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Review Article

A Review on Transferosomes

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ABSTRACT

Transferosomes is a proprietary drug delivery technology, an artificial vesicle suitable for controlled and potentially targeted drug delivery. Transferosomes have recently been introduced, which are capable of delivery of low as well as high molecular weight drugs. This offers several potential advantages like avoidance of first pass metabolism, predictable and extended duration of activity, minimizing undesirable side effects, utility of short half life drugs, improving physiological and pharmacological response and have been applied to increases the efficiency of the material transfer across the intact skin. Composition of transferosomes contains edge activators and phospholipids. Transferosomes penetrate the stratum corneum by intracellular route or the Tran cellular route by the generation of "osmotic gradient". The characterization of Transferosomes is similar to that of other vesicles like liposomes, noisome and micelle.

INTRODUCTION

Transferosomes have been defined as specially designed vesicular particles consisting of at least one inner aqueous compartment enclosed by lipid vesicles; liposomes in morphology, but, functionally, transferosomes are suitably deformable to go through pores much smaller than their own size. The word Transferosomes was introduced by Gregor Cevc in the year 1991.transferosome is a combination of two words transfero and soma. Transfero means tocarry across and soma means body. Transferosomes is an artificial vesicle designed to exhibit the characteristics of cell vesicle or a cell engaged in exocytosis and thus suitable for controlled and potentially, targeted drug delivery. The reason for using vesicles in transdermal drug delivery is based on the fact that they act as drug carriers to deliver entrapped drug molecule across the skin, as well as penetration enhancers because of their composition. Transferosomes can deform and pass through narrow constriction without measurable loss. Transferosomes can pass through tiny pores nearly as efficiently as water, which is 1500 times smaller. Due to the presence of first pass effect or

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medication interactions with other components of Gastro Intestinal tract (GIT) before absorption,an efficacious, successful therapy with no undesirable effects may not be possible in the majority of situations. Patient compliance is poor with these types of therapies. As a result, improved drug delivery methods have been studied in recent years in order to achieve the benefits of conventional treatment while avoiding the drawbacks. One promising method for avoiding pre-systemic metabolism and contact is the use of peptides. The presence of a skin barrier, on the other hand, restricts or amplifies the relaxed penetration of various molecules when they are applied as creams, gels, or ointments. As a result, new carrier or vesicular-based TDDS are needed to increase molecule penetrability through the skin barrier

ADVANTAGES

- They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes.
- They protect the encapsulated drug from metabolic degradation.
- Transferosomes shows greater permeation of the drugs through the skin.
- These serves as carrier for both small and large molecular weight drugs.
- In Transferosomes, percentage of the drug entrapment is more. In case of lipophilic drug near to 90%.Protects the entrapped drug from atmospheric degradation.
- They have high entrapment efficiency this high deformability gives better penetration of intact vesicles.
- They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin.
- Transferosomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility.
- They act as depot, releasing their contents slowly and gradually.
- They can be used for both systemic as well as topical delivery of drug

DISADVANTAGES

- Transferosomes are chemically unstable because of their predisposition to oxidative degradation.
- Purity of natural phospholipids is another criteria militating against adoption of transferosomes as drug delivery vehicles.
- These formulations are very expensive

Factors affecting Transdermal delivery

The factors which affect transdermal delivery of drug are mainly two: biological factors and physicochemical factors

a) Biological factors

Skin age: Children are more sensitive to the absorption of toxins to skin; the young age of skin is more permeable than the old age skin

ii) Condition of skin-Skin condition is altered by the diseased state of the patient. Furthermore acids, alkalis, solvents like methanol and chloroform injures the skin cells and elevates penetration

iii) Metabolism of skin-Skin metabolizes drugs, hormones, steroids and some of the carcinogens. Thus, metabolism of the skin predicts the effectiveness of drug permeated into the skin

iv) Skin site-Nature of SC, thickness of skin, keratins and appendages vary from one site to another site

b) Physicochemical factors

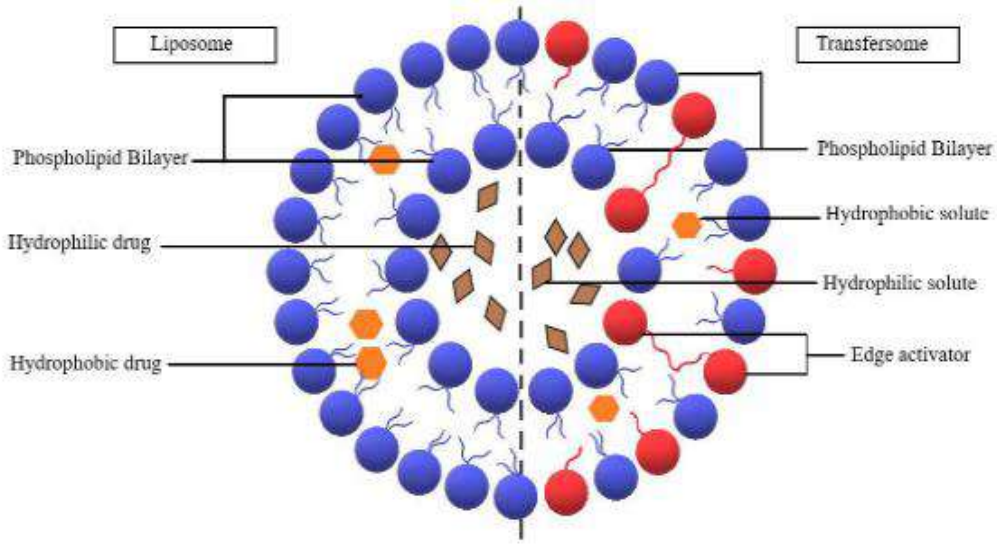
i) Drug concentration - Flux is proportionate to the concentration gradient through the barrier. Thus, concentration gradient will be greater when the drug concentration is more across the barrier

ii) Skin Hydration-Hydration is an important component in increasing the skin permeability. Permeability of the skin increases in contact with water. Hence, humectants are used in formulation of transdermal delivery

iii) Temperature and pH-The permeation of the drug increases with the variation in temperature. The temperature decreases as the diffusion coefficient decreases. The portion of unionized drug determines the drug concentration in skin

iv) Partition coefficient-For highly lipophilic molecules (log K > 3) and for the molecules with intermediate partition coefficient (log K 1 to 3) the intercellular route is the pathway and furthermore ability to partition out of the SC into aqueous region via epidermal tissues, hydrophilic molecules (log K < 1) the transcellular route are likely to dominate

Structure of Transferosomes:



Composition:

Transferosomes are mainly composed of 2 main aggregates like phospholipids and edge activators**.**

Phospholipids: Phospholipids form the membrane and provide stability to vesicles. Therefore, both membranes forming agents i.e. phospholipids and the destabilizing agent. Among phospholipids, soya phospholipids like soya phosphatidylcholine and hydrogenated soya phosphatidylcholine are most commonly used.

Edge activators:

An edge activator consists usually of single chain surfactant of non ionic nature that causes destabilization of the lipid bilayer thereby increasing its fluidity and elasticity. Various edge activators like span 40, span 60, span 80, span 85, tween 20, tween 60, tween 80, sodiumoleate, sodium cholate, sodium deoxycholate, dicetylphosphate (DCP), KG (dipotasium glycrhizinate) etc.have been reported for preparation of transferosomes.

The nature and ratio of different edge activators affect the physicochemical properties of vesicles including their size, entrapment efficiency and zeta potential.

Mechanism of Action of Transferosomes:

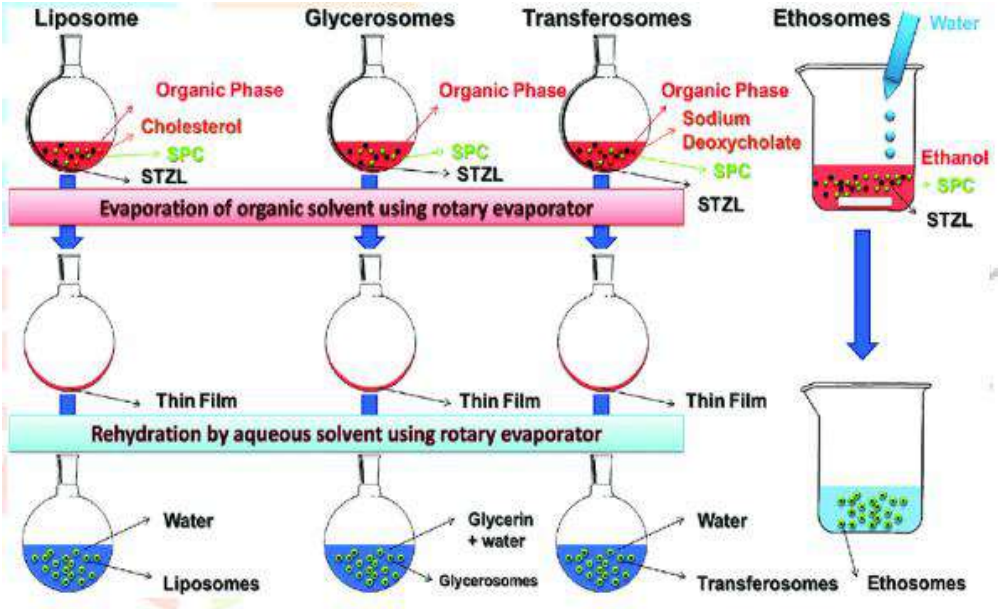
Interaction between the lipid residue and the proximal water makes the lipid to attract water molecules inducing hydration and the lipid vesicles move to the site of higher water concentration. This difference in water content across the skin stratum and epidermis develops transdermal osmotic gradient leading to penetration of transferosomes across the skin. Mechanism of drug penetration the mechanism of drug penetration can be described in three purposed mechanisms. Transferosomes by enforcing its own route induce hydration that widens the hydrophilic pores of the skin causing the gradual release of the drug that bind to the target organ. Transferosomes act as permeation enhancers that disrupt the intercellular lipid from the stratum that ultimately widens the pores and facilitates the molecular interaction and penetration of system across the skin

Method of Preparation of Transferosomes

1. Rotary Film Evaporation Method
2. Reverse Phase Evaporation Method
3. Vortex/Sonication Method
4. Ethanol Injection Method
5. Freeze Thaw Method

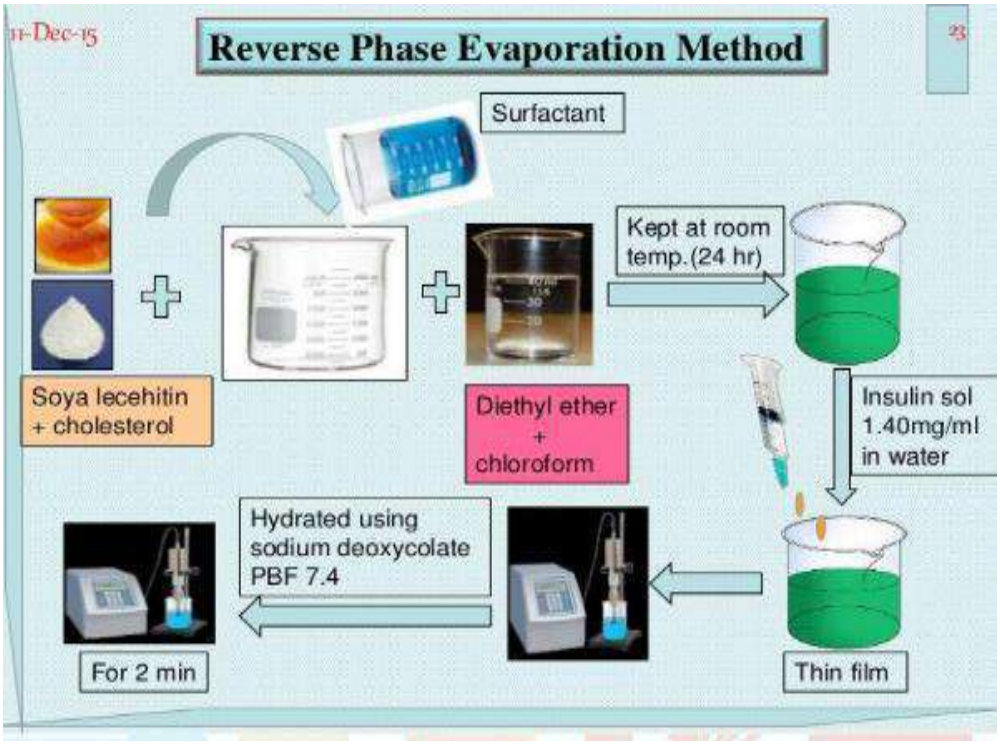
1. Rotary Film Evaporation Method/ Modified Hand Shaking Method:

This method is also known s modified hand shaking method. Lecithin along with the edge activator (surfactant) and drug are dissolved in a mixture of chloroform and ethanol (1:1 ratio). The mixture is subjected to evaporation to remove the organic solvent using temperature above the transition temperature of lipid by hand shaking. The thin lipid film is left overnight to ensure complete removal of the organic solvent. Above prepared thin film is hydrated by using pH6.5 buffer by rotation at 60 RPM for 1hr at corresponding temperature. The resulting vesicles were swollen for 2 hrs at room temperature. To prepare small vesicles, resulting vesicles were sonicated at room temperature.

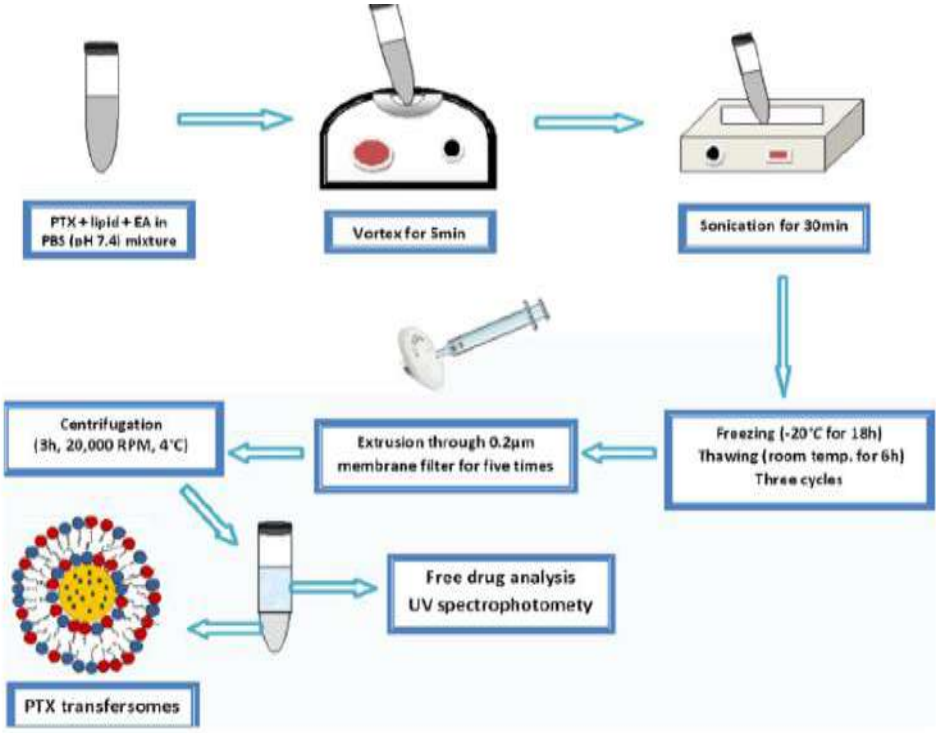


2. Reverse Phase Evaporation Method:

In this method, lipids dissolved in organic solvents are taken in a round bottom flask. Aqueous media containing edge activators is added under nitrogen purging. The drug can be added to the lipid or aqueous medium based on its solubility characters. The formed system is then sonicate until it become a homogeneous dispersion and should not separate for at least 30 minutes after sonication. The organic solvent is then removed under reduced pressure. At this point, the system will convert to a viscous gel followed by the formation of vesicles. The non-encapsulated material and residual solvents can be removed using dialysis or centrifugation

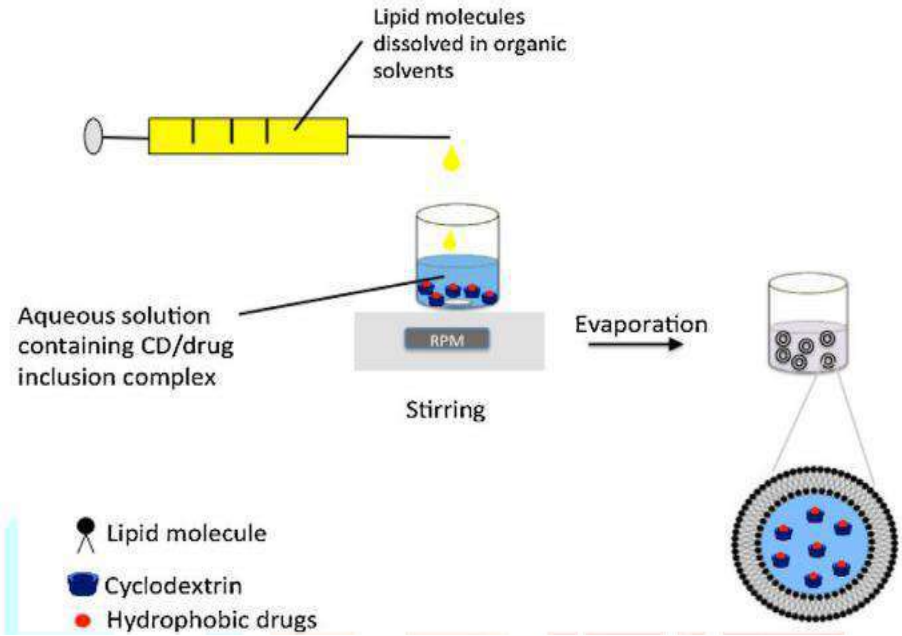


3. Vortex/Sonication Method: In this method, phospholipids and edge activators are mixed by vigorous shaking and agitation in order to suspend them in phosphate buffer. The formed milky suspension is then sonicated using vortex or bath sonicator followed by extrusion through polycarbonate membranes

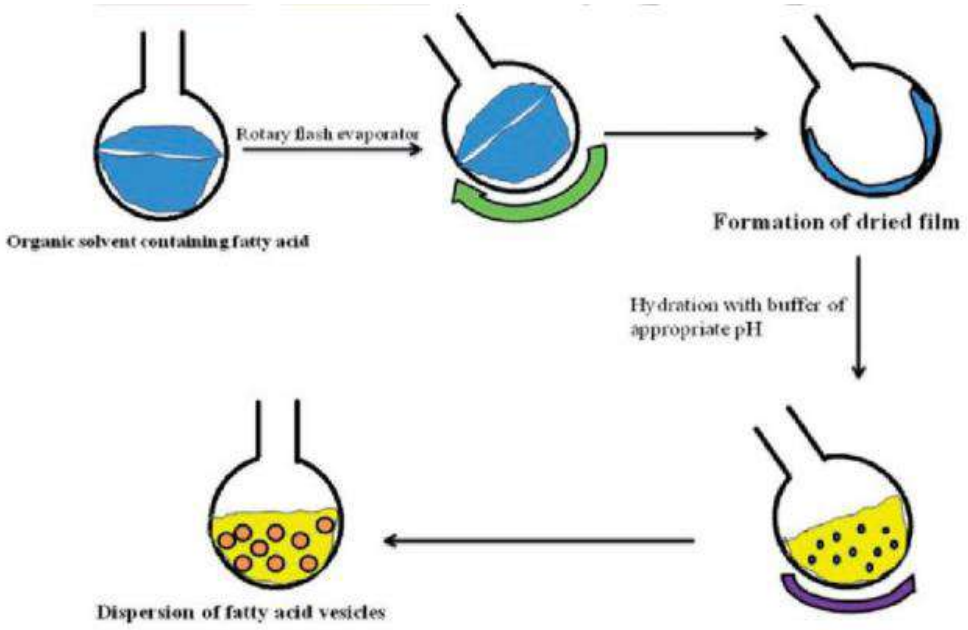


4. Ethanol Injection Method:

This method, Drug along with aqueous solution is heated with continuous stirring at constant temperature Ethanolic solution containing phospholipids and edge activators are injected into an aqueous solution drop wise. When the solution comes in contact with aqueous media the lipid molecules get precipitated and form bilayered structures. This method is more advantageous than other methods



5. Freeze Thaw Method: This method involves the exposure of prepared multi lamellar vesicles suspension to alternate cycles of very low temperature for freezing followed by exposure to very high temperature. The prepared suspension is transferred to a tube and dipped in a nitrogen bath (-30° C) for 30seconds. After freezing, it is exposed to high temperature in a water bath. This process is repeated for 8-9 times



2.Characterization of Transferosomes:

The characterization of transferosomes resembles that of other vesicles like liposomes, niosomes and micelles.

a) Vesicle Size, Size Distribution and Vesicle Diameter
b) Vesicle Shape and Type
c) Number of Vesicle per cubic mm
d) Entrapment Efficiency
e) Drug Content
f) Turbidity Measurement
g) Surface Charge and Charge Density
h) Penetration Ability
i) Occlusion Effect
j) In-vitro Drug Release
k) In-vitro Skin Permeation Studies

3. Applications of Transferosomes:

a) Controlled release of drug
b) Peripheral drug targeting
c) Transport of large molecular weight compounds
d) Delivery of proteins and peptides
e) Delivery of insulin
f) Delivery of interferon
g) Delivery of anesthetics
h) Transdermal immunization
i) Delivery of NSAIDS
j) Delivery of Herbal Drugs
k) Delivery of Anticancer Drugs

4. CONCLUSIONS:

Ultra deformable vesicles like transferosomes are capable of providing an ideal solution to all transdermal drug delivery and transport related problems. Such highly deformable particles can thus be used to bring drugs across the biological permeability barriers, such as skin. They are especially useful for delivery of troublesome molecules like peptides and proteins. The elastic

vesicles deform themselves to penetrate the skin through pores. It is more efficient & safer in composition then others. In this type of delivery, Drug release can also be controlled according to the requirement. The exceptional quality of transferosomes to deform themselves depending on the environmental stress due to the presence of surfactants, often referred to as edge activators makes them very flexible for delivery of a wide range of molecules also having a good scope for targeted delivery. Transferosomes, thus, hold a bright and promising future in transdermal delivery of drugs

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