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A Short Review: Liposomes and Niosomes: Advances in Vesicular Nanocarriers for Targeted Drug Delivery

Jayanthi B[1], Sarojini S[2], Mahamaureeya M P[3]

[1]Department of Pharmacy, Annamalai University

[2]Department of Pharmaceutics, Mayor Radhakrishnan College of Pharmacy

[3]M.R. College of Veterinary Sciences & Research Centre, LUVAS, Haryana, India

Abstract: ***Vesicular drug delivery systems have developed the treatment of cancer, infectious diseases, and chronic disorders by improving bioavailability and reducing systemic toxicity. Liposomes, composed of phospholipids and cholesterol, and Niosomes, composed of non-ionic surfactants and cholesterol, are bilayered nanocarriers capable of encapsulating both hydrophilic and lipophilic drugs. Despite the clinical success of liposomal products like Doxil and mRNA COVID vaccines, limitations such as high cost, oxidation, and stability issues persist. Niosomes emerged as a cost-effective and chemically stable alternative. This review critically analyzes the structure, preparation methods, characterization, recent advances for last few years, clinical applications, and future prospects of liposomes and niosomes. Importance is placed on microfluidics, stimuli-responsive vesicles, and AI-driven formulation design that are shaping next-generation vesicular systems.***

Keywords: Liposomes; Niosomes; Nanovesicles; Drug delivery; Microfluidics; Targeted therapy.

1. Introduction

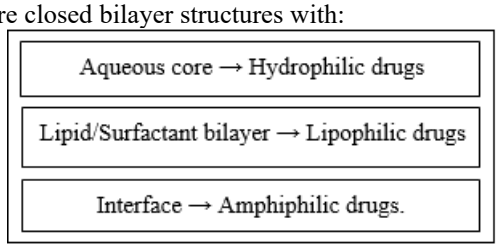
Conventional drug delivery results in <5% of administered drug reaching the target site. This leads to dose-dependent toxicity and poor patient compliance. Vesicular carriers address this by: Protection of drug from degradation Controlled release over 24-72 hrsTargeted delivery via EPR effect or ligand conjugation Liposomes were first described by Bangham in 1965. The first FDA-approved liposomal drug, Doxil in 1995, proved clinical feasibility.

Niosomes were introduced by L'Oreal in 1970s as cosmetic vesicles. They gained pharmaceutical interest after Baillie et al. 1985 due to superior stability. The global liposomal drug delivery market was valued at $6.8 Billion in 2024 and is projected to reach $12.3 Billion by 2030. Niosome market is growing at 9.2% CAGR driven by cosmeceuticals and generics.

2. Structure and Classification

2.1 Common Structural Features

Both are closed bilayer structures with:



2.2 Classification Based on Lamellarity

Table 1: Classification Based on Lamellarity for Liposome & Niosome Preparation

Type	Full Form	Size	Layers	Example Use
MLV	MultilamellarVesicles	0.5-10 µm	Multiple	Depot formulations
SUV	Small Unilamellar Vesicles	20-100 nm	Single	Long circulation
LUV	Large Unilamellar Vesicles	100-1000 nm	Single	Macromolecule delivery
GUV	GiantUnilamellar Vesicles	1000 nm	Single	Research models

2.3 Compositional Difference

- **Liposomes:** Phosphatidylcholine, Phosphatidylethanolamine, Cholesterol, PEG-lipid
- **Niosomes:** Span 20/40/60/80, Tween 20/60/80, Brij, Cholesterol, Charge inducers: DCP, SACholesterol at 30-50 mol% increases membrane rigidity and reduces drug leakage in both.

3. Methods of Preparation

3.1 Liposome Preparation Methods

3.1.1 Thin Film Hydration - Bangham Method

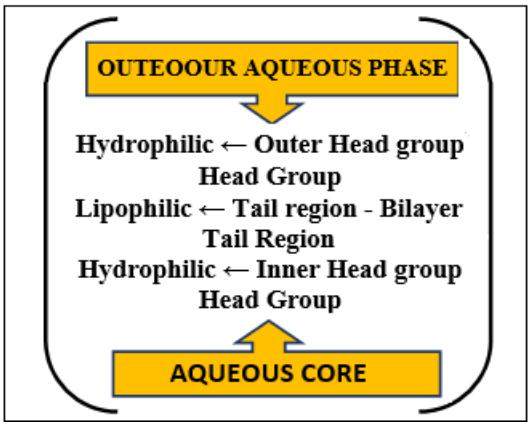


Figure 1: Schematic representation of Thin Film Hydration method

Step 1: Lipid/Surfactant + Cholesterol dissolved in organic solvent.
Step 2: Rotary evaporation to form thin film.
Step 3: Hydration with aqueous buffer.
Step 4: Formation of MLVs.
Step 5: Size reduction to SUVs/LUVs by sonication/extrusion

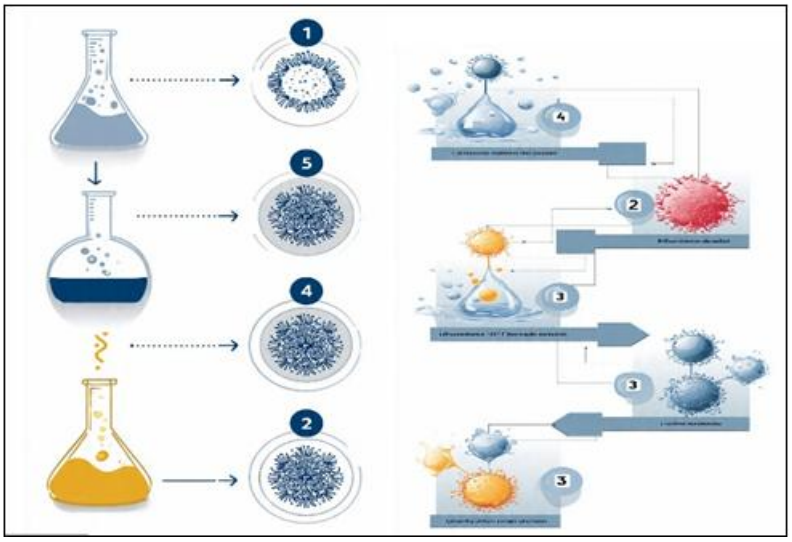


Figure 2: Diagram representation of Thin Film Hydration method

Gold standard lab method. Lipid dissolved in chloroform → rotary evaporate → thin film → hydrate with buffer @ 60°C → MLVs. Size reduction by sonication/extrusion gives SUVs 100nm.

3.1.2 Microfluidics
2023-2025 breakthrough. Lipid in ethanol + aqueous buffer mixed in microchannel. Used for Comirnaty and Spikevax mRNA vaccines. Advantages: reproducible, scalable, narrow PDI <0.2.

3.1.3 Active Loading - pH Gradient
Used for Doxorubicin. Ammonium sulfate gradient gives >90% EE. Key for commercial products.

3.2 Niosome Preparation Methods

3.2.1 Thin Film Hydration
Surfactant:Chol 1:1 in chloroform → film → hydrate with PBS @ 60°C. Span 60 gives most stable niosomes due to high Tc = 53°C.

3.2.2 Bubble Method - Green Technique
Solvent free. Surfactant dispersed @70°C + N2 bubbling. 2024 studies show 40% less residual solvent vs conventional methods.

3.2.3 Microfluidization
High shear 20,000 psi. 2025 paper by Patel et al. reported continuous production of niosomes with 150nm size for transdermal delivery.

Table 2: Comparison of Bubble Method, Thin Film Hydration, and Microfluidics for Niosome/Liposome Preparation

Parameter	Bubble Method Green Technique	Thin Film Hydration Conventional	Microfluidics Advanced 2023-2025
Organic Solvent	No	Yes - Chloroform, Ether	Yes - Ethanol only
Temperature	70°C	60°C for hydration	Room temp - 40°C
Equipment	3-neck flask, N2 cylinder, Water bath	Rotary evaporator, Sonicator	Microfluidic chip, Syringe pumps
Vesicle Type Formed	MLVs	MLVs → SUVs/LUVs after sizing	SUVs/LUVs directly
Size Range	200-500 nm	100-1000 nm	50-200 nm

PDI	0.3-0.5	0.2-0.4	0.1-0.2
Entrapment Efficiency	50-65%	40-80%	60-90%
Processing Time	30 min	2-3 hours	10-15 min
Scalability	Medium - Batch 2L reported 2024	Low - Labor intensive	High - Continuous flow
Cost	Low	Medium	High - Initial setup
GMP Suitability	High - No residual solvent	Low - Solvent removal issue	High - Reproducible
Key Advantage	Solvent-free, Eco-friendly	Lab friendly Narrow size,	Simple, Reproducible
Key Limitation	Needs heat, Only MLVs Solvent toxicity,	Time consuming	Expensive equipment
Best For	Thermostable drugs, Cosmetics	Research, Macromolecules mRNA,	Vaccines, Clinical batches

4. Characterization Techniques

Table 3: Characterization techniques for Niosome/Liposome Preparation.

Parameter	Technique	Acceptance Criteria
Size & PDI	DLS	100-200nm, PDI <0.3
Zeta Potential	Zetasizer	±30 mV for stability
Morphology	TEM, Cryo-SEM	Spherical, unilamellar
EE%	Dialysis + HPLC	60% for liposomes, >50% for niosomes
Drug release	Franz diffusion cell	Sustained 24-48h
Stability	ICH guidelines	3 months @ 4°C, 25°C/60%RH

2024 FDA guidance now recommends "in-vitro release testing IVRT" for generic liposomal products.

5. Advantages and Limitations

5.1 Liposomes

- **Advantages:** Biocompatible, Biodegradable, Clinical validation, can be PEGylated
- **Limitations:** Phospholipid oxidation, High cost $500/g, Leakage, Need cold chain

5.2 Niosomes

- **Advantages:** 10x cheaper, No oxidation, better chemical stability, Easy to sterilize
- **Limitations:** Less biocompatible, Surfactant toxicity at high dose, Limited clinical data

6. Recent Advances 2023-2025

6.1 Stimuli-Responsive Vesicles

- **pH-sensitive:** DOPE + CHEMS for tumor microenvironment pH 6.5
- **Thermo-sensitive:** DPPC: DSPC for hyperthermia triggered release
- **Enzyme-sensitive:** MMP-2 cleavable peptide liposomes 2025

6.2 Targeted Vesicles

Folate-conjugated niosomes for ovarian cancer. HER2 antibody liposomes for breast cancer. 2025 clinical trial NCT05982311 using targeted liposomal siRNA.

6.3 AI in Formulation

2024: Google DeepMind + MIT used ML to predict optimal Span 60: Chol ratio for max EE. Reduced trial runs by 70%.

6.4 Herbal and Nutraceutical Niosomes

Curcumin niosomes showed 8.3x ↑bioavailability vs free drug in 2025 human PK study.

7. Applications

7.1 Oncology

Liposomes: Doxil, Onivyde, Vyxeos

Niosomes: 2024 Phase I trial of Paclitaxel niosomes showed reduced neutropenia vs Taxol

7.2 Infectious Diseases

AmBisome for fungal. 2025: Niosomal Amphotericin B gel for cutaneous leishmaniasis in India.

7.3 Vaccines

mRNA-LNP = modified liposomes. 2024: Self-adjuvanting niosomal vaccine platform for influenza.

7.4 Dermatology and Transdermal

Niosomal gel of Diclofenac, Retinol. Advantage: ↑ skin penetration, ↓ irritation.

8. Marketed Products and Clinical Status

- **Liposomes - FDA Approved:** 20+ products
- **Niosomes:** No FDA approved drug yet. 12 products in Phase I/II as of 2025.
- **Major barrier:** Regulatory path for surfactants.

9. Challenges and Future Perspectives

Scale-up: Microfluidics and continuous manufacturing needed for GMP Regulatory: Need harmonized guidelines for niosomes by USFDA, DCGI Personalized medicine: 3D printed niosomes for patient-specific dose Sustainability: Green surfactants from plant sources 2025 trend.

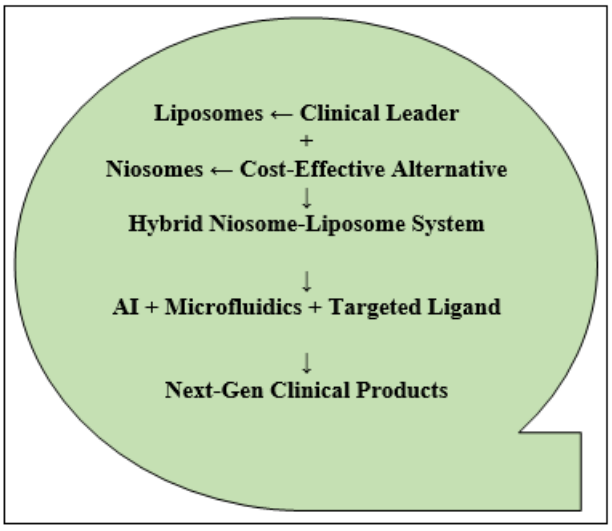


Figure 3: Future Directions in Vesicular Drug Delivery 2025-2030

Table 4: Comparative Overview of Liposomes, Niosomes, and Hybrid Vesicles

Parameter	Liposomes	Niosomes	Hybrid Niosome
Bilayer Composition	Phospholipids+ Cholesterol	Non-ionic Surfactant + Cholesterol Phospholipid	Phospholipid + Surfactant + Cholesterol
Biocompatibility	Excellent - Natural lipids	Good	Excellent
Chemical Stability	Low - Prone to oxidation, hydrolysis	High Stable 2 years	High
Cost of Materials -	High - Purified PC	Low Span/Tween	Medium
Manufacturing	Complex, solvent needed	Simple, Green methods	Moderate complexity
Drug Loading	High for both hydro/lipophilic	Very High	High
Leakage	Moderate	Low	Low
Circulation Time	Long with PEGylation	Moderate	Long
Immunogenicity	Very Low	Very Low	VeryLow
Scalability	Medium	High Bubble method	High Microfluidics
Regulatory Status,	FDA Approved – Doxil, Onpattro	Preclinical/Clinical Trials	Research Stage
Best Application	Injectables, Cancer, Gene therapy	Topical, Oral, Cost-sensitive markets	Targeted, Long-circulating injectables
Key Limitation	Cost + Stability	Clinical data lacking	Optimization needed
Future Role	Gold standard	Emerging markets + OTC	Bridge technology 2026-2030

10. Future Perspectives: Hybrid Systems

To overcome individual limitations, hybrid vesicles incorporating both phospholipids and non-ionic surfactants have been proposed. As summarized in Table 4, these systems aim to combine the biocompatibility and clinical track record of liposomes with the cost-effectiveness and stability of niosomes. Early studies 2023-2024 show that hybrid systems exhibit improved encapsulation efficiency and reduced drug leakage compared to pure niosomes, while maintaining lower cost than pure liposomes. With the advent of microfluidic platforms and AI-driven formulation design, rational development of such hybrids is now feasible.[1] We hypothesize that the first hybrid vesicle product will enter Phase I trials by 2028, particularly for oncology and vaccine applications where both cost and performance are critical.

11. Conclusion

Liposomes remain the clinical leader due to proven safety. However, niosomes offer a compelling alternative for cost-sensitive markets like India. With advances in microfluidics, AI, and targeted ligands, the next 5 years will see niosomes enter clinics. Hybrid "niosome-liposome" systems may combine best of both. Furthermore, hybrid “niosome-liposome” or “niosomal-liposome hybrid” systems that combine the biocompatibility of phospholipids with the stability of non-ionic surfactants may represent the next generation of vesicular carriers, merging the best attributes of both platforms

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