Chapter 7

Oral Noisome and Proniosomes: Mechanistic Insights, Formulation Strategies, and Therapeutic Applications in Enhancing Bioavailability and Targeted Drug Delivery

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Abstract

Oral drug delivery is still the easiest and most popular way to take medicine, but it comes with a lot of problems. Some drugs just don't dissolve well in water, or they can't pass through the gut easily. Others break down because of enzymes or get wiped out by first-pass metabolism, so the body barely absorbs them, and they don't work as well as they should. That's where vesicular systems like liposomes and their dry forms, proniosomes, come in. These carriers, made from non-ionic surfactants and cholesterol, protect drugs from breaking down in the digestive tract and let the medicine release slowly over time. How you put these together really matters. Things like the type of surfactant, how much cholesterol you use, the size of the vesicles, and their surface charge—all these affect how much of the drug gets into your system and how quickly. Modifying the surface, say by adding PEG or coating with chitosan, helps the drug stick to mucosal surfaces, improves how well it passes through, and makes it tougher

against enzymes. Drugs get absorbed better thanks to things like increased endocytosis, tweaks to tight junctions, and transport through the lymphatic system. This review digs into how these vesicular systems are designed, how they help drugs get absorbed, what you need to look for when testing them, and what it takes to actually use them in real-world treatments.

Keywords: Niosomes, proniosomes, oral bioavailability, vesicular drug delivery, lymphatic transport.

1. Introduction

Oral delivery is the most common route but faces challenges like poor solubility, enzymatic breakdown, and first-pass metabolism. Vesicular carriers such as niosomes and proniosomes help overcome these issues by protecting drugs, controlling release, and enhancing gut absorption. Niosomes are vesicles made from non-ionic surfactants and cholesterol, capable of carrying both hydrophilic and lipophilic drugs. Proniosomes are dry powders that easily convert to niosomes upon hydration, offering better handling and stability. Both systems are cost-effective, safe, and improve oral bioavailability. These carriers are especially useful for drugs treating neurological disorders, cancer, and infections. For example, chlorpromazine and trifluoperazine delivered via vesicular gels or nanocarriers avoid first-pass metabolism, stay longer in circulation, and show enhanced therapeutic effects. Factors like surfactant type, particle size, and surface charge affect absorption and guide formulation design. Overall, niosomes and proniosomes are transforming oral drug delivery, making treatments more effective and patient-friendly.

2. Methods and Mechanisms

Niosomes and proniosomes enhance oral drug delivery by protecting

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drugs from gut enzymes and improving absorption through the intestinal wall. Vesicle size, surfactant type, and charge influence uptake via endocytosis, tight junction modulation, or lymphatic transport. Proniosomes are stable powders or gels that convert to niosomes on hydration, making them easier to store and handle. Niosomes are typically prepared by thin-film hydration, while proniosomes use slurry, spray-coating, or freeze-drying. Optimization tools like factorial design help control vesicle size, drug entrapment, and release rate. Characterization includes DLS for size and PDI, zeta potential for stability, TEM for morphology, and in vitro/ex vivo methods (Franz diffusion, dialysis, or tissue studies) for drug release and absorption. These vesicles improve oral bioavailability by enhancing solubility, protecting drugs from enzymes, facilitating cellular uptake, opening tight junctions, enabling lymphatic transport, and inhibiting P-glycoprotein efflux. Pharmacokinetic studies consistently show higher AUC, Cmax, and Tmax. Safety: Non-ionic surfactants are generally safe, but long-term toxicity, especially with chronic use, requires more study. Regulatory Challenges: Lack of standardized tests, variable manufacturing methods, and incomplete toxicology data slow clinical translation. In mental health treatments, such as chlorpromazine and trifluoperazine delivery, these systems bypass first-pass metabolism and maintain steady drug levels, highlighting their potential for chronic therapies.

3. Formulation strategies

Choosing the right components is key: surfactant type and HLB influence bilayer packing, phase transition, and drug entrapment, while cholesterol controls membrane rigidity and release. Edge activators (e.g., Tween-80) improve flexibility in transferosomes, and

polymers like chitosan, HPMC, or Carbopol enhance mucoadhesion or gel formation. Common preparation methods include thin-film hydration for niosomes/transferosomes and slurry, coacervation, spray-coating, or spray-drying for proniosomal powders, with freeze-drying plus cryoprotectants improving stability. Optimization uses Design of Experiments (DOE) to fine-tune particle size, drug entrapment, and release, with process factors (solvent, temperature, agitation, and drying) affecting vesicle properties. Surface modifications like polymer coating, PEGylation, or ligands (peptides, folate) enhance mucoadhesion, mucus penetration, and targeted delivery. Vesicles can be incorporated into in-situ gels, nanogels, capsules, or tablets. Characterization involves DLS (size/PDI), zeta potential (stability), TEM/SEM (morphology), ultracentrifugation/gel filtration (entrapment), and in vitro/ex vivo methods (Franz cells, simulated fluids) for release and permeation studies.

4. Therapeutical Application

Psychiatry & CNS: Intranasal niosomal gels deliver drugs like chlorpromazine directly to the brain, bypassing first-pass metabolism. Transdermal or oral nanogels maintain steady levels for drugs like trifluoperazine.

Oncology: Vesicles enhance tumor targeting, improve drug accumulation in cancer tissue, and reduce systemic side effects. Surface ligands enable precise delivery of poorly soluble drugs.

Infectious Diseases: Encapsulation protects antibiotics and antiparasitic drugs from degradation, improves absorption, and makes proniosomal powders ideal for stable oral formulations.

Vaccines & Immunomodulators: Niosomes/proniosomes deliver antigens to immune cells (e.g., Peyer's patches), boosting local and

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systemic immune responses.

Ocular, Nasal, & Topical: Incorporation into gels (Carbopol, HPMC) prolongs drug retention and provides sustained release.

Metabolic & Systemic Drugs: Improve absorption of poorly soluble drugs, bypass first-pass metabolism, and extend drug action.

Practical Notes: Intranasal/transdermal gels suit CNS drugs; oral proniosomes fit unstable or poorly soluble drugs. Promising results exist, but larger clinical trials are needed.

5. Comparative Evaluation

Niosomes and proniosomes improve poorly absorbed drugs by enhancing solubility, protecting them from enzymatic breakdown, and enabling lymphatic uptake, with surfactant type, cholesterol content, particle size, and surface charge influencing pharmacokinetics (AUC, Cmax, and Tmax). Proniosomes, as stable dry powders, outperform liquid niosomal suspensions and can be made via spray-coating or spray-drying, while liquid niosomes require freeze-drying with cryoprotectants. Proniosomes suit oral solids, converting to niosomes in the GI tract, whereas niosomes and transferosomal nanogels are ideal for mucosal or transdermal delivery due to their flexibility and mucoadhesion. Non-ionic surfactants are generally biocompatible, but safety depends on particle characteristics and residual solvents, with long-term CNS studies still needed. Proniosomes scale efficiently using industrial methods, and tools like QbD and DoE help control particle size, encapsulation, and release. In practice, proniosomes are best for stable oral solids, niosomes for hydrophilic and lipophilic drugs, and transferosomal systems for skin or nasal delivery.

6. Challenges

Safety and Long-Term Biocompatibility The long-term behavior of surfactant-based vesicles is not well understood. Possible concerns include toxicity with repeated use, effects on the gut lining and microbiome, and immune reactions. Most studies only evaluate short-term safety. Stability and Product Integrity Liquid niosomal suspensions may undergo fusion, leakage, or chemical degradation during storage. Proniosomes improve stability, but maintaining vesicle structure and drug content after drying and rehydration remains challenging. Manufacturing and scale-up laboratory methods such as thin-film hydration are difficult to scale for industrial production. Techniques like spray-drying, spray-coating, and quality by design (QbD) approaches are required for consistent large-scale manufacturing. Analytical and Standardization Issues There is no standardized method to measure vesicle size, integrity, drug encapsulation, leakage, or in-body behavior, making it difficult to compare studies and obtain regulatory approval. Clinical and Regulatory Challenges Most current evidence comes from animal studies or small pharmacokinetic trials. Larger clinical studies and clearer regulatory guidelines are needed for broader clinical use.

7. Future Directions

Standardized Characterization Consistent testing methods such as DLS, cryo-TEM, encapsulation efficiency tests, gut stability assays, and in vitro–in vivo correlation models are needed to ensure reliable results and support regulatory approval. Next-Generation Systems Hybrid proniosomes combining lipids, biodegradable polymers, targeting ligands, and stimuli-responsive triggers (pH or enzymes) are being developed for site-specific drug delivery and reduced side

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effects. QbD and Green Manufacturing: Applying Quality by Design (QbD) and using scalable techniques like spray-drying and continuous coating, along with greener solvents, can improve efficiency and sustainability in manufacturing. Targeted Clinical Trials Well-designed clinical trials are required to compare vesicular systems with standard therapies, especially for CNS drug delivery, focusing on efficacy, safety, and patient outcomes. Regulatory Collaboration Early collaboration between researchers, clinicians, and regulatory agencies can establish clear standards and accelerate clinical adoption of these drug delivery systems.

8. Conclusion

Niosomes and proniosomes are promising drug-delivery systems for oral and mucosal administration. By selecting appropriate surfactants and cholesterol and applying tools such as Design of Experiments (DOE) and Quality by Design (QbD), formulations like proniosomal powders, in-situ gels, and nanogels can protect drugs, control release, and improve bioavailability. They are especially useful for poorly soluble drugs, drugs affected by first-pass metabolism, and those requiring intranasal or transdermal brain delivery. However, challenges remain, including stability issues, difficulties in large-scale production, lack of standardized analytical methods, and limited long-term safety data. Future progress depends on QbD-based scale-up, improved standardization, and well-designed clinical trials to translate these systems into clinical practice.

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