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MANAGEMENT OF DISEASE CONDITIONS BY ETHOSOMES OF TOPICAL DELIVERY: AN OVERVIEW

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ABSTRACT

Ethosomes, changed type of liposomes with elevated ethanol content. Ethosomes are made up of phospholipid, ethanol as well as water. They know how to infiltrate the skin and improve the delivery of together compounds to deep skin as well as system. These "soft vesicles" are new vesicular carriers for improved transdermal transport to / through skin. Ethosomes is vesicular medication conveyance framework that increases the penetrability of medication, these variables elevate researchers to pick as definition improvement which keep up sufficient fixation to treat disease conditions. Ethosomes are believed in faster advancement of new safe drugs, reduction in danger while keeping up helpful impacts and are biocompatible. Transdermal medication conveyance remains the most supported method of administration. In any case, stratum corneum shapes the mainly imposing obstruction for the infiltration of medication all the way through the skin, to conquer the stratum corneum boundary; the utilization of lipid vesicles similar to ethosomes in conveyance frameworks has pulled in expanding consideration as of late.

K**eywords:** Ethosomes, Skin, vesicles, Transdermal, Stratum Corneum

INTRODUCTION:

Ethosomes are made up of phospholipid, ethanol as well as water. They know how to infiltrate the skin and improve the delivery of together compounds to deep skin as well as system. This ethanol fluidizes mutually ethosomal lipids along with bilayers of the stratum corneum intercellular lipid. The delicate, soft vesicles at that point infiltrate the scattered lipid bilayers. Ethosomes are delicate; vesicles are primarily made primarily of phospholipids, ethanol (highly concentrated) with water.[1-6] These "soft vesicles" are new vesicular carriers for improved transdermal transport to / through skin. [7, 8]

Vesicles are highlighted for their significance in cellular correlation as well as transport of particles for a long time. Scientists understand the nature of the structure of the wand intended in providing enhanced drug deliverance inside their cavities. Unlike liposomes, it is likely that the product is demonstrated by the effectiveness, encapsulation efficiency for an extensive range of molecules, including lipophilic drugs and precisely in delivering the molecules to and through the skin as reported. [9]

Numerous reports have revealed the success of ethosomes in successful delivery of transdermal agents. It also provides a decent open space for the distribution of medium and widespread molecules. The preparation of the ethosome is simple without the inclusion of complex materials and can be measured along these lines to modern dimensions. These vesicular frameworks are seen as deep archives for providing molecules of lipophilia different to and through *in-vitro* skin and *in-vivo* in the formulation and diagnosis. [10]

MECHANISM OF PENETRATION OF ETHOSOMES

A synergistic mechanism was recommended between ethanol, vesicles, and skin lipids.[11] The enhanced delivery of actives using ethosomes can be ascribed to an interaction between ethosomes and skin lipids. A probable mechanism for this interaction has been proposed.

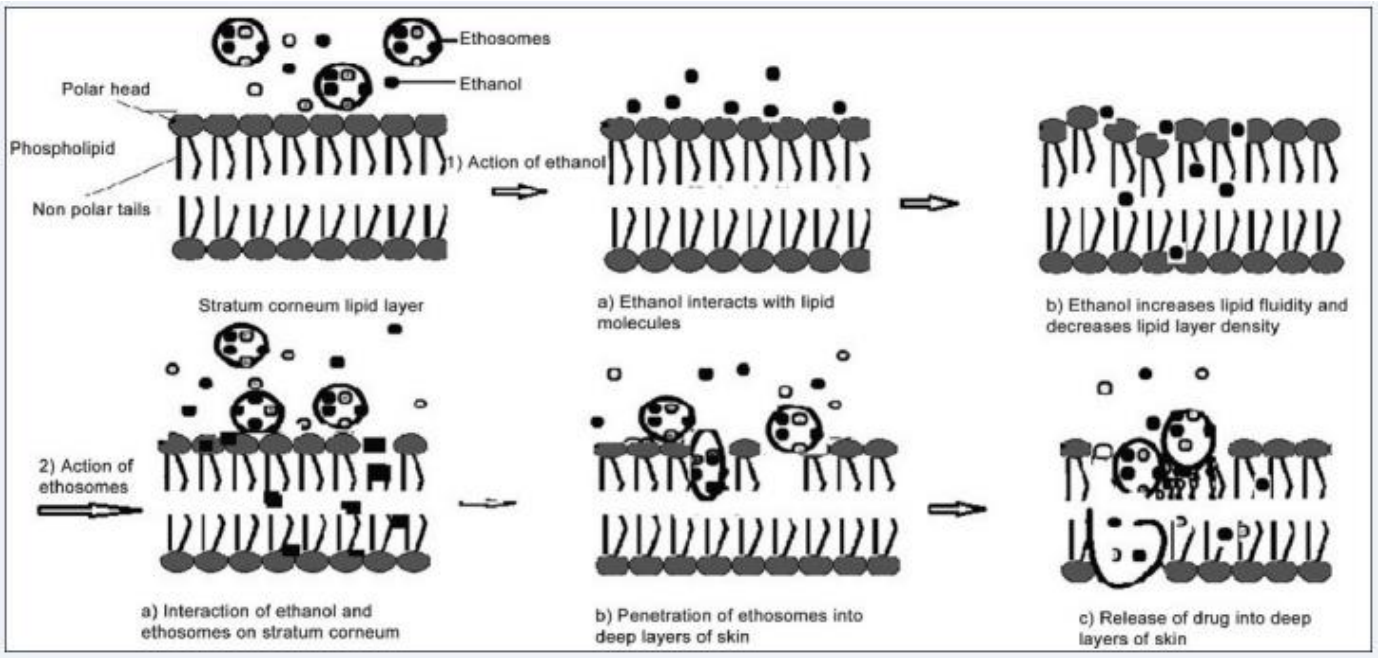

Fig 1 – Mechanism of Penetration of Ethosomes [12]

From Figure 1, it is considered that the first part of the mechanism is due to the ethanol effect, where ethanol interacts with the lipid molecules in the polar head group region resulting in a drop in the transition temperature of the lipids in the stratum corneum, escalating their fluidity and decreasing the density of the lipid multilayer. This is followed by the 'ethosome effect,' which includes lipid penetration and permeation by the opening of new pathways, due to the malleability and fusion of ethosomes with skin lipids, consequential in the release of the drug into the deep layers of the skin. Ethanol may also provide vesicles with soft flexible characteristics, which allow them to penetrate more easily into the deeper layers of the skin. The release of the drug in the deep layers of the skin and its transdermal absorption could then be the result of a fusion of ethosomes, with skin lipids and drug release at various points along the penetration pathway. [13]

Advantages of Ethosomal Drug Delivery

1. Ethosomes helps increase penetration through the skin.

2. Ethosome is a stage used for the transfer of huge and varied group of drugs (peptides, protein molecules).

3. Low hazard profiles - Innovation does not have a huge risk of developing the drug because toxic information is stored in scientific literature.

4. High Stability of Patients – Ethosomes used in semi-solid (gel or cream) form delivering high patient consistence, Interesting, iontophoresis in addition to phonophoresis are usually complex for use that will influence patient compliance.

5. High market attraction meant for products. Easy to manufacture without any modern technical investment needed to produce ethosomes.

6. The ethosomal framework is inactive, non-invasive and accessible for rapid trading.

7. Many programs in pharmaceutical, veterinary, cosmetics. [14]

SUBSTANCES USED IN THE FORMULATION OF ETHOSOMES

Various substances used in the formulation of ethosomes are indicated in Table 1.

Table 1: The addition of various substances used in the formation of Ethosomes [15]

Classes	For example	Use
Phospholipid	Soya phosphatidyl choline, Egg phosphatidyl choline Dipalmityl phosphatidyl Choline	Increased permeability across membranes
Polyglycol	Polyglycol	As a enhancer
Alcohol	Ethanol Isopropyl alcohol	For providing 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, HPMC	As a gel former

MANAGEMENT OF DISEASE CONDITION

Disease conditions where ethosomes act as a carrier are indicated in Table 2.

Table 2: Management of disease condition mentioned below, where Ethosomes act as a carrier [16]

Drug	Use	Comments
Ammonium glycyrrhizinate	Anti-inflammatory	Improved dermal deposition, Exhibiting sustained release, Improved biological anti-inflammatory activity
Azelaic acid	Used to treat mild to moderate acne	Prolong drug release
Acyclovir	Used to treat infections caused by certain types of viruses	Improved drug delivery Increase skin permeation Improved in biological activity Improved in Pharmacodynamic profile.
Bacitracin	Treatment of dermal infection	Reduced drug toxicity Improved dermal Deposition Improved intracellular delivery
Cannabidol	Prevents inflammation and edema	Significant accumulation of the drug in the skin, Improved biological activity

RESEARCHES DONE ON ETHOSOMES

Summarized data of the drug /pigment used in research along with researchers name depicted in Table 3

In 2016 Ahmed *et al.*, developed lornoxicam ethosomal gel, meant for its transdermal conveyance. The formulations of ethosomal set by hot method utilizing phospholipid plus ethanol (20% on the way to 40%) and afterward assessed- figure, entrapment efficiency, vesicular dimension, in-vitro skin penetration, skin retention, drug membrane part interface as well as steadiness. Selected formulation was chosen for further study on the skin when it showed the most surprising drug entrapment percentage (93.96) and a small dimension (100 ± 3.9 nm). The chosen formation with 2% w / w phospholipid in addition to 30% alcohol exhibited the most attractive dose of drug infiltration (74.18%) at the finish of 24 hours. Stability studies conducted at two separate temperatures showed no significant changes in the vesicle entrapment efficiency at the end of three months, indicating that formula is physically-stable.[17]

In 2015 Rathore *et al.*, prepared an updated review of the fluconazole burdened ethosomes gel as well as liposomes gel for the management of deep fungal skin disease.[18]

In 2014 Vijayakumar *et al.*, established and defined the framework of ethosome for local gliclazide transport to overcome oral route problems. Gliclazide ethosomes are created by thinning hydration procedures by changing the composition of drugs, lecithin and propylene glycol. Formulated ethosome with other ethosomal gel were examined and indicated improved outcome.[19]

In 2014 Sujitha *et al.*, developed ethosomes enclosing piroxicam through utilizing phospholipid (1-3 percentage), ethanol (20-40 percentage), propylene glycol (10 percentage) as well as distilled water by

cool technique was formulated and assessed. Prepared ethosomal vesicles examined for vesicular dimensions, figure, entrapment efficiency; *in-vitro* skin diffusion, skin irritation along with stability studies. The results of electron microscopy and size analyser showed the size of the ethosome was circular, unilamellar and nanometric in size. The identified formulation definition represents a maximum entrapment efficiency of 73.59%. At this point, the creation of enhanced ethosome vesicles created for gel using Carbopol.[20]

In 2013 Dhiman et al., established the entrapment efficiency of effective ethosomes using 2.5 g phospholipid concentration with 30 milliliters of ethanol for 12.5 minutes have been found to be extremely limited value 73.9%. The lipid vesicle system of rutin shows the negative zeta potential of -46.0 mV, indicating a high level of stability for rutin ethosomes. *In –vitro* infiltration study of clean rutin and rutin ethosomes has shown that normal ethosomes can penetrate the skin of the ears of pig at the end of 120 minutes than pure rutin. That's why rutin ethosome can facilitate penetration into the ears as compared to the pure rutin.[21]

In 2012 Lakshmi *et al.,* examined the efficacy of ethosomes like new lipid transporters designed for the transdermal deliverance of Alfuzosin Hydrochloride (AH). Taguchi's technology was used to improve the ethosomal formulations. The phospholipid type, phospholipid concentration as well as ethanol concentration was selected as self-determining factors furthermore their influence on the reliant factors (entrapment efficiency as well as flux) was taken into account. Transdermal flux improved by 6.92 times the drug solution. The interaction of vesicle skin is regarded as a manifestation of the changes in body fat. Composite was stable at 4 ° C as reported for 120 days. The outcome recommended that ethosomes be proficient transporters for AH transdermal deliverance.[22]

In 2012 Maheshwari *et al.,* established, assessed and verified the transdermal capacity of the new vesicular nanocarrier: ethosomes in addition to ultradeformable liposomes, composed of clotrimazole (CLT), the anti-fungal bioactive. Ethosomal formulation (ET4) along with ultradeformable liposomal (UL) in combination form (TT3) show the most noticeable entrapment 68.73 ± 1.4% as well as 55.51 ± 1.7%, best nanometric estimate go 132 ± 9.5 nm as well as 121 ± 9.7 nm, and littlest polydispersity record 0.027 ± 0.011 along with 0.067 ± 0.009, individually. The ET4 transdermal formulation provide improved flux 56.25 ± 5.49 μg/cm2/h, moreover reduce the delay time of 0.9 hours against the detailed (50.16 ± 3.84 μg/cm2/h; 1.0 h). Skin interaction as well as FT-IR study findings strongly affect the introduction of ET4 rather than TT3.[23]

In 2010 Maurya *et al.,* researched on transdermal distribution of stavudine, a hydrophobic-based medication used to treat AIDS by ethosomes. The selected structure is included in the HPMC gel furthermore is assessed as drug penetration in addition to mice skin deposition. Improved ethosomes

formulation indicated transdermal flux 25.01 ± 0.34 µg / cm2 / hr crosswise on the skin of the mice contrasted with 2.98 ± 0.21 µg / cm2 / h for the solution of a plain drug, 4.28 ± 0.54 µg / cm2 / h meant for hydroethanolic solution and 9.7 ± 0/21 µg / cm2 / h meant for classical liposome.[24]

In 2010 Sathali *et al.,* established that the ethosomes is a highly motivated vehicle for the delivery of diclofenac potassium, which has been found to be highly effective in elevated entrapment efficiency, improved stability profile as well as anti-inflammatory effects. The improved buildup of diclofenac potassium by means of ethosomal carrier inside the skin may enhance focusing of the drug to the epidermal and dermal destinations, which makes the new door open for diclofenac-potassium in terms of inflammation.[25]

In 2007 Jain *et al.,* researched the component intended for better intercellular as well as intracellular drug deliverance from ethosomes image techniques as well as cell line lessons. Ethosomal formulations arranged utilizing lamivudine as replica drug furthermore characterized *in -vitro, ex-vivo* and *in-vivo.* The optimized ethosomal formulation demonstrated 25 multiple times superior transdermal flux (68.4±3.5 µg/cm2/h) over the rodent skin as contrasted to lamivudine solution (2.8±0.2 µg/cm2/h). Consequences of cell take-up study demonstrated altogether upper intracellular take-up of ethosomes (85.7%±4.5%) when contrasted amid drug solution (24.9%±1.9%). The aftereffects of the categorization studies showed, lipid irritation alongside versatility of ethosomes vesicles is by all accounts the primary benefactor for enhanced skin penetration.[26]

Table 3: Researches done on Ethosomes [17-26]

S. No.	Name of the Drug / Pigment used for Research	Name of Researches
1.0	Lornoxicam	Ahmed et al 2016
2.0	Fluconazole	Rathore et al 2015
3.0	Gliclazide	Vijayakumar et al 2014
4.0	Piroxicam	Suitha et al 2014
5.0	Rutin	Dhiman et al 2013
6.0	Alfuzosin Hydrochloride	Lakshmi et al 2012
7.0	Clotrimazole	Maheshwari et al 2012
8.0	Stavudine	Maurya et al 2010
9.0	Diclofenac Potassium	Sathali et al 2010
10.0	Lamivudine	Jain et al 2007

RECENT STUDY IN ETHOSOMAL FORMULATION:

Development of Terminalia Chebula loaded ethosomal gel for transdermal drug delivery [27] Dried fruits of Terminalia chebula were extracted and preliminary phytochemical evaluation was performed. Ethosome was prepared by cold method using soya lecithin. Ethosomal gel was prepared using carbopol as gelling agent and was evaluated. The prepared gel was evaluated for its pharmaceutical properties and was found to be satisfactory. The *in vitro* drug diffusion of ethosomal gel showed better release compared with that of the gel with extract. *In vitro* anti-arthritic activity exhibited significant effect compared to that of the standard diclofenac.

Ethosomes of Tramadol Hydrochloride (local anaesthetic) were formulated using soya lecithin, cholesterol, ethanol and purified water using ultra shear homogenizer. Ethosomes were evaluated for vesicle size, shape, optical microscopy and *in-vitro* release study. The ethosomes were entrapped in gel matrix of carbopol 980 in different concentration 0.75%, 1.00%, 1.25% and 1.50% w/w. The formulated gel formulation was evaluated with parameter drug content, pH, viscosity, spreadability, *in-vitro* release test, and *ex-vivo* study. The formulations had better *in-vitro* and *ex-vivo* drug release profile which contains Carbopol 980 concentration 1.25%w/w and were stable for 3 Months at room temperature and accelerated storage condition.[28]

CONCLUSION

A conclusion can be drawn from the above review that ethosome is a promising drug delivery system against various disease conditions. The results of all the researches done on ethosomes prove to have better efficiency, compatibility, spreadability, bioavailability, stability, medication retention, proficient transporter capability, release profile, entrapment efficiency and higher transdermal flux. Ethosome can become a versatile and compatible tool for various disease conditions and good candidate for transdermal drug delivery of various drugs since continuous researches conducted with beneficial outcomes proving its upper hand against other competitors.

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