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Lipid-Based Nanocarriers: Unravelling the Potential of Ethosomes in Transdermal Drug Delivery

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ABSTRACT

The stratum corneum (SC) is the foremost barrier of the skin, which restricts the permeation of the drug molecule. Few advanced approaches including liposomes, niosomes, ethosomes, and transferosomes are majorly used to boost the permeation of drug and cosmetic agents across the SC barrier. Among these vesicles, ethosomes are stand out as the best substitute for topical drug delivery. Ethosomal systems are phospholipid based, soft malleable vesicles that can deliver drug of different physicochemical characteristics, both in terms of quantity and depth when compared to other vesicular systems. Because of their unique structure and high content of ethanol, transdermal drug delivery has become easy, improving the drug efficacy and patient compliance. This article reviews various aspects of ethosomes including the ethosomal composition, types, mechanism of penetration, preparation methods, advantages, limitations, ethosomal dosage form, applications. Characterization of ethosomes includes particle size, zeta potential etc and evaluation studies.

INTRODUCTION

The skin is the largest and most easily accessible organ of the body; it serves as a potential route of drug administration for systemic effects.[1] Transdermal drug delivery system encounters the barrier properties of the horny layer (Stratum Corneum) and hence only the lipophilic drugs that have molecular weight <500 Da can pass through it. TDD has some other therapeutic benefits such as sustained drug delivery to provide a steady state plasma profile and hence reduced systemic side effect, thus generating the potential for improved patient compliance, the bypass of first-pass metabolism effect for drug with poor oral bioavailability.[2]

It also behaves as the primary barrier to percutaneous absorption. To improve the permeation of drugs through the skin various mechanisms have been investigated, including use of chemical or physical enhancers, such as iontophoresis, sonophoresis, etc. Liposomes, niosomes, transferosomes and ethosomes also have been reported to enhance the permeability of drug through the stratum corneum barrier. Permeation enhancers increase the permeability of the skin, so that the drugs can cross through the skin easily. Unlike classic liposomes, which are known mainly to deliver drugs to the outer layers of skin, ethosomes can enhance permeation through the stratum corneum barrier. Ethosomes permeate through the skin layers more rapidly and possess significantly higher transdermal flux in comparison to conventional liposomes.[3]

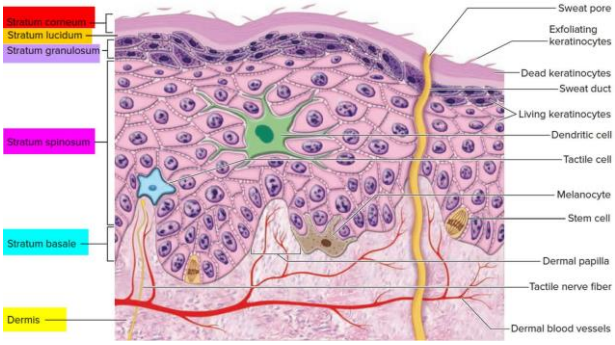


Figure 1: Stratum corneum

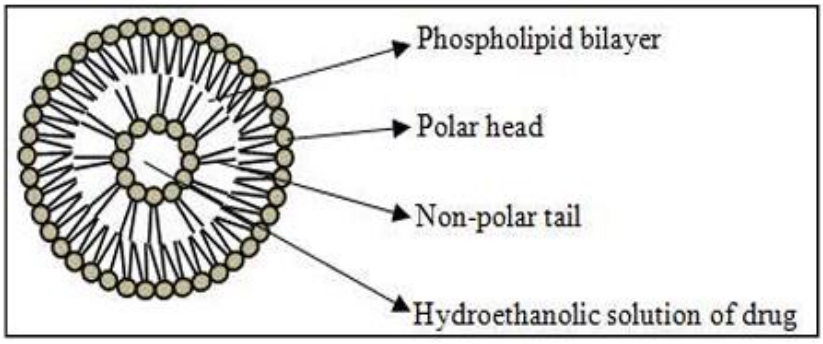


Figure 2: Proposed diagram of Ethosome.

ETHOSOMES

They are mainly used for the delivery of drugs through transdermal route. Drugs can be entrapped in Ethosomes which have various physicochemical characteristics i.e., hydrophilic, lipophilic, or amphiphilic.[4] These are soft, malleable lipid vesicles composed mainly of phospholipids, with higher concentrations (20-45%) of alcohol (ethanol or isopropyl alcohol) than water. Ethosomes were first developed by Touitou et al., 1997, as additional novel lipid carriers composed of ethanol, phospholipids, and water. "Ethosomes are ethanolic liposomes", can be defined as non-invasive delivery carriers that enable to permeation of drug into deeper skin layers and/or the systemic circulation providing an effective intracellular delivery of hydrophilic, lipophilic or amphiphilic molecules as shown in Figure 2.[5]

Types Of Ethosomes.[6]

1.) Classical Ethosomes

Classical ethosomes consist of phospholipids, water and high ethanol concentration. Classical ethosomes are better than conventional liposomes because of small size, negative zeta potential and higher entrapment efficiency.

2.) Binary Ethosomes

Binary ethosomes are formed by introducing another form of alcohol such as propylene glycol and isopropyl alcohol etc to the classical ethosomes.

3.) Transethosomes

Transethosomes are a new form of ethosomal system and have been designed to combine the advantages of classical ethosomes and transfersomes in a single formula. In their structure, they contain basic components such as that of classical ethosomes and a penetration enhancer or an edge activator.

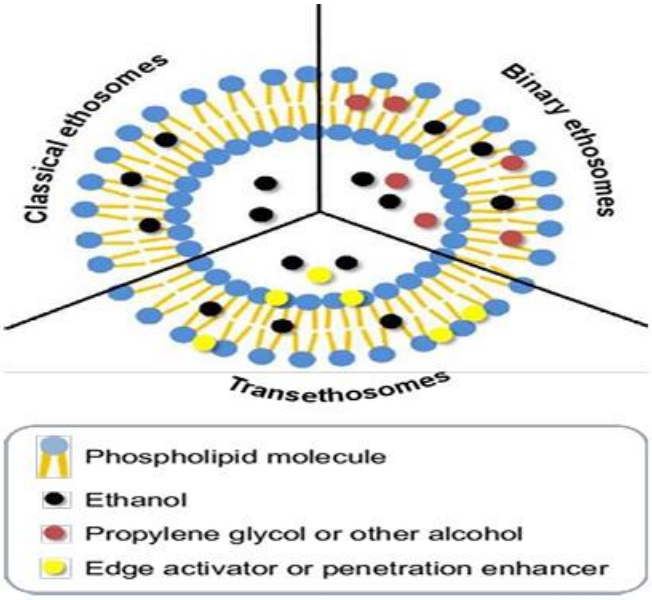


Figure 3: Types of Ethosomes

Advantages of ethosomal drug delivery.

In comparison to other transdermal & dermal delivery systems it predominantly,

- Enhanced permeation of drug through skin for transdermal drug delivery.
- Delivery of large molecules (peptides, protein molecules) is possible.
- It contains non-toxic raw material in the formulation.
- High patient compliance- The ethosomal drug is administrated in semisolid form (gel or cream) hence producing high patient compliance.
- The Ethosomal system is passive, non-invasive and is available for immediate commercialization.
- Ethosomal drug delivery systems can be applied widely in Pharmaceutical, Veterinary and Cosmetic fields.
- Simple method for drug delivery in comparison to Iontophoresis and Phonophoresis and other complicated methods.

- It has a low-risk profile.
- Patient compliance is high.

Limitations Of Ethosomal Drug Delivery. [7,8]

- Rather than a fast bolus-type drug intake, ethosomal administration is designed to provide continuous, sustained pharmaceutical distribution.
- Effective drug solubility in lipophilic and aqueous media for cutaneous micro circulation and systemic circulation.
- The drug's molecular size must be adequate for percutaneous absorption.
- Adhesive might not stick to all skin types.
- It might not be cost-effective.
- Allergy responses to ethanol or other ethosomal components can be identified.
- Ethosomal carriers, in contrast to other carriers (solid lipid nanoparticles, polymeric nanoparticles, and so on), are only required for transdermal administration.
- Because ethanol is flammable, more caution should be exercised when planning, applying, transporting, and storing it.
- Loss of product is observed during the phase transition from organic to water medium.
- It's only for potent chemicals that require a daily dose of long or less.
- The excipients and penetration enhancers that are used in the formulation of ethosomes can cause skin irritation (dermatitis).

Composition.[9]

Ethosomes are vesicular carriers composed of hydro-alcoholic or hydro/alcoholic/glycolic phospholipid in which the concentration of alcohols or their combination is relatively high. (Table 1)

Table 1: Composition of Ethosomes for Transdermal delivery

Additives used in Ethosomal Preparation	Examples	Application
Phospholipid	Soya phosphatidyl choline, Egg phosphatidyl choline, Dipal mityl phosphatidyl choline, Distearyl phosphatidyl choline	Vesicles forming component
Polyglycol	Propylene glycol, Transcutol RTM	As a skin penetration enhancer
Alcohol	Ethanol, Isopropyl alcohol	For providing the softness for vesicle membrane As a penetration enhancer
Cholesterol	Cholesterol	For providing the stability to vesicle membrane
Dye	Rhodamine-123, Rhodamine red Fluorescene Isothiocynate (FITC), 6- Carboxy fluorescence	For characterization study
Vehicle	Carbopol 934	As a gel former

Mechanism Of Drug Penetration.[7,10,11]

Touitou et al. in 2000, illustrated the mechanism of ethosomes wherein they used ethanol as a penetration enhancer. These mainly act by synergistic action of ethanol, vesicular system as well as lipids present in the skin. Skin is mainly composed of stratum corneum, epidermis and dermis. Stratum corneum is the main barrier in drug delivery through skin because in this layer corneocytes are closely packed in a highly ordered manner. This barrier gets disrupted by ethanol, thereby fluidizing both skin lipid layer barrier as well as lipids of the vesicular system. Ethanol also reduces the glass transition temperature of lipids of vesicles and skin. Interaction of ethanol with polar head groups of skin increases the permeation of elastic vesicles deeper in the skin tissues. The mechanism of action of ethosomes is demonstrated in Figure 4.

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 drug absorption probably occurs in the following two phases:

1. Ethanol effect

Ethanol acts as a penetration enhancer through the skin. The mechanism of its penetration-enhancing effect is well known. Ethanol penetrates intercellular lipids and increases the fluidity of cell membrane lipids and decrease the density of lipid multilayer of cell membrane.

2. Ethosome effect

Increased cell membrane lipid fluidity caused by the ethanol of ethosomes results in increased skin permeability. So, the ethosomes permeate very easily inside the deep skin layers, where it got fused with skin lipids and releases the drugs into deep layer of skin.

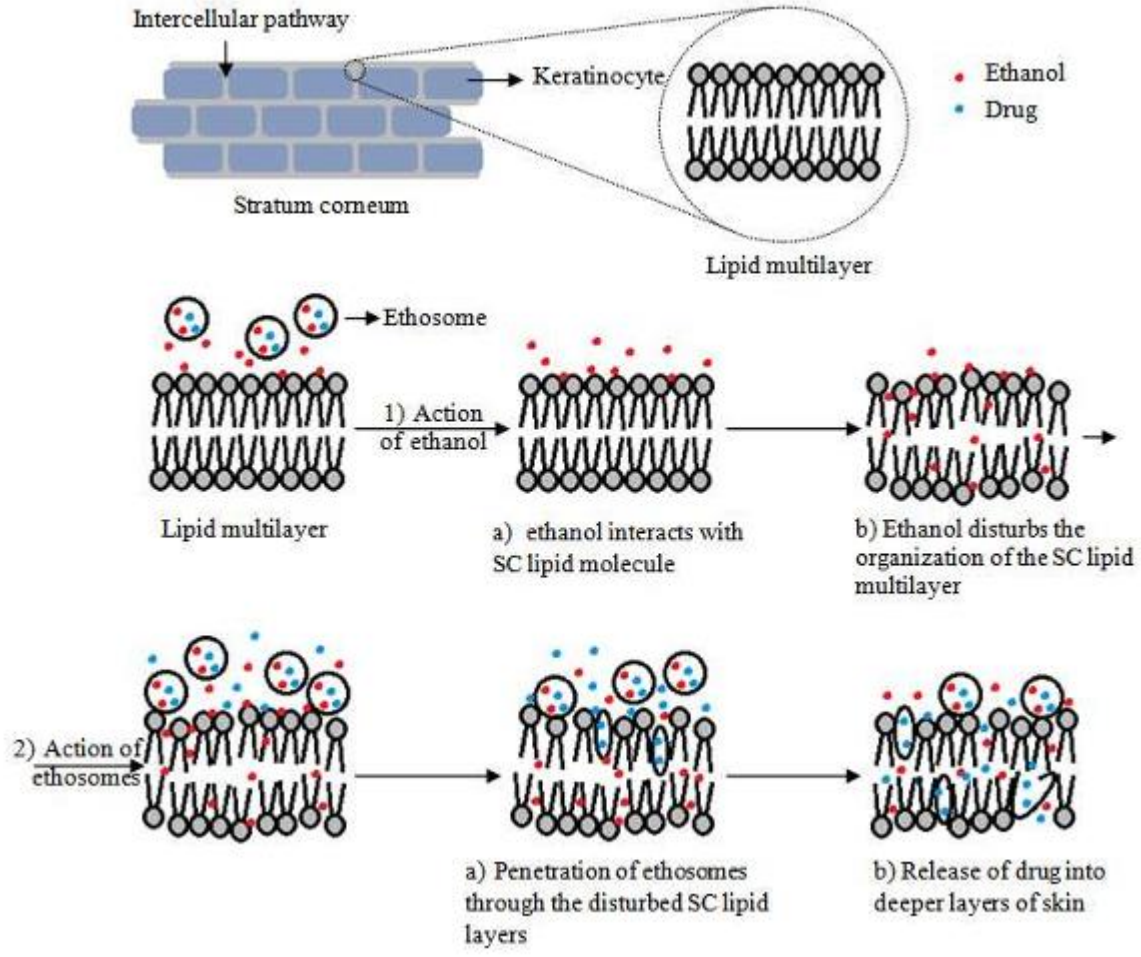


Figure 4: Proposed mechanism for skin delivery of ethosomal system.

Methods Of Preparations of Ethosomes[12,13,14,15]

There are several methods for preparing ethosomes, and may vary depending on the specific conditions and requirements of the ethosome preparation. Their production is relatively simple and cost-effective, making them a suitable alternative to other drug delivery systems. Table 2 highlights the most important methods that can be used to prepare ethosomes.

Hot Method

In this method disperse phospholipid in water by heating in a water bath at 40^0C until a colloidal solution is obtained. In a separate vessel properly mix ethanol and propylene glycol and heat up to 40^0C. Add the organic phase into the aqueous phase. Dissolve the drug in water or ethanol depending on its solubility. The vesicle size of ethosomal formulation can be decreased to the desired extent using probe sonication or extrusion method.

Cold Method

This is the most common and widely used method for the ethosomal preparation. Dissolve phospholipid, drug and other lipid materials in ethanol in a covered vessel at room temperature with vigorous stirring. Add propylene glycol or other polyol during stirring. Heat the mixture to 300c in a water bath. Heat the water up to 300c 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. Finally, the formulation should be properly stored under refrigeration.

Ethanol injection sonication method

Phospholipids are dissolved in ethanol, in a hermetically sealed glass bottle connected with a syringe for the addition of ethanol without its evaporation. The drug is dissolved separately in double-distilled water. The ethanolic solution of lecithin is then added to aqueous drug solution at a flow rate of 200 µL/min and homogenized with ultrasonic probe for 5 min. Later the ethosomal suspension is filtered using 0.45µm filters to collect the drug loaded ethosomes.

Vortex/sonication method edge

This method is a simple and effective common technique used for those preparation. In this method, phospholipids and edge activators are mixed in a phosphate buffer and subjected to forceful shaking and vertexing to ensure an even distribution of the components. The suspension is then sonicated using a vortex or sonicator to create vesicles. The size of the vesicles can be controlled by adjusting the sonication time and intensity. Finally, the suspension is extruded through membranes of various sizes to obtain vesicles of the desired size. This method is versatile, scalable, and can be used to prepare a wide range of drugs, both hydrophilic and hydrophobic. It is also cost-effective and can be easily scaled up for large-scale production.

Rotary film evaporation

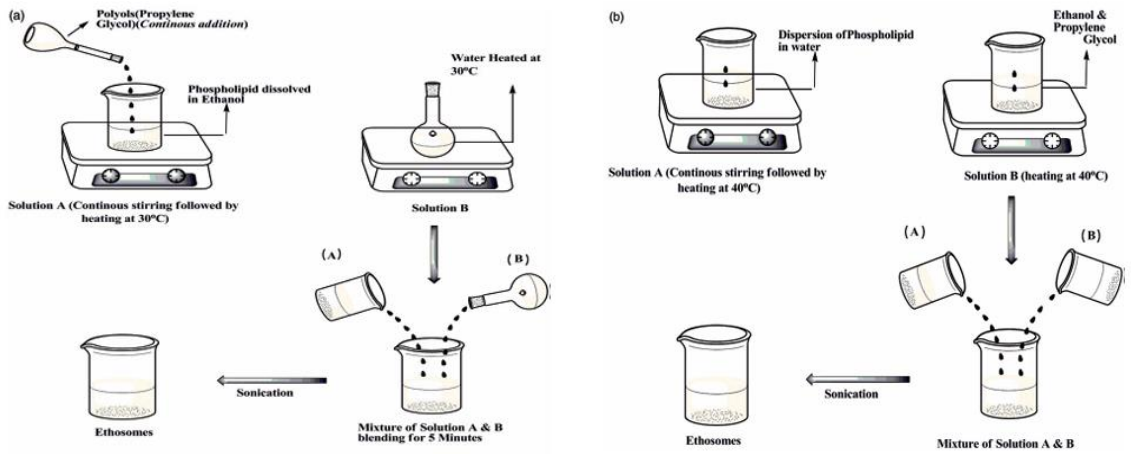
Rotary film evaporation is a useful technique for producing ethosomes for drug delivery applications. Phospholipids are dispersed in an organic solvent within a spherical bottom flask. The organic solvent is evaporated using a rotary evaporator, which leaves a thin film of lipids around the inner walls of the flask. The lipid film is then hydrated using an aqueous medium containing the drug that leads to the formation of lipid bilayer vesicles containing the drug of interest. The size of the ethosomes is controlled using sonication and extrusion.

Classic mechanical-dispersion method

In this method, a lipid mixture consisting of phospholipids and ethanol is first prepared. The drug or active ingredient is then added to the lipid mixture and the mixture is heated to form a clear solution. The clear solution is then cooled and subjected to mechanical dispersion using a high- shear homogenizer or ultrasonicator to form small vesicles, typically in the range of 100– 300 nm in diameter. This process involves subjecting the mixture to high shear stress to break up the lipid bilayers and promote the formation of ethosomes. Finally, the resulting those suspension is filtered through a membrane to remove any large particles or aggregates, and the size and shape of the ethosomes are confirmed using techniques such as dynamic light scattering (DLS) or transmission electron microscopy (TEM).

Transmembrane pH- gradient method

In this method, nonmedicated binary ethosomes are prepared initially followed by active loading of the drug. The phospholipid (e.g., phosphatidylcholine) is dissolved in an alcoholic phase consisting of ethanol and propylene glycol. A citrate buffer solution is gradually added to the solution with continuous stirring at 700 rpm and 30 ± 1°C. The system is cooled to room temperature and the binary ethosomes are ready. Then the drug is actively loaded into the ethosomes and the system is continuously agitated at 700 rpm to effectively disperse and dissolve the drug. A pH gradient can be established between the outer (alkaline) phase and inner (acidic) phase of the ethosomal system by adding sodium hydroxide (NaOH) solution (0.5 M) to adjust the outer pH. The system is then incubated at an appropriate time and temperature to allow the unionized drugs to actively pass through the lipid bilayer of ethosomes and become entrapped in the vesicles.



(a) **(b)**

Figure 5. Schematic representation of the method of preparation of ethosomes by (a) cold process and (b) hot process.

Table 2: Overview of ethosome preparation methods and their key characteristic.

Method	Advantages	Limitations	Cost	Manufacturing scale
Hot method	• Easy and quick method. • High encapsulation efficiency. • Small particle size • Stable at room temperature • Suitable for hydrophilic and hydrophobic drugs	• May cause degradation of the drug. • May result in particle aggregation • High energy consumption • Low drug loading capacity • Poor scalability	Low to moderate	Small to large
Cold method	• Simple and mild preparation method • Good drug loading capacity • Stable at room temperature • Suitable for hydrophilic and hydrophobic drug. • Good scalability	• Low encapsulation efficiency • Large particle size • May require long preparation times	Low to moderate	Small to large
Vortex/sonication method edge	• High encapsulation efficiency • Small particle size • Good drug loading capacity • Stable at room temperature • Suitable for hydrophilic and hydrophobic drug	• May cause degradation of the drug • May result in particle aggregation • High energy consumption • May require specialized equipment	Moderate to high	Small to moderate
Rotary film evaporation	• High drug loading capacity. • Good stability • Suitable for hydrophobic drugs	• May require specialized equipment • High energy consumption • May cause drug degradation	Moderate to high	Small to moderate
Classic Mechanical-dispersion method	• Simple and mild preparation method • Suitable for hydrophilic and hydrophobic drugs	• Low drug loading capacity • Large particle size • Low encapsulation efficiency	Low to moderate	Small to large
Transmembrane pH- gradient method	• Good drug loading capacity • Good stability • Suitable for hydrophobic drugs	• Complex and time-consuming method • Requires specialized equipment and expertise	Moderate to high	Small to moderate

Characterizations of Ethosomes[16,17,18]

1. Visualization

Visualization of ethosomes can be done using transmission electron microscopy (TEM) and scanning electron microscopy (SEM).

2. Vesicle size and Zeta potential Particle size and zeta potential can be determined by dynamic light scattering (DLS) using a computerized inspection system and photon correlation spectroscopy (PCS).

3. Differential scanning calorimetry (DSC)

The transition temperature (Tm) of the vesicular lipid systems was determined by using the Mettler DSC 60 computerized with the Mettler Toledo star software system (Mettler, Switzerland). The transition temperature was measured by using the aluminium crucibles at a heating rate 10 degree/minute, within a temperature range from 20˚C–300˚C.

4. Surface Tension Activity Measurement

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

5. Entrapment Efficiency

The entrapment efficiency of drugs by ethosomes can be measured by the ultra-centrifugation technique.

6. Penetration and Permeation Studies

The depth of penetration from ethosomes can be visualized by confocal laser scanning.

7. Vesicle Stability

The stability of vesicles can be determined by assessing the size and structure of the vesicles over time. Mean size is measured by DLS and structure changes are observed by TEM.

8. Drug Content:

Drug can be quantified by a modified high-performance liquid chromatographic method.

Table 3: Characterization Of Ethosomes

Test	Technique/Instrument
Particle shape	Scanning Electron Microscopy, Transmission Electron Microscopy
Particle size analysis	Optical Microscopy
Drug content	High Performance Liquid Chromatography/UV
Drug Entrapment Efficiency	Ultra-centrifugation technique
In-vitro drug release study	Franz Diffusion cell
Transition Temperature	Differential scanning calorimetry
In-vitro skin permeation study	Franz Diffusion cell

Evaluation of Ethosomes[19,20]

Filter Membrane-Vesicle Interaction Study by Scanning Electron Microscopy [SEM]

It necessitates vesicle suspension filtration (0.2 mL). In diffusion cells, a membrane with a whole size of 50 nm is placed. The top of the filter is exposed to the sun. The top side should be exposed to sunshine, while the bottom should be immersed in a phosphate saline buffer solution (pH 6.5). After 1 hour, the filters are removed, and the samples are prepared for SEM examinations by overnight fixation in Karnovsky's fixative at 4°C, followed by dehydration with ethanol solutions of varied concentrations (30%, 50%, 70%, and 80%) in water (90%, 95%). The filters are then mounted, gold-coated, and evaluated under a scanning electron microscope [SEM].

Skin Permeation, Studies

The test animals' hair was cut short (approximately 2 mm) using scissors and the abdomen skin was removed from the underlying connective tissue with a knife. The skin that had been excised was placed on aluminium foil and any adhering skin was gently teased off using the dermal side of the skin (fat or subcutaneous tissue may be involved). The effective permeation area and receptor cell volume of the diffusion cell were 1.0 cm^2 and 10 mL, respectively. The temperature was held at 32^0C. The temperature is -10C. In the receptor compartment, which contains a saline solution, phosphate buffer was retained (10 mL at pH 6.5). Between the donor's compartment and the receiver's compartment, the skin that had been taken had been mounted. An ethosomal formulation (1.0 mL) was applied to the

epidermal surface of the skin. An ethosomal formulation (1.0 mL) was applied to the epidermal surface of the skin. Samples (0.5 mL) were obtained using the sampling system. High-performance liquid chromatography equipment was used to analyse the data.

Stability Study

The vesicles' stability was tested by storing them at 4°C + 0.5°C. After 180 days, the vesicles' size, zeta potential, and entrapment efficiency were evaluated using the method described before.

Turbidity measurement

The Digital Nephalo-Turbidity Meter was used to determine the turbidity of all of the ethosomal suspensions. The 500 NTU (turbidimetric turbidity unit) range is used in this procedure, with Millipore water as the zero reading. In a 50 mL glass cuvette, the ethosomal formulations were transferred. The holder was then put into the instrument. The turbidity reading was shown on the screen and represented in NTU.

In-vitro release via dialysis membrane

This experiment was carried out using a Franz Diffusion cell. The dialysis membrane was soaked overnight in phosphate buffer 7.4. Between the donor and receiver chambers, the dialysis membrane was clamped down. 5 ml of the ethosomal formulation were uniformly distributed in the donor compartment. 125 mL of phosphate buffer 7.4 was introduced to the receiver compartment. Throughout the experiment, it was stirred continuously at 600 rpm with a Teflon-coated magnetic bead, and the temperature was held at 370 ± 0.5℃. To maintain the sink condition, 5 ml of the receiver fluid was withdrawn at each 1-hour interval and refilled with the same amount. A UV spectrophotometer was used to determine the drug content of withdrawn samples.

Transcellular delivery

Ethosomes as compared to the marketed formulation suggested ethosomes to be an attractive clinical alternative for anti-HIV therapy.

HPLC assay

The amount of drug permeated in the receptor compartment during in vitro skin permeation experiments and in MT-2 cells was determined by HPLC assay using methanol: distilled-water: acetonitrile (70:20:10 vol/vol) mixture as mobile phase 1.

Transdermal Drug Delivery of Hormones

Oral administration of hormones is associated with problems of Temperature, like high first pass metabolism, low oral bioavailability and several dose-dependent side effects. The risk of failure of variance for standard to increase with each pill missed.

Delivery of Anti-arthritis drug

Its oral administration is associated with a number of problems like low bioavailability, first-pass metabolism and GIT degradation.

Delivery of Antibiotics

Ethosomes penetrate rapidly through the epidermis and bring appreciable amount of drugs into the deeper layer of skin and suppress infection at their root.

Statistical Analysis

Statistical significance of all the data generated was tested by employing ANOVA followed by a 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).

Ethosomal Dosage Forms[21]

The ethosomal system has a high alcohol content; therefore, incorporating the system into an appropriate vehicle for dermal/transdermal administration prolongs skin contact time, reduces evaporation of ethanol, enhances drug effectiveness, increases stability and shelf life of the system, and improves patient compliance. The ethosomal system was reported to be loaded into various topical dosage forms, including gels, transdermal patches, and creams.

Ethosomal gels

Gel is a commonly used dosage form for loading the ethosomal system and is usually based on Carbopol or hydroxypropyl methylcellulose as gel-forming agents. The pH, viscosity, spreadability, and extrudability of ethosomal gels are among their distinguishing features. These polymers have been demonstrated to be compatible with ethosomal systems, giving them the necessary viscosity and adhesive characteristics. The skin permeation and deposition of different drugs from ethosomal gels have been studied by many researchers and found to be superior to those of conventional or commercially available gels or creams.

Ethosomal patches and creams

Patches or creams are less commonly used as a vehicle for ethosomal systems, often due to the ease of preparation and compatibility of gel bases with the high alcoholic content of ethosomes, acceptable patient compliance compared to creams, besides the difficulties associated with patch development where specific molds are required. On the other hand, patches offer the delivery of the loaded agents under occlusive conditions that could improve the skin's permeation and deposition. However, in the case of the ethosomal system, the efficiency of delivering the loaded agents under occlusive and nonocclusive conditions showed no significant difference as reported by Godin and Touitou.

Applications of Ethosome[22,23]

Ethosomes are mainly used for delivery of drug through transdermal route. Ethosomes are used in pilosebaceous 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.

There are some common drugs administered by transdermal route like NSAIDS (Diclofenac), Acyclovir, Antibiotics, Cannabidiol, Zidovudine, Ketoconazole.

Applications of ethosomes in various diseases are,[24]

i. Ethosomes for microbial and viral skin infection
ii. Ethosomes for viral and fungal infections
iii. Testosterone ethosomes for hormonal deficiency
iv. Ethosomes for Menopausal syndromes

v. Ethosomes for Erectile dysfunction
vi. Delivery of Peptides through ethosomes
vii. Ethosomes for Parkinsonism disease
viii. Minoxidil ethosomes for hair loss
ix. Anti-Inflammatory and Anti-Arthritis ethosomes
x. Ethosomes for Vaginal delivery
xi. Analgesic and Antipyretic ethosomes
xii. Ethosomes for skin disorders
xiii. Anti-hypertensive ethosomes
xiv. Miscellaneous application

Application of Ethosomes as a Drug Carrier[25]

Drug	**Results**
NSAIDS (Diclofenac)	✓ Selective delivery of drug to desired side for prolong period of time
Acyclovir	✓ Increase skin permeation ✓ Improved in biological activity two to three times ✓ Improved in Pharmacodynamic profile
Insulin	✓ Significant decrease in blood glucose level ✓ Provide control release
Trihexyphenidyl	✓ Improved transdermal flux
Hydrochloride	✓ Provide controlled release ✓ Improved patient compliance ✓ Biologically active at dose several times lower than the currently used formulation
DNA	✓ Better expression of genes ✓ Selective targeting to dermal cells
Antibiotic Cannabidiol Erythromycin	✓ Improved skin deposition ✓ Improved biological activity ✓ Prolonging drug action
Bacitracin	✓ Improved dermal deposition ✓ Improved intracellular delivery ✓ Increased bioavailability Improved transdermal flux ✓ Improved in biological activity two to three times
Anti-HIV agents Zidovudine	✓ Improved in biological activity two to three times ✓ Improved in Pharmacodynamic profile

Future Aspects

The inception of ethosomes has commenced a new revolution in vesicular research for effectual transdermal delivery. The successful commercialization of ethosomes based products has asserted their well-established potential in the market. Though majority of the marketed products include cosmeceuticals, exploration of the system for pharmaceutical products holds tremendous promise. Ethosomes provide better opportunities for non-invasive transport of small, medium as well as large drug molecules. Ethosomal formulations can be prepared in bulk easily and therefore the drug formulations would have found their way into clinics effectively for extensive utilization. Focused investigation on ethosomal variants such as binary ethosomes and composite ethosomes is the future of research based on ethosomes that will allow control over targeted drug release. The ethosomal technology can be extended to introduce the agents into cultured cells and microorganisms. Improvised delivery of bioactive molecules across the skin and cellular membranes by means of an ethosomal carrier gives ways to numerous challenges and opportunities for the research and future development of novel improved therapies. The clinical evaluation of intracellular targeting via ethosomes is still in its infancy. Delivery of quantum dots through human skin via ethosomes is the future aspect of ethosomal system. The modulations of the vesicular system by ligand binding or variation in ethosomal composition hold great potential. Thus, it can be concluded that ethosomal system possesses tremendous potential in the future in providing safe and effective transdermal delivery of therapeutic agents.[26]

CONCLUSION

Ethosome is a non-invasive carrier for the delivery of special drugs with varied physicochemical properties for the skin. It is majorly suitable for local and systemic applications. It is worthy to mention that, ethosomes demonstrate controlled/ sustained drug release, good biocompatibility, reduced toxicity and several advantages in the pharmaceutical field. Notably, simplicity in composition and method preparation of ethosomes make them attractive drug delivery carriers. Especially, the presence of ethanol in vesicles offers several merits as compared to the other lipidic vesicles for topical/ transdermal applications. Even, ethosomes can easily incorporate into different types of dosage forms including gels, patches, and creams. Consequently, it can be concluded that, in years to come, ethosomal formulations would find their place in the therapeutic world due to enhanced permeability for better therapeutic activity.

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