nanoscale niosomal vesicles to improve stability and enhance penetration through the skin barrier.	(65)
Topical pharmaceutical formulation for treatment of chronic pelvic pain	US20240033213	2024	United States (USPTO)	Reports a topical therapeutic system incorporating active agents within niosomal carriers to promote improved permeation and localized therapeutic action.	(66)
Therapeutic topical composition for skin applications	WO2025078919A1	2025	WIPO (International Patent)	Introduces an advanced dermal formulation designed for skin treatment that can accommodate nanovesicular delivery systems to enhance drug transport across the skin.	(67)

Current clinical data and translation status

1. Despite extensive preclinical investigation, the clinical translation of niosomal drug delivery systems remains limited. The majority of reported studies focus on in vitro characterization and animal models, with relatively few formulations progressing to human evaluation. Where clinical data are available, they predominantly involve topical semisolid preparations rather than spray-based delivery systems.
2. For nasal and pulmonary administration, nanospray-dried niosomal formulations are largely confined to preclinical research, often utilizing rodent models or ex vivo tissue to demonstrate enhanced drug deposition and absorption. Although these findings highlight the potential of niosomalnanosprays for non-invasive delivery, they do not yet provide sufficient evidence to support clinical adoption. To date, no fully developed niosomal nasal or ocular spray has received regulatory approval for human use.
3. Key translational barriers include challenges associated with large-scale manufacturing, batch-to-batch reproducibility, and long-term safety evaluation. In addition, regulatory expectations for inhalation and nasal products impose stringent requirements on particle size control, aerodynamic performance, and excipient safety. Addressing these issues will require coordinated efforts integrating formulation science, process engineering, and regulatory strategy to advance nanospray-dried niosomal systems toward clinical and commercial viability[68,69].

Scale-Up and Manufacturing: In addition to improving how nanospray formulations enhance mucosal penetration and bioavailability, great steps forward have also been made in the scale-up of production and manufacturing methods of niosomalnanosprays. With the advancement of drying apparatuses and quality-assurance-testing protocols developed for nanospray formulations, consistent reproducibility and batch-to-batch consistency have been achieved, thus providing for clinical translatability.Scalable methods for producing niosomal nanospray products support the transition from laboratory studies to commercial use and clinical application, allowing for future widespread acceptance of niosomal nanospray-based drug delivery technologies[70-73].

CHALLENGES AND FUTURE DIRECTIONS.

Challenges of Large-Scale Production: One challenge of the commercial large-scale production of niosomal nanospray formulations is the requirement to maintain precise control over several key variables to ensure consistent , maintain consistent size, form and encapsulation efficiency of nanoparticles. In addition, producing uniformity across large batches is key to ensuring that the finished product meets all regulatory guidelines and is of acceptable quality. Current lab-scale techniques may not provide an accurate representation of industrial methods, thus requiring the development of new manufacturing equipment and processes. Some potential methods for large-scale production include continuous flow and microfluidics, both of which are still in need of additional optimization. There is also a need to investigate the economic viability of manufacturing Niosomal Nanospray formulations at a commercial scale in order for them to be economically feasible.[74,75].

Despite promising research outcomes, several challenges remain in the development of niosomal nanospray formulations. These include potential vesicle aggregation during drying, limited large-scale manufacturing processes, and variations in formulation stability during long-term storage. In addition, regulatory guidelines for vesicular nanosystems are still evolving, which may complicate the translation of laboratory findings into commercial pharmaceutical products(76).

Areas for Future Research

1. Enhance the specificity of the targeting of the drug using novel methods for surface modification to enhance the tissue selective capability of the formulation.
2. To develop stimuli responsive niosomes for releasing the drug at defined points in time based on the physiological stimulus that is affecting the patient.
3. Enhance the understanding of the biodistribution and metabolism of niosome formulations and their long
4. term safety.
5. Create predictive in vitro models of niosome formulation performance that better correlate with in vivo performance.
6. Investigate using niosome formulations for Gene Therapy, vaccines, and Diagnostic imaging.
7. Implement Green Synthesis methods to promote a more sustainable environment.
8. Future research should focus on optimizing formulation parameters to improve vesicle stability during the nanospray drying process. Advances in formulation design, process optimization, and quality-by-design approaches may further enhance the reproducibility and scalability of niosomal nanospray systems. Additionally, clinical investigations will be necessary to confirm the therapeutic benefits and safety of these delivery platforms.

CONCLUSION: Niosomal nanovesicular spray systems represent a significant advancement in modern drug delivery research, offering an innovative solution to overcome the limitations associated with conventional topical formulations. By combining the structural advantages of niosomal vesicles with nanospray drying technology, these systems provide improved drug stability, enhanced penetration through biological barriers, and controlled release characteristics. Their ability to encapsulate both hydrophilic and lipophilic molecules further expands their applicability across diverse therapeutic areas. Recent developments in formulation design, surface modification, and quality-by-design approaches have strengthened the potential of these systems as efficient carriers for targeted and non-invasive drug delivery. Despite promising experimental outcomes, important challenges such as large-scale production, regulatory evaluation, and clinical confirmation must still be addressed. Continued

interdisciplinary research integrating pharmaceutical formulation, process engineering, and clinical investigation will be critical to translate niosomal nanospray platforms into reliable and commercially viable therapeutic technologies.

CONFLICT OF INTEREST: The author's declare no conflict of interest.

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