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Review Article

Ethosome as a potential transdermal drug delivery system

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ABSTRACT

Ethosomes are elastic nanovesicles with phospholipid bases that are noninvasive delivery vehicles and have a high ethanol concentration (20–45%). As transdermal drug delivery confers poor penetration, the major obstacle is the low diffusion rate of drugs across the stratum corneum. The sophisticated ethosomal delivery systems enable drugs to reach the deep skin layers and/or the systemic circulation. The development of these new carriers involves the employment of several preparatory processes. Ethosomal dispersions are added to gels, patches, and creams for ease of use and stability. Ethanol is known as an efficient permeation enhancer and has been added in the vesicular systems to prepare elastic nanovesicles. It has the potential to interact with the polar head group region of lipid molecules, lowering the melting point of the stratum corneum lipid and raising lipid fluidity and cell membrane permeability as a result. Ethosomes' special structure allows them to enclose and transmit through the skin highly lipophilic substances like propranolol and trihexyphenidil as well as cationic medicines like testosterone and minoxidil. This article provides a detailed review of the ethosomal structure, mechanism of penetration along with various methods of preparation. Also, the article focuses on the applications of ethosomal carriers and opportunities for the research and future development of novel improved therapies.

1. Introduction

(TDDS) Transdermal drug delivery are the systems used and employed for effectively delivering painless medications beyond the skin. Drugs that endure substantial presystemic metabolism, are not stable in the gastrointestinal tract, or severe side effects can be caused on oral administration may benefit from transdermal drug delivery methods. Additionally, these systems offer better patient compliance, decreased dose frequency, and regulated medication distribution. To regulate the distribution of medications and their subsequent penetration into the skin tissue, therapeutic devices for transdermal delivery developed for topical application onto the skin surface. With this delivery system, self-administration is also an option because it is a non-invasive method of application.[1] Continuous I. V (intravenous) infusion is regarded a preferable method for administering drugs since it not only avoids hepatic "first-pass" metabolism but also keeps the body's pharmacological drug level stable and prolonged. Skin as the drug administration port has been used to provide uninterrupted transdermal infusion of drug into the systemic circulation allows for a close duplication of the advantages of intravenous drug infusion without the risks.[2]

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Scopolamine containing first transdermal patch for the treatment and prevention of motion sickness was approved in 1979 in US. The different types of transdermal delivery systems are used for therapeutic drug delivery for development of continuous infusion long-term for therapeutic agents such as anti-histamine, anti hypertensive, anti-inflammatory, anti-anginal, analgesic, contraceptive drugs and anti-arthritic steroidal.[2]

1.1. Why Ethosomes

Ethosomes are vesicles having size range from 30 nm to several microns which are soft and pliable. According to reports, when made using the same procedure without the use of a size-reduction step, ethosomes are smaller than liposomes in size. The size is reduced because of the high alcohol level, and it gets smaller as the concentration of ethanol rises nearly to 20–45 percent. Ethosome get a net negative charge from ethanol, which reduces their size. The addition of 30% ethanol caused the charge of the vesicles to change from positive to negative.[3]

The groundbreaking work of Touitou et al. and Cevc and Blume in 1924 led to the identification of ethosomes, a brand-new vesicular system made of lipid. Liposomal and ethosomal systems differ from each other in the quantity rather high quantity of ethanol.[4] In an effort to improve and increase the skin permeation and vesicular characteristics of ethosome influence of these ethanol plays a pivotal role, 5–6. Other additional generations of ethosomal systems have been produced since then by adding other compounds to the fundamental ethosomal formula to establish ethosomes as potential carrier system.[5]

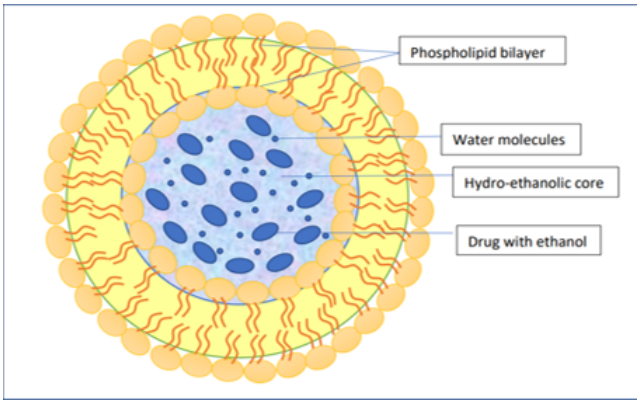

Fig. 1: Structure of Ethosome depicting various layers

1.2. Structure and composition of ethosomes

The hydroalcoholic or hydro/alcoholic/glycolic phospholipid that makes up the ethosomes is a vesicular carrier with a relatively high alcohol concentration or combination of them. Ethosomes contain phospholipids and it has a variety of constituents like phosphatidic acid (PA), hydrogenated phosphatidylcholine (PC), phosphatidylserine (PS), phosphatidylglycerol (PPG), phosphatidylinositol (PI) and phosphatidylethanolamine (PE). They may also contain water, propylene glycol, and other liquids (or other glycols).[4] Through the skin, a high concentration of active substances can be delivered by such a formulation. The ratio of water to alcohol-polyol or alcohol to water can be changed to control drug delivery. Soya phospholipids like Phospholipon 90 (PL-90) is one of the most desired phospholipids. It is often used within a range of 0.5-10% w/w. To the mixture cholesterol can be added in amounts ranging from 0.1 to 1%.[6,7]

Ethanol and isopropyl alcohol are two examples of alcohols that can be employed. Propylene glycol and Transcutol are the two most often utilised glycols. In these formulations, phospholipids may also be mixed with surfactants (non-ionic) like PEG-alkyl ethers. Additionally, cationic lipids such as cocoamide, cetrimide, dodecylamine, POE alkyl amines etc. are also in the list. Between 20 and 50 percent of alcohol may be present in the finished product. Alcohol and glycol mixture content in the non-aqueous phase can range from 22 to 70%.

1.3. Skin permeation mechanism of ethosomes

Ethosomal size is influenced by the content of phospholipid and ethanol. It was established that vesicle size grows when phospholipid concentration increases, ethosome size decreases when ethanol concentration increases.

Percutaneous channel via the stratum corneum and open hair follicles allowed the ethosomes to enter skin. Top layer skin vesicles were split during percutaneous penetration that allow the therapeutically active drugs to progressively permeate while the upper epidermis is maintained by phospholipids.[8] The suggested mechanism depends upon the interaction between phospholipids and ethanol, which increases the rate at which drugs can permeate the ethosomes. Alcohol works well to increase penetration. At physiological temperature, the subcutaneous lipid layer of skin is tightly organized and packed. The Tm of SC lipids is decreased by ethanol, and their fluidity is increased. This results in a disruption of the skin's lipid bilayer organisation and a decrease in skin lipid density. Additionally, ethanol may play the role in malleableization and softening the vesicle bilayer. The disorganized bilayer (SC lipid layer) is more easily penetrated by these flexible, squishy ethosome vesicles. The mechanism for ethosome penetration is described diagrammatically in Figure 2.

1. As it is already known that ethosomes is the ethanol-based liposomal formulation, thus, corelating the mechanism by which the liposomal formulation penetrates various skin layers like lateral diffusion. As the constituents of ethosomes are structurally

similar with the skin lipid for that the exchange between human membrane is the physicochemical phenomenon. Whenever the ethanol is introduced in the vesicle for the flexibility or malleability, the percentage of ethanol is the cause of small shape and high penetrability of ethosomes in the stratum corneum.

2. Ethanol tends to disturb the fat layer of skin which causes the high ability to penetrate the stratum corneum layer.
3. The polar head group region reacts with lipid molecules due to the effect of ethanol. It results in the transition temperature reduction of lipid in the stratum corneum. Which in turn decreasing the density of lipid multilayer and increase the fluidity.
4. Due to fusion and high malleable property of ethosomes with lipid layer of skin the drug release in the deep layer of skin towards systemic circulation.

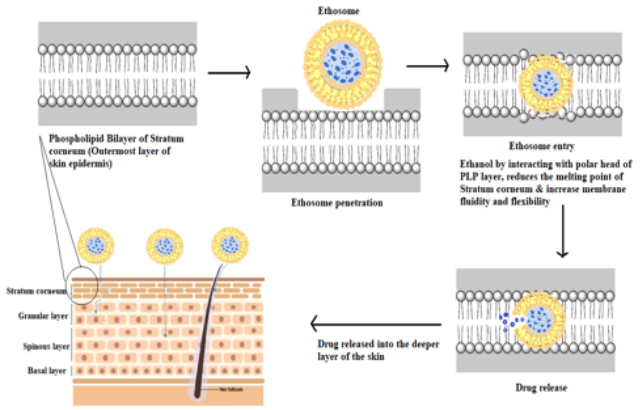

Fig. 2: Mechanism of Ethosome penetration

1.4. *Preparation of ethosomes*

Ethosome preparation relies on basic scale-up processes without the need for expensive equipment at both the pilot and industrial levels. There are three general methods of preparation of ethosomes comprising hot method, cold method and classic method.

1.5. *Hot method*

Phospholipid in a water bath at 30^0C is heated in this technique till a solution (colloidal) is produced. Ethanol and Propylene glycol are mixed and heated to 40°C using a different vessel. The introduction of organic phase and aqueous phase is done once both combinations have reached 40°C. Depending on the nature of the drug if it is hydrophobic or hydrophilic, it dissolves in either ethanol or water. Using the extrusion approach or probe sonication the size of the vesicle of ethosomal formulation can be diminished to the desirable extent.[8–10] The schematic steps are represented in Figure 3.

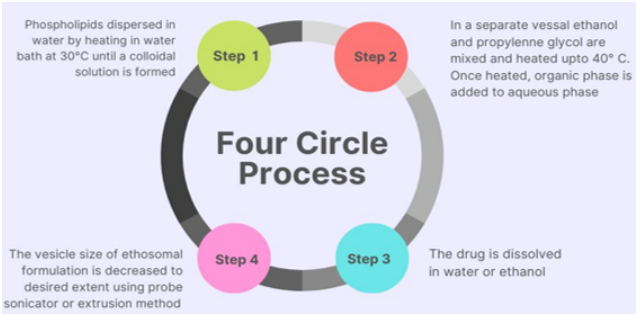

Fig. 3: Schematic representation of hot method

1.6. *Cold method*

The most popular methods for formulation of ethosomes. This method involves two different setups. First setup deals with dissolving ethanol at room temperature with phospholipid and other lipid molecules. Continuous addition of polyols like propylene glycol (PEG) where heidolph mixer is used for vigorous stirring then heating at 30°C in water bath. The second setup is followed by heating water at 30°C in a different vessel. Blending of both the mixtures (from first and second setup) together and stirred for 5 mins using a covered vessel.[11] The vesicle size of ethosomal formulation can be decreased to desirable size with the help of extrusion or sonication method. The formulation is finally refrigerated for storage.[12] The schematic steps are represented in Figure 4.

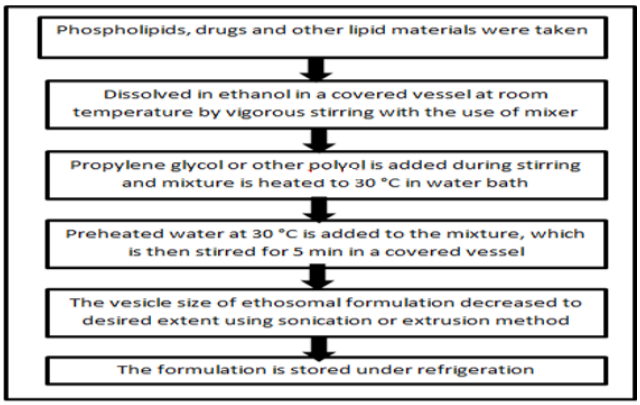

Fig. 4: Schematic representation ofcold process

1.7. *Injection method*

1.7.1. *The ethanol injection–sonication method*

The approach involves injecting aqueous and organic phase together in ethanol containing the dissolved phospholipid

where a syringe system has been used[13] at a flow rate of 200 L/min, followed by 5 minutes of homogenization using probe sonicator.

1.7.2. The thin-film hydration method

An upgrade over the standard liposome preparation technique is thin-film hydration method but in this technique, a hydroethanolic solution hydrates the lipid film. In a dry, clean round-bottom flask, first the phospholipid is dissolved in either a chloroform-methanol mixture at ratios of 3:1[14] or 2:1[15] or chloroform alone.[16] For extraction of organic solvents at temperature higher than the lipid-phase transition temperature rotating vacuum evaporators are used. Then the solvent residue is extracted under vaccum overnight from the deposited lipid film. For hydration of the lipid film a water-ethanol solution or phosphate buffered saline-ethanol solution[17] is then used. Finally, the lipid film is rotated and heated for 30 minutes to an hour during the hydration process.[18]

1.7.3. The reverse-phase evaporation method

To produce large uni-lamellar vesicles this method has been used. By dissolving the phospholipid in diethyl ether, the organic phase is prepared then combining it with the aqueous phase in an ultrasonic bath at 0°C for 5 minutes. This generates water-in-oil emulsion. The organic solvent is withdrawn under reduced pressure resulting a gel formation. The gel upon vigorous mechanical agitation transforms into a colloidal dispersion.[19]

1.7.4. Transmembrane pH-gradient method

Either the organic or aqueous phase is added with the drug, and it is "passively" or spontaneously loaded in the ethosomal system. Actively the drug is loaded in the transmembrane pH-gradient approach, depending upon the differences in the pH-gradient between the internal phase with acidic environment and the ethosomal system with basic external environment. This approach was first utilized to manufacture liposomes.[20,21] and it was afterwards employed by Zhou et al. and Fan et al.[22]

1.8. Characterization of Ethosome

1.8.1. Drug entrapment efficiency

The ability of ethosomes to entrap hydrophilic and lipophilic drugs can be explained and supposed by presence of ethanol and high degree of lamellarity in the vesicles. Moreover, ethosomal formulations have greater entrapment capability compared to liposomes.[23]

Five hundred microliters of ethosomal formulation were placed into a centrifugal filter comprised of two vials the upper to recover retentate and the other to collect filtrate to determine the efficacy of the drug in ethosomal entrapment. Under 8000 rpm ultracentrifugation, upper vial held the ethosome encapsulating drug. The bottom is placed with the free drug. After 20 minutes, a 100 L aliquot extracted from the upper vial. It was diluted, mixed, filtered, and reported for HPLC analysis.

The EE was determined by the formula: EE = CA/TCA × 100

where CA is the amount of drug retained in ethosomes and TCA is the total content of CA.

1.9. Permeation characteristics

Studies like in vitro and in vivo skin permeation have shown that ethosomal formulations can improve the penetration of both hydrophilic and hydrophobic compounds. Several researchers have observed that ethosomal drug formulation penetrate the skin 5-10 times better than typical liposome formulations. Ethanol has long been known for its ability to improve permeability. Ethanol, which was previously thought to be damaging to typical liposomal formulations, offered flexible properties to ethosomes, allowing them to easily permeate deeper skin layers.[24]

2. Vesicle Skin Interaction Study

Different imaging techniques such as fluorescence microscopy, transmission electron microscopy, confocal scanning laser microscopy (CSLM), eosin-hematoxylin staining was employed to evaluate the mechanism of enhanced skin permeability of ethosomal formulation. When utilized together, these imaging tools provided a better understanding of vesicle structural modulation and penetration paths. No structural alterations were identified in cell layers underneath the stratum corneum, indicating that the stiff liposomal formulation had no effect on the stratum corneum's ultrastructure and accumulated solely in the top layer of the skin. These findings demonstrated that liquid state vesicles may act not only in the superficial stratum corneum layers, but also in deeper layers of the SC, whereas gel state vesicles interacted solely with the outermost layers of the SC.[25–27]

3. Applications of Ethosome

Ethosomes are very effective form of delivery of a wide range of drug through the skin Applications of ethosomes in various diseases are discussed below.[28–33]

3.1. Ethosomes for microbial and viral skin infection

Ethosomes got extremely successful rating at delivering antibiotics for skin infections treatment. Antibiotics impact on the treatment of skin infections have been studied in animal models.[34,35] In comparison to the therapy with a hydroethanolic erythromycin solution, when treatment done with ethosomal erythromycin on Staphylococcus aureus infected mice it revealed effective healing of cutaneous infections with no bacterial growth.[34] A study

investigates bacitracin skin permeation ability in vitro and in vivo utilizing bacitracin and fluorescently tagged bacitracin (FITC-Bac) ethosomes.[35] CLSM (confocal laser scanning microscopy) and fluorescent-activated cell sorting (FACS) tests were used to measure the outcomes. Both investigations revealed that ethosomal formulations penetration across the skin easily and faster.[36]

3.2. Ethosomes for menopausal syndromes

Buspirone hydrochloride (BH) has a very poor oral bioavailability of not more than 3.9 percent compared to intravenous administration because of substantial first pass metabolism.[37] BH also has a short half-life of 2.5 hours, necessitating doses frequently.[38,39] Because BH is a hydrophilic cationic molecule, it does not penetrate through the skin sufficiently to reach the blood therapeutic level. Formulations of ethosomes have been done to increase the skin permeability of BH. This also help in the increase in pharmacologic and pharmacokinetic efficiency for menopausal syndrome therapy. According to the findings, BH ethosomes are beneficial and safe for the treatment of menopausal syndrome.[40]

3.3. Ethosome for peptides delivery

Peptides, Proteins are macromolecules that are unable to pass through the SC (subcutaneous) layer. As their oral bioavailability is poor, I. V and S. C routes are considered for their delivery. Insulin being an oligomeric protein have a MW (molecular weight) of 6000 Dalton per monomer that can be administered intravenously to patients with IDDM (insulin-dependent diabetes mellitus). Several studies with focus on nonpassive delivery of insulin through the skin using physical methods such as phonophoresis, iontophoresis and so on.[41,42] Augmentation with phospholipid vesicle that is deformable and its passive delivery has been shown to improve absorption of insulin percutaneously.[43]

3.4. Ethosome for hair loss

A broad population all around the world has been affected and suffering by hair diseases such as excessive hair loss, acne and seborrhea. Focused drug delivery to hair follicles is needful for the efficient treatment of pilosebaceous illnesses. A lipophilic drug Minoxidil is proved to be effective when applied topically to the scalp to cure hair loss. To investigate the targeting to pilosebaceous units ethosomal Minoxidil was formulated and in vivo test was performed in hairless rats. The results demonstrated that minoxidil localized in the pilosebaceous units that indicates minoxidil was delivered more effectively utilizing ethosomal carriers.[44]

3.5. Miscellaneous application

1. Higher deposition of drug in deeper layers of skin by Finasteride ethosomes at a higher flux that is 7.4, 3.2, and 2.6 times higher has been found than those of conventional liposomes, aqueous solution and hydroethanolic solution of drug.
2. Transferosomes and Linoleic acid ethosomes showed promising permeation through human skin in the treatment of topical skin (hyperpigmentation) related disorders.
3. Ethosomes containing iodine as a contrast agent for computed tomography for imagining applications have been studied by some researchers.
4. In a study ethosomes were used for entrapment of new lipophilic excited- state intramolecular proton-transfer dyes for fluorescence spectroscopy.
5. Hair dyes of Transethosomes were developed and showed an effective delivery and higher absorption of black tea extracts to the hair surface as compared to hydroethanolic solutions of the same extract.
6. Ethosomes were also suggested for potential lung targeting for lung disease. Methoxsalen was successfully delivered topically using a nanosized Ethosome-based hydrogel formulation for the treatment of vitiligo.
7. Ethosomes were also studied for the treatment of HIV and hepatitis.
8. Gold nanoparticles have been synthesized in the ethosome bilayer to provide a better pharmacological effect.
9. Ethosomes containing phenyl ethyl resorcinol a skin lightening agent showed higher tyrosinase inhibition activity and melatonin reduction without causing skin irritation.
10. Now a day trending research is going on to enhance the penetration ability by applying microwaves for the treatment of melanoma (skin cancer).

4. Conclusion

Almost two decades from the discovery of ethosomes, different nanocarriers have been demonstrated for their unique capacity to carry therapeutic compounds with varying physicochemical properties via the skin for both local and systemic use. Vast research has resulted in the development of ethosomal systems known as transethosomes. This have been found to have superior characteristics in terms of vesicular system and ability to permeate skin to classical ethosomes. The formulator with transethosomes have the most flexibility in modifying ethosomal properties to meet the study needs by adjusting the penetration enhancers or edge activators. The inclusion of ethosomal systems in proper vehicles such as patches, creams and gels are a crucial step toward improved skin

penetration as well as absorption. This delivery system is the most effective and also the future of all delivery systems.

5. Source of Funding

None.

6. Conflict of Interest

None.

References

1. Nainwal N, Jawla S, Singh R, Saharan V. Transdermal applications of ethosomes - a detailed review. *J Liposome Res*. 2018;29(2):103–13.
2. Patrekar PV, Inamdar S, Mali S, Mujib M, Ahir A, Hosmani A. Ethosomes as novel drug delivery system: A review. *Pharma Innov J*. 2015;4(9):10–21.
3. Nainwal N, Jawla S, Singh R, Saharan V. Transdermal applications of ethosomes - a detailed review. *J Liposome Res*. 2018;29(2):103–13.
4. Kulkarni S, Mishra K, Sharma S, Jain S. Ethosomes - a promising way for transdermal drug delivery. *International Journal of Pharmaceutical Sciences and Research*. 2015;6(9).
5. Abdulbaqi M, Darwis I, Assi A, Khan AK, Khan A. Ethosomal nanocarriers: the impact of constituents and formulation techniques on ethosomal properties, in vivo studies, and clinical trials. *Int J Nanomed*. 2016;11:2279–2304.
6. Anitha PS, Ramkanth K, Sankari UM, Alagusundaram K, Gnanapraksah P, Devaki DR. Ethosomes - A noninvasive vesicular carrier for transdermal drug delivery. *Int J Rev Life Sci*. 2011;1(1):17–24.
7. Barupal AK, Gupta V, Ramteke S. Preparation and Characterization of Ethosomes for Topical delivery of Aceclofenac. *Indian J Pharm Sci*. 2010;72(5):582–6.
8. Limsuwan T, Boonme P, Khongkow P, Amnuaikit T. Ethosomes of Phenylethyl Resorcinol as Vesicular Delivery System for Skin Lightening Applications. *BioMed Res Int*. 2017;p. 1–12.
9. Touitou E. Composition of applying active substance to or through the skin. United States. 1996;5540934. Available from: https://patentimages.storage.googleapis.com/f9/ad/a3/2ba8dd61dda0d0/US5716638.pdf.
10. Mahale N, Khairnar S, Kanawade R, Wale K, Chaudhari S. Ethosomal Drug Delivery System: A Review. *Indo Am J Pharm Res*. 2012;1(5):469–75.
11. Touitou E. Composition for applying active substances to or through the skin. ; 1998. Available from: https://patents.google.com/patent/US5716638A/en.
12. Pandey V, Golhani D, Shukla R. Ethosomes: versatile vesicular carriers for efficient transdermal delivery of therapeutic agents. *Drug Delivery*. 2014;22(8):988–1002.
13. Zhaowu Z, Xiaoli W, Yangde Z, Nianfeng L. Preparation of matrine ethosome, its percutaneous permeation in vitro and anti-inflammatory activity in vivo in rats. *J Liposome Res*. 2009;19(2):155–62.
14. Mishra D, Mishra PK, Dabadghao S, Dubey V, Nahar M, Jain NK. Comparative evaluation of hepatitis B surface antigen-loaded elastic liposomes and ethosomes for human dendritic cell uptake and immune response. *Nanomedicine*. 2010;6(1):110–8.
15. Maheshwari RG, Tekade RK, Sharma PA. Ethosomes and ultradeformable liposomes for transdermal delivery of clotrimazole: a comparative assessment. *Saudi Pharm J*. 2012;20(2):161–70.
16. Park S, Lee H, Gu H. Enhanced skin delivery and characterization of rutin-loaded ethosomes. *Korean J Chem Eng*. 2014;31(3):485–9.
17. Mishra D, Mishra PK, Dubey V, Nahar M, Dabadghao S, Jain NK. Systemic and mucosal immune response induced by transcutaneous immunization using hepatitis B surface antigen-loaded modified liposomes. *Eur J Pharm Sci*. 2008;33(4-5):424–33.
18. Dubey V, Mishra D, Dutta T, Nahar M, Saraf DK, Jain NK. Dermal and transdermal delivery of an anti-psoriatic agent via ethanolic liposomes. *J Control Rel*. 2007;123(2):148–54.
19. Maestrelli F, Capasso G, Gonzalez-Rodriguez ML, Rabasco AM, Ghelardini C, Mura P. Effect of preparation technique on the properties and in vivo efficacy of benzocaine-loaded ethosomes. *J Liposome Res*. 2009;19(4):253–60.
20. Nichols JW, Deamer DW. Catecholamine uptake and concentration by liposomes maintaining pH gradients. *Biochim Biophys Acta*. 1976;455(1):269–71.
21. Cramer JA, Prestegard JH. NMR studies of pH-induced transport of carboxylic acids across phospholipid vesicle membranes. *Biochem Biophys Res Commun*. 1977;75(2):295–301.
22. Fan C, Li X, Zhou Y. Enhanced topical delivery of tetrandrine by ethosomes for treatment of arthritis. *Biomed Res Int*. 2013;p. 161943. doi:10.1155/2013/161943.
23. Kulkarni S, Mishra K, Sharma S, Jain S. Ethosomes - a promising way for transdermal drug delivery. *Int J Pharm Sci Res*. 2015;6(9):3663–70.
24. Godin B, Touitou E. Mechanism of bacitracin permeation enhancement through the skin and cellular membranes from an ethosomal carrier. *J Controlled Rel*. 2004;94:365–79.
25. Sheer A, Chauhan M. Ethosomes as vesicular carrier for enhanced transdermal delivery of Ketoconazole - Formulation and Evaluation. IJPI's. *J Pharm Cosmetol*. 2011;1(3):1–14.
26. Jason DM, Jackson R. Analgesic, antipyretic and antiinflammatory agents and drugs employed in the treatment of gout. *Pharmacol Basis Ther*. 2001;p. 711–20.
27. Talegaonkar S, Tariq M, Alabood RM. Design and development of o/w nanoemulsion for the transdermal delivery of ondansetron. *Bull Pharm Res*. 2011;1(3):18–30.
28. Nainwal N, Jawla S, Singh R, Saharan V. Transdermal applications of ethosomes - a detailed review. *J Liposome Res*. 2018;29(2):103–13.
29. Schoellhammer C, Blankschtein D, Langer R. Skin permeabilization for transdermal drug delivery: recent advances and future prospects. *Expert Opin Drug Deliv*. 2014;11(3):393–407.
30. Jeswani G, Saraf S. Topical Delivery of Curcuma longa Extract Loaded Nanosized Ethosomes to Combat Facial Wrinkles Research Article. *J Pharmaceutics*. 2014;3(1):2–8.
31. Godin B, Touitou E. Mechanism of bacitracin permeation enhancement through the skin and cellular membranes from an ethosomal carrier. *J Controlled Rel*. 2004;94(2-3):365–79.
32. Akhtar N, Pathak K. Cavamax W7 Composite Ethosomal Gel of Clotrimazole for Improved Topical Delivery: Development and Comparison with Ethosomal Gel. *AAPS PharmSciTech*. 2012;13(1):344–55.
33. Prasanthi D, Lakshmi PK. Statistically optimised ethosomes for transdermal delivery of tolterodine tartrate. *Pak J Pharm Sci*. 2013;26(6):1117–39.
34. Godin B, Touitou E. Erythromycin Ethosomal Systems: Physicochemical Characterization and Enhanced Antibacterial Activity. *Curr Drug Deliv*. 2005;2(3):269–75.
35. Godin B, Touitou E, Rubinstein E, Athamna A, Athamna M. A new approach for treatment of deep skin infections by an ethosomal antibiotic preparation: an in vivo study. *J Antimicrob Chemother*. 2005;55(6):989–94.
36. Mohammed M, Makky A, Teaima M, Abdellatif M, Hamzawy M, Khalil M. Transdermal delivery of vancomycin hydrochloride using combination of nano-ethosomes and iontophoresis: in vitro and in vivo study. *Drug Delivery*. 2015;p. 1–7.
37. Tunnicliff G. Molecular Basis of Buspirone's Anxiolytic Action. *Pharmacol Toxicol*. 1991;69(3):149–56.
38. Mahmood I, Sahajwalla C. Clinical pharmacokinetics and pharmacodynamics of buspirone, an anxiolytic drug. *Clin Pharmacokinet*. 1999;36(4):277–87.
39. Sakr A, Andheria M. A comparative multidose pharmacokinetic study of buspirone extended-release tablets with a reference immediate-release product. *J Clin Pharmacol*. 2001;41(8):886–94.
40. Shumilov M, Touitou E. Buspirone transdermal administration for menopausal syndromes, in vitro and in animal model studies. *Int J Pharm*. 2010;387(1-2):26–33.

41. Tachibana K. Transdermal delivery of insulin to alloxan-diabetic rabbits by ultrasound exposure. *Pharm Res*. 1992;9(7):952–6.
42. James V, Walters KA. The importance of skin pH in iontophoresis of peptides, Prediction Percutaneous Penetration. *STS Publishing*. 1993;81(1):1–28.
43. Cevc G. Transfersomes, liposomes and other lipid suspensions on the skin: permeation enhancement, vesicle penetration, and transdermal drug delivery. *Crit Rev Ther Drug Carrier Syst*. 1996;13(3-4):257–388.
44. Dkeidek I, Touitou E. Transdermal absorption of polypeptides. *AAPS Pharm Sci*. 1999;4(11):202–6.

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