

## COMPARATIVE STUDY OF PRONIOSOMES, LIPOSOMES, ETHOSOMES AND TRANSFEROSOMES

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### ABSTRACT

Vesicular medicine delivery systems have been developed as multifaceted platforms for enhancing remedial efficacy, bioavailability, and targeted delivery of hydrophilic and lipophilic medicines. Vesicular carriers- liposomes, proniosomes, ethosomes and transferosomes- give new platforms for transdermal and topical medicine delivery. Proniosomes are greasepaint, surfactant – carpeted phrasings that transfigure into niosomes in the presence of water, working stability problems associated with liposomes and niosomes. Liposomes, made up of phospholipid bilayers, are biocompatible but naturally rigid, confining deep penetration through the skin. Ethosomes introduce high ethanol content (20-45), which enhances bilayer fluidity and improves transdermal saturation. Transferosomes contain edge- activators for ultra- deformability, yielding superior encapsulation effectiveness and deep skin targeting over liposomes and niosomes. Relative studies how transferosomes surpass ethosomes and liposomes in deformability, encapsulation effectiveness ( $\approx 72$  vs.  $\approx 42$ ), and immunogenic response – through ethosomes shine in delivering both hydrophilic and lipophilic medicines. This review examines structural variations, manufacturing process, medicine – lading capacity, permeability, and operations to direct carrier selection in an optimal manner.

**KEYWORDS:** Transdermal delivery, vesicular drug delivery, Nano-carriers, skin permeation, stability, Drug entrapment.

## INTRODUCTION

Nanovesicular systems have transformed drug delivery by improving bioavailability, targeting efficacy, and dosage flexibility. Among them, liposomes initiated early developments because their biocompatible phospholipid bilayers accommodate both hydrophilic and lipophilic drugs. Yet, being rigid and limiting skin penetration encouraged the invention of more flexible carriers.

### Types of Vesicular Drug Delivery Systems

1. Liposomes
2. Virosomes
3. Niosomes
4. Proniosomes
5. Transferosomes
6. Proteasomes
7. Sphingosomes
8. Archaesome
9. Ethosomes

**Proniosomes** are anhydrous form of water-soluble carrier particles which are surfactant coated. They are rehydrated to give niosomal dispersion at the point of use on agitation in hot aqueous media within minutes. Proniosomes are physically stable when stored or transported. Drug entrapped in vesicular structure of proniosomes enhance the drug's lifespan in the systematic circulation and increase the penetration into target tissue and decrease toxicity.<sup>[1]</sup>

**Ethosomes** are the third-generation vesicles, which are high in ethanol content (22-45%). Ethanol inhibits stratum corneum lipids and increases vesicle fluidity – allowing deeper skin penetration and effective delivery of small and large molecules. Ethosomes are soft, pliable vesicles designed for improved delivery of active ingredients. It has been demonstrated that physicochemical features of ethosomes enable this vesicular carrier to deliver active ingredients more effectively through the stratum corneum to the underlying layers of the skin compared to conventional liposomes.<sup>[2]</sup>

**Transferosomes** (elastic liposomes) contain edge- activators (e.g., surfactants such as tween 80), which provides them with ultra – deformability. This facilitates crossing through narrow skin pores through transcellular and intercellular pathways, leading to much enhanced encapsulation ( $\approx 70\%$  vs.  $\approx 40\%$ ) and immune responses similar to injections in certain studies. A transferosome carrier is a man-made vesicle intended to be like a cell vesicle or a cell undergoing exocytosis and hence appropriate for controlled and possibly directed drug delivery.<sup>[3]</sup>

**Liposomes** are synthetic vesicle made up of a bilayer of lipids. Liposomes can be employed as a delivery system for nutrients and drugs. Liposomes may be made by breaking biological membranes. Liposomes consist of natural phospholipids and can also consist of mixed lipid chains which have surfactant activity.<sup>[4]</sup>

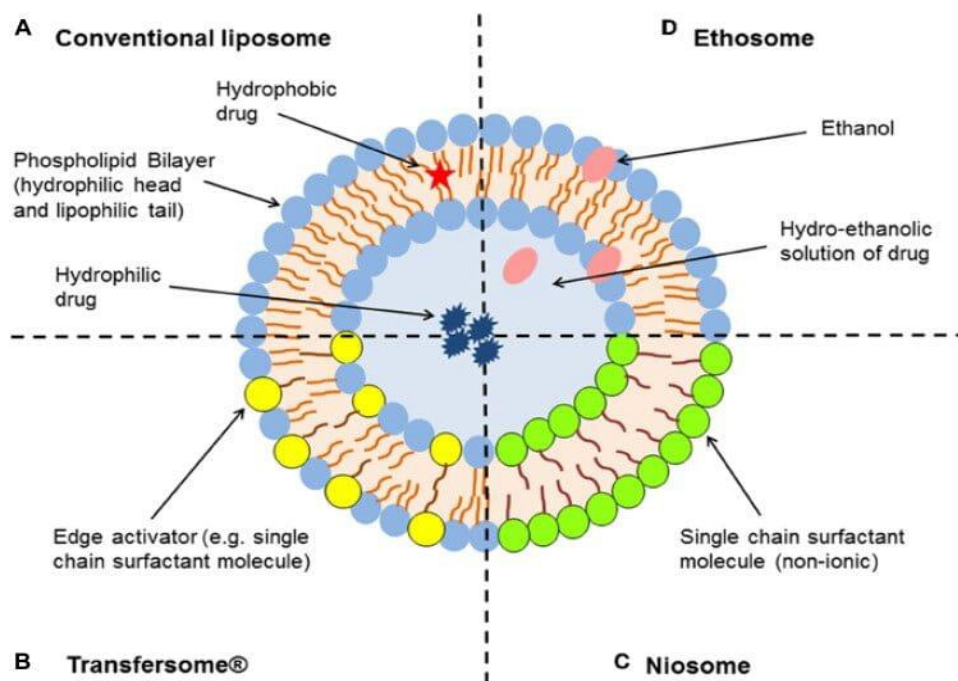


Figure 1: Schematic illustration of liposome, ethosome, transfersomes.<sup>[5]</sup>

## PREPARATION METHODS

### PRONIOSOMES

Proniosomes are dry, free – fluid maquillages are gels that upon hydration give rise to niosomes.

### COMMON METHODS

#### Coacervation phase separation method

- Constituents (nonionic surfactant, cholesterol, lecithin) are dissolved in alcohol.
- A many drops of waterless phase (generally phosphate buffer) are added.
- The admixture is warmed and also stupefied to produce a gel or greasepaint.<sup>[6,7]</sup>

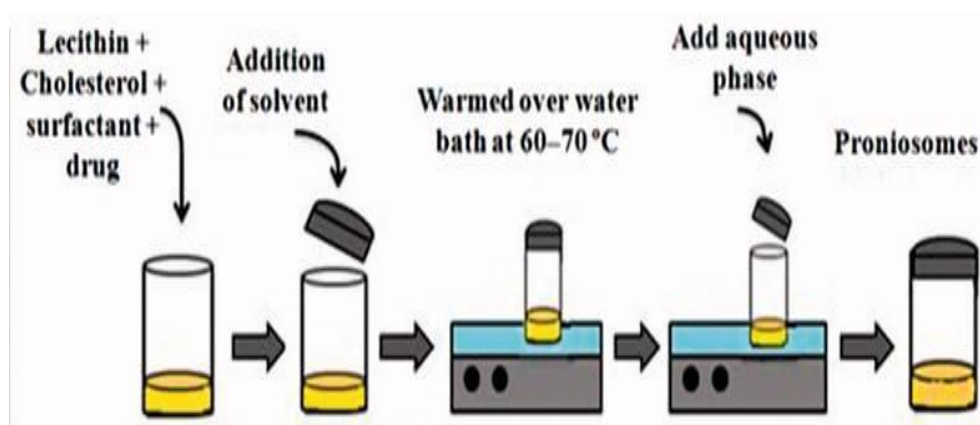


Figure 2: Coacervation phase separation method.<sup>[6,7]</sup>

- Surfactant and lipid factors are blended with a minimum quantum of waterless phase to produce a slurry.
- Maintained at room temperature; hovers niosomes upon rehydration.

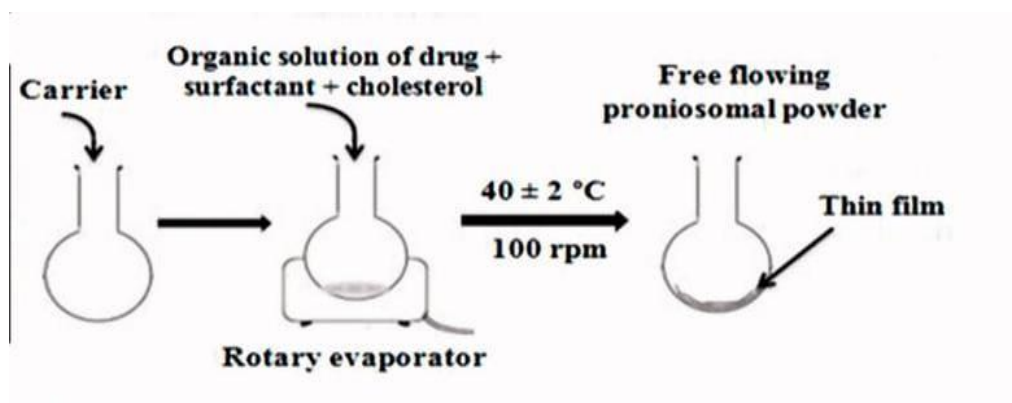


Figure 3: Slurry method.

## LIPOSOMES

Liposomes are spherical vesicles with one or more phospholipid bi layer.

### COMMON METHODS

#### Thin film hydration system

- Phospholipids and cholesterol are dissolved in an organic detergent (e.g., Chloroform).
- The detergent is faded under reduced pressure to produce a thin lipid film.
- The film is doused with waterless medicine result under agitation to produce multilamellar vesicles.
- Optional sonication or extrusion to drop vesicle size.

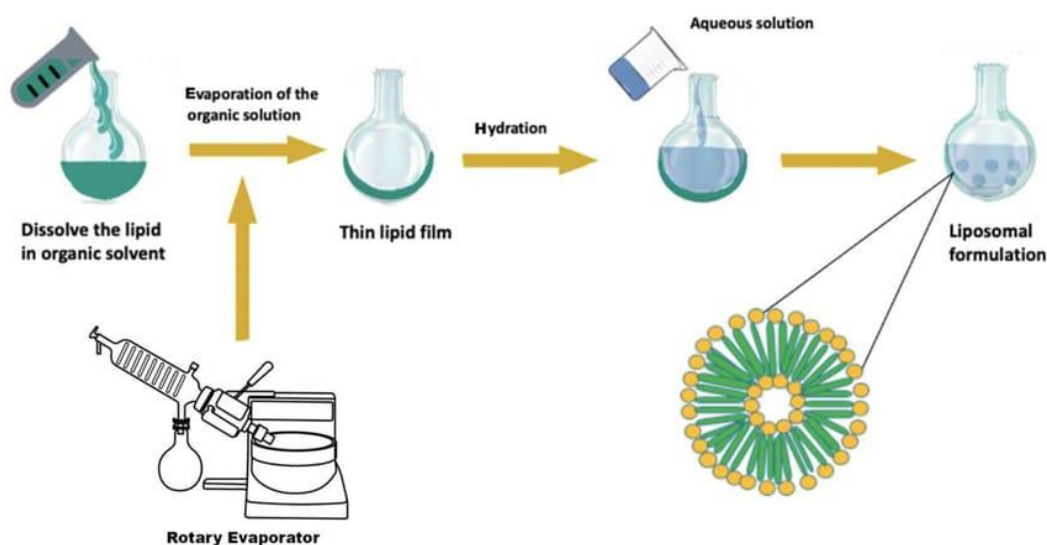


Figure 4: Thin film hydration method.

#### Reverse phase evaporation process

- An oil painting – in - water conflation is produced by using lipid in organic detergent and waterless phase.
- Solvent is faded to produce vesicles.

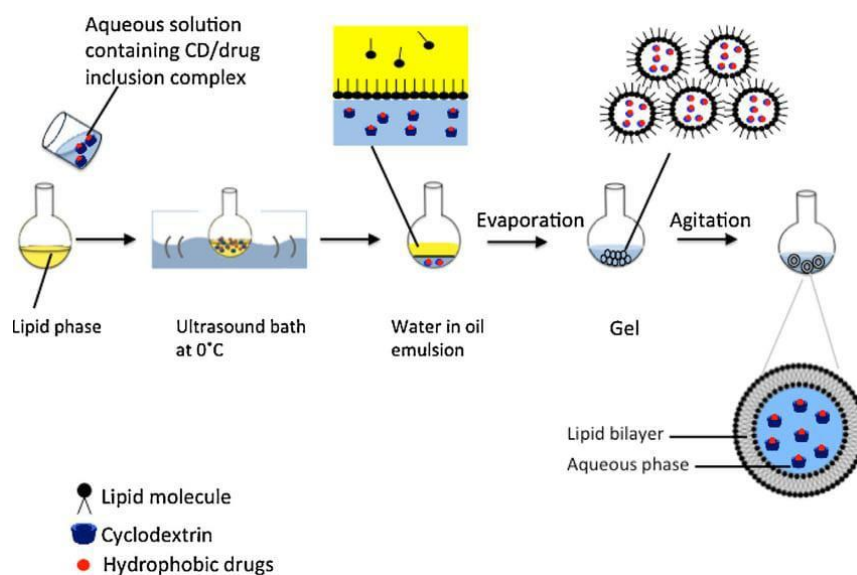


Figure 5: Reverse phase evaporation method.

## ETHOSOMES

Ethosomes are soft, pliable vesicles with phospholipids, high ethanol attention(20- 45), and water.

## COMMON METHODS

### Cold method

- Phospholipids are dissolved in ethanol together with the medicine.
- The expression is stirred while sluggishly adding water at room or cooled temperature.
- Robotic conformation of vesicles occurs.<sup>[9]</sup>

### Hot method

- As in cold system, but constituents are combined at 40- 45C to grease solubilization.

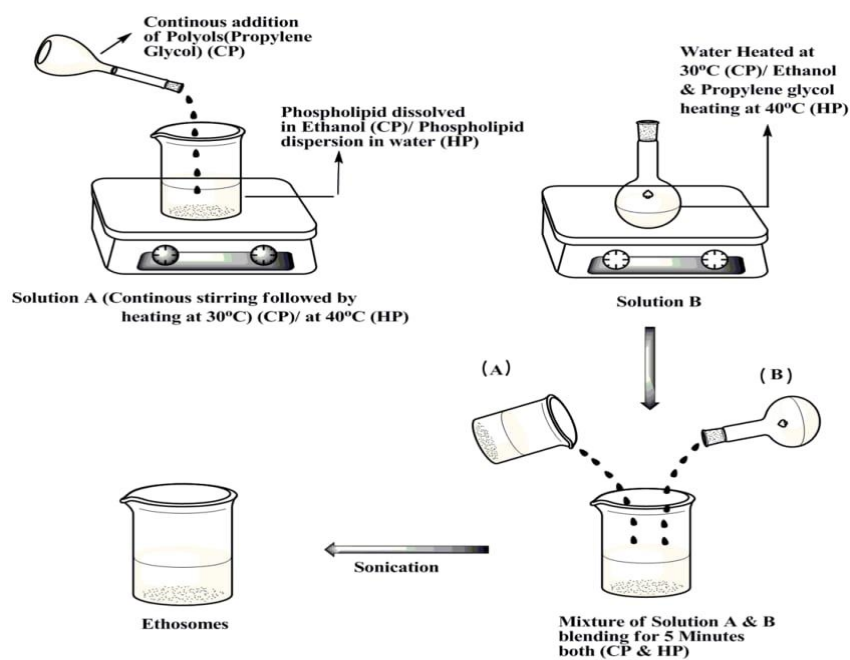


Figure 6: Schematic representation method of (a) Cold method (b) Hot method).<sup>[9,13]</sup>

## TRANSFEROSOMES

Transferosomes are ultra – deformable vesicles that have phospholipids and edge activators (e.g., sodium cholate, Tween 80).

## COMMON METHODS

### Thin film hydration with edge activators

- Analogous to liposome medication.
- Lipids and surfactants are dissolved in organic detergent.
- After forming the thin film, hydration is done using waterless phase with medicine.
- The performing vesicles are sonicated or extruded.

## CHARACTERIZATION<sup>[14,20]</sup>

### 1. Vesicle size and size distribution

- Fashion: Dynamic light scattering( DLS), ray diffraction, SEM, TEM
- Significance it influences saturation, use effectiveness, and medicine release.

### 2. Zeta implicit

- Fashion: Electrophoretic light scattering
- Significance vaticinations physical stability, high absolute values ( $\pm 30\text{mv}$ ) signify good stability.

### 3. Polydispersity indicator (PDI)

- Fashion: DLS
- Importance Provides a measure of uniformity of vesicle size; lower PDI( $< 0.3$ ) is reflective of monodispersity.

### 4. Entrapment Efficiency (%EE)

- Fashion: Centrifugation followed by UV- Vis or HPLC
- Importance Indicates the quantum of medicine reprised in the vesicles.

### 5. Morphological Studies

#### WAYS

- SEM (face structure)
- TEM (Internal structure and lamellarity)
- AFM (3D face topology)
- Importance Confirms vesicle integrity and shape.

### 6. In vitro medicine release

- Fashion: Dialysis membrane system, Franz prolixity cell.
- Significance Evaluates sustained or controlled release eventuality.

### 7. Ex vivo skin saturation

- Fashion: Franz prolixity cell using beast or mortal skin.
- Importance Determines transdermal or dermal medicine delivery effectiveness.

**8. Stability studies**

- Parameters Storage at different temperatures (4C, 25C, 40C) and moisture (RH 60- 75).
- Measure over 1- 6 months.
- Importance Determines physical and chemical stability on a time scale.

**9. PH Measurement**

- Fashion: Digital PH cadence
- Importance Guarantees comity with the skin ( $\approx 5.5- 7.0$ )

**10. Density and Rheological parcels (Specific to Proniosomal gel)**

- Fashion: Brookfield viscometer
- Importance Determines ease of operation and spreadability.

**11. Deformability indicator (Specific to Transferosomes)**

- Fashion: Extrusion fashion using membranes of lower severance size.
- Significance Measures capability to access through pores in the skin.

**12. Ethanol Content Analysis (Specific to Ethosomes)**

- Fashion: Gas chromatography or HPLC
- Importance Verifies ethanol attention, which is essential for ethosomal exertion. Liposomes are globular vesicles with one or further phospholipid bi subcaste.

**COMPARATIVE STUDY OF PRNIOSONES VS LIPOSOMES, ETHOSOMES, TRANSFEROSOMES**

Aspect	Proniosomal gel	Liposome	Ethosome	Transferosome
	Forms niosomes on hydration from dry gel	Formed by hydration of phospholipids in aqueous media	Formed by mixing phospholipids and ethanol in aqueous phase	Formed by hydration of phospholipid with edge activators
Stability	High stability due to dry storage form longer shelf life	Moderate stability prone to oxidation/ Hydrolysis	Moderate stability ethanol can enhance preservation but may cause leakage	Moderate edge activators may affect membrane integrity over time
Particle size	Typically nanosized upon hydration	Variable size uni or multilamellar vesicles	Smaller size (often<200nm) due to ethanol effect	Small size with high deformability size 100 to 300nm
Encapsulation efficiency	Good for hydrophilic and lipophilic drug	Good for hydrophilic (aqueous core) and lipophilic drugs	Good especially for Liphophilic drugs due to ethanol presence.	Good encapsulation with improved permeation
Drug release	Sustained and controlled release improved permeation	Controlled release systemic or topical use	Enhanced permeation and rapid release due to ethanol	Controlled release with enhanced penetration through skin
Skin penetration	Enhanced due to surfactant properties moderate flexibility	Moderate vesicle may remains on the surface or penetrate slightly	High penetration due to ethanol disrupting lipid bilayers of skin	Very high penetration due to ultra flexible deformable vesicles
Flexibility /deformability	Moderate niosomes less deformable than transfersomes	Rigid compared to ethosomes and transfersomes	More flexible than liposomes due to ethanol content	Highly deformable can squeeze through skin pores smaller than vesicle size



Toxicity and irritation	Low toxicity; non-ionic surfactants minimize irritation	Generally biocompatible; low toxicity	Ethanol may cause some irritation at high concentration	Edge activators may cause mild irritation but generally safe
Applications	Transdermal topical delivery; improved stability	Systemic and topical delivery; gene/drug delivery	Transdermal and topical delivery with enhanced skin penetration	Transdermal delivery of large molecules, peptide, vaccines
Preparation complexity	Simple; dry gel easier to handle	Moderate complexity; hydration and size control	Moderate; ethanol handling and optimization required	More complex; formulation requires precise surfactant balance
Shelf life	Longer shelf life; dry form stable	Moderate; refrigeration often needed	Moderate: ethanol helps but can affect stability	Moderate; sensitive to formulation and storage conditions
Cost	Cost-effective; simpler ingredients	More expensive due to phospholipids	Higher due to ethanol and phospholipids	High due to specialized surfactants and formulation <sup>8</sup>

## CONCLUSION

Vesicular drug delivery systems like proniosomes, liposomes, ethosomes, and transfersomes have converted the drug delivery sedulity by perfecting remedial effectiveness, reducing side goods, and enhancing patient compliance.

In relative terms, proniosomes are more stable and accessible to store than liposomes and ethosomes; ethosomes have the topmost skin permeability; transfersomes are most flexible and transdermal effective; and liposomes are still the most biocompatible but technically delicate. The drug and the system must be named predicated on the parcels of the drug, target point, delivery route, and clinical need. The incorporation of these vesicular systems in personalized medicine and nanotechnology could potentially increase their remedial value indeed more in the future.

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