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Review on Background of Future Prospects of Transfersome in Drug Delivery System

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ABSTRACT: Now a day, Noval drug delivery system has creating a new interesting development of various drug delivery system. The transdermal route of drug delivery system has gained interest of pharmaceutical research it acts as sidestep to the number of problems associated with oral route of administration and parenteral drug delivery system due to its poor patient compliance. Mainly, these include ionotrophoresis, elecrophoresis, sonophoresis, chemical permeation enhancers, microneedles, and vesicular systems (liposomes, niosomes, elastic liposomes like ethosomes and transfersomes). Compounds with molecular weights greater than 500Da and ionized compounds generally don't undergo the skin; only a limited number of medicines are capable of being administered by this route. physical and chemical means of crossing the lipophilic stratum corneum, there are several advantages over conventional routes like avoiding first pass metabolism, predictable and extended duration of activity, minimizing undesirable side effects, utility of short half-life drugs, improving physiological and pharmacological response and also to extend the efficiency of the drug material transfer across the intact skin by use of penetration enhancers, ionotrophoresis, sonophoresis and use of colloidal carriers like lipid vesicles and non-ionic surfactant vesicles. Characterization of transfersome is examined by known the vesicle size, morphology, drug content, entrapment efficient, Penetration ability, occulsion effect, surface charge, invitro drug release, invitro skin penetration, SEM, TEM, FTIR etc., Transfersome are more conventional vesicles and more deformable.

KEY WORDS: Transfersomes, Novel drug delivery, Lipid bilayer, Phospholipid vesicles, Carrier system.

I. INTRODUCTION:

Transfersome is a novel drug delivery and a special type of liposomes, consisting of phosphatidyl choline and an edge activator. This system also takes advantages of phospholipids vesicles as transdermal drug carrier. An edge activator consists usually of single chain surfactant of non-ionic nature that cause de- stabilization of the lipid bilayer thereby increasing its fluidity and elasticity. Flexibility of transfersomes membrance can be altered by mixing suitable surface active agents in the proper ratio. Surfancants such as sodium cholate, sodium deoxycholate, span 80, tween 80, have been used as edge activator. They are self-optimized aggregates, with the ulterfelxible membrane, which deliver the drug reproducibly either into or through the skin. The system has several order magnitudes of elasticity and flexibility over liposomal drug delivery which makes it favourable for efficient skin penetration and hence for the novel drug delivery sys- tem. 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 concept of rational membrane design a special type of composition bodies, so called transfersomes have been developed, which overcome the filteration problem and penerate the skin barrier along the transcutaneous moisture gradient. Liposomes facilitate drug transport through the skin by three possible meachanism: adsorption to the skin surface with a subsequent transferring of the drug directly from vesicles to skin, fusion with the lipid matrix of the corneum, thereby increasing drug partitioning into the skin, and lipid exchange between the liposomal membrane and cell wall, facilitating the diffusion of the drug across the membrane.

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VARIOUS TYPES OF VESICLES:

1. Liposomes
2. Niosomes
3. Pharmacosomes
4. Collidosomes
5. Herbosomes
6. Sphingosomes
7. Cubosomes

Liposomes:

They are usually unilamellar and range of 50-250nm. Consists of one or more lipid bilayer enclosed by Internal aqueous volume. Liposomes are capable of carrying drugs differ in physicochemical properties such as polarity, charge, size. They are hollow spheres. The main component is dipalmitoyl phosphatidyl choline improve stability and Increase the solubility of insoluble drugs. Both water soluble and insoluble drug can be delivered[4].

Niosomes:

Nonionic surfactant vesicles uptained by hydrating mixture of cholesterol and nonionic surfactants, used as a carriers of hydrophilic-amphiphilic and lipophilic drug moieties. they are biodegradables, biocompatible, non-immunogenic and flexibility in their structural characterization. They are osmotically active and stable and enhance the skin penetration of drugs[5].

Pharmacosomes:

It is amphiphilic phospholipid complex of medicine bearing active hydrogen that bind to phospholip- ids. Impart better biopharmaceutical properties to the drug, results in improved bioavailability. Developing the pharmacosomes of the drug has found to improve the aborption and minimize the gastro intestional toxicity. Various NSAID'S, protein, cardiovascular, anti-neoplastic drugs are used to prepare [6].

Ethosomes:

It is phospholipid nanovesicles used for dermal and transdermal delivery of molecules. They are com- posed of multiple, concentric layer of flexible bilayer, with a relative high concentration of ethanol (20- 45%), glycols and water. They have high penetration of the horny layer of the skin, which enchances the permeation of encapsulated drug. Because of their unique structure, ethosomes are able to efficiently encapsulated and deliver into the skin highly lipophilic molecules such as testosterone, cannabinoids and ibuprofen, as well as hydrophilic drugs such as clindamycin phosphate, buspirone Hcl[4].

Collidosomes:

Hollow-shells of fused particles at interface of emulsion droplets. The shell of Collidosomes consistes of coagulated or fused colloid particles adsorbed on the surface of octanol-in-water emulsion drops and removal of oil after fusing monolayers. The final hollow shells are obtained by removal of central, spherical colloidal particles collidosomes membrane offer great potential in controlling the permeability of the en-trapped species and permit the selective and time release[8].

II. ADVANTAGES OF TRANSFERSOMES:

Transfersomes can deform and passes through a narrow constriction. High entrapment efficiency and high deformability leads to better penetration of vesicles. It can act as a carrier for low also as high relative molecular mass drugs e.g: analgesic, anesthetic, corticosteroids, steroid hormone, anticancer, insulin, gap junction protein, albumin, interferons, NSAID's, pepties, herbal drugs. It possesses a hydrophobic and hydrophilic moiety together and results in high solubility of drug molecules. It acts as depot, releasing their contents slowly and gradually. Biocompatible and biodegradable similar to liposomes, they are made up of natural phospholipid and EAs. They protect the encapsulated drug from metabolic degradation. Easy to scale up and short, simple.

Avoid first-pass metabolism, which is a major drawback in oral drug administration and results in optimized bioavailability of the drug. Have the advantage of being made from pharmaceutically acceptable ingredients using standard methods but need to be designed and optimized on a case-by-case basis. It has a capable of increasing the transdermal flux [5,12,46].

Limitation of transfersomes:

Transfersomes are chemically unstable due to their predisposition to oxidative degradable but expensive [1].

Composition of Transfersomes:

Transfersomes are generally composed of;

The most ingredients, an amphipathic ingredient (e.g., soy phosphatidylcholine, egg

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phosphatidylcho- line, etc.) which will be a mix of lipids, which are the vesicle-forming components that make the lipid bi- layer. 10–25% surfactants; the foremost commonly used edge activators in transfer-some preparations are surfactants as sodium cholates; sodium deoxycholate; Tween 20, 60, 80; Span 60, 65 and 80 and dipotassium glycyrrhizinate are biocompatible bilayer-softening compounds, increase the vesicles' bilayer flexibility and improve permeability.

About 3–10% alcohol (ethanol or methanol), as the solvent and, finally, hydrating medium consist with either water or a saline phosphate buffer (pH 6.5–7)[5,7,12].

In an aqueous environment, the phospholipids self-assemble into flexible lipid bi-layers and close to form vesicles. The total amount of surfactants and the proper ratios of individual surfactants to phospholipids are responsible for the control of vesicles' membrane flexibility and minimizing the risk towards vesicle ruptures in the skin. This result promotes transfersomes to follow the natural osmotic gradient. The penetration enhancing effect of these vesicles depends on the concentrations and the types of surfactants, the types of lipids, the size shape and elasticity of the vesicles [13].

DRUGS CAN BE SUITABLE FOR TRANSFEROSOMES:

NSAIDS: Ibuprofen, naproxen, curcumin

Antifungal: Fluconazole, Itraconazole, Nystatin, Voriconazole

Steroids: Oestradiol, Norgestrone, Hydrocortisone

Proteins: Human serum albumin, integral membrane proteins. Others: Interferons-α, interleukins-2, insulin

The isolation of a "yellow coloring-matter" from the rhizomes of turmeric (turmeric) and named as Curcumin, which may be a member of the Zingiberaceae (Zingi-beraceae). Accumulating preclinical studies have shown that curcumin can interfere with an increasing number of molecular targets, pathways and pro- cesses involved in cancer[14].

POLYMERS USED FOR THE DEVELOPMENT OF TRANSFEROSOMES[16]:

Lecithin, Soyaphosphatidyl Choline, Disteroyl Phosphatidyl Choline, Dipalmitoyl Phosphati-Dylcholine, Cholesterol, Deoxycholic Acid, Tween 80 &20, Span 20& 80, Ethanol, Methanol, Chloroform.

III. METHOD OF PREPARATION:

Thin Film Hydration Technique/Rotary Evaporation-Sonication Method:

The phospholipids and edge activator (vesicle-forming ingredients) are dissolved during a flask em- ploying a volatile organic solvent mixture (example: chloroform and methanol during a suitable (v/v) ratio). The lipophilic drug can be incorporated in this step. In order to form a thin film, the organic solvent is evapo- rated above the lipid transition temperature under reduced pressure using a rotary vacuum evaporator. Keep it under vacuum to get rid of the ultimate traces of the solvent. The deposited thin film is hydrated employing a solution with the acceptable pH (example: pH 7.4) by rotation for a respective time at the corresponding tem- perature. The hydrophilic drug incorporation can be done in this stage. The resulting vesicles are swollen at room temperature and sonicated in a bath or probe sonicator to obtain small vesicles. The vesicles are homogenized by extrusion through a sandwich of 200 nm to 100 nm polycarbonate membranes[2,16].

Vortexing-Sonication Method:

The phospholipids, edge activator and therefore the drug are mixed during a phosphate buffer. It is then sonicated, using a bath sonicator, for a respective time at room temperature and then extruded through polycarbonate membranes (example: 450 and 220 nm)[17].

Modified Handshaking Process:

The modified handshaking method has the same basic principle as the rotary evaporation sonication method. In the modified handshaking process, the organic solvent, the lipophilic drug, the phospholipids and edge activator are added during a flask. All the excipients should completely dissolve within the solvent and acquire a transparent transparent solution. The organic solvent is removed by evaporation while hand-shaking instead of using the rotary vacuum evaporator. In the meantime, the round-bottom flask is partially immersed in the water bath maintained at a high temperature (example: 40–60 ◦C), thin lipid film is formed inside the flask wall. it kept overnight for complete evaporation and form film, then hydrated with the acceptable solu-tion with gentle shaking at a temperature above its phase change temperature. The hydrophilic drug incorpo- ration can be done in this stage[16].

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Suspension Homogenization Method:

Transfersomes are prepared by mixing an ethanolic phospholipid solution with an appropriate amount of edge activator. Prepared suspension is mixed with buffer to yield a complete lipid concentration. The resulting formulation is then sonicated, frozen and thawed respectively two to threetimes[18].

Centrifugation Process:

Phospholipids, edge activator and lipophilic drug are dissolved in the organic solvent. Solvent re- moved by rotary evaporator under reduced pressure. The deposited lipid film is hydrated with the acceptable solution by centrifuging at temperature. The hydrophilic drug incorporation can be done in this stage. The resulting vesicles are swollen at room temperature [19].

Reverse-Phase Evaporation Method:

The phospholipids and edge activator are added to a round-bottom flask and dissolved in the organic solvent mixture (example: diethyl ether and chloroform). The lipophilic drug is often incorporated during this step. The solvent is evaporated by rotary evaporator to obtain the lipid films. The lipid films, re dissolved in the organic phase mostly composed of isopropyl ether and/or ether. Subsequently, the aqueous phase is added to the organic phase, resulting in a two-phase system. The hydrophilic drug incorporation is wiped out this stage. This system is subjected to sonication using a bath sonicator until a homogeneous w/o (water in oil) emulsion is formed. The organic solvent is slowly evaporated using rotary evaporator to form a viscous gel, which then becomes a vesicular suspension[20,21].

High-Pressure Homogenization Technique:

The phospholipids, edge activator and the drug are uniformly dispersed in PBS or dis-tilled water containing alcohol and followed by ultrasonic shaking and stirred simultaneously. The mixture is treats with intermittent ultrasonic shaking. The resulting mixture is then homogenized using a high-pressure homogenizer. Finally, the transfersomes are stored in appropriate conditions[22,23].

Ethanol Injection Method:

The organic phase is produced by dissolving the phospholipid, edge activator and therefore the lipophilic drug in ethanol with magnetic stirring for the respective time, until a transparent solution is obtained. The aqueous phase is produced by dissolving the water-soluble substances within the phosphate buffer. The hydrophilic drug incorporation is wiped out this stage. Both solutions are heated up to 45–50 ◦C. Subsequently, the ethanolic phospholipid solution is injected drop by drop into the aqueous solution with continuous stirring for the respective time. Solvent (Ethanol) is removed by vacuum evaporator and then sonicating for particle size reduction[24,25].

IV. OPTIMIZATION FORMULATION CONTAINING TRANSFERSOMES:

There are various process variables which could affect the preparation and properties of the transfersomes. The preparation procedure is optimized and validated. The process variables depend upon the procedure involved in manufacturing of formulation. The preparation of transfersomes involves various process variables Like,

1. Lecithin
2. Surfactant ratio
3. Effect of various solvents
4. Effect of various surfactants
5. Hydration medium

Optimization was done by selecting entrapment efficiency of drug, During the preparation of a particular sys- tem, the other variables were kept constant[1,15].

TRANSFERSOMES FOR SKIN:

The vesicular transfersomes are more elastic than the quality liposomes and thus compatible for the skin penetration. Transfersomes overcome the skin penetration difficulty by squeezing themselves along the intracellular sealing lipid of the corneum. Because of the high vesicle deformability, this allows the entry. Mechanical stress of surrounding, during a self-adapting manner. Flexibility of transfersomes membrane is influence by mixing suitable surface-active components in the proper ratios with phospholipids. The resulting flexibility of transfersome membrane minimizes the risk of complete vesicle break in the skin and allows to follow the natural water gradient across the epidermis, when applied under non-occlusive condition. Transfersomes can penetrate the whole stratum corneum spontaneously along two routes in the intracellular lipid that differ in their bilayers

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properties[17,26].

The mechanism of penetration is generation of "osmotic gradient" due to evaporation of water while applying the lipid suspension (Transfersomes) on the skin surface. Transfersomes have strong bilayer de- formability and therefore they have increased affinity to bind and retain water. An ultradeformable and highly hydrophilic vesicle always seeks to avoid dehydration; involve a transport process related to but not identical with forward osmosis. Transfersome uptake is driven by the hydration gradient that exists across the epider- mis, stratum corneum, and ambient atmosphere[27,45].

CHARACTERIZATION OF TRANSFERSOMES:

1. **Entrapment efficiency:** 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. The EE expressed in percentage entrapment[26].

EE= Amount entrapped*100

Total amount added

2. **Drug Content:** The drug content can be determined using a modified high performance liquid chromatography method (HPLC) method using a UV detector, column oven, auto sample, pump, and computerized analysis program[28].
3. **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 over time. Mean size is measured by DLS and structural changes are observed by TEM[17].
4. **Occlusion effect:** Occlusion of skin is considered to be helpful for permeation of drug in case of traditional topical preparations. Occlusion affects hydration forces as it prevents evaporation of water from skin[28].
5. **Turbidity measurement:** The turbidity measurements were diluted with distilled water to give a total lipid concentration of 0.312m. Sonicate for 5 min. Measure turbidity at 274 nm with UV visible spectrophotometer[29].
6. **Vesicle size distribution and zeta potential:** Vesicle size, size distribution and zeta potential were de- termined by Dynamic Light Scattering Method using a computerized inspection system by Malvern Zetasizer[30].
7. **Number of vesicle per cubic mm:** It is an important parameter for optimizing the composition and other process variables. Transferosome formulations can be diluted for 5 times with 0.9% sodium chloride solution and studied with optical microscopy[31].

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

8. **Degree of deformability or permeability measurement:** In the case of transfersomes, the permea- bility study is one of the important and unique parameters 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. The degree of deformability can be determined using the followingformula,

$$D = J * \frac{rv}{rp}$$

J= the amount of the suspension extruded during 5min; rv = the size of the vesicle;
rp = pore size of the barrier[8].

9. **Surface charge and charge density:** Surface charge and charge density of transfersomes can be determined using zetasizer[33].
10. **Penetration ability:** Penetration ability of Transfersomes can be evaluated using fluorescence microscopy[34].
11. **Confocal scanning laser microscopy study:** Conventional light microscopy and electron microscopy both face problem of fixation,

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sectioning and staining of the skin samples. Often 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 emit- tedby these markers used for following purpose:

For investigating the mechanism of penetration of transfersomes across the skin.
For determining histological organization of the skin (epidermal columns interdigitation), shapes and architecture of the skin penetration pathways.
For comparison and differentiationof the mechanism of penetration of transfersomeswith liposomes, niosomes and micelle[35].
Different fluorescence markers used in CSLM study are[47]

1. Fluorescein- DHPE (1, 2- dihexadecanoyl- sn-glycero- 3- phosphoethanolamine- N- (5-fluores- denthiocarbamoyl), triethyl-ammonium salt)
2. Rhodamine - DHPE (1,2–dihexadecanoyl–sn–glycerol-3ogisogietgabikanube NLissamineTmrhodamine – B - sulfonyl), triethanol - amine salt)
3. NBD- PE (1, 2- dihexadecanoyl- sn-glycer 3-phosphoethanolamine- N- (7-nitro- Benz2- xa-1,3- dia- zol 4- yl) triethanolamine salt),
4. Nile red.

12. **In-vitro drug release:** In this study, it is performed for examine the permeation rate. Time needed to achieve steady state permeation and therefore the permeation flux at steady state and the information from in-vitro studies are won't to optimize the formulation before costlier in vivo studies are performed. To determine drug release, suspension is incubated at 32^0C and samples are taken at different times intervals and the free drug is separated by mini column centrifugation. The amount of drug released is calculated indirectly by the amount of drug entrapped at zero times as the initial amount[36].

13. In-vitro Skin Permeation Studies:

Modified Franz diffusion cell with a receiver compartment volume of 50ml and effective diffusion area of 2.50cm^2 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 fat layer of the skin was removed by rubbing with a cotton swab. Skin was kept in isopropyl alcohol solution and stored at 0-4 ^{0}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 com- partment was crammed with 50ml of phosphate buffer (pH 7.4) Saline maintained at 37± 0.5^{0}C and stirred 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 with- drawn and immediately replaced by an equal volume of fresh phosphate buffers (pH 7.4) to maintain sink conditions. Correction factors for every aliquot were considered in calculation of release profile. The samples were analyzed by any instrumental analytical technique[37,43].

14. Stability studies of transfersomes:

After measuring the initial percentage entrapment of the drug in the optimized formulation, the three batches of the same formulation were stored in sealed glass ampoules (one each) at refrigeration temperature (4±2°C), room temperature (25±2°C) and body temperature (37±2°C) for a period of at least 3 months. The percentage entrapment of the drug and % drug content was determined in the formulations after 15, 30, 45 and 90 days to know the amount of drug leaked out. The percent drug lost was calculated taking the initial entrapment of drug as 100%[44].

FACTORS AFFECTING TRANSFERSOMES PROPERTIES:

1. Effect of phospholipids: Edge activator ratio:

Phospholipid: Edge activator should be optimized ratio because they greatly affect the entrapment efficiency, vesicle size, permeation ability. EE reduced in higher surfactant concentration due to the arrangement eg: surfactant

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molecules within the lipid bilayer vesicular vesicles membrane permeability and increase fluidity and cause the leakage of entrapped drug[38].

2. Effect of various solvents:

Solvents are selected based on the solubility of the formulation ingredient and compatibility (such as ethanol, methanol). Solvents used in the formulation can also apply their function as penetration enhancers that improving drug flux through the membrane[17,38,39].

3. Effect of various Edge activators:

Various type of edge activator (such as Tween 80, Span 80, and Sodium deoxycholate) affects the deformability and entrapment efficiency of vesicles. The vesicles size de-creases by increasing the surfactant concentra- tion, the hydrophilicity of the surfactant head group, carbon chain length and the hydrophilic lipophilic balance (HLB). High concentration of surfactant (more than 15%), leads to reduction of vesicle size[40].

4. Effect of hydration medium:

The hydrating medium may consist of either water or saline phosphate buffer (pH 6.5–7). The pH level of the formulation should be suitable to achieve a balance between the formulation properties and biological applications, as well as the route of administration. The lipid bi-layer of transfersomes mimics the phospholipid layer of the cell membrane, and only unionized drugs remain membrane bound to the phospholipid bilayer and penetrate through the intracellular route. It is important to use the suitable pH of the hydration medium, which keeps the drug unionized to increase the entrapment and permeation of the drug[41,42].

V. CONCLUSION:

Transfersomes can undergo even tiny pores (100 mm) nearly as efficiently as water, which is 1500 times smaller. Ultra-deformable vesicles can provide the solution for the transport related problems. It enhanced delivery of bioactive materials through the skin by means of a vesicular carrier opens new challenges and opportunities for the event of novel improved therapies. It concluded that the new ultraflexible drug car- rier (transfersomes) can overcome all the issues related to the transdermal delivery as transfersomes itself.

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TABLE 1: ADDITIVES USED IN TRANSFERSOMES FORMULATION

S. No.	Class	Example	Use
1	Phospholipids	Soya Phosphatidyl choline, egg phosphatidyl choline, dipalmitoylphosphatidyl choline	Vescicles forming component
2	Surfactants	Sod.cholate, Sod/deoxycholate, Tween-80, Span-80, Tween 20	Vescicles forming component
3	Solvents	Ethanol, methanol, isopropyl alcohol, chloroform	As a solvent
4	Buffering agent	Saline phosphate buffer (pH 6.4), phosphate buffer pH 7.4	As a hydrating medium
5	Dye	Rhodium-123, Rhodamine-DHPE, Fluoresce- in-DHPE, Nile-red	For CSLM study

TABLE 2: APPLICATION OF DRUGS IN TRANSFERSOMES

S. No.	Name of drug	Inference
1	Curcumin	Better permeation for anti-inflammatory activity
2	Indinavir sulphate	Improved influx for activity against acquired immune deficiency syndrome (AIDS)
3	Ketoprofen	Improved penetration for anti-inflammatory activity
4	Insulin	Induce therapeutically significant hypoglycemiawith good effica- cy and reproducibility
5	Capsaicin	Increase skin penetration
6	Colchicine	Increase skin penetration
7	Vincristine	Increase entrapment efficiency and skin permeation
8	Interferon-α	Efficient delivery means (because delivery other route is diffi- cult). Controlled release. Overcome stability problem.
9	Norgesterol	Improved transdermal flux
10	Tamoxifen	Improved transdermal flux
11	Methotrexate	Improved transdermal flux
12	Oestradiol	Improved transdermal flux
13	Tetracaine, Lignocain	Suitable means for the noninvasive treatment of local pain on direct topical drug application.
14	Corticosteroids	Improved site specificity and overall drug safety.
15	Hydrocortisone	Biologically active at dose several times lower than currently used formulation.
16	Triamcinolone acetonide	Used for both local and systematic delivery.
17	Human serum albumin	Antibody titer is similar or even slightly higher than subcutaneous injection.
18	Stavudine	Improved the in vitro skin delivery of stavudine for antiretroviral activity
19	Tetanus toxoid	For transdermal immunization

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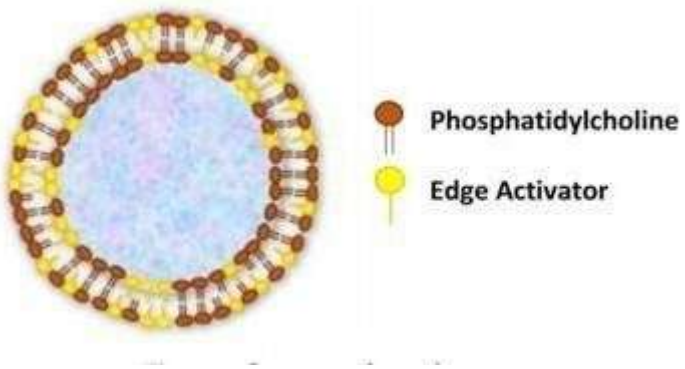

Fig.1: Structure of Transfersomes

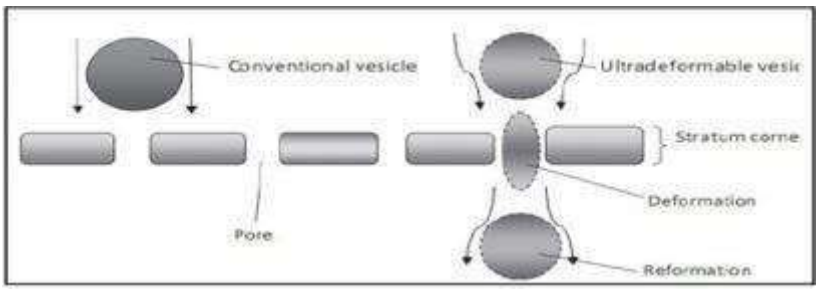

Fig.2: Meachanism of transfersomes

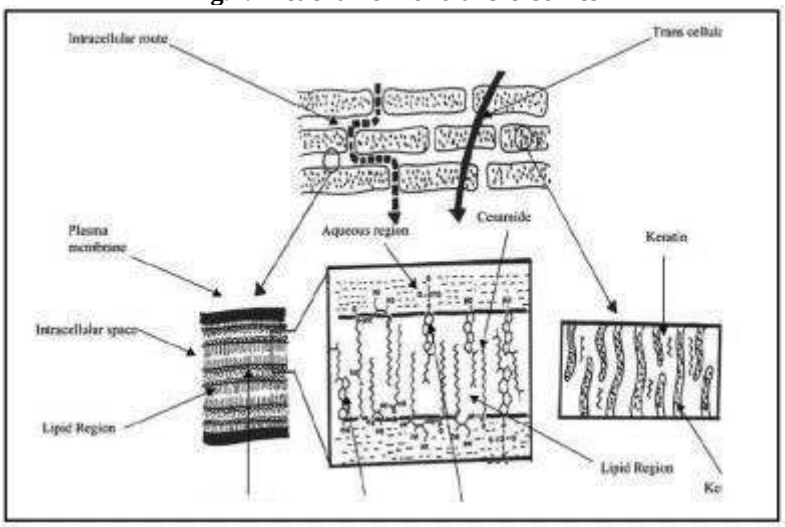

Fig.3: Micro routes for drug penetration across the human skin

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Undertaking to be signed by all authors while submitting manuscript
We the undersigned herewith submit a manuscript entitled REVIEW ON BACKGROUND OF FUTURE PROSPECTS OF TRANSFERSOMES IN DRUG DELIVERY SYSTEM author by M. JEEVAJOTHI, PRIYANKA SINHA, GRACE RATHNAM AND U. UBAIDULLA for consideration for
publication as a Review Article in the Indian J. .
Pharmaceutical Sciences.
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