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Transfersomes: As Helping Hand for Trandermal Drug Delivery System

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ABSTRACT: With oral and parenteral drug delivery systems, poor patient compliance in regular clinical practise is a frequent issue. So, pharmaceutical research has developed considerable interest in the transdermal route of drug delivery. But the skin, the stratum corneum, & the outermost envelope of the skin are the major hurdle in transdermal drug delivery. Different techniques have recently been used to improve the transdermal delivery of bioactive materials. In particular, iontophoresis, electrophoresis, sonophoresis, enhancers of chemical permeation, micro needles and vesicular system (liposomes, niosomes, elastic liposomes such as ethosomes and transfersomes) are Transfersomes together have an infrastructure consisting of hydrophobic and hydrophilic moieties and can therefore accommodate drug molecules with a wide solubility. The high and self-optimizing deformability of the typical membrane of composite transfersomes, which are adaptable to ambient tress, enables the ultra-deformable transfersomes, when pushed against or attracted into narrow pore, to adjust their membrane composition locally and reversibly. Without observable loss, transfersomes can deform and move through narrow constrictions (from 5 to 10 times less than their own diameter). This high deformability gives the intact vesicles better penetration. They can serve as a carrier for medicines of low and high molecular weight, such as analgesics, anaesthetics, corticosteroids, sex hormones, anticancer medications, insulin, protein gap junction, and albumin.

Keywords
: Transfersomes, transdermal vesicles, osmotic gra dient, ultra-deformable vesicles

I. INTRODUCTION

Transferosomes and fundamental concept of transferosomes was launched by Gregor Cevc in the year 1991. In a board sense, transferosome is a stress responsive, elastic and an extremely adaptable aggregate. It exits as an ultra-deformable complex having a hydrated core surrounded by a complex layer of lipid. Transferosome is a tradework registered by the German company IDEA AG, which refers to its proprietary drug delivery technology. The name means “carrying body” and is derived from the Latin word `transferre`, meaning `to carry across` and the Greek word `soma` , meaning `a body`. A Transferosome carrier is an artificial vesicle designed to exhibit the characteristics of a cell engaged in exocytosis, and thus suitable for controlled and potentially, targeted drug delivery . Transferosome are complex vesicles that have extremely flexible & self-regulating membranes, which makes the vesicles very deformable. Transferosome vesicle can cross microporous barriers efficiently, even if the prous are much smaller than the vesicles size.

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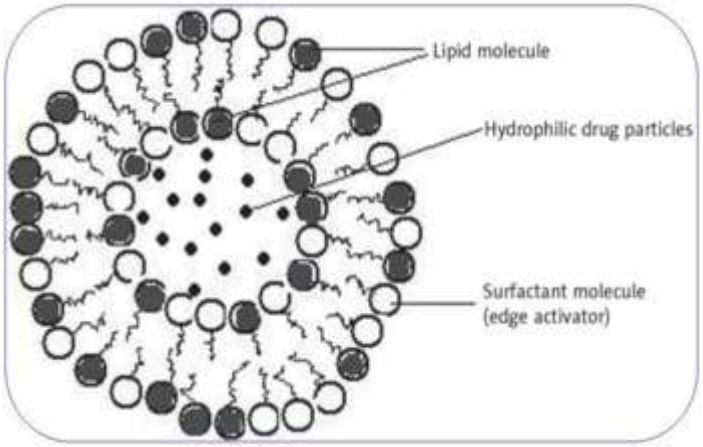

Fig:Transferosomes

Drug Delivery via the route is an interesting option in this respect because transdermal route is convenient and safe. They offers several advantages over conventional drug delivery system like avoidance of first pass metabolism, predictable and extended duration of action, minimizing undersirable side effects utility of short half-life drugs, improving physiological and pharmacological response, avoiding the fluctuation in drug levels, inter-and intra-patient variations and important its provides patients convenience. Low stratum corneum permeability restricts the utility of topical medications, considering substantial research and development efforts in transdermal systems and the advantages of these routes. To overcome this, various methods have been assessed to increase stratum corneum permeability. To date many physical and chemical approaches have been applied to increase the efficacy of the material to transfer across the intact skin, by use of the penetration enhancers iontophoresis, iontophoresis and the use of colloidal carriers such as lipid vesicles (liposome and proliposomes) and non-ionic surfactant vesicles (noisome and proniosomes). Vesicular system used in transdermal drug delivery such as liposomes, niosomes, or microemulsions usually remains confined to the skin surface and therefore do not transport drugs efficiently through the skin. By using the concept of rational membrane design a special type of composite bodies, so-called Transferosomes have been developed, Which overcome the filtration problem and the penetrate the skin barrier along the transcutaneous gradient.Tranferosomes is recent novel drug delivery system and are special types of liposomes, consisting of phosphatidylcholine and an edge activator. This system also takes advantages of phospholipids vesicles as transdermal ldrug carrier. They are self-optimized aggregates with the ultra-flexible membrane, which deliver the drug reproducibly either into or through the skin. The system delivers the drug with high efficiency depending on the choice of administration or application . This system has several order magnitude of elasticity and flexibility over liposomal drug delivery which makes it favorable for efficient skin penetration and hence for the novel drug delivery system. They overcome the skin penetration difficulty by squeezing themselves along the intracellular sealing lipid of the stratum corneum. With the application of mechanical stress, they canenter through stratum corneum in self-adapting manner because of their high vesicles deformability. Flexibility or elasticity of transferosomes membrane is achieved by mixing suitable surface-active components (edge activator) in the proper ratios. The resulting flexibility of transfersomes membrane minimizes the risk of complete vesicle rupture in the skin and allows them to follow the natural water gradient across the epidermis, when applied under nonexclusive condition. They can penetrate the intact stratum corneum spontaneously by either intracellular lipids or transcellular route. The strong and self-optimizing deformability of the traditional membrane of composite bodies, adaptable to ambient stress, enables the ultra-deformable transfers to alter the composition of the membrane locally and reversibly when pressed against or attracted by narrow pore. When applied on the skin, the carriers searches and exploits hydrophilic pathways or ‘pores’ between the cells, where it opens wide enough to permit the entire vesicle to pass through stratum corneum along with drug molecule, deforming itself extremely to accomplish

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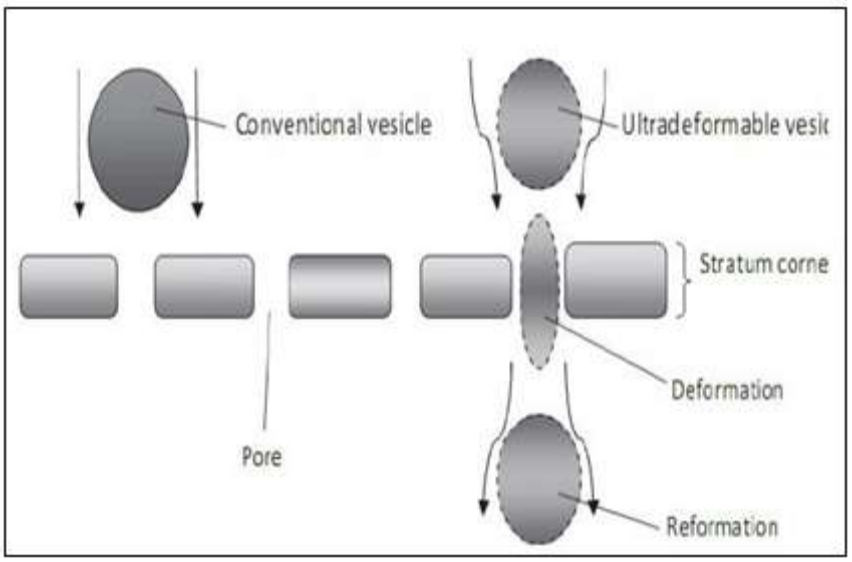
this without losing its vesicular integrity. This enables them to cross various transport barriers efficiently.

Transferosomes are ultra-deformable, self-optimized aggregates for transdermal application containing a mixture of lipids and biocompatible membrane softeners. While the basic organisation is largely similar to liposomes, the Transfer some differs by its smoother, more deformable and better adjustable artificial membrane, because of the evaporation of a transfersome vesicle, when applied to an open biological surface, they penetrate the stratum corneum by either intracellular route or the transcellular route by the generation of 'osmotic gradient'Transferosomes vesicles can transport molecules that are too big to diffuse through skin E.g.: systemic delivery of therapeutically meaningful amounts of macromolecules, such as insulin or interferon. Other uses involve the transport of small molecule drugs with some physicochemical properties that would otherwise stop them from spreading around the Nowadays, Transferosome can be used to target subcutaneous peripheral tissue. The Non-steriodal anti-inflammatorydrug (NSAID) ketoprofen in a transferosome formulation in the trade mark Diractin gained marketing approval by the Swiss regulatory agency (Swiss Medic) in 2007. Topical immunization using cationic transferosome based DNA vaccine offers all the advantages of DNA vaccines and in addition overcome the disadvantages of classical invasive methods of vaccinations. Owing to their low skin permeability, breaking of vesicles, drug leakage, aggregation and vesicle fusion, the liposomal and noisome systems are not appropriate for transdermal delivery. A new type of carrier system called "Transferosome" has recently been developed to address this issue, which is capable of transdermal delivery of low and high molecular weight drugs. Transferosomes are specially optimised, ultra-deformable (ultra-flexible) supra molecular lipid aggregates that can penetrate the intact preservation of the skin. At least one internal aqueous compartment is composed of each transferosome. Due to the insertion of "edge activators" into the vesicular membrane, which is surrounded by a lipid bilayer with specially formulated properties. As edge activators, surfactants such as sodium cholate, sodium deoxycholates, span 80, and tween 80 were used. Transferosomes are vesicles composed of phospholipids as the main ingredients (soy phosphatidycholine, egg phosphatidycholine, dipalmithylphosphatidycholine, etc), 10-25 percent versatile surfactants (sodium cholate, tween 80), 3-10 percent alcohol as a solvent (ethanol, methanol) and h-10 percent alcohol as a solvent (ethanol, methanol) and h-10 percent alcohol as a solvent (ethanol, methanol) The name means "to bring across" and the Greek word for "body". Transferosome carriers are artificial vesicles that are engineered to be like vesicles or cells that are involved in exocytosis and are therefore ideal for drug delivery that is regulated and potentially targeted.



Schematic Diagram Of The Two Microroutes Of Penetration.

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ADVANTAGES OF TRANSFEROSOMES

- Transferosomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as result can accommodate drug molecules with wide range of solubilities. They can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without significant loss.
- This system 's high deformability gives better penetration of intact vesicles. They can act as a carrier for medicines such as analgesics, anaesthetic, corticosteroids, sex hormones, anticancer, insulin and albumin that are both low and high molecular weight.
- As they are made from natural phospholipids similar to liposomes, they are biocompatible and biodegradable.
- They have high entrapped efficiency, in case of lipophilic drug near to 90%.
- They protect the encapsulated drug from metabolic degradation examples: protein and peptides.
- They act as depot, releasing their content slowly and gradually & can be used for both systemic as well as topical delivery of drug. They are easy to scale up, as procedure is simple and avoid unnecessary use or pharmaceutically unacceptable additives.
- At first glance, transferosomes appear to be remotely related to lipid bilayered vesicles, liposomes.However in functional terms, transferosomes differ vastly from commonly used liposome in that they are much more flexible and adaptable.
- The extremely high flexibility their membrane permits transferosomes to squeeze themselves even through pores much smaller than their own diameter.
- Transferosomes have a hydrophobic and hydrophilic structure and can thus accommodate drug molecules with a wide range of solubility..
- Without measurable loss, transferosomes can deform and move through narrow constrictions (from 5 to 10 times less than their own diameter).
- They can act as a carriers for low as well as high molecular weight drugs e.g. analgesic, synesthetic, corticosteroids, sex hormone. They have high entrapment efficiency, in case of lipophilic drugs close to 90%.

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.
- The formulations of transferosomes are costly.

II. COMPOSITION OF TRANSFEROSOME

The transfersome is composed of two main aggregates namely,

- An amphipathic ingredient (such as phosphatidylcholine) that self-assembles in aqueous solvents into a lipid bilayer that closes into a clear lipid vesicle.
- The second bilayer softening factor (such as a biocompatible surfactant or an amphiphile drug) is significantly enhanced by lipid bilayer flexibility and permeability. Transfersome vesicles can therefore easily and quickly adapt their shape to the environment by adjusting the local concentration of each bilayer portion to the local stress encountered by the bilayer, as shown in The resulting optimised flexibility and permeability. The Transfersome therefore differs primarily from such more traditional vesicles by its "softer", more deformable, and better adjustable artificial membrane.

MECHANISM OF ACTION

At least one amphipathic aggregate (such as phosphatidylcholine) is composed of the carrier aggregate, which is self-assembled in aqueous solvents into a lipid bilayer which closes into a simple lipid vesicle. By adding at least one bilayer softening component (such as biocompatible surfactant or amphiphile drug) to lipid bilayer flexibility and permeability, the resulting optimised flexibility and permeability can then adapt its shape to the environment quickly and easily by changing the local concentration of each bilayer component to the local stress encountered by the b vesicle artificial membrane.

The increased transferosome affinity to bind and hold water is another beneficial consequence of high bilayer deformability. An ultra-deformable and highly hydrophilic vesicle often seeks to avoid dehydration; this may require a transport mechanism linked to, but not equivalent to, for example, a transferosome vesicle applied to an open biological surface, such as non-occluded skin, tends to penetrate its barrier and migrate to

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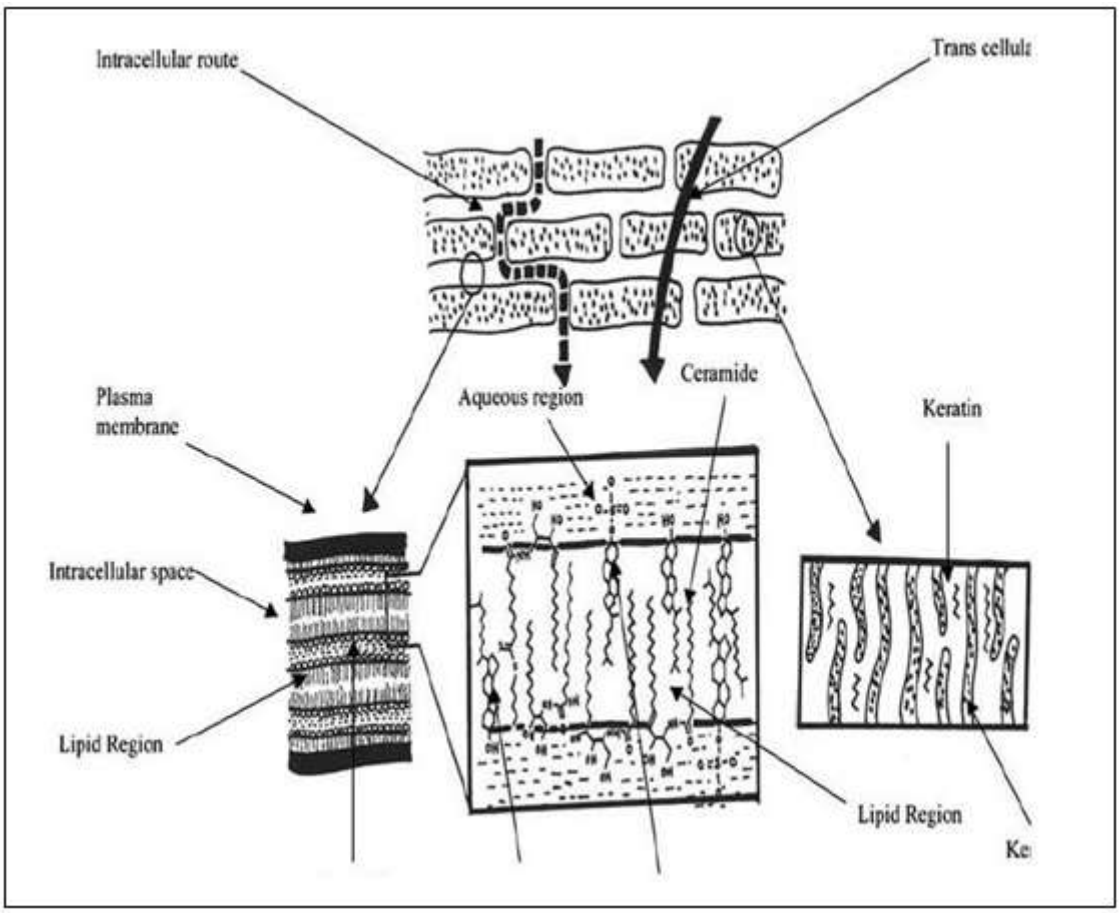
the deeper water-rich strata to protect its penetration into the place.

The Transferosome has to find and implement its own path through the organ since it is too big to diffuse through the skin. As a consequence, the use of Transferosome vesicles in transmission relies on the ability of the carrier to expand and resolve the hydrophilic pores in the skin or some other barrier (e.g. plant cuticle). If the vesicle is deliberately taken up by the cell in the process called endocytosis, the subsequent, incremental release agent from the drug carrier helps the drug molecules to disperse and eventually bind fusion with the cell.



Diagrammatic Representation of The Stratum Corneum And The Intercellular And Transcellular Routes Of Penetration.

PROPENSITY OF PENETRATION

The magnitude of the transport driving force, of course, also plays an important role: Flow =Area x (Barrier) Permeability x (Trans- barrier) force. Therefore, the chemically driven lipid flow across the skin always decreases dramatically when lipid solution is replaced by the same amount of lipids in a suspension.

Optimization of Formulation Containing Transfersomes

Techniques for optimization are plentiful in the pharmaceutical field. Techniques of optimization have both a depth of understanding and an opportunity to investigate and defend formulating and processing factor ranges. There are various process variables that could influence the transfersomes' planning and properties..

The preparation procedure for transfersome was first optimized and validated. The process variables in the formulation depend on the formulation process involved in the output. The preparation of transfersome involves various process variables such as,

1. Lecithin: surfactant ratio
2. Effect of various solvents
3. Effect of various surfactants

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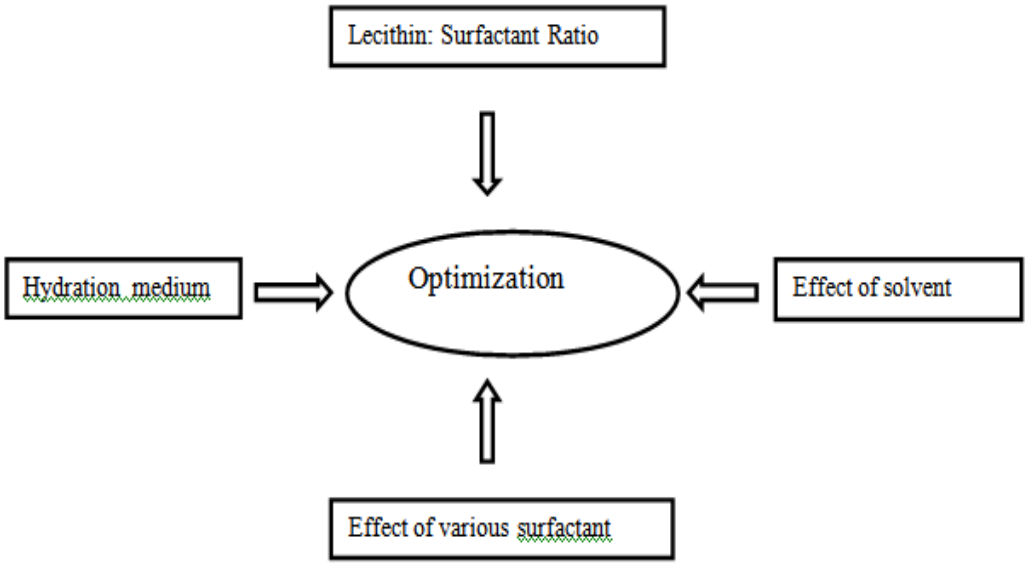
4. Hydration medium
5. Optimization was performed by choosing the drug's trapping efficiency

Process variables affecting optimization technique in transferosome formulation:



MATERIAL FOR TRANSFEROSOMES

Transferosomes is a self-adaptable and optimized mixed lipid aggregate and composed of phospholipids like phosphatidylcholine which self assembles into lipid bilayer in aqueous environment and closes to forma vesicle. A bilayer softening component (such as a biocompatible surfactant or an amphiphile drug) is added to increase lipid bi layer flexibility and permeability. This second element is known as the edge activator.

An edge activator typically consists of a single chain surfactant that induces lipid bilayer destabilisation, thus increasing its fluidity and elasticity. The newer elastic vesicles were introduced by Van den berg in 1998, consisting of ionic surfactant as the edge activator 30. Transferosome membrane versatility can be altered by combining appropriate surface active agents in the appropriate ratios. The resulting optimised transferosome vesicle, versatility and permeability, can therefore easily and quickly adapt its shape to surrounding stress by changing the local concentration of each bi layer portion to the local stress encountered by the bi. This versatility also minimises the risk of complete vesicle rupture in the skin and enables transfersomes to adopt the natural water gradient ac. Vesicles composed of phospholipids as the main ingredients (soya phosphatidylcholine , egg phosphatidylcholine, dipalmithylphosphatidycholine, etc) ,10-25% surfactant for providing flexibility (ethanol, methanol) and hydrating medium consisting of saline phosphate buffer (pH 6.5-7). Dye like Rhodamine 123,Nile red for Confocal Scanning Laser Microscopy.

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Materials commonly used for the preparation of transferosome are summarized in Table below:

Ingredients	Examples	Functions
Phospholipid	Soya Phosphatidylcholine Egg Phosphatidylcholine Disteryl Phosphatidylcholine	Vesicles forming Component
Surfactant	Sodium Cholate Sodium Deoxy Cholate Tween 80 Span 80	For Providing Flexibility
Alcohol	Ethanol Methanol	As a Solvent
Dye	Rhodamine-123 Rhodamine-DHPE Fluorescein-DHPE Nil-red 6 Carboxyl fluorescence	For Confocal Scanning Laser Microscopy (CSLM) Study
Buffering Agent	Saline phosphate buffer (pH 6.5) 7% v/v ethanol Tris buffer (pH 6.5)	As a hydrating medium

III. METHODS OF PREPARATIONS OF TRANSFEROSOMES

1.Thin film hydration technique:

For the preparation of transferosomes thin film hydration technique is used, which comprised of mainly three steps.

(a)The organic solvent was evaporated using a rotary evaporator above the lipid transition temperature. The last traces of the solvent were removed overnight under a vacuum. At 60 RPM / min, the deposited lipid films were hydrated with buffer by rotation.

(b)The thin film is hydrated with buffer solution (pH 6.5) by rotation at 60 rpm for 1 hour at the corresponding temperature. The resulting vesicles were swollen for 2 hr.at room temperature.

(c)To prepare small vesicles, resulting vesicles were sonicated at room temperature or 50C for 30 min, using a bath sonicator or probe sonicator. The sonicated vesicles were homogenized by manual extrusion 10 min 10 times through a sandwich of 200 and 100nm polycarbonate membranes.

2.Modified Hand Shaking (lipid film hydration technique):

The method comprise of the following steps

(a)Drug, Phosphatidylcholine and Edge activator (Surfactant) were dissolved in ethanol: chloroform (1:1) mixture. Organic solvent was extracted by evaporation while shaking hands above the temperature of lipid transformation (43C). The film was kept overnight for complete evaporation of solvent.

(bThe film was then hydrated at the corresponding temperature with a phosphate buffer (pH 7.4) with gentle shaking for 15 minutes. The transferosomes suspension further hydrated upto at 1 hour at 2-8C.

IV. CHARACTERISATION OF TRANSFEROSOME:

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

1. **Vesicle Size, Size Distribution and Vesicle Diameter:**

Transmission electron microscopic studies are used to study the vesicular shape. The size of thevesicle and size distribution is generally determined using light scattering technique. The diameter of the vesicle is determined by photon correlation spectroscopy or dynamic light scattering DLS method. The samples are prepared using distilled water, and diluted with filtered saline after passing through a membrane filter of 0.2mm

2. **Vesicle Shape and Type:**

The visualization is carried out using TEM. Also, they can be visualized by phase contrast microscopy without sonication using optical microscopy method. Dynamic light scattering technique can also be used.

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3. Number of vesicle per cubic mm:

This character is very important for not only for optimizing the composition of the system but also other process variables. The formulation is diluted five times with 0.9% sodium chloride solution, without sonication. This solution is then studied by using haemocytometer with optical microscope. The transferosomes in at least 80 small squares can be counted by application of the formula:

Total no. of Transferosomes per cubic mm = Total no. of Transferosomes counted X dilution factor X 4000/Total no. of squares counted.

4. Entrapment Efficiency:

It is expressed as the amount of the drug entrapped in percent of that what is added. It is determined by separating the unentrapped drug by mini column centrifugation followed by disruption of the vesicles using 0.1 % Triton X-100 or 50% n-propanol. The entrapment efficiency is expressed as :

Entrapment efficiency = (amount entrapped/ total amount added)*100

5. Drug Content:

Instrumental analytical methods are used to determine the drug content like modified HPLC using a UV detector. The choice of the other parameters depend on the pharmacopoeial analytical method.

6. Confocal Scanning Laser Microscopy Study:

Conventional methods of light microscopy and electron microscopy have problems when it comes to fixing, sectioning and staining the sample. There is an incompatibility generally observed between the sample and the processing techniques. The misinterpretations that arise from such studies can be corrected by using Confocal Scanning Laser Microscopy (CSLM). The technique involves the use of lipophilic fluorescences markers and the light emitted by these markers is then used for:

- Understanding the mechanism by which the transferosome penetrate the skin.
- Determining the arrangement of the skin and the organization of the skin penetration pathway.
- Understanding the similarities and dissimilarities in the mode of penetration of transferosomes with other vesicles like liposome, noisome, micelles etc.
- The fluorescein- DHPE (1, 2-dihexadecanoyl-snglycero-3-phosphoethanolamine-N-(5 fluores denthiocarbamoyl), triethyl-ammounium salt)
- Rhodamine- DHPE (1,2-d (7-dihexadecanoyl-snglycero-3ogisogietgabikanube Lissamine tmrhodamine-B-sulfonyl), triethanol-amine salt)
- NBD-PE (1,2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine-N- (7-nitro-Benz-2-xa-1,3-diazol-4-yl) triethanolamine salt)
- Nile red

7. Turbidity Measurement:

Turbidity of the drug is measured in the solution from using a nephelometer.

8.Surface Charge and Charge Density:

A zeta sizer is used to determine the surface charge and charge density.

9.Penetration Ability:

This is generally evaluated using fluorescence microscopy.

10.Occlusion Effect:

It is considered to be helpful for permeation of topical preparation s. Hydrotaxis appears to be the major driving force responsible for the permeation of tranfersomes. Occlusion effect is important to study as it prevents evaporation of water from skin thus affecting hydration forces.

11.In-vitro Drug Release:

Determined by calculating the permeation rate. The formulation is incubated at 32 C . The free drug from the samples which are drawn at regular intervals is obtained by mini column centrifugation. The calculation for amount of drug released is done indirectly from the amount of drug that was entrapped at zero time as 100%.

12.In-vitro Skin Permeation Studies:

Modified franz diffusion cell having a volume of 50 mL and receiver compartment which has an effective area of 2.50 cm2 is generally used. Goat skin in phosphate buffer (pH 7.4) is used which is freshly collected from slaughter house. Hair is removed from the skin and the skin is allowed to hydrate in normal saline. The skin has to be cleaned of the adipose tissues using a cotton swab.

The skin can be stored in IPA at low temperatures. While mounting,the skin should be placed with the stratum corneum facing towards the

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donor compartment. The stirring is carried out at a rate of 100rpm. Formulation equivalent to 10 mg of drug is used. At regular intervals interval 1 mL of aliquot is drawn and is replaced immediately with fresh phosphate buffer (pH 7.4). Analysis of samples is done using instrumental techniques after including the correction factors.

13.Skin Deposition Studies of Optimized Formulation:

After the end of permeation study (at the end of 24 h), the goat skin surface is washed five times with a solution containing ethanol :PBS (pH 7.4) in the ratio 1:1 and the excess drug present on the surface should be removed by using giving washings with water.

The skin is subjected to homo-genisation after it is cut into small piece with the same ethanol and pH 7.4 buffer solution and is then left room temperature for 6 hrs. After shaking it for 5 min and centrifugation it for 5 min at 5000 rpm, the drug content is analysed using appropriate dilutions with phosphate buffer solution (pH 7.4). The result is compared using a student's test, with that of that control.

14.In Vivo Fate of Transferosomes and Kinetics of Transferosomes Penetration:

Transferosomes enter the deeper skin after penetrating through and outermost skin layers From this later skin area, they are usually washed out into the blood circulation through the lymph, and through the latter throughout the body, so if applied under suitable transferosomes, all such body tissues that are accessible to subcutaneously injected liposomes can be reached. The most important single factors in this process are:

(a).Carriers in-flow

(b). Carrier accumulation at the targets site

(c).Carrier elimination

15. Physical Stability:

The initial proportion of the drug trapped in the formulation was developed and stored in sealed glass ampoules. The ampoules were placed at 4 to 20 C months. Samples from each ampoules were analysed after 30 days to determine drug leakage. Percent drug lose was calculated by keeping the initial entrapped of drug as 100%.

V. APPLICATION OF TRANSFERSOMES

Different drugs are successfully loaded on to transfersomes which provides targeted as well as controlled drug delivery to the various body tissues (Table).

Table: Application of transfersomes

Sr.no.	Name of drug	Inference
1	Curcumin[28]	Better permeation for anti-inflammatory activity
2	Indinavir sulfate[30]	Improved influx for activity against acquired immune deficiency syndrome (AIDS)
3	Ketoprofen[45]	Improved penetration for anti-inflammatory activity
4	Insulin[40]	induce therapeutically significant hypoglycemia with good efficacy and reproducibility
5	Capsaicin43, 44	Increase skin penetration
6	Colchicine[46]	Increase skin penetration
7	Vincristine[46]	Increase entrapment efficiency and skin permeation
	1. Interferon-α[41]	Efficient delivery means (because delivery other route is difficult). Controlled release. Overcome stability problem.
	2. Norgesterol[47]	Improved transdermal flux

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3.	Tamoxifen[17]	Improved transdermal flux
4.	Methotrexate[38]	Improved transdermal flux
5.	Oestradiol[39]	Improved transdermal flux
6. Lignocain[34]	Tetracaine,[39]	Suitable means for the noninvasive treatment of local pain on direct topical drug application.
7.	Corticosteroids[22]	Improved site specificity and overall drug safety.
8.	Hydrocortisone[22]	Biologically active at dose several times lower than currently used formulation.
9. acetonide[22]	Triamcinolone	Used for both local and systemic delivery.
10.Human albumin[17]	serum	Antibody titer is similar or even slightly higher than subcutaneous injection.
11.Stavudine[29]		Improved the in vitro skin delivery of Stavudine for antiretroviral activity
12.Tetanus toxoid[48]		For transdermal immunization

Delivery of proteins and peptides:

Transfersomes have been commonly used as a carrier for protein delivery and peptides are massive biogenic molecules that are very difficult to transport into the body and are fully degraded in the GI tract when administered orally. There are the reasons why these peptides and proteins by injections still have to be inserted into the body. In order to enhance these conditions, various methods have been developed. The bioavailability of the transferosomes is very similar to that of the same protein suspension resulting from subcutaneous injection. After repeated epicutaneous application, transferosomal preparations of this protein have induced a powerful immune response, such as adjuvant immunogenic bovine serum albumin in transferosomes, which is as active immunologically after many dermal difficulties as the corresponding injected proteo-transferosomes preparations.

Delivery of insulin

The effective means of non-invasive therapeutic use of such large molecular weight drugs on the skin is through transferosomes. Insulin is normally administered via an uncomfortable subcutaneous route. All these problems are solved by the encapsulation of insulin into transferosomes (transfersulin). The first symptom of systemic hypoglycemia is observed after application of transfersulin to the intact skin after 90 to 180 minutes, depending on the 40-minute duration.

Delivery of interferons:

Transferosomes have also been used as an interferon carrier, such as leukocytic derived interferon-alpha (INF-alpha) is a naturally occurring antiviral, antiproliferative protein, and some transferosomes have the potential to provide controlled release of the medication administered and improve the stability of labile drugs as drug delivery systems.

Hafer et al analysed the formulation of transferosme-containing interleukin-2 and interferone-alpha for potential transdermal use. They recorded transferosome-trapped IL-2 and INF-alpha delivery at appropriate concentrations for immunotherapy.

Delivery of corticosteroids:

Transferosomes have also been used for corticosteroid delivery purposes. Transferosomes, by improving the epicutaneously administered drug dose, enhance the site specificity and overall drug safety of corticosteroid delivery into the skin. Corticosteroids based on transferosomes are biologically active at a dosage many times lower than the formulations commonly used to treat skin diseases.

Transdermal immunization:

Transdermal immunisation using transferosomes loaded with soluble protein such as integral membrane protein, human serum albumin, gap is another most important application of transferosomes. This method provides at least two advantages: firstly, they are applicable without injection and secondly, they give rise to very high titer levels and probably relatively high IgA levels.

Delivery of anesthetics:

The use of anaesthetics in suspension of highly deformable vesicles, transferosomes, induces topical anaesthesia under suitable conditions, with the maximum resulting insensitivity to pain being almost as extreme (80%) as that of comparable subcutaneous bolus injection, but the impact of transferosomal anaesthetics.

Delivery of NSAIDS:

There are several GI side effects associated with NSAIDS. These can be solved using ultra-deformable vesicles by transdermal delivery. Studies on Diclofenac and Ketoprofen have been performed. Ketoprofen was obtained marketing approval by the Swiss regulatory agency (SwissMedic) in the Transfersome formulation in 2007; According to IDEA, the drug is scheduled to be marketed under Other therapeutic products based on Transfersome technology are in clinical research

Delivery of Anticancer Drugs:

Using transfer technology, anti-cancer drugs such as methotrexate have been studied for transdermal delivery. The findings were positive. This has created a new approach to treating, in particular, skin cancer.

Delivery of Herbal Drugs:

In this relation, transfersomes can penetrate stratum corneum and supply the nutrients locally to maintain its functions resulting in skin maintenance, Xiao-Ying has prepared transfersomes of capsaicin, which shows better topical absorption compared to pure capsaicin.

VI. CONCLUSION

Ultra-deformable vesicles can provide the novel solution for the transport related problems.They are free from the rigid nature of traditional vesicles, and even large molecules can be transported. They are working on a variety of mechanisms that function together to provide an excellent transport system for drug carriers. Transfersomes can move almost as efficiently through even tiny pores (100 mm) when tested in artificial systems as water, which is 1500 times smaller. Drug laden transfersomes (up to 100 mg cm2h-1) can bring unparalleled amounts of drugs per unit of time through the skin. Ultra-deformable vesicles hold great prospective in delivery of huge range of drug substances which includes large molecules like peptides, hormones and antibiotics, drugs with poor penetration due to unfavorable physicochemical characters, drugs for quicker and targeted action, etc. All above discussed properties of this technology strongly advocate its good future in transdermal drug delivery.

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