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### TRANSFEROSOMES: MTRANSDERMAL DRUG DELIVERY – EMERGING TRENDS AND APPLICATIONS IN DRUG DELIVERY AND THERAPEUTICS

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#### ABSTRACT

Transfersomes are also called as transfersomes, ultra deformable vesicles for transdermal applications, consisting of a lipid bilayer with phospholipids An edge activator. Depending upon the lipophilicity of the activesubstance it canbe encapsulated within thecore or amongst the lipid bilayer.Most transfersomescontains phosphatide choline(C18) as it is the most abundant lipid component of the cell membrane. The most common edge activators are surfactants. Application of quality by design(Quds) specifically design of experiments is crucial to understand the interplay among all these factors not only during the preparation add labs scale but also in the scaleup process. Clinical trials of a licensed topical ketoprofen transfersomal gel have shown promising results in the alleviation of symptoms in ortriorities with non-severe skin and subcutaneous tissue disorders.

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## INTRODUCTION

Skin is considered as the largest organ of the body making up 16% of the body weight and consists of 3 functional layers: epidermis, dermis and subcutaneous. It has many different functions one major task of the skin is to protect the organism from water loss and mechanical, chemical, microbial and physical influences. Transdermal drug delivery system (TDDS) can be used as an alternative delivery of drug into this systemic circulation. Transdermal drug delivery offers many advantages as compared to traditional drug delivery better alternative to achieve constant plasma levels.

A novel vesicular drug carrier system called transfersomes which is composed of phospholipid polydispersity, surfactant and water for enhanced transdermal delivery.

### Definition and History:

Transfersomes are a form of elastic or deformable vesicle.

Which were first introduced in the early 1990s. Transfersomes are advantageous as phospholipid vesicles for transdermal drug delivery. Because of their self-optimised, they are able to deliver the drug reproducibly either into or through the skin, depending on the choice of administration or application with high efficiency.

Drug delivery via the transdermal route is an interesting option in this respect because a transdermal route is convenient and safe. They offer several advantages over conventional drug delivery system like avoidance of first pass metabolism and extended duration of action, minimising undesirable side effects and pharmacological response, avoiding the fluctuation in drug levels inter and intra patient variations it provides convenience.

### Composition of Transfersomes:

Transfersomes is a novel elastic or ultra-deformable vesicular drug carrier system composed of phospholipid, surfactant and water for the enhancement of transdermal delivery. It crosses skin barrier by squeezing themselves along the intracellular space of the stratum corneum. Transfersomes is a self-adaptable and optimised mixed lipid aggregate and composed of phospholipids like phosphatidylcholine which self-assembles into a lipid bilayer in aqueous environment and closes to form a vesicle. Consequently, Soy phosphatidylcholine has a very low phase transition temperature of less than 0°C in water systems. This may be the reason behind its ability to fluidise the lipid bilayers of the horny layer, which can be determined by measuring the increase of trans epidermal water loss (TEWL) after application for a short while.

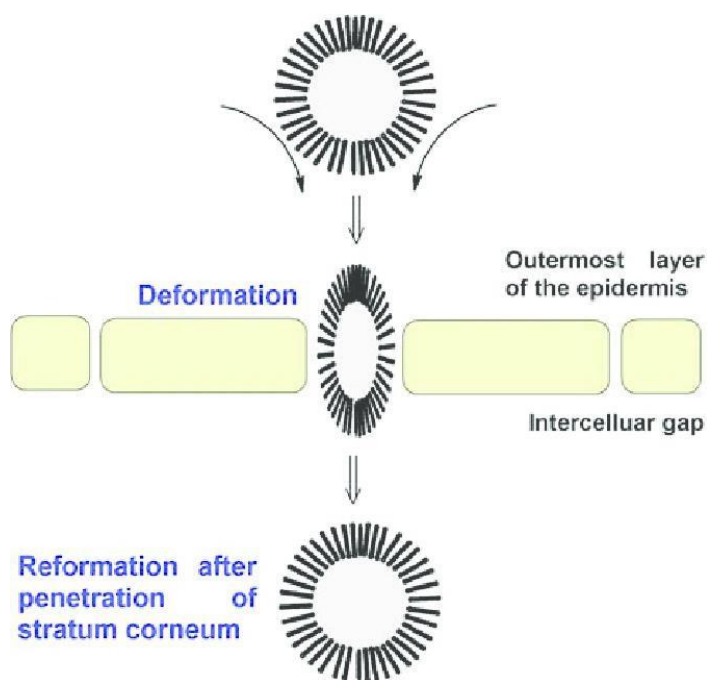
The slight increase of TEWL coincides with the penetration of phosphatidylcholine and active agents which are co-formulated with phosphatidylcholine a lipid bilayer softening component is added to increase flexibility and permeability. This second component is called as edge activator and it consists usually of single chain surfactant of non-ionic nature that causes destabilization of the lipid bilayer thereby increasing its fluidity and elasticity.

### Mechanism of Penetration of Transfersomes:

Transfersomes when applied under suitable conditions can transfer 0.1 mg of lipid per hour and cm<sup>2</sup> area across the intact skin. This value is substantially higher than that which is typically driven by the transdermal concentration gradients. The reason for this high flux rate is naturally occurring "transdermal osmotic gradient". The osmotic gradient is developed due to the skin and maintains a water activity difference in viable part of the epidermis (75% water content) and nearly completely dry stratum corneum, near to the skin surface (15% water content).

All polar lipids attract some water due to energetically favourable interaction between hydrophilic lipid residues and proximal water. Most lipid bilayers thus spontaneously resist and induced dehydration. Consequently all lipid vesicles made from the polar lipid vesicles move from the rather dry location to the sites with a sufficiently high water concentration. So when lipid suspension (transfersomes) is placed on the skin surface that is partly dehydrated by the water evaporation loss and then the lipid vesicles feel this "osmotic gradient" and try to escape complete drying by moving along this gradient.

Transfersomes vesicles can therefore adapt its shape to ambient easily and rapidly by adjusting local concentration of each bilayer component to the local stress.



Figureno:1 Mechanism of penetration of transfersomes.

Ref: Mehdi Rajabhi; Mechanism of transfersomes through skin

#### Structural representation of one Transfersomes unit

Transfersomes can be deform and pass through the narrow constriction without measurable loss (from 5-10 times lesser than their own diameter). They can even pass through tiny pores (100nm) nearly as efficiently as a water which is 1500 times smaller.

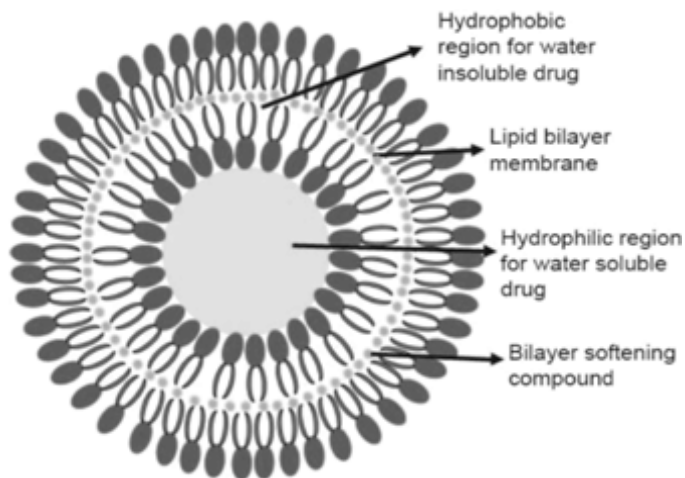


Fig no: 2 Structure of transfersomes.

Ref: Priyanka Karunanidhi; A review on skin targeted delivery of bio actives as ultra deformable vesicles

#### Advantages of Transfersomes:

It consists of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with a wide range of solubility.

Transfersomes have elastic properties and pass through intracellular spaces.

They also act as a carrier for low and as well as high molecular weight drugs. For example - analgesic, sex hormones, insulin, an aesthetic etc.

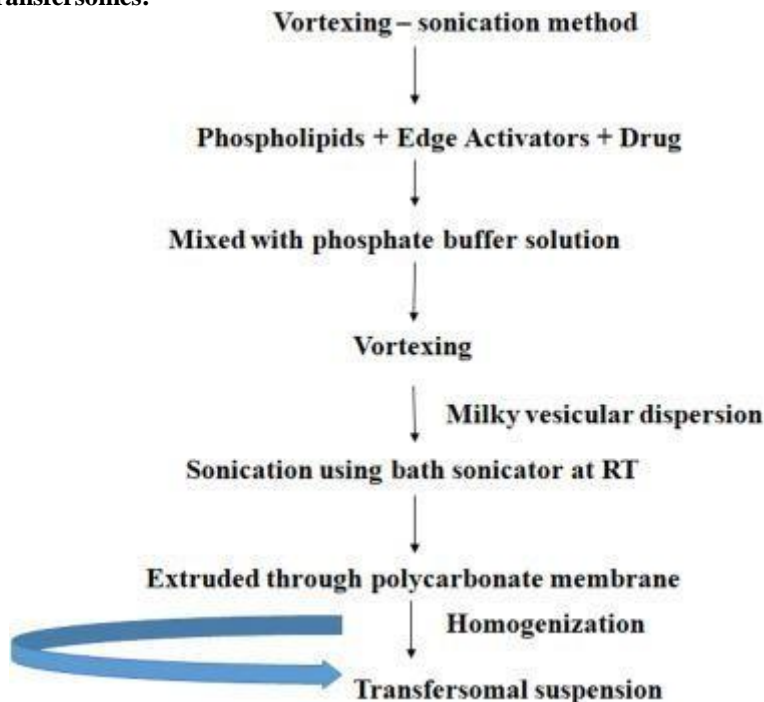
They are biocompatible and biodegradable.

They have high entrapment efficiency, if the drug is near to 90%. They protect the encapsulated drug from metabolic degradation.

By releasing their contents slowly they act as a depot. They can be used for both systemic and topical drug delivery.

**Limitations:**

- Transfersomes are chemically unstable, and highly susceptible to oxidative degradation.
- Their formulations are expensive.

**Methods for preparation of transfersomes:****Figno:3methodofpreparation.**

Ref: Biswarup Das: Transfersomes: a Nano vesicular approach for drug delivery.

**1. Overtaxing-sonication method:**

In this method the mixed lipids such as phosphate decholine etc. are blended in a buffer and vortexes to attain a milky suspension. The suspension is solicated through poly-carbonate membranes.

**2. Suspensionhomogenisationmethod:**

In this method transfersomes are prepared by mixing and ethologic soyabean phosphatidecholine solution with an appropriate amount of edge active molecule. This suspension is mixed with Tri ethanolamine HCL buffer to yield a total lipid concentration.

**3. Modifiedhandshakingprocess:**

In this process transfersomes are prepared by modified hand shaking “lipid film hydration technique”. Organic solvent was removed by evaporation while hand shaking above lipid transition temperature at 43°C.

At in liquid film was formed inside the flask wall with rotation and was kept overnight forcomplete evaporation of solvent then the film was hydrated with phosphate buffer ph. 7.4 gently shaking for 15 minutes at corresponding temperature.

**4. Aqueous lipid suspension method:**

In this process, depending upon the type the composition is preferred. This would ensure the high flexibility of the vesicle membrane by comparing to standard vesicles in fluid phase. Specifically the vesicles size ranges from 100 to 200nm prepared by using soy phosphatidyl choline with standard size around 30% .This could be prepared by suspending the lipids in aqueous phase where in the drug is dissolved.

**5. Centrifugationprocess:**

In this process the phospholipids, surfactants and the drug are dissolved in alcohol and then the solvent is removed by rotary evaporation under the pressure at 40°C.

Finally traces of solvents are removed and deposited. Lipid film is hydrated with the buffer by centrifuging at 60 rpm for one hour at room temperature the resulting vesicles are swollen for 2 hours.

**Characterization of Transfersomes:**

The mechanical properties and transportability of a vesicle can be studied by measuring stress or deformation vesicle bilayer elasticity and permeability changes.

**>Entrapment efficiency:**

It can be determined by separating the entrapped drug. After separating the vesicle can be ruptured.

**>Vesicle diameter:**

Size of vesicle is one of the key issues during the manufacturing process of the transfersomes. It gives important information about the control of the preparation technique and can be utilised for optimization process.

**>Con focal scanning laser microscopy (CSLM) study:**

- For investigating the mechanism of penetration of transfer some across the skin.
- For determining his to logical organisation of the skin, shape and architecture of the skin penetration pathways.
- For comparison and differentiation of the mechanism of the penetration of transfersomes with liposomes niosomes and micelles.

**>Turbidity measurement:**

Turbidity of the drug in a queous solution can be measure dusing nephelometer.

**>Vesicle shape and type:**

Transfersomes vesicles can be visualized by TEM, phase contrast microscopy.

**>Number of vesicles percubic mm:**

Formulations are diluted five times with 0.9% NaCl solution.

*Total no. of transfersomes per cubic mm = total no. of transfersomes counted × dilution factor × 4000.*

**>Penetration ability:**

Fluore scence microscopy used to evaluate penetration ability of transfersomes.

**>Occlusion effect:**

Occlusion of skin is considered to be helpful for permeation.

**Applications:**

1. **Delivery of Insulin:** Insulin is generally administered by subcutaneous route that is inconvenient. Encapsulation of insulin into transfersomes overcomes the larger size along with showing 50% response as compared to subcutaneous injection.
2. **Delivery of corticosteroids:** Transfersomes based corticosteroids are biologically active at dose several times lower than the currently used formulation for the treatment of skin disease.
3. **Delivery of proteins and peptides:** Transfersomes have been widely used as a carrier for the transport of proteins and peptides, these when gives orally they are completely degraded in GI tract and delivery suffers because of their large size.
4. **Delivery of herbal drugs:** They can penetrate stratum cornea and supply nutrients to maintain it functions resulting maintenance of skin.
5. **Delivery of anti-cancer drugs:** Anticancer drugs like methotrexate were tried for transdermal delivery using transfersomes technology. The results were favourable. This provided a new approach for treatment especially of skin cancer.
6. **Delivery of an aesthetics:** Maximum resulting pain insensitivity is nearly as strong (80%) as that of a comparable subcutaneous bolus injection, but the effect of transfersosomal an aesthetics last longer.

## CONCLUSION

Transfersomes are specially optimised particles or vesicle, which can respond to an external stress by rapid and energetically inexpensive shape transformations. Transfersomes hold great prospective in delivery of huge range of drugs substances which includes large molecules like peptides, hormones, and antibiotics, drug with poor penetration due to unfavourable physico-chemical characters. It is clear that transfersomes can deliver enhanced amounts of both small and large therapeutic agents into and through the skin.

Transfersomes are complex lipid molecules therefore, enhanced delivery of NSAIDs, herbal drugs, anti-cancer drugs etc... through the skin by means of an ultra-deformable vesicular carrier open new challenges and opportunities for the development of novel improved therapies. The fewer drugs loading tag to transdermal system must be challenged used novel transfersomes carrier.

## Summary:-

Novel drug delivery systems are now a days creating a new interest in development of drug deliveries. Vesicular drug delivery system is also a part of these novel drug delivery systems. TDDS is the permeability of the skin, it is permeable to small molecules, lipophilic drug and highly impermeable to the macromolecules and hydrophilic drugs.

Transfersomes have recently been introduced which are capable of transdermal delivery of low as well as high molecular weight drugs. This offers several potential advantages over conventional routes like avoidance of firstpass metabolism, predictable and duration of activity side effects etc... it is suitable for controlled and targeted drug delivery and it can accommodate drug molecules with wider range of solubility. Transfersomes thus differs from such more conventional vesicles primarily by its softer, more deformable, better adjustable artificial membrane.

Overall, the scope of this review article encompasses a thorough examination of transfersomes as a novel drug delivery system for transdermal delivery, covering their composition, mechanism of action, preparation methods, characterization techniques, applications, and future prospects.

## Marketed Formulation:

ENHANCEMENT METHOD	BRANDNAME	COMPANYNAME	DRUG PRODUCT AVAILABLE UNDER CONSIDERATION
Microprojection	Macroflux®	Alza	Vaccines, Therapeutic proteins.
Ultrasound	SonoDerm®	Imarx	Large molecules
Needless Injectors	Intraject®	Weston Medical	Vaccines
Medicated Tattoos	Med-Tat®	Lippman Ltd.	Acetaminophen, Vitamin C

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## Completing Interest:

Authors declare no competing interest.

## Ethical Consideration:

NIL

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