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# Transfersomes – A Review

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**ABSTRACT**

Transdermal drug delivery appears to be the most vital drug delivery system because of its merit over conventional systems. Various strategies can be used to augment the transdermal delivery which includes iontophoresis, electrophoresis, sonophoresis, chemical permeation enhancers, microneedles, and vesicular system (liposomes, niosomes, elastic liposomes such as ethosomes and transfersomes).The transfersomal system was much more efficient among all these strategies. These can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without measurable loss. The system can be characterized by *in vitro* for vesicle shape and size, entrapment efficiency, degree of deformability, number of vesicles per cubic mm.The deformability characteristic of transfersomes gives better permeation of drugs.They can act as a carrier for low as well as high molecular weight drugs eg: analgesics, anaesthetics,corticosteroids, sex hormone, insulin.[1-3]

## INTRODUCTION

The term transfersome and the underlying concept were introduced in 1991 by Gregor Cevc. In broadest sense, a transfersome is a highly adaptable and stress-responsive, complex aggregate. Its preferred form is an ultra deformable vesicle possessing an aqueous core surrounded by the complex lipid bilayer. Interdependency of local composition and shape of the bilayer makes the vesicle both self-regulating and self-optimising. This enables the transfersome to cross various transport barriers efficiently, and then act as a drug carrier for non-invasive targeted drug delivery and sustained release of therapeutic agents.[4,5]

Delivery via the transdermal route is an interesting option in this respect because a transdermal route is convenient and safe. This offers several potential advantages over conventional routes (Shaw et al., 1999) 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, avoiding the fluctuation in drug levels, inter-and intra-patient variations, and most importantly, it provides patients convenience. Today many chemical and physical approaches have been applied to increase the efficacy of the material transfer across the intact skin, by use of the penetration enhancers, enhancers, iontophoresis, sonophoresis and the use of colloidal carriers such as lipid vesicles (liposomes and proliposomes) and nonionic surfactant vesicles (niosomes and proniosomes).[6]

Transfersomes were developed in order to take the advantage of phospholipids vesicles as transdermal drug carrier. These self-optimized aggregates, with the ultra-flexible membrane, are able to deliver the drug reproducibly either into or through the skin, depending on the choice of administration or application, with high efficiency. These vesicular transfersomes are several orders of magnitudes more elastic than the standard liposomes and thus well suited for the skin penetration. Transfersomes overcome the skin penetration difficulty by squeezing themselves along the intracellular sealing lipid of the stratum corneum as shown in fig 1. There is provision for this, because of the high vesicle deformability, which permits the entry due to the mechanical stress of surrounding, in a self-adapting manner.[7-9] Flexibility of transfersomes membrane is achieved by mixing suitable surface-active components in the proper ratios (Cevc et al, 1991). The resulting flexibility of transfersome membrane minimizes the risk of complete vesicle rupture in the skin and allows transfersomes to follow the natural water gradient across the epidermis, when applied under nonocclusive condition.

Transfersomes can penetrate the intact stratum corneum spontaneously along two routes in the intracellular lipid that differ in their bilayers properties (Schatzlein et al, 1995). The following figure shows possible micro routes for drug penetration across human skin intracellular and transcellular (Panchagnula, 1997).[10-12]

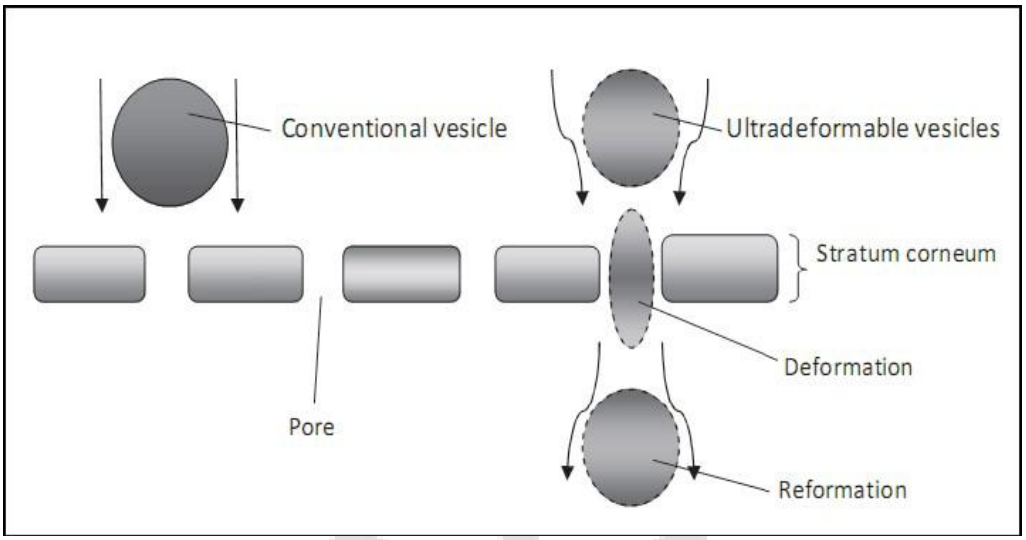


**Fig 1: Schematic Diagram of the Two Microroutes of Penetration.**

The high and self-optimizing deformability of typical composite transfersomes membrane, which are adaptable to ambient stress allow the ultra-deformable transfersomes to change its membrane composition locally and reversibly, when it is pressed against or attracted into narrow pore. The transfersomes components that sustain strong membrane deformation preferentially accumulate, while the less adaptable molecules are diluted at sites of great stress. This dramatically lowers the energetic cost of membrane deformation and permits the resulting, highly flexible particles, first to enter and then to pass through the pores rapidly and efficiently. This behaviour is not limited to one type of pore and has been observed in natural barriers such as in intact skin (Bain *et al*, Cevc *et al*., 1996).[13,14]

**Salient features and limitations of transfersomes**

Transfersomes possess an infrastructure consisting of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility as shown in fig 2. Transfersomes can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without measurable loss. This high deformability gives better penetration of intact vesicles.[15]

They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anaesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin. They are biocompatible and biodegradable as they are made from natural phospholipids similar to liposomes. They have high entrapment efficiency, in case of lipophilic drug near to 90%. They protect the encapsulated drug from metabolic degradation. They act as depot, releasing their contents slowly and gradually. They can be used for both systemic as well as topical delivery of drug. Easy to scale up, as procedure is simple, do not involve lengthy procedure and unnecessary use or pharmaceutically unacceptable additives (Jain.,2001).[16-18]

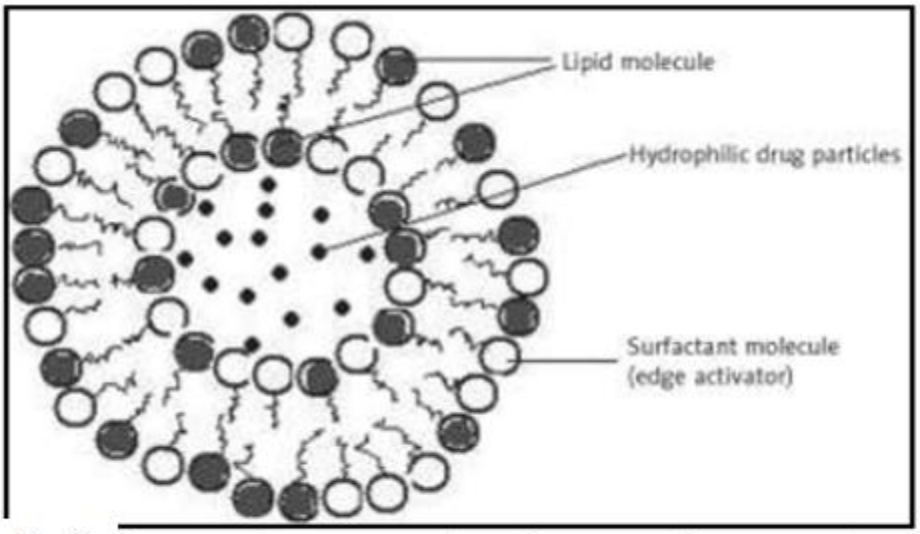


**Fig. 2** Structural representation of one transfersome unit

**Silent features of Transfersomes**

**Anatomy and Physiology of Human Skin**[19-23]

The skin is the largest organ of the body, accounting for about 15% of the total adult body weight. It performs many vital functions, including protection against external physical, chemical, and biologic assailants, as well as prevention of excess water loss from the body and a role in thermoregulation. The skin is continuous, with the mucous membranes lining the body surface.

The skin of an average adult body covers a surface area of approximately 2 $m^2$ and receives about one third of the blood circulating through the body and serves as a permeability barrier against the transdermal absorption of various chemical and biological agent. It is one of the

most readily available organs of the body with a thickness of only a few millimetres (2.97 ±0.28 mm). The skin

- Separates the underlying blood circulation network from the outside environment.
- Serves as a barrier against physical, chemical and microbiological attacks.
- Acts as a thermostat in maintaining body temperature.
- Plays role in the regulation of blood pressure.
- Protects against the penetration of UV rays.

As skin is major factor in determining the various drug delivery aspects like permeation and absorption of drug across the dermis. It is quite worthwhile to highlight some important characteristic of skin. The diffusion resistance of the skin is greatly dependent on its anatomy and ultrastructure. Figure 1 shows the stratified organization of the skin. The composite structure of the skin is indicated by three distinct layers: the epidermis, dermis and subcutaneous fat layer **(Figure 3).**

For the purpose of transdermal drug delivery, we can examine the structure and function of human skin categorized into following four main layers:

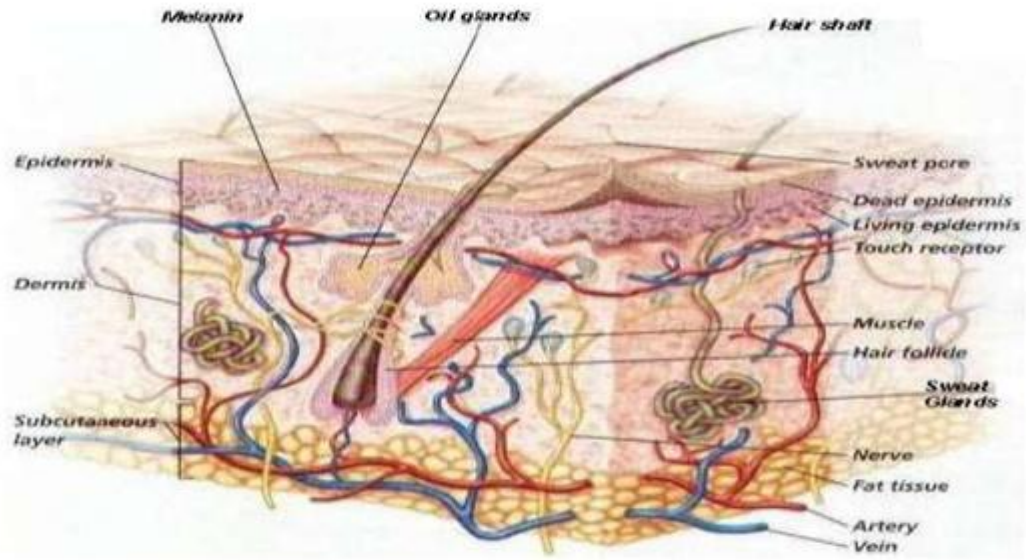


**Fig. 3 : Standard organization of skin**

**Subcutaneous Fat Layer**

The subcutaneous fat layer or hypodermis, bridges between the overlying dermis and the underlying body constituents. In most areas of the body this layer is relatively thick, typically

in the order of several millimetres. This layer of adipose tissue principally serves to insulate the body and to provide mechanical protection against physical shock. The subcutaneous fatty layer can also provide a readily available supply of high-energy molecules, whilst the principal blood vessels and nerves are carried to the skin in this layer.

**Dermis**

The dermis has numerous structures embedded within it: blood and lymphatic vessels, nerve endings, pilosebaceous units (hair follicles and sebaceous glands) and sweat glands (eccrine and apocrine). Thus provides physiological support for the epidermis. The dermis (or corium)is typically 3–5 mm thick and is the major component of human skin. It is composed of a network of connective tissue, predominantly collagen fibrils providing support and elastic tissue providing flexibility, embedded in a mucopolysaccharide gel. In terms of transdermal drug delivery, this layer is often viewed as essentially gelled water and thus provides a minimal barrier to the delivery of most polar drugs, although the dermal barrier may be significant when delivering highly lipophilic molecules.

**Epidermis**

The epidermis is further classified into a number of layers. The stratum germinativum is the basal layer of the epidermis. Above the basal layer are the stratum spinosum, the stratum granulosum, the stratum lucidum and finally, the stratum corneum.

**Stratum Corneum**

The stratum corneum or the horny layer is the rate limiting barrier that restricts the inward and outward movement of chemical substances consists of flattened keratin-filled cells (e.g., corneocytes). Upon reaching the stratum corneum, these cells are cornified and flatten. The corneocytes are then sloughed off the skin at a rate of about one cell layer per day, a process called desquamation. The main source of resistance to penetration and permeation through the skin is the stratum corneum. Stratum corneum is approximately 15-20 m thick over much of the human body and corneocytes are composed of cytoplasmic protein matrices comprising keratin embedded in the extracellular lipid. In the simplest sense, therefore, the skin may be represented as a bilaminated membrane; and to reach the dermal vasculature (and rapid systemic distribution), a penetrating molecule must traverse both, the lipophilic

environment of the stratum corneum and the aqueous environment of the underlying viable epidermis and upper dermis.

**Composition and Mechanism of Action**

The carrier aggregate is composed of at least one amphipathic (such as phosphatidylcholine), which in aqueous solvents self-assembles into lipid bilayer that closes into a simple lipid vesicle. By addition of at least one bilayer softening component (such as a biocompatible surfactant or an amphiphile drug) lipid bilayer flexibility and permeability are greatly increased. The resulting, flexibility and permeability optimized, Transfersome vesicle can therefore adapt its shape to ambient easily and rapidly, by adjusting local concentration of each bilayer component to the local stress experienced by the bilayer as shown in fig 4. In its basic organization broadly similar to a liposome), the Transfersome thus differs from such more conventional vesicle primarily by its "softer", more deformable, and better adjustable artificial membrane.[24]

Another beneficial consequence of strong bilayer deformability is the increased Transfersome affinity to bind and retain water. An ultra deformable and highly hydrophilic vesicle always seeks to avoid dehydration; this may involve a transport process related to but not identical with forward osmosis. For example, a Transfersome vesicle applied on an open biological surface, such as non-occluded skin, tends to penetrate its barrier and migrate into the water-rich deeper strata to secure its adequate hydration. Barrier penetration involves reversible bilayer deformation, but must not compromise unacceptably either the vesicle integrity or the barrier properties for the underlying hydration affinity and gradient to remain in place.[25-26]

Since it is too large to diffuse through the skin, the Transfersome needs to find and enforce its own route through the organ. The Transfersome vesicles usage in drug delivery consequently relies on the carrier's ability to widen and overcome the hydrophilic pores in the skin or some other (e.g. plant cuticle) barrier. The subsequent, gradual agent release from the drug carrier allows the drug molecules to diffuse and finally bind to their target. Drug transport to an intracellular action site may also involve the carrier's lipid bilayer fusion with the cell membrane unless the vesicle is taken up actively by the cell in the process called endocytosis (Wikipedia).

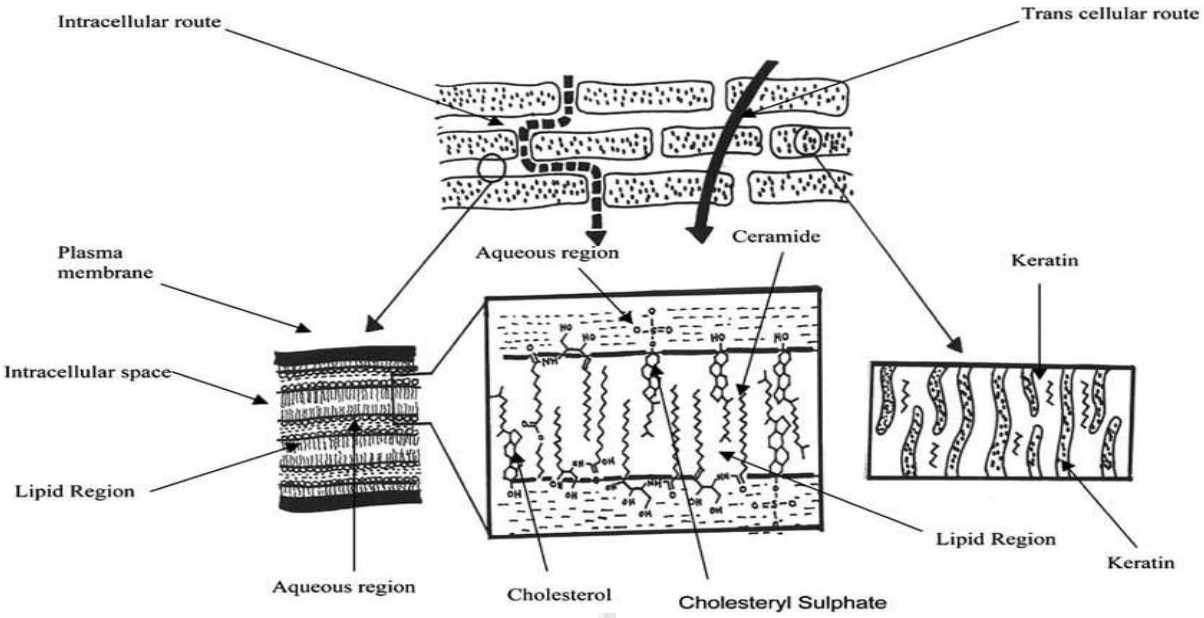


**Fig 4: Diagrammatic Representation of The Stratum Corneum And The Intercellular And Transcellular Routes of Penetration** (Heather., 2005).

## MATERIALS AND METHODS[27]

Materials which are widely used in the formulation of transferosomes are various phospholipids, surfactants, alcohol, dye, buffering agent etc. Different additives used in the formulation of transferosomes are summarized in table no. 1 (Wearner *et al*., 1988, Rand *et al*., 1988, Cevc *et al*., 1997, Cevc *et al*1998., Gamal *et al*., 1999)

| **Class** | **Example** | **Uses** |
|---|---|---|
| Phospholipids | Soya phosphatidylcholine, egg phosphatidylcholine, dipalmitoyl phosphatidylcholine | Vesicles forming agent |
| Surfactant | Sod. cholate, Sod. deoxycholate, Tween -80,Span-80 | For providing flexibility |
| Alcohol | Ethanol, methanol | As a solvent |
| Buffering agent | Saline phosphate buffer (pH 6.4) | As a hydrating medium |

**Preparation of Transfersomes**

**A. Thin film hydration technique is employed for the preparation of transfersomes which comprised of three steps:**

1. A thin film is prepared from the mixture of vesicles forming ingredients that is phospholipids and surfactant by dissolving in volatile organic solvent (chloroform methanol). Organic solvent is then evaporated above the lipid transition temperature (room temp. for pure PC vesicles, or 50°C for dipalmitoylphosphatidylcholine) using rotary evaporator. Final traces of solvent were removed under vacuum for overnight.

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

3. To prepare small vesicles, resulting vesicles were sonicated at room temperature or 50°C for 30 min. using a bath sonicator or probe sonicated at 4°C for 30 min. The sonicated vesicles were homogenized by manual extrusion 10 times through a sandwich of 200 and 100 nm polycarbonate membranes

**B. Modified hand shaking, lipid film hydration technique is also founded for the preparation of transfersomes which comprised following steps**

1. Drug, lecithin (PC) and edge activator were dissolved in ethanol: chloroform (1:1) mixture. Organic solvent was removed by evaporation while handshaking above lipid transition temperature (43°C). A thin lipid film was formed inside the flask wall with rotation. The thin film was kept overnight for complete evaporation of solvent.

2. The film was then hydrated with phosphate buffer (pH 7.4) with gentle shaking for 15 minute at corresponding temperature. The transfersome suspension further hydrated up to 1 hour at 2-8°C.

**Characterization of Transfersomes**[28-30]

The characterization of transfersomes is generally similar to liposomes, niosomes and micelles (Nanda *et al*., 2005, Jain *et al*., 1998).

**Entrapment Efficiency**

The entrapment efficiency is expressed as the percentage entrapment of the drug added. Entrapment efficiency was determined by first separation of the unentrapped drug by use of mini-column centrifugation method. After centrifugation, the vesicles were disrupted using 0.1% Triton X-100 or 50% n-propanol. The entrapment efficiency is expressed as: Entrapment efficiency= (amount entrapped/ total amount added)*100.

**Vesicle Diameter**

Vesicle diameter can be determined using photon correlation spectroscopy or dynamic light scattering(DLS) method. Samples were prepared in distilled water, filtered through a 0.2 mm membrane filter and diluted with filtered saline and then size measurement done by using photon correlation spectroscopy or dynamic light scattering (DLS) measurements (Gamal *et al.,* 1999).

**Number of Vesicle per Cubic Mm**

This is an important parameter for optimizing the composition and other process variables. Transferosome formulations (without sonication) can be diluted five times with 0.9% of sodium chloride solution and studied with optical microscopy by using haemocytometer.

**Degree of Deformability or Permeability Measurement**

In the case of transfersomes, the permeability study is one of the important and unique parameter for characterization. The deformability study is done against the pure water as standard. Transfersomes preparation is passed through a large number of pores of known size (through a sandwich of different microporous filters, with pore diameter between 50 nm and 400 nm, depending on the starting transfersomes suspension). Particle size and size distributions are noted after each pass by dynamic light scattering (DLS) measurements.

**Turbidity Measurement**

Turbidity of drug in aqueous solution can be measured using nephelometer.

**Surface Charge and Charge Density**

Surface charge and charge density of transferosomes can be determined using zeta sizer.

**Penetration Ability**

Penetration ability of transferosomes can be evaluated using fluorescence microscopy.

***In vitro* Drug Release**

Modified Franz diffusion cell with a receiver compartment volume of 50ml and effective diffusion area of 2.50 cm2 was used for this study. In vitro drug study was performed by using goat skin in phosphate buffer solution (pH 7.4). Fresh Abdominal skin of goat were collected from slaughterhouse and used in the permeation experiments. Abdominal skin hairs were removed and the skin was hydrated in normal saline solution. The adipose tissue layer of the skin was removed by rubbing with a cotton swab. Skin was kept in isopropyl alcohol solution and stored at 0-40˚C. To perform skin permeation study, treated skin was mounted horizontally on the receptor compartment with the stratum corneum side facing upwards towards the donor compartment of Franz diffusion cell. The effective permeation area of donor compartment exposed to receptor compartment was2.50cm2 and capacity of receptor compartment was 50ml. The receptor compartment was filled with50ml of phosphate buffer (pH 7.4) saline maintained at 37 ± 0.5˚C and stirred by a magnetic bar at 100RPM. Formulation (equivalent to 10mg drug) was placed on the skin and the top of the diffusion cell was covered. At appropriate time intervals 1 ml aliquots of the receptor medium were withdrawn and immediately replaced by an equal volume of fresh phosphate buffers (pH 7.4) to maintain sink conditions. Correction factors for each aliquot were considered in calculation of release profile. The samples were analyzed by any instrumental analytical technique.

***In Vivo* Fate of Transfersomes and Kinetics of Transfersomes Penetration**[31,32]

After having penetrated through the outermost skin layers, transfersomes reach the deeper skin layer, the dermis. From this latter skin region they are normally washed out, via the lymph, into the blood circulation and through the latter throughout the body, if applied under suitable conditions. Transfersomes can thus reach all such body tissues that are accessible to the subcutaneously injected liposomes. The kinetics of action of an epicutaneously applied agent depends on the velocity of carrier penetration as well as on the speed of drug (re) distribution and the action after this passage. The most important single factors in this process are:

1. Carrier in-flow
2. Carrier accumulation at the targets site
3. Carrier elimination

The onset of penetration-driving force depends on the volume of the suspension medium that must evaporate from the skin surface before the sufficiently strong trans-cutaneous chemical potential chemical potential or water activity gradient is established. Using less solvent is favourable in this respect. The rate of carrier passage across the skin is chiefly determined by the activation energy for the carrier deformation.

The magnitude of the penetration driving force also plays a big role. This explains, for example, why the occlusion of an application site or the use of too strongly diluted suspension hampers the penetration process. Carrier elimination from the subcutis is primarily affected by the lymphatic flow, general anaesthesia or any other factor that affects this flow, consequently, is prone to modify the rate of transcutaneous carrier transport. While it has been estimated that approximately 10% of the cardiac blood flow pass through each gram of living skin tissue, no comparable quotation is available for the lymph. Further, drug distribution is also sensitive to the number of carrier used, as this may affect the rate of vehicle degradation and / or filtration in the lymph nodes.

The lag between the time of application and the time of drug appearance in the body, therefore, is always quite long, complex and strongly sensitive to the type of drug and formulation administration. In the best case, the skin penetration lag amounts to approximately 15 min. if rapidly exchanging agents such as local analgesics are detected right under the skin permeability barrier. Less rapidly exchanging molecules or molecules measured in the blood compartment are typically detected with a lag time between 2 and 6 hr. depending on the details of drug formulation. Molecules that do not diffuse readily from the carriers or agents delivered with the suboptimal carriers normally fall in this category. The kinetics of vesicle penetration into and across the skin can be controlled to a large extent by fixing the physicochemical characteristics of the drug carrier suspension.

Kinetics of the transfersomes penetration through the intact skin is best studied in the direct biological assays in which vesicle associated drugs exert their action directly under the skin surface. Local analgesics are useful for this purpose, for determining the kinetics of penetration, various lidocaine loaded vesicles were left to dry out on the intact skin.

Corresponding subcutaneous injection is used as control. The animal's sensitivity to pain at the treated site after each application was then measured as a function of time. Dermally applied standard drug carrying liposomes or simple lidocaine solution have never caused any analgesic effect. It was necessary to inject such agent preparations to achieve significant pain suppression. In contrast to this, the lidocaine-loaded transfersomes were analgesically active even when applied dermally. Maximum analgesic effect with the latter type of drug application was typically observed 15 minutes after the drug application. A marked analgesic effect was still noticeable after very long time. The precise reach as well as kinetics of transfersomes penetration through the skin are affected by: drug carrier interaction, application condition or form, skin characteristics, applied dose (Planas *et al*., 1992).

**Transfersomes vs Other Carrier Systems**[33]

At first glance, transfersomes appear to be remotely related to lipid bilayers vesicle, liposomes. However, in functional terms, transfersomes differ vastly from commonly used liposomes in that they are much more flexible and adaptable. The extremely high flexibility of their membrane permits transfersomes to squeeze themselves even through pores much smaller than their own diameter. This is due to high flexibility of the transfersomes membrane and is achieved by judiciously combining at least two lipophilic/amphiphilic components (phospholipids plus biosurfactant) with sufficiently different packing characteristics into a single bilayer. The high resulting aggregate deformability permits transfersomes to penetrate the skin spontaneously. This tendency is supported by the high transfersomes surface hydrophilicity that enforces the search for surrounding of high water activity. It is almost certain that the high penetration potential of the transfersomes is not primarily a consequence of stratum corneum fluidization by the surfactant because micellar suspension contains much more surfactant than transfersomes (PC/Sodium cholate 65/35 w/w %, respectively). Thus, if the penetration enhancement via the solubilization of the skin lipids was the reason for the superior penetration capability of transfersomes, one would expect an even better penetration performance of the micelles. In contrast to this postulate, the higher surfactant concentration in the mixed micelles does not improve the efficacy of material transport into the skin. On the contrary, mixed micelles stay confined to the topmost part of the stratum corneum even they are applied nonocclusively (Chapman *et al*., 1998).

The reason for this is that mixed micelles are much less sensitive to the trans-epidermal water activity gradient than transfersomes. Transfersomes differ in at least two basic features from

the mixed micelles, first a transfersomes is normally by one to two orders of magnitude (in size) greater than standard lipid micelles. Secondly and more importantly, each vesicular transfersomes contains a water-filled core whereas a micelle is just a simple fatty droplet. Transfersomes thus carry water as well as fat-soluble agent in comparison to micelles that can only incorporate lipoidal substances (Gompper *et al*., 1995, Wearner *et al*., 1988). To differentiate the penetration ability of all these carrier systems (Rand *et al*., 1989) proposed the distribution profiles of fluorescently labelled mixed lipid micelles, liposomes and transfersomes as measured by the Confocal Scanning Laser Microscopy (CSLM) in the intact murine skin. In all these vesicles the highly deformable transfersomes transverse the stratum corneum and enter into the viable epidermis in significant quantity.

**Application of Transfersomes**[34]

**1. Delivery of insulin:**

Transfersomes is the successful means of non invasive therapeutic use of such large molecular weight drugs on the skin. Insulin is generally administered by subcutaneous route that is inconvenient. Encapsulation of insulin into transfersomes (transfersulin) overcomes these entire problems. After transfersulin application on the intact skin, the first sign of systemic hypoglycaemia are observed after 90 to 180 min, depending on the specific carrier composition.

**2. Delivery of corticosteroids:**

Transfersomes have also used for the delivery of corticosteroids. Transfersomes improve the site specificity and overall drug safety of corticosteroid delivery into skin by optimizing the epicutaneously administered drug dose. Transfersomes based corticosteroids are biologically active at dose several times lower than the currently used formulation for the treatment of skin diseases.

**3. Delivery of proteins and peptides:**

Transfersomes have been widely used as a carrier for the transport of proteins and peptides. Protein and peptide are large biogenic molecules which are very difficult to transport into the body, when given orally they are completely degraded in the GI tract. These are the reasons why these peptides and proteins still have to be introduced into the body through injections.

Various approaches have been developed to improve these situations. The bioavailability obtained from transferosomes is somewhat similar to that resulting from subcutaneous injection of the same protein suspension. The transferosomal preparations of this protein also induced strong immune response after the repeated epicutaneous application, for example the adjuvant immunogenic serum albumin in transferosomes, after several dermal challenges is as active immunologically as is the corresponding injected protea-transferosomes preparations.

**4. Delivery of interferons:**

Transferosomes have also been used as a carrier for interferons, for example leukocytic derived interferone-α (INF-α) is a naturally occurring protein having antiviral, antiproliferative and some immunomodulatory effects. Transferosomes as drug delivery systems have the potential for providing controlled release of the administered drug and increasing the stability of labile drugs. Hafer et al studied the formulation of interleukin-2 and interferone-α containing transferosmes for potential transdermal application .they reported delivery ofIL-2 and INF- α trapped by transferosomes insufficient concentration for immunotherapy.

**5. Delivery of Anticancer Drugs:**

Anti-cancer drugs like methotrexate were tried for transdermal delivery using transferosomes technology. The results were favourable. This provided a new approach for treatment especially of skin cancer.

**6. Delivery of anaesthetics:**

Application of anaesthetics in the suspension of highly deformable vesicles, transfersomes induces atopical anaesthesia, under appropriate conditions, with less than 10 min. Maximum resulting pain insensitivity is nearly as strong (80%) as that of a comparable subcutaneous bolus injection, but the effect of transfersomes anaesthetics last longer.

**7. Delivery of NSAIDS:**

NSAIDS are associated with number of GI side effects. These can be overcome by transdermal delivery using ultra-deformable vesicles. Studies have been carried out on diclofenac and ketoprofen. Ketoprofen in a transfersomes formulation gained marketing

approval by the Swiss regulatory agency (Swiss Medic) in 2007; the product is expected to be marketed under the trademark Diractin. Further therapeutic products based on the transfersomes technology, according to IDEA AG, are in clinical development.

**8. Delivery of Herbal Drugs:**

Transfersomes can penetrate stratum corneum and supply the nutrients locally to maintain its functions resulting maintenance of skin in this connection the transfersomes of capsaicin has been prepared by Xiao-Ying et al, which shows the better topical absorption in comparison to pure capsaicin.

## CONCLUSION

Transfersomes are specially optimized particles or vesicles, which can respond to an external stress by rapid and energetically inexpensive, shape transformations. Such highly deformable particles can thus be used to bring drugs across the biological permeability barriers. When tested in artificial systems transfersomes can pass through even tiny pores (100mm) nearly as efficiently as water, which is 1500 times smaller.

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