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ETHANOLIC VESICLES: A NOVEL APPROACH TO ENHANCE TRANSDERMAL DRUG DELIVERY

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ABSTRACT

Transdermal drug delivery is the approach in which the drug is embedded into the reservoir within the patch and it pass through the skin into the blood stream. The various techniques has developed to disrupts the skin barrier and deliver drug into the body through the intact skin. Liposomes in the Transdermal drug delivery system limits their use at clinical and industrial level due to its unstable nature. Ethosomes have the ability to reach into the deep into skin. It contains the ethanol in high concentration . ethosomes act by the ethanol effect and ethosomes effect. Ethosomes are flexible and also pass through the narrow constrictions. This article covers the basic information regarding the advantages of ethosomes, mechanism of penetration , method of preparation, evaluation parameter, it also covers the information like formulation aspect of ethosomes, challenges and opportunities and marketed formulation. The applicability of ethosomes in various fields like cosmetics, analgesics, anesthetics, corticosteroids, anticancer agents, insulin.

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INTRODUCTION

Transdermal drug delivery

Transdermal patch (Skin patch) uses a special membrane to control the rate at which the liquid drug contained in the reservoir within the patch can pass through the skin and into the bloodstream. Some drugs must be combined with substances, such as alcohol, that increase their ability to penetrate the skin in order to be used in a skin patch[1].

Transdermal drug delivery is gaining importance due to its noninvasive procedure for administration. The transdermal drug delivery overcomes a number of limitations of oral drug delivery such as degradation of drugs by digestive enzymes, irritation of gastrointestinal mucosa and first pass effect. Also due the pain on administration associated with parenteral route, patients highly prefer transdermal route. Hence transdermal dosage forms enjoy being the most patient compliant mode of drug delivery. Transdermal drug delivery system (TDDS) showed promising result in comparison to oral drug delivery system as it eliminates gastrointestinal interferences and first pass metabolism of the drug[3].

The Skin:

The skin is a multi-layered structure made up of stratum corneum (SC), the outermost layer, under which lies the epidermis and dermis. Within these layers of skin are interspersed fibroblasts, hair follicles and sweat glands that originate in the dermis blood supply. The almost insurmountable nature of SC is a major challenge for systemic delivery of percutaneously applied drugs. Furthermore, it is even more difficult for anything to penetrate to the deeper strata of skin[4].

The stratum corneum or the horny layer is the rate-limiting barrier that restricts the inward and outward movement of chemical substances. The interior of the cells is crisscrossed with densely packed bundles of keratin fibres. Due to this, the dry composition of the horny layer is 75-85% protein, most of which is the intracellular keratin and a part being associated with a network of cell membranes. The bulk of the remainder of the substance of the stratum corneum is a complicated mixture of lipids which lies between regions, the mass of intracellular protein and the intercellular lipoidal medium. The epidermis rests on the much thicker dermis. The dermis essentially consists of about 80% of protein in a matrix of muco-polysaccharide "ground substance". A rich bed of capillaries is encountered 20 m or so into the dermal field. Also contained within the dermis are lymphatics nerves and the epidermal appendages such as hair follicles, sebaceous glands and sweat glands. Excepting the soles of the feet, the palms of the hand, the red portion of the lips and associated with one or more sebaceous glands which are outgrowths of epithelial cells[5].

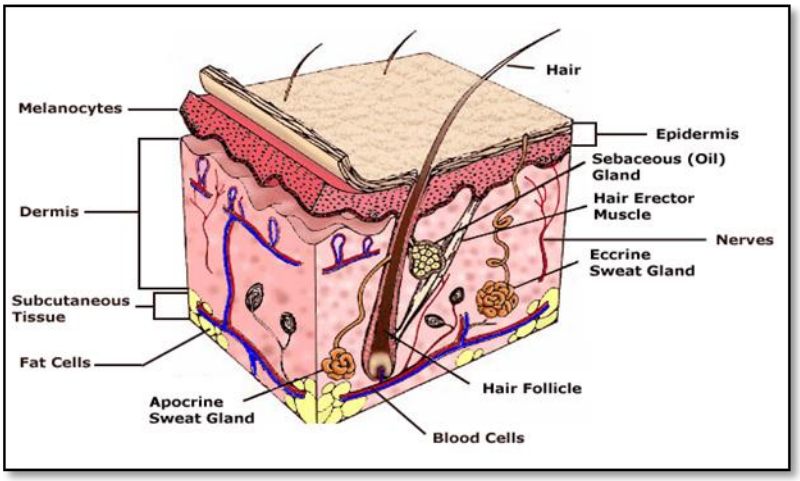


Fig 1: Structure of skin.

During the past several decades, researchers have developed numerous techniques to weaken or disrupt the skin barrier and deliver drugs into the body through the intact skin. Chemical skin permeation enhancers, iontophoresis, sonophoresis, electroporation, microneedles, and many other methods have been investigated to increase the efficacy of transdermal transport. Owing to their limited efficacy, resulting skin irritation, complexity of usage, and/or high cost, none of these methods have been broadly applied to date. For transdermal and topical drug delivery system to be effective, the drug must obviously be able to penetrate the skin barrier and reach the target site[6].

Lipid-based suspensions such as liposomes, niosomes, and microemulsions, have also been proposed as low- risk drug carriers, but they do not offer much value in transdermal drug delivery because they do not deeply penetrate the skin, but rather remain on the upper layers of skin strata. Several researchers have developed novel elastic lipid vesicular systems in order to deeply and easily penetrate through the skin. Phospholipids, ethanol, bile salts and many surfactants have been used to prepare these elastic vesicles. The high flexibility of vesicular membranes allows these elastic vesicles to squeeze themselves through the pores in stratum corneum, which are much smaller than their vesicular sizes. In 1992, Cevc et al. introduced the first generation elastic lipid vesicular carrier, Transfersomes, mainly consists of phospholipids and an edge activator (non-ionic surfactant). They were reported to penetrate intact skin and able to deliver the drug into and across the skin, when applied under non-occlusive conditions.

The vesicular approach i.e. liposome in transdermal drug delivery system has been studied for many purposes but the unstable nature limits their use at clinical and industrial levels. In order to increase the stability of liposomes concept of proliposomes has been proposed. But because of poor skin permeability, breaking of vesicles, leakage of drug, aggregation and fusion of vesicles, these systems are not much successful for effective transdermal drug delivery[7].

Recently an innovative flexible vesicular system, ethosomes has been developed for topical/ transdermal delivery of a drug. This system has wonderful property to permeate intact through the human skin due to its high elasticity properties, which has an immense consequence for design of carrier system to be applied topically both for local and systemic delivery of hydrophilic and lipophilic drugs[7].

Ethosomes:

Ethosomes are noninvasive delivery carriers that enable drugs to reach the deep skin layers and/or the systemic circulation. These are soft, malleable vesicles tailored for enhanced delivery of active agents. The size of ethosome vesicles can be modulated from tens of microns to nanometres. This carrier presents interesting features correlated with its ability to permeate intact through the human skin due to its high deformability[9].

Ethosomal carriers are systems containing soft vesicles, ethanol at relatively high concentration and water. It was found that ethosomes penetrate the skin and allow enhanced delivery of various compounds to the deep strata of the skin or to the systemic circulation[10].

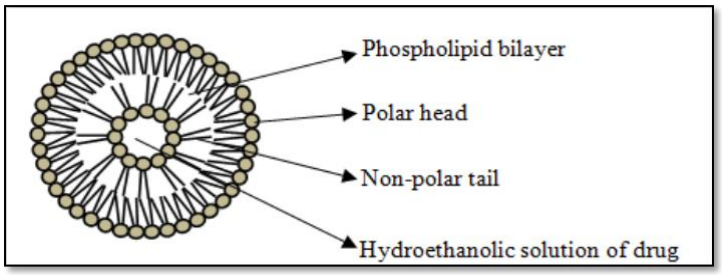


Fig2: Structure of Ethosomes.

Ethosomes composition[10]:

Ethosomes are vesicular carrier comprise of hydroalcoholic or hydro/alcoholic/glycolic phospholipid in which the concentration of alcohols or their combination is relatively high. Typically, Ethosomes may contain phospholipids with various chemical structures like phosphatidylcholine (PC), hydrogenated PC, phosphatidic acid (PA), phosphatidylserine (PS), phosphatidylethanolamine (PE), phosphatidylglycerol (PPG), phosphatidylinositol (PI), hydrogenated PC, alcohol (ethanol or isopropyl alcohol), water and propylene glycol (or other glycols). Such a composition enables delivery of high concentration of active ingredients through skin. Drug delivery can be modulated by altering alcohol: water or alcohol-polyol: water ratio. Some preferred phospholipids are soya phospholipids such as Phospholipon 90 (PL-90). It is usually employed in a range of 0.5-10% w/w. Cholesterol at concentrations ranging between 0.1 1% can also be added to the preparation. Examples of alcohols, which can be used, include ethanol and isopropyl alcohol. Among glycols, propylene glycol and Transcutol are generally used. In addition, non-ionic surfactants (PEG-alkyl ethers) can be combined with the phospholipids in these preparations. Cationic lipids like cocoamide, POE alkyl amines, dodecylamine, cetrimide etc. can be added too. The concentration of alcohol in the final product may range from 20 to 50%. The concentration of the non-aqueous phase (alcohol and glycol combination) may range between 22 to 70%.

Table no 1: Components of Ethosomes[12]

Class	Example	Uses
Phospholipid	Soya phosphotidyl choline Egg phosphotidyl choline Dipalmityl phosphotidyl choline Distearyl phosphotidyl choline	Vehicle forming component
Polyglycol	Propylene glycol Transcytol RTM	As a skin penetration enhancer
Alcohol	Ehanol Isopropyl alcohol	For providing softness to the vesicle membrane as a penetration enhancer
Cholesterol	Cholesterol	Stabilization of memebrane
	Rhodamine-123 Rhodamine red Fluroecence isocynate 6 carboxy fluroscence	For characterization study
Vehicle	Carbopol 934	Gel provider

Mechanism of drug penetration[13]:

The enhanced delivery of actives using ethosomes over liposomes can be ascribed to an interaction between ethosomes and skin lipids. A possible mechanism for this interaction has been proposed. It is thought that the first part of the mechanism is due to the 'ethanol effect whereby intercalation of the ethanol into intercellular lipids increasing lipid fluidity and decreases the density of the lipid multilayer. This is followed by the 'ethosome effect', which includes inter lipid penetration and permeation by the opening of new pathways due to the malleability and fusion of ethosomes with skin lipids, resulting in the release of the drug in deep layers of the skin.The main advantage of ethosomes over liposomes is the increased permeation of the drug. The mechanism of the drug absorption from ethosomes is not clear.

The mechanism of drug absorption from ethosomes followed by two phases.

1. Ethanol effect
2. Ethosomes effect

1. Ethanol effect:

Ethanol act as a enhance penetration through the skin. Ethanol penetrates in the intercellular lipids and increased fluidity of cell means due to decreased the density of lipid multilayer cell membrane

2. Ethosome Effect:

Ethanol increased lipid fluidity of ethosomes result increased skin permeability. Ethosomes easy to permeate inside deep layer which fused with skin lipids and release the drug layer of skin.

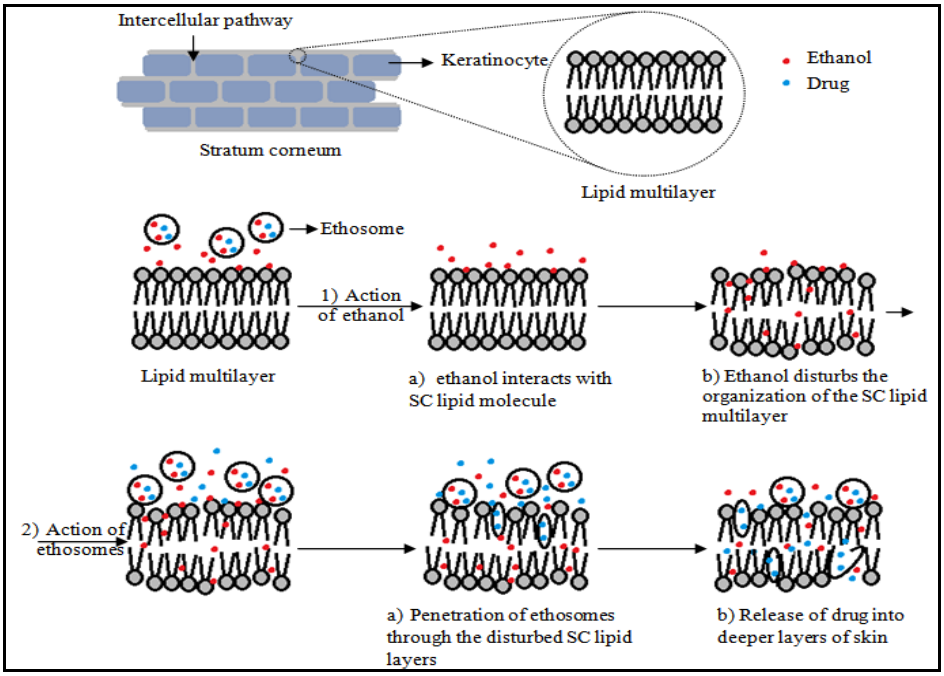


Fig3: Proposed mechanism for skin delivery of ethosomal systems.

Advantages

1. Ethosomal system is passive, non invasive and is available for immediate commercialization.
2. Enhanced permeation of drug through skin for transdermal drug delivery.
3. Delivery of large molecules (peptides, protein molecules) is possible.
4. It contains nontoxic raw material in formulation.
5. Ethosomal drug delivery system can be applied widely in Pharmaceutical, Veterinary, Cosmetic fields.
6. Ethosomes are platform for the delivery of large and diverse group of drugs (peptides, protein molecules)
7. Low risk profile-Technology has no large-scale drug development risk since toxicological profiles of the ethosomal components are well documented in the scientific literature.
8. Relatively smaller size as compared to conventional vesicles.

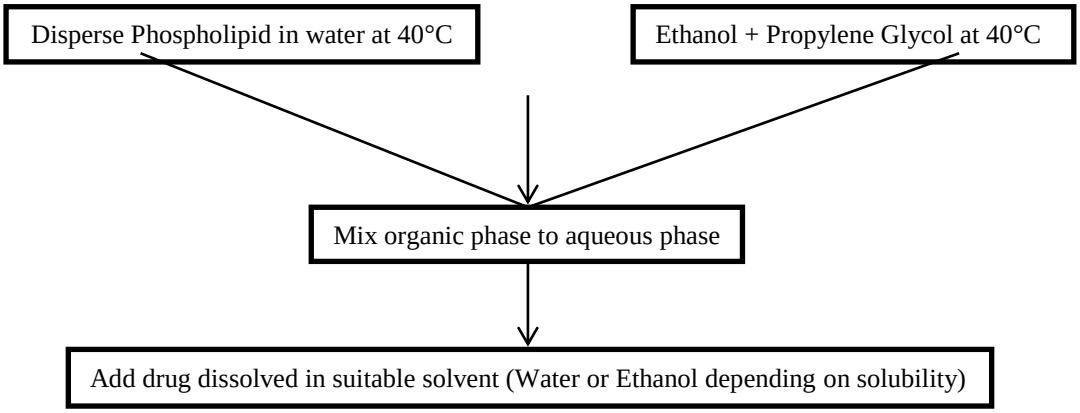
Limitations

1. Ethosomes having Poor yield .
2. In case if shell locking is ineffective then the ethosomes may coalescence and fall apart on transfer into water.
3. Loss of product during transfer form organic to water media.

METHODS OF PREPARATION[5,6,12]

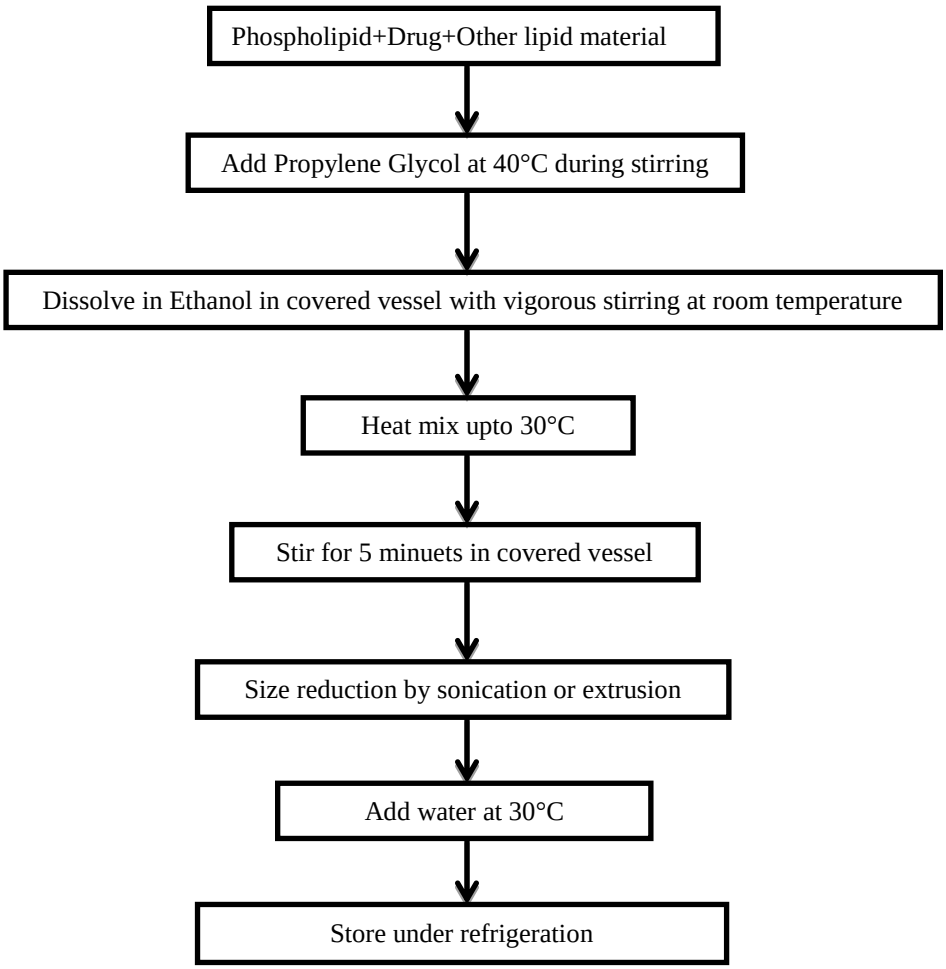
1. Hot method
2. Cold method
3. Classic Mechanical Dispersion Method
4. Classic Method

1. Hot method



In hot method, phospholipid is dispersed in water by heating in a water bath at 40^0C until a Colloidal solution is obtained. In a separate vessel ethanol and propylene glycol are mixed and Heated to 40 °C. Organic phase was added to aqueous phase and stirred for 5 min. The Vesicle size of ethosomal formulation was decreased to desire extent using sonication. The vesicle size of ethosomal formulation can be decreased to the desire extent using probe sonication or extrusion method .Finally, the formulation was stored properly.

Cold method



This is the most common and widely used method for the ethosomal preparation. Phospholipids, drug and other lipid materials are dissolved in ethanol in a covered vessel at room temperature by vigorous stirring with the use of mixer. Add propylene glycol or other polyglycol during stirring. Heat the mixture up to 30°C in a water bath. Heat the water up to 30°C in a separate vessel and add to the mixture and then stir it for 5 min in a covered vessel. The vesicle size of ethosomal formulation can be decreased to desire extend using sonication or extrusion method.

Classic Mechanical Dispersion Method

Soya phosphatidylcholine is dissolved in a mixture of chloroform: methanol (3:1) in round bottom flask. The organic solvents are removed using rotary vacuum evaporator above lipid transition temperature to form of a thin lipid film on wall of the flask. Finally, traces of solvent mixture are removed from the deposited lipid film by leaving the contents under vacuum overnight. Hydration is done with different concentration of hydroethanolic mixture containing drug by rotating the flask at suitable temperature.

Classic Method

The phospholipid and drug are dissolved in ethanol and heated to 30ºC±1ºC in a water bath. Double distilled water is added in a fine stream to the lipid mixture, with constant stirring at 700 rpm, in a closed vessel. The resulting vesicle suspension is homogenized by passing through a polycarbonate membrane using a hand extruder for three cycles.

CHARACTERISATION

Table no.2: Methods for the Characterization of Ethosomal Formulation.

Parameter	Methods
Visualization of vesicles	Scanning electron microscopy
	Transmission electron microscopy
Entrapment efficiency	Fluorescence spectrophotometry
	Mini column centrifugation method
Vesicle size and size Distribution	Dynamic light scattering method
Vesicle Skin interaction study	Confocal laser scanning microscopy
	Fluorescence microscopy
	Transmission electron microscopy
	Eosin-Hematoxylin staining
Phospholipidethanol Interaction	Differential scanning calorimeter
	31P NMR
Zeta potential	Zeta meter
Turbidity	Nephalometer
Degree of deformability	Extrusion method
In vitro drug release Study	Franz diffusion cell with artificial or biological membrane, Dialysis bag Diffusion
Stability study	Transmission electron microscopy
	Dynamic light scattering method

Vesicle shape[2]

Transmission electron microscopy (TEM) and Scanning electronic microscopy (SEM) are used to characterize the surface morphology of the ethosomal vesicles. Prior to analysis, mount the ethosomes onto double sided tape that has previously been secured on copper stubs and coated with platinum, then analyzed at different magnifications.

Entrapment Efficiency [5]

Entrapment efficiency of ethosomal vesicles can be determined by centrifugation method. The vesicles were separated in a high speed cooling centrifuge at 20,000 rpm for 90 minutes in the temperature maintained at 4 °C . The sediment and supernatant liquids were separated amount of drug in the sediment can be determined by lysing the vesicles using methanol. From this, the entrapment efficiency can be determined by the following equation,

$$\text{Entrapment Efficiency} = DE / DT \times 100$$

Where,

DE - Amount of drug in the ethosomal sediment

DT - Theoretical amount of drug used to prepare the formulation (equal to amount of drug in supernatant liquid and in the sediment)

Transition Temperature[12]

The Transition temperature (T) of vesicular lipids can be measured in duplicate by DSC in an aluminum pan at a heating rate of 10 °C per min, under a constant nitrogen stream.

Drug content[12]

Drug content of the ethosomes can be determined using UV spectrophotometer. This can also be quantified by a modified high performance liquid chromatographic method.

Surface tension measurement[12]

The surface tension activity of drug in aqueous solution can be measured by the ring method in a Du Nouy ring tensiometer.

Vesicle Stability studies[2]

The ability of ethosomal preparations to retain the drug (i.e drug-retentive behavior) can be checked by keeping the preparations at different temperatures, i.e., 25 ± 2°C (room temperature, RT), 37 ± 2°C and 45 ± 2°C for different periods of time (1, 20, 40, 60, 80 and 120 days). The ethosomal preparations were kept in sealed vials (10 ml capacity) after flushing with nitro-gen. The stability of ethosomes was also determined quantitatively by monitoring size and morphology of the vesicles using DLS and TEM.

Skin permeation studies[12]

The ability of the ethosomal preparation to penetrate into the skin layers can be determined by using confocal laser scanning microscopy (CLSM).

EVALUATION TEST[12]

Vesicle-Skin Interaction Study by Fluorescence Microscopy

Fluorescence microscopy was carried according to the protocol used for TEM and SEM study. Paraffin blocks are used, were made, 5-µm thick sections were cut using microtome (Erma optical works, Tokyo, Japan) and examined under a fluorescence micro Cytotoxicity Assay MT-2 cells (T-lymphoid cell lines) were propagated in Dulbecco's modified Eagle medium (HIMEDIA, Mumbai, India).Which containing 10% fetal calf serum, 100 U/mL penicillin, 100 mg/mL streptomycin and 2 mmol/L L-glutamine at 37°C under a 5% CO2 atmosphere.Cytotoxicity was expressed as the cytotoxic dose 50 (CD50) that induced a 50% reduction of absorbance at 540 nm.

Filter Membrane-Vesicle Interaction Study by Scanning Electron Microscopy

Vesicle suspension (0.2 mL) was applied to filter membrane having a pore size of 50 nm and placed in diffusion cells. The upper side of the filter was exposed to the air, whereas the lower side was in contact with PBS (phosphate buffer saline solution), (pH 6.5). The filters were removed after 1 hour and prepared for SEM studies by fixation at 4°C in Karnovsky's fixative overnight followed by dehydration with graded ethanol solutions (30%, 50%, 70%, 90%, 95%, and 100% vol/vol in water).Finally, filters were coated with gold and examined in SEM (Leica, Bensheim, Germany)

Skin Permeation Studies

The hair of test animals (rats) were carefully trimmed short (<2 mm) with a pair of scissors, and the abdominal skin was separated from the underlying connective tissue with a scalpel. The excised skin was placed on aluminium foil, and the dermal side of the skin was gently teased off for any adhering fat and/or subcutaneous tissue. The effective permeation area of the diffusion cell and receptor cell volume was 1.0 cm2 and 10 mL, respectively. The temperature was maintained at 32°C ± 1°C. The receptor compartment contained PBS (10 mL of pH 6.5). Excised skin was mounted between the donor and the receptor compartment. Ethosomal formulation (1.0 mL) was applied to the epidermal surface of skin. Samples (0.5 mL) were withdrawn through the sampling port of the diffusion cell at 1-, 2-, 4-, 8-, 12-,16-, 20-, and 24-hour time intervals and analyzed by high performance liquid chromatography (HPLC) assay.

Vesicle-Skin Interaction Study by TEM and SEM

From animals ultra thin sections were cut (Ultracut, Vienna,Austria), collected on formvar-coated grids and examined under transmission electron microscope. For SEM analysis, the sections of skin after dehydration were mounted on stubs using an adhesive tape and were coated with gold palladium alloy using a fine coat ion sputter coater. The sections were examined under scanning electron microscope.

HPLC Assay

The amount of drug permeated in the receptor compartment during in vitro skin permeation experiments and in MT-2 cell was determined by HPLC assay using methanol: distilled-water :acetonitrile (70:20:10 vol/vol) mixture as mobile phase delivered at 1 mL/min by LC 10-AT vp pump (Shimadzu, Kyoto, Japan). A twenty microliter injection was eluted in C-18 column (4.6×150 mm, Luna, 54, Shimadzu) at room temperature. The column eluent was monitored at 271 nm using SPDM10A vp diode array UV detector. The coefficient of variance (CV) for standard curve ranged from 1.0% to 2.3%, and the squared correlation coefficient was 0.9968.

Statistical Analysis

Statistical significance of all the data generated was tested by employing ANOVA followed by studentized range test. A confidence limit of $P < .05$ was fixed for interpretation of the results using the software PRISM (GraphPad, Version 2.01, San Diego, CA).

Drug Uptake Studies

The uptake of drug into MT-2 cells (1×106 cells/mL) was performed in 24-well plates (Corning Inc) in which 100 µL RPMI medium was added. Cells were incubated with 100 µL of the drug solution in PBS (pH 7.4), ethosomal formulation, or marketed formulation, and then drug uptake was determined by analyzing the drug content by HPLC assay.

Stability Study

Stability of the vesicles was determined by storing the vesicles at 4°C ± 0.5°C. Vesicle size, zeta potential, and entrapment efficiency of the vesicles was measured after 180 days using the method described earlier.

APPLICATIONS

Ethosomes are novel drug carrier can overcome the various problems related to the drug molecules such as low solubility, low permeability, low bioavailability, drug related to the high side effects, low therapeutic efficacy, high extensive first pass metabolism , and it is also used to target drug delivery and transdermal drug delivery and delivery of special drug molecule such as larger molecule as protein & peptide and DNA

Ethosomes solve problem of limited solubility

Example- Glimepiride is practically insoluble in water, this poor aqueous solubility & slow dissolution may lead to irreproducible clinical response or therapeutic failure due to sub therapeutic plasma drug levels. Low oral bioavailability results in wasting of a large portion of an oral dose. To circumvent these drawbacks glimepiride entrapped in vesicular carrier system to improve therapeutic efficacy of glimepiride via transdermal route.

Ethosomes avoid first pass metabolism:

Example- Oral delivery of hormones is associated with problems like high first pass metabolism, low oral bioavailability and several dose dependent side effects, increased risk of failure of treatment if the pill is missed. The skin permeation potential of testosterone ethosomes across rabbit pinna skin with marketed transdermal patch of testosterone (Testoderm patch, Alza) compared and it was observed nearly 30 times higher skin permeation of testosterone from ethosomal formulation as compared to that of marketed formulation of testosterone. Both in vitro and in vivo studies demonstrated improved skin permeation and bioavailability of testosterone from ethosomal formulation. Further, testosterone non patch formulation was designed to reduce the area of application. With the ethosomal testosterone formulation, area of application required to produce the effective plasma concentration was 10 times less than that required by commercial gel formulation.

Ethosomes used as targeted site specific delivery:

Example- Barupal , et al; prepare and characterized ethosomes of accelofenac which may deliver the drug to targeted site more efficiently than marketed gel preparation & also overcome the problems related with oral administration f drug . prepared ethosomes & evaluated as vesicle size, shape, surface morphology, entrapment efficiency and in vitro drug permeation study.it was observed that it permeate very efficiently & also have good stability profile of ethosomes.

Ethosomes are more beneficial than conventional formulations (ointment & tinctures):

Example- Apigenin, a flavonoid abundant in vegetables & fruits including parsley & onion, has been reported to have numerous pharmacological properties & anti-inflammatory, antioxidant & anticarcinogenic effects. Recent studies have demonstrated that apigenin could play an important role in the treatment of skin inflammation induced by free- radicals generated by UV, x-ray & γ radiation. It may inhibit cyclooxygenase-2 (cox-2) a key enzyme in the synthesis of prostaglandins from archidonic acid. But poor water solubility & unsatisfactory cutaneous permeability of apigenin after topical administration using conventional formulation (eg- ointments or tinctures) limits its therapeutic value. Ethosomes, a novel type of liposomes containing 20 – 50% of ethanol (v/v) have the potential to fulfill these therapeutic requirement because they can enhance drug loading by increasing apigenin's solubility & transdermal absorption. Present study investigated that apigenin-loaded ethosomes showed higher skin deposition than liposomes or deformable liposomes both in vitro & in vivo. Ethosome-mediated apigenin delivery produced the strongest effect on UVB –induced skin inflammation by suppressing cox-2 levels.

Ethosomes are used in pilosabeceous targeting:

Ethosomes the high ethanol containing vesicles are able to penetrate the deeper layers of the skin and hence appear to be vesicles of choice for transdermal drug delivery of hydrophilic and impermeable drugs through the skin. Example- The ethosomal system dramatically enhanced the skin permeation of minoxidil in vitro compared with either ethanolic or hydroethanolic solution or phospholipid ethanolic micellar solution of minoxidil.

Delivery of problematic drug molecules:

Example- Oral delivery of large biogenic molecules such as peptides or proteins and insulin is difficult because they are completely degraded in the GIT tract hence transdermal delivery is a better alternative. But conventional transdermal formulation of biogenic molecules such as peptides or protein and insulin has poor permeation. Formulating these above molecules into ethosomes significantly increase permeation and therapeutic efficacy.

Ethosomes also used in cosmetic:

The advantage of ethosomes in cosmeceuticals is not only to increase the stability of the cosmetics and decrease skin irritation from the irritating cosmetic chemicals, but also for transdermal permeation enhancement, especially in the elastic forms. Topical administration of many antioxidants is one of the several approaches to diminish oxidative injury in the skin for cosmetic and cosmeceutical applications. A USA company, Osmotics Inc., reported new cellulite cream called lipoduction prepared by using ethosome technology that penetrated the skin lipid barrier and delivered ingredients directly into the fat cells .

PATENTED MARKETED FORMULATION[12]

- Ethosome was invented and patented by Prof. Elka Touitou along with her students of department of Pharmaceutics at the Hebrew University School of Pharmacy 44, 45.
- Novel Therapeutic Technologies Inc (NTT) of Hebrew University have been succeeded in bringing a number of products to the market based on ethosome delivery system.

1. Noicellex TM an anti – cellulite formulation of ethosome is currently marketed in Japan.
2. Lipoduction TM another formulation is currently used in treatment of cellulite containing pure grape seed extracts (antioxidant) is marketed in USA.
3. Physonics is marketing anti – cellulite gel Skin Genuity in London.
4. Nanominox© containing monoxidil is used as hair tonic to promote hair growth is marketed by Sinere.

FUTURE PERSPECTIVE [12]

- Introduction of ethosomes has initiated a new area in vesicular research for transdermal drug delivery.
- Different reports show a promising future of ethosomes in making transdermal delivery of various agents more effective.
- Further, research in this area will allow better control over drug release in vivo, allowing physician to make the therapy more effective.
- Ethosomes offers a good opportunity for the noninvasive delivery of small, medium and large sized drug molecules.
- The results of the first clinical study of acyclovir ethosomal formulation support this conclusion. Multiliter quantities of ethosomal formulation can be prepared very easily.
- It, therefore, should be not before long that the corresponding drug formulation would have found their way into clinics to be tested for wide spreadusage.
- Special emphasis given to skin delivery of proteins & other macromolecules & for transcutaneous immunization.
- Thus, it can be a logical conclusion that ethosomal formulations possess promising future in effective dermal/transdermal delivery of bioactive agents.

List of abbreviations

TDDS -Transdermal drug delivery system
SC -stratum cor nium
NTT - Novel Therapeutic Technologies
HPLC -high performance liquid chromatography
SEM -scanning electron microscopy
CLSM - confocal laser scanning microscopy

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