Exploring Ethosomes : Innovations and Applications in Drug Delivery.

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ABSTACT:

Ethosomes are lipid-based vesicular carriers that have emerged as a promising drug delivery system for enhancing skin penetration of therapeutic agents. Composed mainly of phospholipids, ethanol, and water, ethosomes exhibit unique properties that enable them to encapsulate and transport both hydrophilic and lipophilic drugs effectively. Ethanol, a key component, disrupts the lipid bilayer of the stratum corneum, facilitating deep penetration into the skin layers. Ethosomes are therefore particularly valuable in transdermal drug delivery, offering a non-invasive alternative to conventional administration methods

This review explores the structural properties, mechanisms of action, and preparation techniques of ethosomes, comparing them with other lipid-based carriers like liposomes and niosomes. It discusses factors influencing their performance, including composition, vesicle size, and drug loading capacity, and emphasizes their potential for delivering a broad range of therapeutic molecules, including peptides, proteins, and small drugs. Additionally, the review highlights recent advancements and applications of ethosomes in dermatology, anti-inflammatory treatments, and systemic drug delivery.

The development of ethosomes offers significant advantages, including improved bioavailability, reduced systemic side effects, and sustained drug release profiles. However, challenges remain, particularly in terms of formulation stability and large-scale manufacturing. Future research is needed to optimize ethosomal formulations, explore new therapeutic applications, and address potential limitations, paving the way for more effective and patient-friendly transdermal drug delivery solutions. Ethosomes have shown promise in treating various conditions, including psoriasis, acne, fungal infections, and inflammatory disorders, by targeting deeper skin layers or systemic circulation. The development of ethosomal formulations has attracted significant research interest due to their non-invasive nature.

Keywords : skin taegeting ,transdermal,Nanotechnology penetration enhancers ,phospholipid vesicles ,bilayer phospholipid

INTRODUTION :

- A evolved variant of liposomes, ethersomes have demonstrated efficacy as epidermal transporters. Water, ethanol, and lipids such as make up the majority of ethersomes, which are fatty vesicles.

- Ethosomes are composed of a the lipids membrane on the outside and a fluid-filled center that holds the therapeutic compound's ethanol fermentation solution (Fig. 1). The outcome when bilayers made of are fluidized by ethanol

- assists in the development of novel circulatory systems with enhanced delivery: dermal absorption and characterization qualities. The flexible nature of these vesicles enables components (drugs, medications, or active agents) to penetrate wider epidermal phases [1,2]. J The oversight Allowance, 1964(3), 403-18-22, 1999. Liposome-based

administration of medicines has not been very successful in epidermal preparations due to their transitory nature and limited absorption [3-4–5].

- Niosomes, a unique circular transport, were developed to solve the inadequate quality of liposomes, which was becoming an issue. Given this, niosomes and liposomes seemed unsuccessful to solve the problems of poor pores in the skin.

- Therefore, ethanolic vesicles were developed to enhance the skin's ability to absorb medications. Ethamomes have a larger capillary motion and skin accessibility, and they span in dimension from tens of tiny to inches. Ethosomal techniques can be divided into three categories based on their composition. Conventional ethosomes Subcutaneous drug administration has been documented using ethosomes [6-7-8-9-]

- Hydration phospholipids, and slightly larger quantities of alcohol (ethanol and isopropyl alcohol) are all found in fatty tubes called ethersomes.

- They are a somewhat modified form of the well-known drug carrier liposome and are a novel carrier system used for the delivery of drugs with low penetration through the biological membrane, primarily skin. [10] Soft vesicles called ethersomes are composed of water, phospholipids, and ethanol (in larger amounts).

- Ethamomes can be anywhere from numerous of millimeters and miniatures (μ) across [11]. Ethamomes have a significantly larger percutaneous flow and more rapid penetration of the barrier phases than conventional liposomes. [12, 13-14].

- However, it's still unclear how exactly ethosomes improve penetration into deeper skin layers. It has been proposed that deeper distribution and penetration in the skin lipid bilyers are caused by the synergistic effects of phospholipid combination and high ethanol concentration in vesicular formulations. Transdermal medication delivery is the primary application for ethersomes. One of the most crucial methods of administering drugs is transdermal distribution.
- medication penetration through the skin is the primary problem limiting the use of the transdermal method for medication delivery. Drug permeability is selective in human skin. medicines that are hydrophilic in nature cannot penetrate the skin, whereas lipophilic medicines can.
- Drugs that dissolve in water either exhibit extremely little or no penetration. Numerous methods have been studied to increase medication penetration through the skin, including the use of chemical or physical enhancers like sonophoresis and iontophoresis.
- It has also been shown that liposomes, niosomes, transferosomes, and ethosomes increase a drug's permeability across the stratum corneum barrier. Drugs can more easily pass through the skin thanks to penetration enhancers, which increase the skin's permeability.
- In contrast to traditional liposomes, [15-16]. Ethamomes, which are mostly recognized for delivering medications to the skin's outer layers, can improve penetration through the stratum corneum barrier.[17–18] Drug molecules with different physicochemical properties, such as hydrophilic, lipophilic, or amphiphilic, can be entrapped by ethersomes.[19,20] Drug delivery is noninvasive and reaches the systemic circulation or deep skin layers.

- These are pliable, squishy vesicles designed to improve active drug distribution. Their main components include phospholipids (phosphatidylcholine, phosphatidylserine, and phosphatitidic acid) in addition to a high ethanol and water content. The high ethanol content makes the ethosomes distinctive.
- Ethamomes' ethanol improves the vesicle's ability to penetrate the stratum corneum since it changes the structure of the skin's lipid bilayer

- integrated into its membrane. Additionally, due to its high ethanol content, the lipid membrane is less densely packed than that of traditional vesicles, yet it is just as stable, allowing for a more flexible shape and better medication dispersion in stratum corneum lipids.

- Ethosomes are pliable, soft lipid vesicles that are mostly made of phospholipids and contain 20–45% more alcohol (ethanol or isopropyl alcohol) than water. Touitou et al. (1997) initially created ethersomes as new lipid carriers made of water, phospholipids, and ethanol. "Ethosomes are ethanolic liposomes," which are noninvasive delivery vehicles that allow drugs to enter deeper epidermal layers and/or the systemic circulation, effectively delivering hydrophilic, lipophilic, or amphiphilic compounds intracellularly [21].

- the ethosomes are a special formulation for medication administration into deep dermis because of their high ethanol content [22].It is well recognized that ethersomes are crucial for regulating a drug's release rate over time, protecting it from elimination systems, such as the immune system. Ethamomes exhibit reduced vesicle size, increased entrapment efficiency, and enhanced stability as compared to traditional liposomes

- . Depending on [23–24] The dimension of ethosomes may vary from microns (μ) to tens of nanometers (nm). They have a significantly higher transdermal flux and get the skin layers faster.

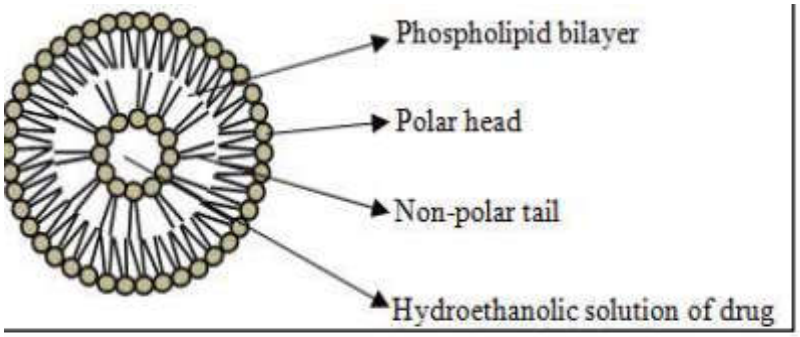


Figure 2: Proposed diagram of Ethosome.

- Ethanolic vesicles are called ethersomes. Because ethanol is present in the vesicular structure, Touitou created a novel vesicular system that he called ethosomes [25].Vesicular sys tEthosomes are non-invasive delivery vehicles that allow medications to enter the systemic circulation or deep into the skin layers [26.27].

- Drugs can now be delivered transdermally thanks to ethersomes. The tremendous elasticity of the human skin allows this system to pass through it undamaged. Alcohol in relatively high concentrations (20–45%), water, and phospholipid make up the majority of ethersomes, which are soft, flexible lipidvesicles. Tauitou and her associates created ethersomes for the first time in 1997 [28].

- This vesicle is soft. Ethamomes can be anything from tens of nanometers to microns in size. Ethosomes penetrate the layers of the skin quicker and have a significantly greater transdermal travel.

- In addition to delivering the medication to the deep layer of the skin, etherosomes also fulfill the necessary requirements for Ethersomes meet the requirements for the safe and efficient administration of hydrophilic or lipophilic drugs itransporting the drug to transporting the drug to the deep layer of the skin [29–30].

- Great molecular weight, hydrophilic, and lipophilic chemicals are among the many types of chemicals that ethersomes can capture. In both occlusive and non-occlusive circumstances, ethersomes can transport the medication via the skin [31].

- Medicines with both systemic and local applications may be administered through the skin, the biggest organ in the human body. Yet, the stratum corneum, the topmost layer of the skin, serves as a barrier to prevent the body in absorbing aqueous and big size medications
- [32].Ethersomes are a kind of cellular drug carrier that has gained interest considering that they can enhance drug penetration by making the cell membrane more permeable and fluid. They consist of a monolayer of ethanol and phospholipids.[33] Since they can improve the absorption of drugs by making the nucleus membrane more fluid and permeable, ethersomes have drawn interest as a kind of vesicular drug distribution method. Because of their phospholipid monolayer, they are a flexible and efficient substitute for conventional transdermal drug delivery methods. as well as the capacity to move both hydrophilic and hydrophobic substances, including ethanol

- The Wiley Online Library's Terms and Conditions [34](https://onlinelibrary.wiley.com/terms-and-conditions) contain utilization rules. [35] Free to access articles must adhere to the applicable Innovative Public License. Ethamomes can be classified into various types based on their composition and method of production, including lipid-based ethosomes, protein-based ethosomes, [36] ethosomes centered on polymer compounds, [37] ethosomes centered on particles, [38–39]

  - 5 and dendrimer-based ethosomes.[40] The therapeutic value of ethosomes in drug transport has been shown in a number of preliminary and medical studies.

  - The use of ethersomes has allowed for the efficient delivery of medications such as diclofenac [41], terbinafine [42], and [43] through the skin as well as other routes of treatment, such as the orally and olfactory pathways.13. Additionally, the usage of ethosome has been associated with increased bioavailability, reduced toxicity, and improved pharmacological efficacy.[45–46] Because of their potential for transdermal drug delivery and growing importance in the pharmaceutical industry, a comprehensive evaluation of the current level of ethosome research is becoming increasingly important.

- An outline of the several kinds of ethosomes, their fabrication process, physicochemical characteristics, and drug loading and release mechanisms may be found in such a review. as

well as their uses in drug delivery for cosmetic purposes. It can also point up future research paths and draw attention to the potential and difficulties related to the use of ethosomes.

Ethosomes composition

- Ethamomes essentially resemble liposomes in their lipid bilayer, however they are different from liposomes in that they contain a higher amount of ethanol.

- Ethamomes are composed of hydroalcoholic or hydro/glycolicphospholipid, which has a rather substantial amount of alcohol. Standard phosphate lipid discovered in ethosomes include phenolcholine (PC), hydrogenation PC, phosphate (PA), phosphates of (PS), phosphate-bonded a solution of (PE), phosphate glucose (PPG), phosphate-containing the substance (PI), modified PC, substances (ether or a mixture of is spirits), liquid, and propylene glycol, among others (or other glycols).

- One of the ethosomes' constituent hydroalcoholic or hydro/glycolicphospholipids has an average amount of alcohol level. Examples of phospholipids that are frequently present in ethosomes include phenol choline (PC), hydrogenation PC, phosphate (PA), phosphates of (PS), phosphate the ethanolamine (PE), phosphate-bonded glucose (PPG), phosphate-containing the drug (PI), modified PC, spirits (ethanol or a mixture of is alcohol), fluids, and propylene glycol (or other glycols).

  - It is possible to combine the phospholipids in the formulations using non-ionic compounds solvents like (PEG-alkyl ethers) and basic fatty acids (cocoamide, POE alkyl amines, dodecylamine, cetrimide, etc.) [48]. The amount of alcohol and glycol combination in the non-aqueous state might range from 22 to 70%. A summary includes multiple substances used in the production of ethosomes (table 1) Ethosomal drug distribution can be altered by adjusting the alcohol to water or alcohol to polyol to water ratio.

  - Ethersomes, which are vehicles composed of hydroalcoholic or hydro/alcoholic/glycolic phospholipid, contain comparatively large quantities of alcohols or their mixture [49–50].

- Water and alcohol are present in high concentrations in ethersomes, which are vesicular carriers made of hydroalcohalic or hydrolglycolic phospholipids. The ethosome is distinct due to its high ethanol content. The final product contains between 20 and 30 percent alcohol.

- Phaspholipids such phasphatic acid, phosphatidyl glucose, phosphatidyls a substance called in, liquor, water, phosphatidyl a mineral called modified phasphotidyl the vitamin choline and propylene glycol are found in the ethosome.

- It is possible to change the medicine's administration by connecting the liquor you hydrate fluid: ite phaspholipids include soyaphaspholipids such as phaspholipon90 (PL-90). lipids within the often-used interval of 0.5–10% w/w lipids, with a related range of 0.1–1%. A SIX ILLUMINE Alcohols such as ethanol and isopropyl alcohol, together with carbs like synthetic glycerin and transcutol, are commonly used.

- The phosphate are usually synthesized using lipids which are as coca-amide POE alkyl amine, dodecylamine, cetrimide, etc., however non-ionic surfactants are sometimes utilized.

METHODS OF PREPARATION ETHOSOMES

There are two extremely easy and practical ways to produce ethersomes: the hot approach and the cold approach.

A.The Cold Approach

This is the method most commonly used to create ethosomes. In the cold method, the drug is dissolved and Ethanol (and a mixture of glycols) at ambient level, along with lecithin (and all other fatty ingredients). Following that, this mixture is gradually heated to 30°C. For a while, the ethanol-based combination is brought to a constant degree while the water mixture is added and stirred. The size of the ethosomes' compartments can be decreased by sonicating or extruding the ethanolic mixture2. For the duration of the process, ethanol should not evaporate. Last but not least, the formulas are stored in a refrigerator. In [51], the diagrammatic version of the cold approach is presented.

B. Hot method

The phospholipids are first dissolved in water and heated to 40°C in this procedure. Etha Ethanol (and a mixture of glycols) at ambient level, along with lecithin (and all other fatty ingredients). Following that, this mixture is gradually heated to 30°C. For a while, the ethanol-based combination is brought to a constant degree while the water mixture is added

nol and propylene glycol are heated to the same temperature as the aqueous phase at the same time. Depending on its characteristics The drug is soluble in either water or ethanol. The organic phase is introduced to the aqueous phase and then sonicated to reduce the size of the particles (29, 32, 43). An overview of the heating technique for ethosome preparation is given in Fig. 3.

C injection Method:

Various amounts of lecithin, ethanol, isopropyl alcohol, and propylene glycol were used to create ethersomes. The phospholipids and medicine are dissolved by ethanol and propylene glycol. A thermoregulated magnetic stirrer is used to heat the mixture to 30 degrees. A fine stream of double-distilled water is supplied to the solution gradually in a closed vessel.

at a rate of 200 µl per minute while being continuously mixed at 700 rpm. Throughout the experiment, the temperature is kept at 30 degrees Celsius. Five more minutes are spent mixing. The ethosomes that have been prepared are kept at 4º C. This process involves preparing ethersomes, which are then sonicated using a probe sonicator at 4ºC in three cycles of five minutes each, with a five-minute break in between [52].

method characteristics and composition:

- **Classical ethosomes**
- **Transethosomes**
- **Binary Ethosomes**

Classical Ethosomes: Classical Ethosomes: A modified form of liposome, classical ethosomes are composed of lipids with fluid, and a significant amount of ethanol (about 45%w/v). Because of their reduced size and improved skin penetration, they are thought to be better than traditional liposomes for transdermal medication delivery. It also had a higher entrapment efficiency and a negative ζ-potential.[53]

Transethosomes: Transethosomes, a subsequent version of ethosomal pathways developed by Song et al., combine the traits of ethosomes and transfers into just one equation. This ethosomal system has a unique stimulator or access boost, like surfactants, as well as to the basic components of traditional ethosomes. Multiple studies have shown that the properties of transethosomes are better than those found in typical ethosomes.[54–55]

Binary Ethosomes: Zhou et al. created these kinds of ethosomes by combining several kinds of alcohol, like isopropyl alcohol (IPA) and propylene glycol (PG), with the traditional ethosomes [56].

Different additives employed in formulation of ethosomes

Class	phospholipid	polyglycol	alcohol	cholesterol	Dye	vehicle
examples	The the fatty acid found in legumes and eggs,	ethylene glycerol is a solvent and Rtf transcutol	Acetate spirits is created with methanol	cholesterol	Rhodamine-123, Rhodamine	Carbopol D 934
uses	part that forms microspheres	At being absorbed of the epidermis	Providing the softyness for vesicle	supplying the cavity with strength	To a research in characterisation	As a gel former

Characterization of Ethosomes .

INSTRUMENT /TECHNIQUE	TEST
Scanning Electron Microscopy	Particle shape
Optical Microscopy	Particle size analysis

High performance liquid choromatogeapy /UV	Accuracy of Medication Enchantment
Franz diffusion cell	In vitro skin permeation study
Franz diffusion cell	In vitro skin permeation study
Differntial scanning calorimetry	Transition temperature

[57,58]

Visualization: Two techniques for observing ethersomes are scanning microscopy with electrons (SEM) and transmission electron microscopy (TEM).[59] Zeta potential and vesicle size: It is possible to ascertain the particle size of the ethosomes using energetic light scattering (DLS) and photon correlation spectroscopy (PCS). The ethosome suspension's zeta potential can be measured with zeta meters [60–61].

PH Measurement: Using a pH meter, the formulation's pH was measured by fully submerging the glass electrode into the semisolid formulation until the electrode was covered [62].

Transition Temperature: Vesicular lipid systems' transition temperature can be determined using differential scanning calorimetry (DSC) [63].
The entrapment effectiveness of the ethosomes can be evaluated by the ultracentrifugation method [64]
Drug Content: A UV spectrophotometer and a modified high-performance liquid chromatographic technique can be used to quantify drugs [65–66].

Surface tension measurement - A ring approach for determining a drug's surface tension is the Du Novy ring tensiometer [67].

Ethosome application

A. Antiviral medicine Administration: Acyclovir is a form of antiviral medication used to treat Herpes labialis. Due to its inadequate skin penetration the traditional marketed formulation of acyclovir has a low level of therapeutic efficacy. By adding the medication to ethosomes, these drawbacks were resolved. In addition to extending the medication release and transdermal flux, this offered sufficient zero order delivery.[68–69]

B. Topical delivery of DNA: To express genes in skin cells, DNA molecules can be topically delivered via ethersomes. In their investigation, Touitou et al. produced and administered an ethosomal formulation encapsulated with a transfecting construct driven by GFP-CMV to the dorsal skin of naked mice for 48 hours. After 48 hours, the treated skin was removed, and CLSM detected the penetration of green fluorescent protein (GFP), demonstrating the efficacy of ethosomes as a transdermal vaccination agent.[70]

C. Transdermal delivery of hormones: Hormones administered orally had a number of drawbacks, including low oral bioavailability, many dose-dependent adverse effects, and significant first-pass metabolism. When hormones like testosterone were added to an ethosomal formulation, the skin penetration was about 30 times greater than with other commercially available oral preparations (Testoderm patch, Alza).[71]

D. Delivery of antibiotics: Topical application of antibiotics can overcome the severe allergic reactions and other negative effects associated with conventional oral antibiotic therapy. By releasing a significant amount of medication into the skin's deeper layers, ethersomes can get around these issues [72].

E. Pilosebaceous targeting: Pilosebaceous units are thought to be target areas for the treatment of conditions relating to hair follicles, such as alopecia and acne. Because it is fat soluble and can accumulate seven times as much on mice's skin, an ethosomal version of minoxidil is used to treat baldness.

F. Drug Targeting: long-term, targeted distribution of medications like Diclofenac (NSAIDS).[73]

G. Delivery of anti-parkinsonism agent: When compared to its liposomal version, the ethosomal form of the psychoactive drug trihexyphenidyl hydrochloride (THP) demonstrated superior skin penetration capacity.[74]

H. Delivery of anti-arthritis drug: Topical administration of anti-arthritis medications can solve issues with oral traditional therapy and is a better option for site-specific drug delivery. By promoting skin penetration and accumulation, the cannabidol ethosomal formulation exhibits noticeably enhanced anti-inflammatory action. Similarly, when taken orally, piroxicam, which is used to treat rheumatoid arthritis, can cause serious adverse effects include ulcers and bleeding in the stomach. To stop enzymes from breaking down systemically active medications like piroxicam, transdermal drug administration in ethosomal formulation is an alternate method.[75]

Advantages of Ethosomes

- It is feasible to deliver big molecules, such as peptides and protein molecules.
- Its formulation uses non-toxic basic ingredients
- Better drug penetration through the skin for transdermal delivery
  Formulated with non-toxic raw elements.
- Ethosomal drug delivery methods have significant potential applications in the pharmaceutical, veterinary, and cosmetic sectors.
- When the ethosomal drug is given in a semisolid form, like a gel or cream, high patient compliance occurs.
- A straightforward approach to medication delivery as opposed to more complex techniques like iontophoresis and phonophoresis.
- The Ethosomal system may be commercialized right away and is passive and non-invasive [76–77].
- Large molecules (peptides, protein molecules) can be delivered; transdermal drug delivery is made possible by improved drug penetration via the skin.
- Its formulation includes non-toxic raw materials.
- High patient compliance is a result of the ethosomal medication being administered in a semisolid form, such as a gel or cream.
- Ethosomal drug delivery systems are widely applicable in the sectors of cosmetics, veterinary medicine, and pharmaceuticals.
- A straightforward approach to medication delivery as opposed to more complex techniques like iontophoresis and phonophoresis[78].

Disadvantages of ethosomal drug delivery

- Precipitation can result from clumps of ethersomes with weak shells.
- Sufficient drug solubility in aqueous and lipophilic media to enter the dermal microcirculation and enter the systemic circulation.

• Dermatitis or skin irritation brought on by medication delivery system boosters and excipients.
• Ethosomal administration is typically intended to provide steady, sustained medication delivery rather than a quick bolus-style drug input.
• Only strong medications (daily dose of -10 mg or less) can be administered; drugs that require high blood levels cannot.
low yield in practice.

Mechanism of drug penetration

How drugs are absorbed from ethosomes is unknown. The next two stages are when medication absorption is most likely to take place.
Alcohol's impact: Alcohol improves skin penetration. Its mechanism of action to improve penetration is widely understood. Ethanol lowers the density of the lipid multilayer of the cell membrane and increases the fluidity of the lipids in the intercellular space [79].
The impact of ethersomes: Skin permeability increases as ethosomes' ethanol improves the lipid fluidity of cell membranes. Consequently, the ethosomes readily penetrate the deep layers of the skin, where they mix with skin lipids to liberate the medications.[80]

[81]

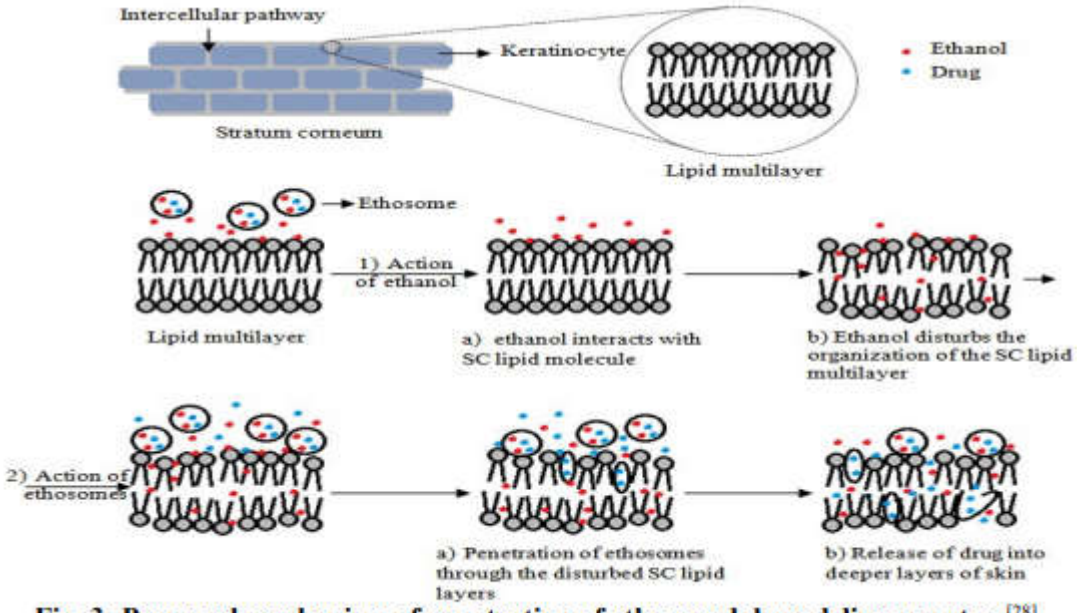
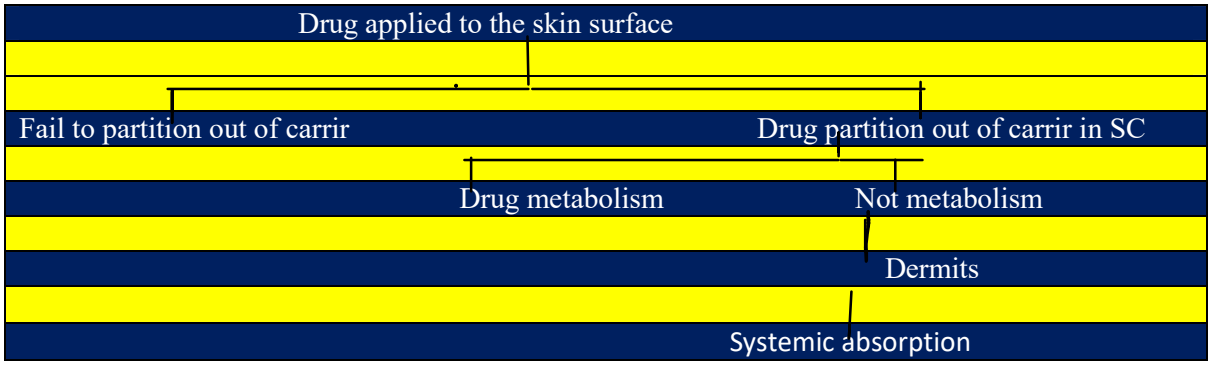


Fig. 3: Proposed mechanism of penetration of ethosomal drug delivery system[28].

[82]



Stability of Ethosomes

A UV spectrophotometer and a modified high-performance liquid chromatographic technique can be used to quantify drugs [65–66]. Ethersome stability is higher than that of conventional liposomes [22]. During storage, liposomes frequently combine and grow to form larger vesicles. There is a serious chance that the drugs may spill out of the receptacles due to this fusion and rupture during storage. Although the absence of magnetism in impartial liposomes likely contributes to the tendency to collect, ethanol changes the net charge of ethosomes, making them negatively charged. A UV spectrophotometer and a modified high-performance liquid chromatographic technique can be used to quantify drugs [65–66]. The vesicles are more stable from clumping and loss of drug because it offers some steric stabilization. Because of the membranes' fluidity, the entrapment effectiveness increases as the volume of ethanol climbs from 20% to 45%. However, vesicles become unstable at greater levels of ethanol (>45%), and the porousness of the vessel wall is probably increased, reducing the efficiency of entrapment [83].

Comparative studies of liposomes, transferosomes and ethosomes.:

There is a strong relationship between liposomes, transferosomes, and ethosomes. Table 3 lists their comparative research for topical and transdermal products. Transdermal and topical Products that were promoted Ambisone, Decorin, Nanominox, and Daunoxome Transferosomes TM (Idea AG)

Characters	composition	characteristion	flexibility	Permeation mechanism	Extent of skin permation	Route of administration	Marketeted product
liposomes	**Phospolipid and cholestrol**	**Microscopic vesicles**	**rigid**	**Diffusion**	**Very less penetration**	**Oral,parantral,topical**	**Ambisone,daunoxome**
transferosomes	**Phosolipid and edge activators**	**Ultra - flexible vesicles**	**High deformability due to surfactant**	**Deformation of vesicle for penetration**	**Can easily penetrates**	**Topical and tansdarmal**	**transdermal**
Ethosomes	**Phospholipid and ethanol**	**Elastic vesicles**	**Elasticity due to ethanol**	**Lipid perturbatio**	**Can easily penetrates**	**Topical and transdermal**	**Nanominox ,decorin cream**

Marketed products based on the Ethosomal drug delivery system

Trima, a pharmaceutical company, in collaboration with Yissum, a study research organization of the Hebrew University of Jerusalem, and Professor Elka Touitou. Dermal and oral illnesses caused by the Herpes simplex virus were treated with the solution [84].However, the manufacturing company's website no longer has the product details. Some authors have also mentioned other ethosomal-based products including Decorin cream, Skin Genuity, Cellutight EF, and Nanominox.[85] Despite being manufactured a few years ago, there is now no comprehensive information about these products or their manufacturers on the internet.[86]

Future perspective

The stratum corneum serves as the primary restrictions layer that prevents medication absorption during topical administration. Numerous techniques have been found to improve medication absorption through the skin, and in recent years, lipid vehicle-based augmentation has attracted a lot of attention. Research on employing lipid vesicles to enhance medicine delivery via the skin will continue. The discovery of ethosomes has opened up a new field of study in vesicles. Ethosomes have demonstrated encouraging results and the ability to more efficiently distribute a variety of medicines. Ethamomes can be used to deliver tiny, medium, and large therapeutic molecules non-invasively and with better control over drug release. As an alternative formulation for problematic medications, ethersomes may be an effective method for the dermal/transdermal delivery of a variety of substances.[87]

With the advent of ethosomes, vesicular research for transdermal medication administration has entered a new field. According to several reports, ethosomes have a bright future in improving the efficacy of transdermal distribution of different medicines. More study in this field will enable doctors to better regulate drug release in vivo and increase the efficacy of treatment. The non-invasive administration of tiny, medium, and large therapeutic molecules is a promising use for ethersomes. This conclusion is supported by the findings of the first clinical study of the acyclovir-ethosomal formulation. It is relatively easy to make ethosomal mixture in multiliter amounts. It stands to reason that ethosomal formulations have a bright future in the efficient transdermal and dermal administration of bioactive substances [88].

Conclusion

It is logical to believe that ethosomes can provide enhanced cutaneous penetrating because they have been demonstrated to be considerably more successful than liposomes at delivering medications to the skin. Ethersomes have been shown to be capable of encasing aqueous and cationic drugs, proteins, and peptides. Ethosomal carriers present both new obstacles and chances for the creation of innovative, more potent therapies. Ethersomes—which contain intriguing and unique vesicular systems—have recently surfaced in the field of medical devices and administering drugs. This carrier has interesting properties pertaining to its ability to penetrate human skin intact because of its high deformability. [89]

REFERENCES

1.Godin B, Touitou E. Ethosomes: new prospects in transdermal delivery. Crit Rev Ther Drug Carrier Syst. 2003;20(1):63–102

2.Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes

3. Patel MC, Patel HK, Suthar RM, Patel SR. Liposomes: as a topical drug delivery system. Int J Pharm Chem Sci.

4.Yarosh DB. Liposomes in investigative dermatology.

5.Photodermatol. Photoimmunol. Photomed. 2001; 17(5):203-212. (1):1-0.

6. Deo MR, Sant VP, Parekh SR, Khopade AJ, Banakar U V

7. Lasch J, Laub R, Wohlrab W. How deep do intact liposomes penetrate into human skin? J. Control. Release. 1992;18(1):55-58..

8. Touitou E I, Composition of applying active substance to or through the skin. US patent 5 934, 1996, July

9. Rakesh R, Anoop KR Ethosomes for transdermal and topical drug delivery. Int. J. Pharm. Pharm. Sci.

10**.** Touitou E, inventor. Composition of applying active substance to or through the skin. US patent 5 540 934. July 30, 1996

11. Patel S, Ethosomes: A promising tool for transdermal delivery of drug, Pharma Info.Net, 5(3), 2007

12. Touitou E, inventor. Composition of applying active substance to or through the skin. US patent 5 540 934. July 30, 1996.

13. Touitou E, inventor. Composition of applying active substance to or through the skin. US patent 5 716 638. October 2, 1998. 5. Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A, Levi-Schaffer F, Intracellular delivery mediated by an ethosomal carrier. Biomaterials, 22, 2001, 3053-3059.

14. Jain S, Umamaheshwari RB, Bhadra D, Jain NK, Ethosomes: a novel vesicular carrier for enhanced transdermal delivery of an anti-HIV agent, Ind J Pharma Sci, 66, 2004, 72-81.

15. . Size determination of liposomes, Liposomes-A practical approach, edited by RRC New (Oxford University Press, NewYork) 1990, 154

16. Heeremans JLM, Gerristen HR, Meusen SP, Mijnheer FW, Gangaram RS, Panday G, Prevost R, Kluft C, Crommelin DJA, The preparation of tissue type plasminogen activator (t- PA) containing liposomes: entrapment efficacy and ultracentrifugation damage, J Drug Target, 3, 1995, 301

17. Preparation of liposomes and size determination, Liposomes-A practical approach, edited by RRC New (Oxford University Press, New York) 1990, 3611.

18.Asbill CS, El-Kattan AF, Michniak B, Enhancement of transdermal drug delivery: chemical and physical approaches, Crit Rev Therapeut Drug Carrier Sys, 17, 2000, 621

19.Verma, DD, Fahr A, Synergistic penetration effect of ethanol and phospholipids on the topical delivery of Cyclosporin A, J. Control Release, 97, 2004, 55-66.

20. Bhalaria MK, Naik S, Misra AN, Ethosomes: A novel delivery system for antifungal drugs in the treatment of topical fungal diseases, Indian Journal of Experimental Biology 47, 2009, 368-375thosomal

21. López-Pinto JM, González-Rodríguez ML, Rabasco AM. Effect of cholesterol and ethanol on dermal delivery from DPPC liposomes. Int J Pharm 2005;298(1):1–12

22. Nagadevi B, Kumar KS, Venkanna P, Prabhakar D. Formulation and characterisation of Tizanidine hydrochloride loaded ethosomes patch. Int J Pharm Pharm Sci 2014;6(4):199–205

23. Shukla T, Verma A, Upmanyu N, Mishra SS, Shilpi S. Development and characterization of clopidogrel-loaded ethosomal transdermal patch for antiplatelet effect. Asian J Pharm 2016;10(4):S480–86.

24. Vijayakumar KS, Parthiban S, Senthilkumar GP, Tamiz Mani T. Gliclazide loaded ethosomes as transdermal drugmethod of preparation, composition and application techniques like sonication

25 .Touitou.E, Godin B. Ethosomes for skin delivery. Journal of Drug Delivery Science and Technology 2007;17:303-308

26. Kumar Lalit. Verma Shivani, Singh Kuljit, Prasad Deo Nandan and Jain Amit Kumar. Ethanol based vesicular carriers in transdermal drug delivery: Nanoethosomes and Transethosomes in Focus. Nano World Journal 2016;2:41-51

27. Rathore A.R, Khambete H, and Jain S. Preparation and characterization of Repaglinide loaded ethosomal gel for the treatment of NIDDM. International Journal of Pharmaceutical & Biological Arcvhives 2013;4:385-390

28. Patel Ravi b, Patel Tejas B, Suhagia B.N, Patel Mehul N, Patel Mayur, and Patel Parth. Ethosomes an emerging targeted drug delivery system a review. International Journal of Pharmaceutical Sciences and Research 2014;2:941-961

29. Bugwan Samridhi, Kumar Pravin, Ashawat Mahendra Singh, Pandit Vinay. Recent advances and technological aspects of ethosomes: a laconic review. World Journal of Pharmacy and Pharmaceutical Sciences 2019;2:460-472.

30. Bhagya Rekha. Formulation and characterization of atorvastatin ethosomal gel. jounal of drug development and delivery 2018;1:13-20

31. Kulkarni Sunisha, Mishra Kaushal Prasad, Sharma Shyam Bihari and Jain Suman.Ethosomes a promising way for transdermal drug delivery. International Journal of Pharmaceutical Sciences and Research 2015;6:3663-3670.

32. Cevc G, Vierl U. Nanotechnology and the transdermal route: a state of the art review and critical appraisal. J Control Release. 2010;141(3):277-299. doi:10.1016/j.jconrel.2009.10.020

33.Shinde P, Page A, Bhattacharya DS. Ethosomes and their monotonous effects on skin cancer disruption. Front Nanotech. 2023;5:1. doi:10.3389/fnano.2023.1087413Njpx.2019.10002

34. Meng S, Chen Z, Yang L, et al. Enhanced transdermal bioavailability of testosterone propionate via surfactant-modified ethosomes. Int J Nanomedicine. 2013;8:3051-3060. doi:10.2147/IJN.S46748 14732165, 2024, 1, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jocd.15895, Wiley Online Library on [07/08/2024].

35. Singh S, Sharma N, Zahoor I, et al. Decrypting the potential of nanotechnology-based approaches as cutting-edge for management of hyperpigmentation disorder. Molecules. 2022;28(1):220. doi:10.3390/molecules28010220

36. Sharma T, Thakur S, Kaur M, Singh A, Jain SK. Novel hyaluronic acid ethosomes based gel formulation for topical use with reduced toxicity, better skin permeation, deposition, and improved pharmacodynamics. J Liposome Res. 2022;33:1-15. Advance online publication. doi:10.1080/08982104.2022.2087675

37. Niu XQ, Zhang DP, Bian Q, et al. Mechanism investigation of ethosomes transdermal permeation. Int J of Pharma: X. 2019;1:100027. doi:10.1016/j.ijpx.2019.100027

38 . An Y-H, Park MJ, Lee J, et al. Recent advances in the transdermal delivery of protein therapeutics with a combinatorial system of chemical adjuvants and physical penetration enhancements. Adv Therap. 2020;3:1900116. doi:10.1002/adtp.201900116 liposome-based ethosomes.

39. Radwan Y, Karaly AH, El-Sherbiny IM. Nanovesicles for delivery of antiviral agents. Viral Infections and Antiviral Therapies. Academic Press; 2023:493-518. doi:10.1016/B978-0-323-91814-5.00001

40. How KN, Yap WH, Lim CLH, Goh BH, Lai ZW. Hyaluronic acidmediated drug delivery system targeting for inflammatory skin diseases: a mini review. Front Pharmacol. 2020;11:1105. doi:10.3389/fphar.2020.01105

41. Ghanbarzadeh S, Arami S. Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transfersomes. Biomed Res Int. 2013:616810. doi:10.1155/2013/616810 PMID: 23936825; PMCID: PMC3725948,

42. Paiva-Santos AC, Silva AL, Guerra C, et al. Ethosomes as nanocarriers for the development of skin delivery formulations. Pharm Res. 2021;38(6):947-970. doi:10.1007/s11095-021-03053-5 and tamoxifen

43. Sarwa K, Suresh P, Rudrapal M, Verma V. Penetration of tamoxifen citrate loaded ethosomes and liposomes across human skin: a comparative study with confocal laser scanning microscopy. Curr Drug Deliv. 2014;11:332-337. doi:10.2174/1567201811666140115113127

44. Elsayed MMA, Abdallah OY, Naggar VF, Khalafallah NM. Lipid vesicles for skin delivery of drugs: reviewing three decades of research. Int J Pharm. 2007;332(1–2):1

45. Raghuvanshi A, Shah K, Dewangan HK. Ethosome as antigen delivery carrier: optimisation, evaluation and induction of immunological response via nasal route against hepatitis B. J Microencapsul. 2022;39(4):352-363. doi:10.1080/02652048.2022.2084169

46. Benson HA. Transdermal drug delivery: penetration enhancement techniques. Curr Drug Deliv. 2005;2(1):23-33.

47. Sarwa K, Suresh P, Rudrapal M, Verma V. Penetration of tamoxifen citrate loaded ethosomes and liposomes across human skin: a comparative study with confocal laser scanning microscopy. Curr Drug Deliv. 2014;11:332-337. doi:10.2174/1567201811666140115113127

48.Elsayed Mustafa MA et al. Deformable liposomes and ethosomes: mechanism of enhanced skin delivery. Int j pharm 2006; 322: 60-66

49. Sultana Syeda Shabana and A Krishna Sailaja. Ethosomes a novel approach in the design of transdermal drug delivery system. International Journal of Medicine and Pharmaceuticle Research 2015;2:17-22

50. Agarwal S, Gautam G. And Rajpoot N. A review on ethosomes: an advanced approach to transdermal drug delivery system. International Research Journal of Pharmacy 2019;10:14-20.

51.Touitou E I, Composition of applying active substance to or through the skin. US patent 5 540 934, 1996, July 30 Alkilani AZ, McCrudden MTC, Donnelly RF. Transdermal drug delivery: Innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. Pharm., 2015;7(4):438-470Wilson V, Siram K, Rajendran S, Sankar V. Development and evaluation of finasteride loaded ethosomes for targeting to the pilosebaceous unit. Artif. Cells, Nanomed. Biotechnol. October 2017:1-10.

52.Saeed G, Arami S (2013). Enhanced transdermal delivery of diclofenac sodium via conventional liposomes, ethosomes, and transfersomes. BioMed res Int. 2013 article ID:616810

53. Abdulbaqi IM, Darwis Y, Khan NAK, Assi RA, Khan AA. Ethosomal nanocarriers: the impact of constituents and formulation techniques on ethosomal properties, in vivo studies, and clinical trials. Int J Nanomedicine 2016;11:2279–304

54. Akhtar N, Pathak K. Cavamax W7 Composite Ethosomal Gel of Clotrimazole for Improved Topical Delivery: Development and Comparison with Ethosomal Gel. AAPS Pharm Sci Tech 2012;13(1):344–5

55. Sudhakar CK, Jain S, Charyulu RN. A Comparison Study of Liposomes, Transfersomes and Ethosomes Bearing Lamivudine. Int J Pharm Sci Res 2016;7(10):4214–21

56. Abdulbaqi Ibrahim M, Darwis Yusrida, Khan Nurzalina Abdul Karim, Assi Reem Abou Khan Arshad A. Ethosomal nanocarriers the impact of constituents and formulation

57. Mistry A, Ravikumar P and Pathare S. Ethosomes unique elastic vesicular carrier an overview. International Journal of Pharmaceutical Sciences and Research 2015;6:4129-4136

58. Patrekar Prasad V, Inamdar Suhel J, Mali Sachin S, Mujib Mulla T, Ahir Amita A, Hosmani Avinash H. Ethosomes as novel drug delivery system a review. The Pharma Innovation Journal 2015;4:10-21

59. Waghmare Suchita. G, B.Dr.Satish, Nikhade Rasika R, Kannao Shweta U. Vesicular Carrier for Transdermal Drug Delivery System Ethosomes. World Journal of Pharmaceutical Research 2015;4:750-762.

60. Jaiswal Pankaj Kumar, Kesharwani Shikha, Kesharwani Roohi, Patel Dilip K. Ethosome a new technology used as topical & transdermal delivery system. Journal of Drug Delivery & Therapeutics 2016;6:7-17

61. Sujatha V, Vishnuvaravidyadhar T, Parvathi M, Reddy Suryaprakash. A review on transdermal drug delivery system by ethosomes. PharmaTutor 2014;2:50-55

62. Dave Vivek., Pareek Ashutosh., Paliwal Sarvesh. Ethosome: a novel approach of transdermal drug delivery system. International journal of advanced research in pharmaceutical & BioSciences 2012; 2:439- 452

63. L Pingale Prashant, S Boraste Sahebrao, P muthal Amol, Y Ghegade Raosaheb. Ethosomes newer trend in transdermal drug delivery a review. International Journal of Pharma Research and Health Sciences 2018;6:2586-90.

64. Pandey Nidhi. Proniosomes and ethosomes new prospect in transdermal and dermal drug delivery system. International Journal of Pharmaceutical Sciences & Research 2011;2:1988-1996

65. Trivedi Sagar S, Gautam Suresh A, Ambatwar Ramesh V, Pounikar Sheetal D, Wadher Kamlesh J, Umekar Milind J. Ethosomes as a carrier in drug delivery recent approaches and applications. Research Pharmaceutica 2018;2:1-5.

66. Gangurde PA. And Saudagar RB. Ethosomes novel drug delivery. International Journal of Pharma and Chemical Research 2017;3:25-31

67. C Monisha, Ganesh GNK and L Mythili, Radhakrishnan Kayalvizhi. A review on ethosomes for transdermal application research. Journal of Pharmacy and Technology 2019;12:3133-3143

68. Horwitz E, Pisanty S, Czerninski R, Helser M, Eliav E, Touitou E. A clinical evaluation of a novel liposomal carrier for acyclovir in the topical treatment of recurrent herpes labialis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1999;87(6):700–5.

69. Touitou E, Godin B, Dayan N, Weiss C, Piliponsky A, LeviSchaffer F. Intracellular delivery mediated by an ethosomal carrier. Biomaterials 2001;22:3053–9.

70. Fang JY, Hong CT, Chiu WT, Wang YY. Effect of liposomes and niosomes on skin permeation of enoxacin. Int J Pharm 2001;219:61–72.

71. Ainbinder D, Touitou E. Testosterone ethosomes for enhanced transdermal delivery. Drug Deliv 2005;12:297–303

72. Mohammed MI, Makky AMA, Abdellatif MM. Formulation and characterization of ethosomes bearing vancomycin hydrochloride for transdermal delivery. Int J Pharm Pharm Sci 2014;6(11):190– 4.

73. Vijayakumar MR, Sathalia AH, Arun K. Formulation and Evaluation of Diclofenac Potassium Ethosomes. Int J Pharm Pharm Sci. 2010; 2(4): 82–6

74. Dayan N, Touitou E. Carriers for skin delivery of trihexyphenidyl HCl: ethosomes vs liposomes 2000;21:1879–85

75. Sujitha B, Krishnamoorthy B, Muthukumaran M. Formulation and Evaluation of Piroxicam Loaded Ethosomal Gel for Transdermal Delivery. Int J Adv Pharm Gen Res. 2014; 2(1): 34–45

76. Aggarwal Divya, Nautiyal Ujjwal. Ethosomes A review. International Journal of Pharmaceutical and Medicinal Research 2016;4:354-363

77. Bansal Saurabh, Kashyap Chandan Prasad, Aggarwal Geeta and Harikumar SL. A comparative review on vesicular drug delivery system and stability issues. International journal of research in pharmacy and chemistry 2012;2:704-713

79. Akiladevi D, Basak Sachinandan. Ethosomes a noninvasive approach for transdermal drug delivery. International Journal of Current Pharmaceutical Research 2010;2:1-4

80. Gupta N.B, Loona S, and Khan M.U. Ethosomes as elastic vesicles in transdermal drug delivery an overview. International Journal of Pharmaceutical Sciences and Research 2012;3:682-687.

81. Rakesh R, Anoop KR. Ethosomes for transdermal and topical drug delivery. International Journal of Pharmacy and Pharmaceutical Sciences 2012;4:17-24.

82. S hahwal V, Samnani A, Dubey B, Bhowmick M, "Ethosomes: an overview". Int.J. Bio Adv Res 2011, 2: 161-168.

83. Dayan N, Touitou E. Carrier for skin delivery of trihexyphenidyl HCl: Ethosomes vs liposomes. Biomaterials. 2002; 21(18):1879-85

84 .Yissum [website on the Internet]. Available from: http://www.yissum. co.il. Accessed November 14, 2015.

85. Mbah CC, Builders PF, Attama AA. Nanovesicular carriers as alternative drug delivery systems: ethosomes in focus. Expert Opin Drug Deliv. 2014;11(1):45–59.7,

86. Sudhakar CK, Nitish U, Sanjay J, Charyulu RN. Ethosomes as noninvasive loom for transdermal drug delivery. In: Haghi AK, editor. Nanomedicine and Drug Delivery. Oakville (ON): Apple Academic Press; 2012:1–16.

87. Santosh Shelke1, Sadhana Shahi2 , Suwarna Kale1 , Vandana Patil1 , Dipali DeshpandeWorld Journal of Pharmaceutical Sciences ISSN (Print): 2321-3310; ISSN (Online): 2321-3086 Published by Atom and Cell Publishers © All Rights Reserved Available online at: http://www.wjpsonline.org

88. agentsPankaj Kumar Jaiswal1, Shikha Kesharwani1 , Roohi Kesharwani1 , Dilip K. Patel2 1Chandra Shekhar Singh College of Pharmacy, Kaushambi, Allahabad, U.P., India 2Department of Pharmaceutical Sciences, s

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