ETHOSOMES AS NOVEL VESICULAR CARRIERS FOR ENHANCED DRUG DELIVERY
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Abstract
Dermal route has been recognized as one of the highly potential route of systemic drug delivery. Skin is main target of topical and transdermal preparation. Ethosomes are the ethanolic phospholipid vesicles which are used mainly for transdermal drug delivery of drugs. Ethosomes have higher penetration rate through skin. It contain soft vesicle, composed of hydroalcoholic or hydroglycolic phospholipid in which concentration of alcohol is relatively high. Ethosomes are novel carrier for enhanced skin delivery. The use of lipid vesicles in delivery system for skin treatment has attracted increasing attention in recent year in comparison to oral drug delivery system as it eliminates the gastrointestinal interference and first pass metabolism. The concentration of ethanol in ethosomes is about 15 to 45% it increase in fluidity of the membrane. The purpose of writing this review on ethosomes drug delivery was compile the focus on various aspect of ethosomes including mechanism of penetration, preparation, characterization, evaluation test and application. Unique structures of ethosomes are able to encapsulate. The delivery through the skin highly lipophilic molecules such as cannabinoids, testosterone and minoxidil as well as cationic drug such as propranolol and trihexyphenidil. Ethosomes provide number of important benefits including improving the drug’s efficacy, enhancing patient compliance and comfort and reducing the total cost of treatment.

Key words: Dermal, Ethosome, Penetration, Vesicle.

Introduction
The human skin covers the external surface of the body and is largest organ of the body in both surface area and weight. In adult the skin covers an area of about 2 square meters (22 square feet) and weighs 4.5-5 kg (10-11 lb), about 16% of total body weight. It range in thickness from 0.5 mm (0.02 in.) on eyelids to 4.0 mm (0.16 in.) on the heels (Tortora and
Human skin has selective permeability for lipophilic drug having molecular weight < 500 Dalton. Skin form a covering layer against the external environment and reduced the water loss from internal tissue. It also perform an ancillary functions such as synthesis and metabolism and production of sweat enable temperature control excretion of waste products by means of sweating (Scheuplein, Blank, 1971). Skin is act as thermostat which maintain the body temperature. It acts as barrier against physical, chemical and microbial attacks. Human skin consist of main three layer epidermis, dermis and subcutaneous tissue. Human skin is an effective, selective barrier to chemical permeation. Epidermis (specially the stratum corneum) most small water soluble non electrolyte diffuse into systemic circulation thousand times more rapidly when horny layer is absent. Thus to maximise drug flux we usually try to reduce this barrier’s hindrance (Barry, 2001). Stratum corneum is the most formidable barrier to passage of most of the drug except for highly lipophilic, low molecular weight drug. To overcome the stratum corneum such as Iontophoresis, sonophoresis etc. Stratum corneum is the outermost layer of the epidermis. It consists of 10 to 25 layers of dead, elongated, fully keratinized corneocytes, which are embedded in a matrix of lipid bilayers (Menton and Eisen, 1971).

**Fig.1 Structure of human skin**
Fig. 2 Proposed mechanism of drug absorption through skin.

The skin protect from the antigen stimuli by means of immune system known as skin associated lymphoid tissue (Lynch, Robert, et. al., 1987). Stratum corneum is the most formidable barrier to passage of most drugs except for highly lipophilic drug, low molecular weight drug.

Ethosomes are noninvasive drug delivery carrier passed through skin and reach to systemic circulation. These are soft, malleable vesicles tailored for the enhanced the delivery of active agent. High amount of ethanol makes the ethosomes unique. Ethanol is known for its disturbances the skin lipid bilayer.

**Silent Feature of Ethosomes**

1. Ethosomes provides a mode for passive noninvasive delivery.
2. These carriers are suitable for large molecules like lipophilic, hydrophilic, molecules, peptides and other macromolecules.
3. They can act as carrier for low as well as high molecular weight substance e.g. analgesic, corticosteroids and sex hormone.
4. They are biocompatible and biodegradable.
5. Due to high content of ethanol it possesses high entrapment efficiency and high cell transfection efficiency.
6. It act as depot formulation hence sustain release is obtained.
7. Easy to scale up, procedure is simple, does not involve lengthy procedure and unnecessary use of pharmaceutically unacceptable additives.
8. High Patient compliance. Ethosomes drug is administered in semisolid form (gel or cream).

10. Low risk profile- The technology has no large scale development drug risk.

11. High market attractiveness for products with proprietary technology. Relatively simple to manufacture with no complicated technical investments required for production of Ethosomes.

**Limitations of Ethosomes**

1. Poor yield (Laib and Rauth, 2008).

2. In case if shell locking is ineffective then the ethosomes may coalesce and fall apart on transfer into water.

3. Loss of product during transfer form organic to water media (Swarnlata, Rahul, et al., 2011).

**Ethosome Composition**

Ethosome is composed of hydroalcoholic phospholipid or hydroglycolic phospholipid in which concentration of alcohol is relatively high. It is mainly composed of Phospholipids, phospholipids are amphipathic (have affinity for both aqueous and non-aqueous moiety) these molecules have hydrophobic/nonpolar tail and hydrophilic/polar head. Hydrophilic tail is composed of two fatty acids chain containing 10-24 carbon atoms, 0-6 double bonds in each chain. Hydrophilic head end of molecules is mainly phosphoric acid bound to water soluble molecules. The hydrophilic and hydrophobic domain/segment within the molecules geometry of the amphiphilic lipid orient and self-organize in order supramolecules structure when confront membrane (Lasic, 1995). It contain the phospholipid which various chemical structure like Phosphatidylcholine (PC), Hydrogenated PC, Phosphatic acid (PA), Phosphatidylserine (PS), Phosphatidylethanolamine (PE), Phosphatidyglycerol (PPG), Phosphatidylinositol (PI). 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%.

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**Fig.3: Composition of ethosomes.**
Composition of Ethosome (Touitou, 1996).

Table no. 1 Additives used in ethosomal preparation.

<table>
<thead>
<tr>
<th>Class</th>
<th>Examples</th>
<th>Uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phospholipid</td>
<td>Soya phosphatidylcholine (0.5-10% w/w.)</td>
<td>Vesicles forming component</td>
</tr>
<tr>
<td></td>
<td>Egg phosphatidyl choline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Dipalmitylphosphatidyl choline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distearylphosphatidyl choline</td>
<td></td>
</tr>
<tr>
<td>Polyglycol</td>
<td>Propylene glycol</td>
<td>As a skin penetration enhancer.</td>
</tr>
<tr>
<td></td>
<td>Transcutol RTM</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>Ethanol</td>
<td>For providing the softness for vesicle membrane</td>
</tr>
<tr>
<td></td>
<td>Isopropyl alcohol</td>
<td>As a penetration enhancer</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Cholesterol (0.1-1%).</td>
<td>For providing the stability to vesicle membrane.</td>
</tr>
<tr>
<td>Dye</td>
<td>Rhodamine-123, Rhodamine red FluoresceneIsothiocyanate (FITC)</td>
<td>For characterization study.</td>
</tr>
<tr>
<td></td>
<td>6- Carboxy fluorescence</td>
<td></td>
</tr>
<tr>
<td>Vehicle</td>
<td>Carbopol934</td>
<td>As a gel former</td>
</tr>
</tbody>
</table>

Mechanism of Drug Penetration of Ethosomes

Ethosomes
↓
Ethanol cause skin disruption
↓
Increase lipid fluidity
↓
More permeation through skin
↓
Ethosomes permeates inside
↓
Fuse with skin lipids
↓
Release the drug in deep skin layer
Mechanism of Drug Permeation

Ethanols affect the stratum corneum lipid multi-layer which are densely packed and highly ordered at physiological temperature. Ethanols interact with lipid molecules in polar head group region resulting in reduction in Tm of stratum corneum lipids, thus increasing their fluidity. Ethanol is penetration enhancer act by affecting the intercellular region of stratum corneum thus it permeation. A possible mechanism for the interaction between skin and ethosomes 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 ‘ethosomes 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.

Penetration enhancing effect of ethanol could be attributed to (Jain, 2006).

1. Increase in thermodynamic activity due to evaporation of ethanol known as "push effect"
2. "Pull effect" in which penetration of drug molecules is increase due to reduction in barrier properly of stratum corneum by ethanol.

There are two types of effect (Verma, Fahr, 2004).

Ethanol effect: Increase the fluidity of cell membrane lipid and decrease the density of lipid multilayer of cell membrane. Ethosomes effect: increase cell membrane lipid fluidity caused by ethanol of ethosomes results increase skin permeability so the ethosomes permeates very easily inside the deep skin layer where it got fused with skin lipids and release the drugs into deep skin.

![Fig.4 Influence of high alcohol on skin.](image-url)
Method of Preparation


**Phospholipid**

Ethanol

Drugs

Slowly add double distilled water in a fine stream with constant mixing at 700 rpm

Ethanolic solution of phospholipid

Sonication or extrusion

**Ethosomes Preparation** (Vyas, 2009).

There are four methods which can be used for formulation and preparation. Hot method and cold method are the two conventional methods used for the preparation of ethosomes are very simple and convenient and do not involve any sophisticated instrument or complicated process. Classic mechanical dispersion and transmembrane pH gradient active loading method are also reported in various literature (Zhou, Wei, et al., 2010).

**Hot method**

In this method phospholipid is dispersed in water by heating in a water bath at 40°C until a colloidal solution is obtained. In a separate vessel ethanol and propylene glycol are mixed and heated to 40°C. Once both mixtures reach 40°C, the organic phase is added to the aqueous one. The drug is dissolved in water or ethanol depending on its hydrophilic/hydrophobic properties (Touitou, 1998). The vesicle size of ethosomal formulation can be decreased to the desire extent using probe sonication or extrusion method (Sheer, Chauhan, 2011).
Fig. 5: Hot method for the preparation of ethosomes.

**Cold method**

This is the most common method utilized for the preparation of ethosomal formulation. In this method phospholipid, drug and other lipid materials are dissolved in ethanol in a covered vessel at room temperature by vigorous stirring with the use of mixer. Propylene glycol or other polyol is added during stirring. This mixture is heated to 30°C in a water bath. The water heated to 30°C in a separate vessel is added to the mixture, which is then stirred 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 is stored under refrigeration (Shree and Chauhan, 2011).

- Phospholipid + Drug
  - Dissolved in ethanol
    - Add propylene glycol
      - Mixture is heated to 30°C ± 1°C
        - Double distilled water is added with constant stirring for 5 min.
          - Vesicle size is controlled by using sonication and extrusion method
            - Formation is stored in refrigerator
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 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 (Dubey, Mishra, et al., 2007). (Jain, Tiwari, 2012).

```
Phospholipid+CHCl₃+CH₃OH+drug dissolved
↓
Organic solvent removed by rotary vacuum evaporation
↓
Finally hydration done
↓
Trace solvent remove under vacuum over night
↓
Ethosomes are obtained
```

Classic method

The phospholipid and drug are dissolved in ethanol and heated to 30°C±1°C 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 (Jain and Tiwari, 2007).

```
Phospholipid+ dissolved in ethanol
↓
Heat to 30°C
↓
Add double dissolved water
↓
Stir at 700 rpm
↓
Formed vesicles homogenized passing through poly carbonate
↓
Ethosomes obtained
```
### Characterisation of Ethosome

The parameters and methods used for characterization of ethosomes are listed in below table.

**Table no. 2 Characterization of ethosomes.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vesicle shape (morphology) (Nikalje and Tiwari, 2012).</td>
<td>Transmission electron microscopy</td>
</tr>
<tr>
<td></td>
<td>Scanning electron microscopy</td>
</tr>
<tr>
<td>Entrapment efficiency (Maghraby, Williams, et al., 2000).</td>
<td>Mini column centrifugation method</td>
</tr>
<tr>
<td></td>
<td>Fluorescence spectrophotometry</td>
</tr>
<tr>
<td>Vesicle size (Nikalje and Tiwari, 2012). and size distribution</td>
<td>Dynamic light scattering method</td>
</tr>
<tr>
<td></td>
<td>Photon correlation spectroscopy (PCS)</td>
</tr>
<tr>
<td>Zeta potential (Kapilkanwar, 2012).</td>
<td>Zeta meter</td>
</tr>
<tr>
<td>Vesicle Skin interaction study</td>
<td>Confocal laser scanning microscopy</td>
</tr>
<tr>
<td></td>
<td>Fluorescence microscopy</td>
</tr>
<tr>
<td></td>
<td>Transmission electron microscopy</td>
</tr>
<tr>
<td></td>
<td>Eosin-Hematoxylin staining</td>
</tr>
<tr>
<td>Phospholipid-ethanol interaction</td>
<td>$^{31}$P NMR</td>
</tr>
<tr>
<td></td>
<td>Differential scanning calorimeter</td>
</tr>
<tr>
<td>Degree of deformability</td>
<td>Extrusion method</td>
</tr>
<tr>
<td>Surface Tension Activity Measurement (Cevc, Schatzlein, et al., 1995).</td>
<td>Du Nouy ring tensiometer</td>
</tr>
<tr>
<td>Turbidity</td>
<td>Nephelometer</td>
</tr>
<tr>
<td>In vitro drug release study</td>
<td>Franz diffusion cell with artificial or biological membrane, Dialysis bag diffusion</td>
</tr>
<tr>
<td>Drug deposition study</td>
<td>Franz diffusion cell</td>
</tr>
<tr>
<td>Skin permeation studies (Toll, Jacobu, et al., 2004).</td>
<td>Confocal laser scanning microscopy (CLSM)</td>
</tr>
<tr>
<td>Stability study (Geest, Swartzendruber, et al., 1997).</td>
<td>Dynamic light scattering method</td>
</tr>
<tr>
<td></td>
<td>Transmission electron microscopy</td>
</tr>
<tr>
<td>Drug content (Dayan and Touitou, 2002).</td>
<td>UV spectrophotometer</td>
</tr>
<tr>
<td></td>
<td>High performance liquid chromatography</td>
</tr>
<tr>
<td>Transition Temperature (Fry, White, et al., 1978).</td>
<td>Differential scanning calorimeter (DSC)</td>
</tr>
<tr>
<td>Elasticity Measurement (Crook, 1997).</td>
<td>extrusion method</td>
</tr>
</tbody>
</table>
Evaluation Test of Ethosomes (Nikalje and Tiwari, 2012; Lopen-pinto, Gonzalez-Rodriguez, et al., 2005; Kumar, Radhika, et al., 2010; Tyagi and Kumar, 2013).

The evaluation test can be carried out by following methods.

**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, Blenheim, Germany).

**Vesicle-Skin Interaction Study by TEM and SEM**

From animals ultra-thin sections were cut (Ultracut, Vienna, Austria), collected on formvacated 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.

**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) containing 10% fetal calf serum, 100 U/mL penicillin, 100 mg/mL streptomycin and 2 mMol/LL-glutamine at 37°C under a 5% CO2 atmosphere. Cytotoxicity was expressed as the cytotoxic dose50 (CD50) that induced a 50% reduction of absorbance at 540 nm.

**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 aluminum 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 cm$^2$ 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.

**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.

**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.

**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.

**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).

**Cytotoxicity Assay:**

MT-2 cells (T-lymphoid cell lines) were propagated in Dulbecco's modified Eagle medium (HIMEDIA, Mumbai, India) 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.
The application of ethosomes can be described in the following table.

**Table no.3: Application of Ethosomes.**

<table>
<thead>
<tr>
<th>Dug</th>
<th>Application</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir</td>
<td>Treatment of Herpetic infection</td>
<td>-Improved drug delivery&lt;br&gt;-Provide noninvasive mean of therapeutic use&lt;br&gt;-high Transdermal flux</td>
</tr>
<tr>
<td>Minoxidil</td>
<td>Hair growth promotion effect</td>
<td>-Higher skin retention&lt;br&gt;-high entrapment efficiency.&lt;br&gt;- pilosebaceous targeting.</td>
</tr>
<tr>
<td>Testosterone</td>
<td>Treatment of male hypogonodism</td>
<td>-Enhance skin permeation&lt;br&gt;-High entrapment efficiency.&lt;br&gt;-Greater Transdermal delivery as compared to marketed patches.</td>
</tr>
<tr>
<td>TrihexylenidylHCl</td>
<td>Treatment of Parkinsonian syndrome</td>
<td>-Increased drug entrapment Efficiency&lt;br&gt;-reduced side effect &amp; constant systemic levels</td>
</tr>
<tr>
<td>Insulin</td>
<td>Treatment of Diabetes</td>
<td>-Improved therapeutic efficacy of drug&lt;br&gt;-significant decrease in blood glucose level</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Efficient healing of <em>S. aureus</em> -induced deep dermal infections</td>
<td>-Improved drug penetration and Systemic effect.&lt;br&gt;- Complete inhibition of infection&lt;br&gt;-prolong action of drug</td>
</tr>
<tr>
<td>Cannabidol</td>
<td>Prevents inflammation and edema</td>
<td>-Significant accumulation of the drug in the skin&lt;br&gt;-improved Transdermal flux</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>Treatment of dermal infections</td>
<td>-efficient delivery to deep skin strata.&lt;br&gt;- Reduced drug toxicity</td>
</tr>
<tr>
<td>Zidovudine</td>
<td>Treatment of AIDS</td>
<td>-Improved transdermal flux</td>
</tr>
<tr>
<td>Name of product</td>
<td>Uses</td>
<td>Manufacturer</td>
</tr>
<tr>
<td>-----------------</td>
<td>----------------------------------------------------------------------</td>
<td>-----------------------------------</td>
</tr>
<tr>
<td>Cellutight EF</td>
<td>Topical cellulite cream, contains a powerful combination of ingredients to increase metabolism and break down fat</td>
<td>Hampden Health, USA</td>
</tr>
<tr>
<td>Decorin cream</td>
<td>Anti-aging cream, treating, repairing, and delaying the visible aging signs of the skin including wrinkle lines, sagging, age spots, loss of elasticity, and hyperpigmentation</td>
<td>Genome Cosmetics, Pennsylvania, US</td>
</tr>
<tr>
<td>Nanominox</td>
<td>First minoxidil containing product, which uses ethosomes. Contains 4% Minoxidil, well-known hair growth promoter that must be metabolized by sulfation to the active compound</td>
<td>Sinere, Germany</td>
</tr>
<tr>
<td>Noicellex</td>
<td>Topical anti-cellulite cream</td>
<td>Novel Therapeutic Technologies, Israel</td>
</tr>
<tr>
<td>Skin genuity</td>
<td>Powerful cellulite buster, reduces orange peel</td>
<td>Physonics, Nottingham, UK</td>
</tr>
<tr>
<td>Supravir cream</td>
<td>For the treatment of herpes virus, formulation of Acyclovir drug has a long shelf life with no stability problems, stable for at least three years, at 25°C. Skin permeation experiments showed that the cream retained its initial penetration enhancing properties even after three years</td>
<td>Trima, Israel</td>
</tr>
</tbody>
</table>
Conclusion

The main limiting factor of Transdermal drug delivery system i.e. epidermal barrier can be overcome by ethosomes to significant extent. Ethosomes open new opportunities to transcutaneous immunization (TCI) and gene therapy. Thus it can be logical conclusion that ethosomes can become a promising drug delivery carrier in future for not only topical treatment of local and systemic disorder, but also for cosmetic and cosmeceutical field. Ethosomes have been found to be much more efficient at delivering drug to the skin than either liposomes or hydroalcoholic solution.

Future Prospective

Ethosomal carrier open new challenge and opportunities for development of novel improved therapy. Future research in this area will allow better control over drug release in vivo, allowing physicians to make the therapy more effective. Ethosomal formulation possess promising future in effective transdermal delivery of bioactive agents. Introduction of ethosomes has marked a new era in vesicular research for transdermal drug delivery. Ethosomes offer good opportunity for invasive delivery of small, medium and large sized drug molecules. Multiliter quantities of ethosomal formulation can be prepared very easily.

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27. Touitou E; Composition of applying active substance to or through the skin, US patent, 5,716,638, 1996.


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