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Review Article

Transferosome: A Nobel Approach for Transdermal Drug Delivery System

Pallav Namdeo, Ashish Garg*, Sweta Garg

Department of P.G. Studies and Research in Chemistry and Pharmacy, Rani Durgavati University, Jabalpur, 482001, M.P.

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Abstract

Objective: Transdermal drug delivery appears to be the most vital drug delivery system because of its merit over conventional systems. **Material and Method:** 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. With oral and parenteral drug delivery systems, or patient compliance is a frequent problem observed in daily clinical practice. Transport of drug across the skin is best route of drug delivery, because the skin is largest human organ with total weight 3 kg and a surface of 1.5-2.0 m^2. But the big hurdle in transdermal delivery of drug is the skin, the stratum corneum, the outermost envelop of the skin. **Conclusion:** Recently, various strategies have been used to augment to the transdermal delivery. Mainly, they include iontophoresis, electrophoresis, sonophoresis, chemical permeation enhancers, microneedles, and vesicular system (liposomes, niosomes, elastic liposomes such as ethosomes and transfersomes). Transfersomes possess an infrastructure consists of hydrophobic and hydrophilic moieties together and as a result can accommodate drug molecules with wide range of solubility. Transfersomes can deform and pass through narrow constriction (from 5 to 10 times less than their own diameter) without measurable loss. Transfersomes penetrate through the pores of stratum corneum which are smaller than its size and get into the underlying viable skin in intact form due to its deformable nature. The system can be characterized by *in vitro* for vesicle shape and size, entrapment efficiency, degree of deformability, number of vesicles per cubic mm. This high deformability gives better penetration of intact vesicles. They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormones, anticancer, insulin, gap junction protein, and albumin. The present review highlights the formulation aspects, characterization, and therapeutic applications of transfersomes.

***Keywords*:** includes iontophoresis, electrophoresis, sonophoresis, chemical permeation enhancers, microneedles, and vesicular system.

Introduction

Transdermal Drug Delivery is one of the most efficient routes for the delivery of drug into systemic circulation.

**Address for Corresponding Author:*
Ashish Garg
Department of P.G. Studies and Research
in Chemistry and Pharmacy,
Rani Durgavati University,
Jabalpur, 482001, M.P.
Email: ashish.garg071010@gmail.com

The aim of successful formulation is to deliver the active substance attarget organ with minimal discomfort and side effects. In this respecttransdermalroute ispreferred because of avoidance ofhepatic first pass metabolism, typical peak trough plasma profile,ease of administration. However, the improvement in permeability of drug throughthe skin is always a difficult problem because of barrier function of human skin epitheliato exogenous substances.Therefore the

major challenge in topical administration is to increase the penetration of drug into the skin. 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 fornon-invasive targeted drug delivery and sustained release of therapeutic agents. 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 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). 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. 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 (Lever et al., 1990; Chung et al., 2003; Koh et al., 2004). Flexibility of transfersomes membrane is achieved by mixing suitable surface-active components in the proper ratios. 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 (Chapman et al., 1998; Gompper et al., 1995). 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 (Batisse et al., 2002; Ting et al., 2004; Boinpally et al., 2002). Vesicular systems show importance because of their ability to give sustained release action of drugs. These systems exhibit several advantages which include:

Advantages

- Transdermal medication delivers a steady infusion of a drug over an extended period of time.

- An equivalent therapeutic effect can be elicited via transdermal drug input with a lower daily dose of the drug than is necessary, e.g. the drug is given orally.
- Self administration is possible with these systems.
- They are easily and rapidly identified in emergencies (e.g. unresponsive, unconsciousor comatose patient) because of their physical presence, features and identifying markings.
- They can be used for drugs with narrow therapeutic window.
- Longer duration of action resulting in a reduction in dosing frequency. Increased convenience to administer drugs which would otherwise require frequent dosing.
- Improved bioavailability.
- More uniform plasma levels and maintain plasma concentration of potent drugs.
- Reduced side effects and improved therapy due to maintenance of plasma levels up to the end of the dosing interval.
- Flexibility of terminating the drug administration by simply removing patch from the skin.
- Improved patient compliance and comfort via non-invasive, painless and simpleapplication.
- Avoid inter and intra patient variation and enhance therapeutic efficacy.

Disadvantages

- Many drugs especially drugs with hydrophilic structures permeate the skin too slowly to
- be of therapeutic benefit.
- The barrier function of the skin changes from one site to another on the same person,
- from person to person and also with age.
- Only small, lipophilic drugs can be delivered currently through the skin.
- Drug molecule must be potent because patch size limits amount that can be delivered.
- Not suitable for high drug doses.
- Adhesion may vary with patch type and environmental conditions.
- Skin irritation and hypersensitivity reactions may occur.
- Drugs that require high blood levels cannot be administered.
- Along with these limitations the high cost of the product is also a major drawback for the wide acceptance of this product (Randen et al., 2011; Sharma et al.,2011; Patel et al.,2011; Vinod et al., 2010). Transfersomes have a unique structure which is capable of entrapping hydrophilic, lipophilic, amphiphilic drugs**.** Vesicles are colloidal particle shaving a water filled core surrounded by a wall of lipids and surfactants (amphiphiles) arranged in bilayer. If the proportion of water is increased, these amphiphiles can form one or more concentric bilayers. Hydrophilic drugs find a place in the internal aqueous environment while amphiphilic, lipophilic drugs get entrapped in the bilayered wall with electrostatic and/or hydrophobic forces. The flexible or deformable vesicles are called elastic vesicles or transfersomes.

Characteristics 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.
- Transfersomes can deform and pass through narrow constriction (from 5 to10 times less than their own diameter) without measurable loss.
- This high deformability gives better penetration of intact vesicles.
- They can act as a carrier for low as well as high molecular weight drugs e.g. analgesic, anesthetic, corticosteroids, sex hormone, anticancer, insulin, gap junction protein, and albumin.

- 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.

Limitations of transfersomes

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

Mechanism of penetration of transfersomes

The mechanism for penetration is the generation of "osmotic gradient" due to evaporation of water while applying the lipid suspension (Transfer-somes) on the skin surface. The transport of these elastic vesicles is thus independent of concentration. The trans-epidermal hydration provides the driving force for the transport of the vesicles. As the vesicles are elastic, they can squeeze through the pores in stratum corneum (though these pores are less than one-tenth of the diameter of vesicles).

- Interaction between hydrophilic lipid residues and proximal water makes the polar lipids to attract water molecules induce hydration, lipid vesicles move to the site of higher water concentration. The difference in water content across skin stratum and epidermis develop transdermal osmotic gradient that leads to penetration of transfersomes across skin.
- Transfersomes by enforcing its own route induce hydration that widen the hydrophobic pores of skin, through the widen pores there is gradual release of drug occurs that binds to targeted organ.
- Transfersomes act as penetration enhancers that disrupt the intercellular lipids fromstratum which ultimately widens the pores of skin and facilitate the molecular interaction and penetration of system across skin.

Necessity of transfersomes for skin delivery

Transfersomes are advantageous as phospholipids vesicles for transdermal drug delivery. Because oftheir self-optimized and ultra-flexible membrane properties, 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. The vesicular transfersomes are 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.

Composition of transfersomes

The transfersome is composed of two main aggregates namely,

1. Firstly, an amphipathic ingredient (phosphatidylcholine), in which the aqueous solvents self-assembles into lipid bilayer that closes into a simple lipid vesicle.
2. Secondly, a bilayer softening component (such as a biocompatible surfactant or amphiphile drug)that increases lipid bilayer flexibility and permeability. The resulting, flexibility and permeability optimized, transfersome vesicle can therefore adapt its shape easily and rapidly, by adjusting local concentration of each bilayer component to the local stress experienced by the bilayer Figure 2.Therefore, the transfersome thus differs from such more conventional vesicle primarily by its "softer", more deformable, and better adjustable artificial membrane. 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 1.

Table 1. Different additives used in the formation of transferosomeand their uses.

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

Method of preparation of transfersomes

To prepare vesicles capable of different shape adaptability, the relative concentration of surfactants, which act as membrane- softening and -destabilizing agents (such as cholateorpolysorbate), is varied.

Vortexing-Sonication Method

In the vortexing-sonication method, mixed lipids (i.e. phospha-tidylcholine, EA and The therapeutic agent) are blended in a phosphate buffer and vortexed to attain a milky suspension. The suspension is sonicated, followed by extrusion through poly-carbonate membranes (Chapman et.al., 1998) Cationic transfersomes have also been prepared by this method, which involves mixing cationic lipids, such as DOTMA, with PBS to obtain a concentration of 10mg/ml followed by the addition of sodium deoxycholate (SDC). The blend is vortexed and sonicated, followed by extrusion through a polycarbonate (100-nm) filter (Gompper et.al., 1995)

Rotary Evaporation-Sonication Method

The rotary evaporation–sonication method involves dissolution of phosphatidylcholine and EA in a blend of chloroform and methanol (2:1, v/v), followed by the removal of organic solvent using rotary evaporation under reduced pressure at 4008C. The film deposited is hydrated with a solution of the therapeutic agent in a suitable aqueous phase while rotating the flask for one hour at room temperature. The vesicles produced are left to swell for two hours at room temperature, followed by 30 min of sonication in a bath sonicator so as to decrease their volume. Extrusion of vesicles then occurs through a sandwich of 450- and 220 nm polycarbonate membranes, with the resulting vesicles being stored at 408°C.

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 1hr at the corresponding temperature. The resulting vesicles were swollen for 2hr at room temperature.
3. To prepare small vesicles, resulting vesicles were sonicated at room temperature or 50°Cfor 30 min. using a bath sonicator or probe sonicated at 4°C for 30 min. The sonicated a vesicle were homogenized by manual extrusion 10 times

through a sandwich of 200 and 100nm polycarbonate membranes.

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

The characterization of transfersomes is generally similar to liposomes, niosomes and micelles

Entrapment efficiency

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

Drug content

The drug content can be determined using one of the instrumental analytical methods such as modified high performance liquid chromatography method (HPLC).

Vesicle morphology

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. Transfersomes vesicles can be visualized by TEM, phase contrast microscopy, etc. The stability of vesicle can be determined by assessing the size and structure of vesicles overtime. Mean size is measured by DLS and structural changes are observed by TEM.

Vesicle size distribution and zeta potential

Vesicle size, size distribution and zeta potential were determined by Dynamic Light Scattering Method (DLS) using a computerized inspection system by Malvern Zetasizer.

Number of vesicles per cubic mm

This is an important parameter for optimizing the composition and other process variables. Non-sonicated transfersome formulations are diluted five times with 0.9% sodium chloride solution. Haemocytometer and optical microscope can then be used for further study. The transfersomes in 80 small squares are counted and calculated using the following formula:

Total number of transfersomes per cubic mm =Total number of Transfersomes counted × dilution factor × 4000

Confocal scanning laser microscopy study

Both the conventional light microscopy and electron microscopy techniques faces problem of fixation, sectioning and staining of the skin samples. The structures to be examined are actually incompatible with the corresponding processing techniques; these give rise to misinterpretation, but can be minimized by Confocal Scanning Laser Microscopy (CSLM).In this technique lipophilic fluorescence markers are incorporated into the transfersomes and the light emitted by these markers used for following purpose:

1. To investigate the mechanism of penetration of transfersomes across the skin.
2. To determine histological organization of the skin (epidermal columns, inter digitation), shapes and architecture of the skin penetration pathways.
3. To compare and differentiate the mechanism of penetration of transfersomes with liposomes, niosomes and micelles. Different fluorescence markers used in CSLM study are as

1. Fluorescein- DHPE (1, 2- dihexadecanoyl- snglycero-3- phosphoethanolamine- N- (5- fluoresdenthiocarbamoyl), triethyl- ammonium salt)
2. Rhodamine- DHPE (1, 2- dihexadecanoyl- snglycero-3ogisogietgabikanube-Lissamine Tmrhodamine-B- sulfonyl,triethanol- amine salt)
3. NBD- PE (1, 2-dihexadecanoyl- sn-glycero- 3- phosphoethanolamine- N- (7-nitro- Benz- 2- xa- 1,3- diazol- 4- yl) triethanolamine salt)
4. Nile red (Schatzlein et al., 1995)

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 transfersomes can be determined using zetasizer.

Penetration ability

Penetration ability of transfersomes can be evaluated using fluorescence microscopy.

Occlusion effect

Occlusion of skin is considered to be helpful for permeation of drug in case of traditional topical preparations. But the same proves to be detrimental for elastic vesicles. Hydrotaxis (movement in the direction) of water is the major driving force for permeation of vesicles through the skin, from its relatively dry surface to water rich deeper regions. Occlusion affects hydration forces as it prevents evaporation of water from skin.

Physical stability

The initial percentage of the drug entrapped in the formulation was determined and were stored in sealed glass ampoules. The ampoules were placed at 4 ± 20°C (refrigeration), 25 ± 20°C (room temp),and 37 ± 20°C (body temp) for at least 3 months. Samples from each ampoule were analyzed after 30days to determine drug leakage. Percentage drug lose was calculated by keeping the initial entrapment of drug as 100%.

***In vitro* drug release**

In vitro drug release study is performed for determining the permeation rate. Time needed to attain steady state permeation and the permeation flux at steady state and the information from in-vitro studies are used to optimize the formulation before more expensive in vivo studies are performed. For determining drug release, transfersomes suspensionis incubated at 320°C and samples are taken at different times and the free drug is separated by mini column centrifugation. The amount of drug released is then calculated indirectly from the amount of drug entrapped at zero times as the initial amount (100% entrapped and 0% released).

***In vitro* skin permeation studies**

Modified Franz diffusion cell with a receiver compartment volume of 50ml and effective diffusion area of 2.50cm2 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 was 2.50cm^2 and capacity of receptor compartment was 50ml. The receptor compartment was filled with 50ml of phosphate

buffer (pH 7.4) saline maintained at 37± 0.50°C and stirred by a magnetic bar at 100rpm. 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.

Skin deposition studies of optimized formulation

At the end of the permeation experiments (after 24hr), the skin surface was washed five times with ethanol: PBS pH 7.4 (1:1), then with water to remove excess drug from surface. The skin was then cut into small pieces. The tissue was further homogenized with ethanol: buffer solution pH 7.4 (1:1) and left for 6hr at room temperature. After shaking for 5 minutes and centrifuging for 5 minutes at 5000rpm, the drug content was analyzed after appropriate dilutions with appropriate phosphate buffer solution.

***In vivo* fate of transfersomes and kinetics of transfersomes penetration**

Once the transfersomes passes the outermost skin layers, they will go into blood circulation via the lymph and distributed throughout the body, if applied under suitable conditions. Transdermal transfersomes can supply the drug to all such body tissues that are accessible to the subcutaneously injected liposomes. The kinetics of action of anepicutaneously applied agent depends on the velocity of carrier penetration as well as on the speed of drug distribution and the action after this passage. The most important single factors in this process are:

I. Carrier in-flow.

II. Carrier accumulation at the targets site.

III. 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 or water activity gradient is established. Using less solvent is favorable in this respect. The rate of carrier passage across the skin is chiefly determined by the activation energy for the carrier deformation. If penetration of transfersomes involves the occlusion of an application site or the use of too strongly diluted suspension then it will hamper the penetration process. Carrier elimination from the sub cutis is primarily affected by the lymphatic flow, general anesthesia or any other factor that affects this flow, consequently, is prone to modify the rate of transcutaneous carrier transport. 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 wasthen 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 analgesic ally 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 (Schatzlein et al., 1995).

Application of Transferosomes

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 transfer 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 isas active immunologically as is the corresponding injected 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. The formulation of interleukin-2and interferone-α containing transferosmes for potential transdermal application .they reported delivery of IL-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 tobe marketed under the trademark Diractin. Further therapeutic products based on thetransfersomes 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 which shows the better topical absorption in comparison to pure capsaicin.

Conclusion

Transfersomes are specially optimized particles or vesicles, which can respond 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 a sufficiently as water, which is 1500 times smaller. Ultra deformable vesicles can provide the novel solution for the transport related problems. They are free from the rigid nature of conventional vesicle and can transport even the large molecules. They work on number of mechanisms working together to provide an excellent carrier system for the drug transport. When tested in artificial systems. Transfersomes can pass through even tiny pores (100 mm) nearly as efficiently as water, which is1500 times smaller.

Drug loaded transfersomes can carry unprecedented amount of drug per unit time across the skin (up to 100mg cm^2h). 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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