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TRANSFEROSOMES – A NOVEL DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT

Transport of the drug through skin is best route of drug delivery because the skin is largest organ in human body. Drug carries which are used in transdermal drug delivery such as liposomes, niosomes, or microemulsions pose a problem that they remains mostly confined to the skin surface and therefore do not transport drugs efficiently through the skin. Because of the deformable nature of transfersomes, it penetrates through the pores of stratum corneum which are smaller than its size and get into the underlying viable skin in intact form. Vesicle shape and size, entrapment efficiency, degree of deformability, number of vesicles per cubic mm can be characterised by in vitrostudies.Thus, they act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin.

INTRODUCTION:

Transdermal route offers many potential benefits over typical routes like rejection of first pass metabolism, predictable and extended length of activity, minimizing undesirable aspect effects, utility of short half-life medication, physiological and medical specialty response, avoiding the fluctuation in drug levels, inter-and intra-patient variations, and most significantly, it provides patients convenience [1, 2]. In the previous few years, the sac systems are promoted as a mean of sustained or controlled unleash of medication. These vesicles area unit are mostpopular over different formulations owing to their specific characteristics like lack of toxicity, biodegradation,capability ofencapsulating each hydrophilic and lipophilic molecules, capability of prolonging the existence of the drug within the circulation by encapsulation in sac structures, capability of targeting the organs and tissues, capability of reducing the drug toxicity and increasing its bioavailability [3]. The percutaneous route of drug delivery has gained nice interest ofpharmaceutical analysis, because it circumvents variety of issues related to oral route of drug administration. Recently, varied ways are accustomed augment the percutaneous delivery of bioactives. Mainly, they embody electrolysis, EMDA, chemical permeation enhancers, micro needles, sonophoresis, and sac system like liposomes, niosomes, elastic liposomes like ethosomes and transferosomes. Among these ways transferosomes seem promising . A completely unique sac drug carrier system known as transfersomes that consists of lipids, surfactant, and waterfor increased percutaneous delivery. Transferosomes square measure a kind of elastic or deformable sac, that were 1st introduced within the early 1990's [4, 5]. Transferosomes square

measure advantageous as phospholipids vesicles for percutaneous drug delivery. Due to their self-optimized and radical versatile membrane properties, they're ready to deliver the drugreproducibly either into or through the skin, counting on the selection of administration or application, with high potency. The sac transferosomes square measure additional elastic than the quality liposomes and so well matchedfor the skin penetration. Transferosomes overcome theskinpenetration issue by compressing themselves on the animate thing protection supermolecule of the stratum corneum layer [6].

Advantages: Transferosomes will deform and undergo slender constriction (from five to ten times but their own diameter) while not measurable loss.

1. They have high entrapment efficiency, near to90%.
2. This high offers entrapment efficiency higher penetration of intactvesicles.
3. They'll act as a carrier for low also as high Molecular weight compounds e.g. analgesic, anesthetic,corticosteroids,steroid,anticancer,insulin,gapjunctionsupermolecule,andsimple protein.
4. Transferosomes possess associate infrastructure consisting ofhydrophobicand hydrophilic moieties along and as a result will accommodate drug molecules with big selection of solubility.
5. They act as depot, which release their contents slowly and step bystep
6. They'll be used for Systemic as well as topical delivery ofdrug.
7. They're biocompatible and perishable as they're made of natural phospholipidsalmost likeliposomes.
8. They defend the encapsulated drug from metabolicdegradation
9. Preparation procedure is simple, don't involve prolonged procedure and supernumerary use or pharmaceutically unacceptable additives [2, 3,7].
10. High deforming ability which ensures deeper penetration in skinlayers

Limitations of Transferosomes: Transferosomes are chemically unstable due to their oxidativedegradation**.**

1. Purity of natural phospholipids is another criteria militating against adoption of transferosomesas drug deliverysystems
2. Transferosomes formulations are costly and Expensive [1, 3,7].

Transferosomes V/S Other carrier system: At first glance, transferosomes appear to be remotely related to lipid bilayers vesicle, liposomes. However in functional terms, transferosomes differ vastly from commonly used liposomes in that they are much more flexible and adaptable (Table 1). The extremely high flexibility of their membrane permits transferosomes to squeeze themselves even through pores much smaller than their own diameter. This is due to high flexibility of the transferosomes membrane and is achieved by judiciously combining at least two lipophilic/amphiphilic components (phospholipids plus bio surfactant) with sufficiently different packing characteristics into a single bilayer. The high resulting aggregate deformability permits transferosomes to penetrate the skin spontaneously. This tendency is supported by the high transferosomes surface hydrophilicity that enforces the search forsurrounding of high water activity. It is almost certain that the high penetration potential of the transferosomes is not primarily a consequence of stratum corneum fluidization by the surfactant because micellar suspension contains much more surfactant than transferosomes (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 transferosomes, one would expect an even better penetration performance of the micelles. According 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 non occlusively. Transferosomes differ in at least two basic features from the mixed micelles, first a transferosomes is normally by one to two orders of magnitude (in size) greater than standard lipid micelles. Secondly and more importantly, each vesicular transferosomes contains a water filled core whereas a micelle is just a simple fatty droplet. Transferosomes thus carry water as well as fat-

soluble agent in comparison to micelles that can only incorporate lipoidal substances.

Table 1: Comparison of different vesicles

Methods	Advantage	Disadvantage
Liposomes	Phospholipid vesicle, biocompatible, biodegradable	Less skin penetration less stable
Proliposomes	Phospholipid vesicle, more stable than liposomes	Less penetration, cause aggregation and fusion of vesicles
Physical methods e.g. iontophoresis	Increase penetration of intermediate size charged molecule	Only for charged drugs, transfer efficiency is low (less than 10 %)
Niosomes	Non – ionic surfactants vesicles	Less skin penetration easy handling But will not reach up to deeper skin
Proniosomes	Greater stability, will convert into noisome in situ, stable	Less skin penetration easy handling But will not reach up to deeper skin
Transferosomes and Protransferosomes	More stable, hjgh penetration due to high deformability, biocompatible and biodegradable, suitable for both low and high molecular weight and also for lipophilic as well as hydrophilic drugs and reach up to deeper skin layers.	None, but for some limitations

Table 2: Different additives used in formulation of transferosome.

Class	Example	Uses
Phospholipids	Soya phosphatidyl choline, Dipalmitoyl phosphatidyl choline, Distearoyl phosphatidyl choline	Vesicles forming component
Surfactant	Sodium cholate, Sodium dexoxycholate, 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
Dye	Rhodamine- 123, Rhodamine-DHPE, Fluorescein_DHPE Nilered	For CSLM study

Table 3: List of drugs used for transferosomes

Drug	Inference
Oestradiol	Improved transdermal flux
Norgesterol	Improved transdermal flux
Hydrocortisone	Biologically active at dose several times lower than currently used formulations
Human serum albumin	Antibody titer is similar or even slightly higher than subcutaneous injection
Interferon- α	Controlled release, Overcome stability problem
Insulin	High encapsulation efficiency. Transfer across the skin with an efficiency of > 50%. Provide noninvasive means of therapeutic use.

To differentiate the penetration ability of all these carrier systems proposed the distribution profiles of fluorescently labelled mixed lipid micelles, liposomes and transferosomes as measured by the Confocal Scanning Laser Microscopy (CSLM) in the intact murine skin. In all these vesicles the highly deformable transferosomes transverse the stratum corneum and enter into the viable epidermis in significant quantity [1, 2, 7].

Preparation of Transferosomes

Thin film hydration technique is used for the preparation of transferosomeswhich comprised of threesteps: A thin film is made from the mixture of vesicles fromphospholipids and chemical agent by dissolving in volatile organic solvent (chloroform-methanol). Evapouration of organic solvent takes place above the lipid transition temperature (room temp. for pure PC vesicles, or 50°C for dipalmitoyl phosphatidyl choline) using rotary evaporator. Final tracesof solvent were removed by applying vacuum for about 8 hours. A prepared thin film is hydrated with buffer (pH 6.5) by rotation at rotation at 60 rpm for 1 hr at the corresponding temperature. The ensuing vesicles were swollen for 2 hours at room temperature, Toprepare small vesicles, these vesicles were sonicated at temperature or50°Cfor 30 minutes employing a bath sonicator or probe sonicated at 4°C for 30 minutes. The sonicated vesicles were homogenized by manual extrusion 10 times through a sandwich of 100nm and 200 nm polycarbonate membranes [1, 8, 9]. Modified hand shaking, lipid film hydration technique is also founded forthe preparation of transferosomes which comprised followingsteps: Drug, lecithin (PC) and edge activator were dissolved in ethanol: chloroform (1:1)mixture. Organic solvent was removed by evaporation while hand shaking 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. 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 [1, 10,11].

Application of Transfersomes

1. Delivery of Insulin: Transferosomes are successful in delivering large MolecularWeight drugs such as insulin. Administering insulin by subcutaneous route is inconvenient. Encapsulation of insulin in transferosomes (transfersulin) overcomes this problem.Aftertransfersulin application on the intact skin, the first sign of systemic hypoglycemia are observed after 90 to 180 min, depending on the specific carrier composition
2. Delivery of corticosteroids: Transferosomes are used for the delivery ofcorticosteroids.
3. Transferosomes improves the site specificity and overall drug safety of

corticosteroids into skin. Transferosomes containing corticosteroids are biologically active at lower doses compared to the currently used formulation for the treatment of various skin diseases [6]

4. Delivery of proteins and peptides: Transfersomes have been used as a carrier for the transport of proteins and peptides. Proteins 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. Peptides are not formulated as injections because they get degraded in the body. Various approaches have been developed to improve these situations. Thebioavaibility obtained from transferosomes is somewhat similar to that obtained from subcutaneous injection of the same protein suspension. The transferosomal preparations of this protein also induced strong immune response after the repeated application on skin, for example the adjuvant immunogenic serum albumin in transferosomes, after several dermal challenges is active immunologically as it is corresponding proteo-transferosomespreparations.
5. Deliveryofinterferons:Transferosomesh avealsobeenusedasacarrierforinterferons, for example leukocytic derived interferone-α (INF-α) is a naturally occurring protein having antiviral, antiproliferive and some immunomodulatory effects. Transferosomes as drug delivery systems are capable of providing controlled release of the administered drug and increasing the stability of unstabledrugs.
6. Delivery of Anticancer Drugs: Anti cancer drugs like methotrexate were tried for transdermal delivery using transfersome technology. The results were favorable.This introduced a new approach for treatment of skin cancer[1].
7. Delivery of anesthetics: Topical anesthesia is induced by Transferosomes, under appropriate conditions, with less than 15 min. Effect of transferosomal anesthetics last longer compared to others[1].
8. NSAIDS Delivery: NSAIDS are associated with number of GI side effects. Theselimitations can be rectified by transdermal delivery by using ultra-deformable vesicles. Studies have been carried out on Diclofenac and Ketoprofen. Ketoprofen in a Transfersome formulation gained marketing approval by the Swiss regulatory agency (SwissMedic) in 2007; the product is expected to be marketed under the trademark Diractin. Further therapeutic products based on the Transfersometechnology.
9. 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 beenprepared.

CONCLUSION:

Transfersomes are specially designed optimized particles or optimized vesicles, which generally respond to the external stress by shape transformations. These highly deformable particles can be used to bring drugs across the permeability barriers, such as skin. Transfersomes can pass through even tiny pores (100 mm) nearly as efficiently as water, which is 1500 times smaller when tested externally.

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