

## Transfersomes for Transdermal Drug Delivery System

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### Abstract

Transdermal drugs delivery system (TDDS) have become important as an alternative to oral and parenteral drug administration because they can improve patient compliance, prevent first-pass hepatic metabolism and provide sustained drug release. However, the stratum corneum layer is the main barrier to drug permeation in transdermal delivery. To overcome this limitation, transfersomes have been suggested as a very promising type of vesicular carriers. Transfersomes are ultra-deformable and elastic lipid vesicle. They are mainly composed of phospholipids and edge activators. The flexible structure of them helps them to pass to the narrow intercellular spaces to the skin without losing their integrity and thus they improve the drug penetration. They can also be used to deliver hydrophilic and lipophilic drugs into deeper skin layers and systemic circulation. Transfersomes successfully study for the delivery of anti-inflammatory drug, corticosteroids, anticancer agents, peptides proteins, vaccines and herbal compounds. They are valuable and efficient carriers in transdermal drug delivery systems.

**Keywords:** Transfersomes, Transdermal drug delivery, Vesicular carriers, Edge activators, Skin permeation, Elastic liposomes

### I. Introduction

Delivery of drugs through skin has been a focus of pharmacological studies due to the non-invasive nature of this mode of administration and its simplicity<sup>(1; 17)</sup> Many benefits associated with transdermal drug delivery include avoiding drug breakdown in the gastrointestinal tract, preventing first-pass effect, sustaining drug delivery, and improving compliance among others. Although this method of drug administration poses many benefits, its effective use is hindered by the nature of the skin as a good barrier to external substances.<sup>(1)</sup>

Stratum corneum, which is the top layers of the skin, forms the major barriers to the diffusion of drugs molecules through the skin.<sup>(1) (2)</sup> There are only a few molecules with certain physicochemical characteristics including low molecular weight, optimum lipophilicity, and high potency that diffuse

passively through the skin. Several advanced vesicular systems such as liposomes, niosomes, ethosomes, and transfersomes have been discovered in order to enhance skin permeation.<sup>(3)</sup> From all these, transfersomes are among the most efficient vesicular systems which can effectively facilitate transdermal delivery of the drugs.<sup>(4)</sup> Transfersomes are highly deformable vesicles that have the capacity to cross the intact skin layer better than conventional liposomes. Due to the flexibility and elasticity, transfersomes enable effective and efficient penetration of drugs through the skin layer.<sup>(5)</sup> The word Transfersomes has originated from the Latin word 'transferres' means to carry across and Greek word "somas" means body. Transfersomes are ultra-deformable vesicular carriers and are used for improving the penetration of drugs through the skin.<sup>(8)</sup> Transfersomes are made up of phospholipids, edge activators, and aqueous phase. Transfersomes are sometimes also known as elastic liposomes due to their high deformability as compared to conventional liposomes.<sup>(7)</sup>

### II. Need for Transdermal Drug Delivery System

The oral route is the most popular route of drug administration. However, many drug administered orally suffers from bad bioavailability due to degradations in the gastrointestinal tract or hepatic first-pass metabolisms. Parenteral administration, although effective, is invasive and often associated with pain, risk of infection, and reduced patient compliances.<sup>(12)</sup>

- Avoids first-pass metabolisms
- Reduces gastrointestinal side effects
- Provide controlled and sustained releases of drug
- Improves patient compliance

### III. Skin as a Barrier to Drug Delivery

Skin is one of the largest organs in the human body. It serves as a barrier against mechanical injury, pathogens, chemicals, and dehydrations. It has three main layers, the epidermis, the dermis, and the hypodermis. Among these, the stratum corneum is the major barrier of transdermal drug transport. It consists of dead

keratinized cells in a lipid matrix, referred to as a “brick and mortar” structure. This setup makes it

hard for most drugs to get through the skin. <sup>(2) (3)</sup>

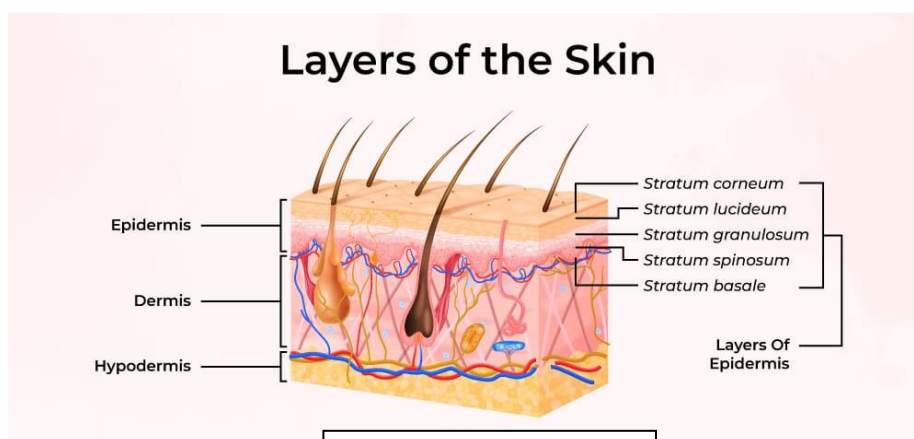


Fig.1 Structure of skin

#### IV. Composition of Transfersomes

Table no.1; Composition of Transfersomes:<sup>(17)</sup>

| S.No. | Component        | Component                                                  | Property                                                   |
|-------|------------------|------------------------------------------------------------|------------------------------------------------------------|
| 1.    | Phospholipids    | Phosphatidylcholine, Soy Lecithin, Egg Phosphatidylcholine | Form the basic bilayer structure of transfersomes          |
| 2.    | Edges Activator  | Tween 80, Span 80, Sodium Cholate, Sodium Deoxycholate     | Increases flexibility and deformability of vesicles        |
| 3.    | Solvents         | Chloroform, Methanol, Ethanol                              | Used for dissolving lipid components during formulation    |
| 4.    | Hydration medium | Phosphate Buffer Saline (PBS), Distilled Water             | Used for hydration of the thin lipid film to form vesicles |

#### V. Structure of Transfersomes

Transfersomes are generally sphericals or oval vesicles consisting of one or more phospholipid bilayer enclosing an aqueou core. Hydrophilics

drugs are entrapped in the hydro core, whereas lipophilic drug are incorporated into the lipids bilayer. <sup>(19)</sup>

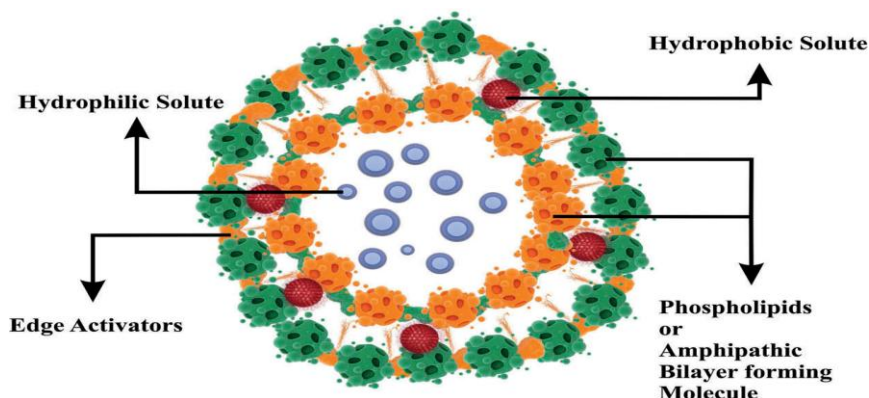


Fig. No. 2 Structure of Transfersome

## VI. Mechanism of Skin Penetration by Transfersomes

Transfersomes penetrate the skin through a unique mechanism involving both osmotic gradient and vesicle deformability<sup>(3) (5)</sup>

### 6.1 Hydration Gradient:

The outer surface of the skin is relatively dry, while the deeper layers are more hydrated.

### 6.2 Deformability:

Due to their elastic nature, transfersomes can squeeze through narrow pores and intercellular pathways much smaller than their own diameter without rupturing.

### 6.3 Lipid Interaction:

Transfersomes may also interact with the skin lipids and disturb the ordered structure of stratum corneum, thereby increasing permeability.

### 6.4 Drug Release:

Once the transfersomes reach deeper layers of skin, the entrapped drug is released either locally or into systemic circulation.

## VII. Methods of Preparations of the Transfersomes

Several methods are used for the preparations of transfersomes depending on the nature of the drug and desired vesicle characteristics.

### Thin Films Hydration Method

This process is also known as the rotary evaporation technique. Desired quantity of phospholipids and edge activator is weighed and added into a suitable solvent such as solvent and chloroforms. The prepared solution is then transferred into the rotary flask, which is rotated at constant temperature and reduced pressure. When all the organic solvents are evaporated as a result of it, a thin film is formed on the bottom of the flask. The film is then hydrated with an aqueous medium containing a drug for the complete swelling of lipid vesicles. Particles of the desired sizes are obtained by sonication or extrusion processes<sup>(8) (13)</sup>

### Thin Film Hydration Method for Transfersomes

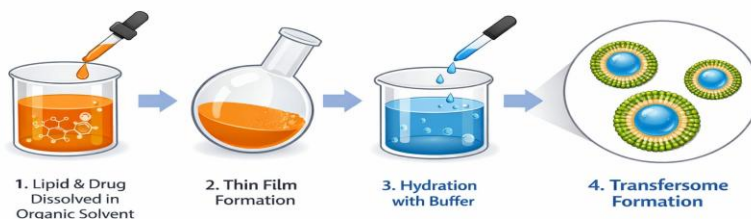


Fig. no.3 Thin Film Hydration Method

### Reverse Evaporation Method

Dissolve the phospholipid and edges activators in an organics solvents (chloroform/ether) to form the oil phase. Dissolve the phospholipids and edges activators in an organic solvent (chloroform/ether) to form the oil phase <sup>(7), (13)</sup> Sonicate the mixture to make a stable emulsion. Remove the organic solvent under reduced pressure using a rotary evaporators at controlled temperature. The emulsion collapses into a viscous gel, which, upon further hydration, forms transfersomal vesicles. Sonicate or extrude vesicles to achieve desired size.

### Ethanol Injection Method

Dissolve phospholipids and edges activators in ethanol. the concentration depends on the final vesicle size and drug loading. Prepare an aqueous solution of the drug in distilled water or PBS. Using a syringe, slowly inject the ethanol-lipid solution into the aqueous phase under continuous stirring (typically magnetic stirring). Lipids spontaneously form vesicles due to rapid diffusion of ethanol into water. The ethanol acts as a co-solvent, increasing lipid solubility and helping vesicle formation. Ethanol is removed by rotary evaporation or dialysis to avoid toxicity and achieve the final transfersome suspension. Vesicles can be sonicated or extruded to achieve uniform size (usually 100–300 nm. <sup>(14)</sup> The thin films hydration method is the most commonly used method for preparations of transfersomes.

## VIII. Characterization and Evaluation of Transfersomes

Evaluation of transfersomes is essential to determine their quality, stability, and effectiveness.

Important parameters include:

- Vesicle sizes and size distributions
- Zeta potentials
- Entrapments efficiencies
- Deformability index
- Morphologies (TEM/SEM)
- In vitro drug release
- Ex vivo skin permeations study
- Stability studie

## IX. Applications of Transfersomes

Transfersomes have been used for a wide ranges of therapeutic applications such as:

- Anti-inflammatory drugs
- Corticosteroids
- Anticancer drugs
- Peptides and proteins

- Herbal drugs
- Cosmeceutical agents

## X. Limitations of Transfersomes

- Chemical instability of phospholipids
- Possibility of oxidation
- High production cost
- Difficulty in large-scale manufacturing
- Requirement of careful storage conditions
- Potential leakage of entrapped drug over time

## XI. Recent Advances and Future Prospects

Recent research focuses on nano-transfersomes, transfersomal gels, surface-modified transfersomes, herbal transfersomes, peptide and vaccine delivery, and combination systems such as transfersomal patches and films. <sup>(18)</sup>

Transfersomes hold significant promise for future drug delivery applications, especially for non-invasive therapy and patient-friendly formulations.

## XII. Conclusion

Transfersomes represent a highly promising vesicular carrier system for transdermal drug delivery. Their ultra-deformable nature enables them to overcome the skin barrier more efficiently than many conventional vesicles. Due to their flexibility, biocompatibility, and versatility, transfersomes have gained substantial attention in modern pharmaceutical research.

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