Available online on 15.02.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Review Article

Ethosomes: A Revolutionary Approach in Advanced Drug Delivery Systems

Manpreet, Shubham Sachdeva *, Harwinder Kaur, Ritika Garg, Jitender Singh

Department of Pharmaceutics, Lord Shiva College of Pharmacy, Sirsa, Haryana

Article Info:

Article History:

Received 13 Nov 2024
Reviewed 30 Dec 2024
Accepted 24 Jan 2025
Published 15 Feb 2025

Cite this article as:

Manpreet, Sachdeva S, Kaur H, Garg R, Singh J, Ethosomes: A Revolutionary Approach in Advanced Drug Delivery Systems, Journal of Drug Delivery and Therapeutics. 2025; 15(2):186-192 DOI: http://dx.doi.org/10.22270/jddt.v15i2.6993

Abstract

Ethosomes, a novel vesicular carrier system, have emerged as a promising approach in the field of drug delivery. These lipid-based carriers, characterized by their high ethanol content, exhibit unique properties that enhance the delivery of therapeutic agents across biological barriers, particularly the skin. Ethosomes overcome the limitations of conventional delivery systems by improving drug solubility, stability, and permeation. Their ability to encapsulate both hydrophilic and lipophilic drugs makes them versatile carriers for a wide range of pharmaceutical applications, including transdermal, dermal, and systemic delivery. This review explores the composition, preparation methods, mechanisms of action, and therapeutic applications of ethosomes, highlighting their potential to revolutionize drug delivery practices. Furthermore, challenges in their large-scale production and future prospects are discussed to provide a comprehensive understanding of this innovative technology.

Keywords: Ethosomes, transdermal drug delivery, lipid-based vesicles, enhanced skin permeation, nanocarriers

*Address for Correspondence:

Mr. Shubham Sachdeva, Asstt. Professor, Department of Pharmaceutics, Lord Shiva College of Pharmacy, Sirsa, Haryana

Introduction

Human skin acts as an effective and selective barrier to chemical permeation, which limits the entry of water-soluble molecules and drugs. Despite these challenges, skin-based drug delivery offers notable advantages, including avoidance of first-pass metabolism, reduced fluctuations in plasma drug levels, targeted delivery for localized effects, and improved patient compliance.[1] The stratum corneum, the outermost layer of the epidermis, consists of bundled keratins stabilized by a cell envelope of cross-linked proteins and covalently bound lipids. This structural composition makes it a formidable barrier, particularly to water-soluble drugs.

Human skin acts as a highly selective barrier to chemical permeation, particularly limiting the penetration of water-soluble molecules and drugs. Despite these challenges, transdermal drug delivery offers several advantages, including bypassing first-pass metabolism, reducing plasma drug level fluctuations, providing localized effects, and improving patient compliance. The stratum corneum, the outermost layer of the epidermis, consists of bundled keratins and a lipid matrix, making it an effective barrier, especially against hydrophilic drugs.

Various strategies have been developed to enhance drug permeation, including physical and chemical methods. Physical approaches such as iontophoresis, sonophoresis, and microneedles have demonstrated efficacy but often involve complex procedures affecting patient compliance[2]. Chemical penetration enhancers, including surfactants and organic solvents, can disrupt skin integrity, leading to irritation[3]. Consequently, vesicular systems, such as liposomes and ethosomes, have gained attention as non-invasive alternatives for drug delivery[4].

The epidermis, specifically the stratum corneum, plays a pivotal role in controlling drug permeation. In its absence, small water-soluble and non-electrolytic molecules can diffuse into systemic circulation up to a thousand times more rapidly. Therefore, various strategies have been developed to enhance drug flux by mitigating the barrier function of the skin. Technological advancements over recent decades have introduced both physical and chemical methods to overcome the skin's barrier properties.[5]

Physical approaches, such as iontophoresis, sonophoresis, and microneedles, have demonstrated efficacy but often require complex procedures that may affect patient compliance. Chemical penetration enhancers, including surfactants and organic solvents, can irritate or damage the skin, compromising its natural barrier function. Consequently, there is an increasing preference for drug delivery systems that maintain the skin's integrity while facilitating drug penetration.[6]

Vesicular systems, such as liposomes and ethosomes, have gained considerable attention for their ability to enhance skin permeation without causing irritation. Over the past decade, the topical delivery of drugs using liposomal formulations has shown significant promise.[7] Deformable liposomes and transferosomes, introduced by Ceve and Blume in 1992, represent the first generation of elastic vesicles capable of penetrating intact skin and delivering therapeutic concentrations of drugs under non-occlusive conditions. These vesicles are composed of phospholipids and non-ionic surfactants, which encapsulate the drug and facilitate its transport into and across the skin.[8]

Ethosomes build upon this concept, offering enhanced deformability and penetration efficiency. Their high ethanol content disrupts the lipid structure of the stratum corneum, further improving drug delivery to deeper skin layers and systemic circulation. This makes ethosomes a superior choice for non-invasive therapeutic applications, ensuring effective delivery of both hydrophilic and lipophilic drugs.[9]

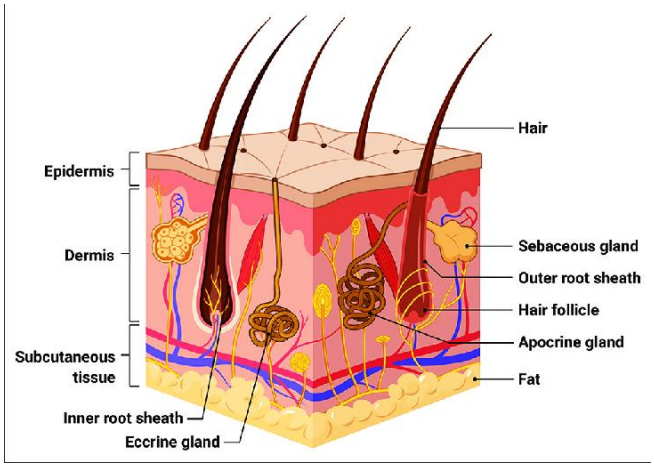

Figure 1: Structure of skin

Ethosomes

Ethosomes have emerged as a cutting-edge drug delivery system, offering significant advancements in transdermal and topical applications. These vesicular carriers, composed of phospholipids, ethanol, and water, enable the delivery of both hydrophilic and lipophilic drugs through the skin. By enhancing permeability and stability, ethosomes overcome the limitations of conventional delivery systems, making them particularly effective in treating skin disorders, fungal infections, and systemic diseases. This review provides a comprehensive analysis of the structure, preparation methods, mechanisms, applications, and future prospects of ethosomes, highlighting their transformative potential in pharmaceutical sciences.[10]

Ethosomes are phospholipid-based nanocarriers containing high concentrations of ethanol (20-45%), which enhances skin permeability by disrupting the stratum corneum lipid matrix[11]. Compared to conventional liposomes, ethosomes offer superior deformability, allowing them to penetrate deeper into the skin, facilitating both topical and systemic drug delivery[12].

Ethosomes: Composition and Structure

Ethosomes consist of three primary components:

Phospholipids: Form the vesicle bilayer and provide biocompatibility.

Ethanol (20-45%): Enhances vesicle flexibility and disrupts skin lipids to facilitate drug penetration.

Water: Acts as a solvent and stabilizer for ethosomal vesicles[13].

This composition allows ethosomes to encapsulate hydrophilic, lipophilic, and amphiphilic drugs, making them versatile carriers for dermatological and transdermal applications[14].

This composition allows ethosomes to encapsulate a wide range of drugs, including hydrophilic, lipophilic, and amphiphilic molecules, making them versatile carriers for diverse therapeutic applications.[15]

Ethosomes enhance transdermal drug delivery through a dual mechanism:

1. Ethanol Effect: Ethanol increases skin permeability by disrupting intercellular lipid organization in the stratum corneum[16].

2. Flexible Vesicular System: The deformable ethosomes penetrate through the skin layers and deliver drugs into deeper tissues[17].

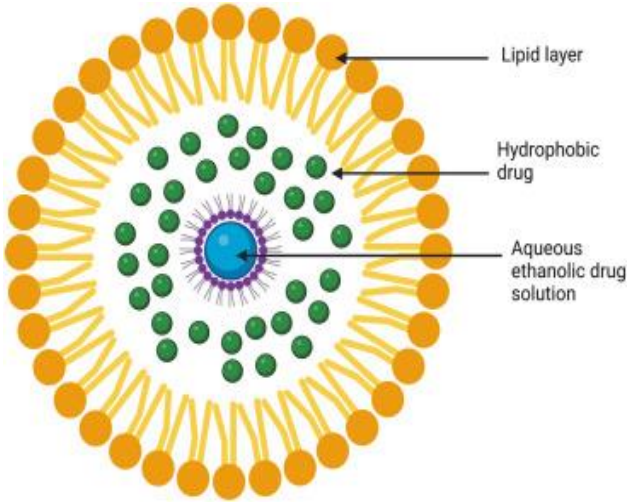

Figure 2: Structure of ethosomes[48]

Table 1: Different composition of ethosomes

Class	Example	Uses
Phospholipids	Soya phosphatidyl choline Egg phosphatidyl choline Dipalmityl phosphatidyl choline Distearyl phosphatidyl choline	Vesicles forming component[49]
Polyglycol	Propylene glycol Transcutol RTM	As a skin penetration enhancer[50]
Alcohol	Ethanol Isopropyl alcohol	For providing the softness for vesicle membrane As a penetration enhancer[51]
Cholesterol	Cholesterol	For providing the stability to vesicle membrane[49]
Dye	Rhodamine-123[53] Rhodamine red Fluorescene Isothiocynate (FITC)[54]	For characterization study[52]
Vehicle	Carbopol O934[55]	As a gel former[56]

Advantages of Ethosomes

Ethosomes offer several advantages over conventional drug delivery systems:

- **Enhanced Skin Permeation:** Ethanol facilitates drug penetration across the stratum corneum[18].
- **Sustained Drug Release:** Provides prolonged therapeutic effects, reducing dosing frequency[19].
- **Non-Invasive and Patient-Friendly:** Improves patient compliance compared to injections or oral medications[20].
- **Encapsulation of Both Hydrophilic and Lipophilic Drugs:** Increases versatility for different drug molecules[21].
- **High Encapsulation Efficiency:** Ethosomes can encapsulate drugs of varying solubilities, providing flexibility in formulation.
- **Improved Bioavailability:** By bypassing the hepatic first-pass metabolism, ethosomes enhance systemic drug bioavailability.
- **Controlled Drug Release:** Sustained drug release profiles can be achieved, improving therapeutic outcomes. [22]

Method of Preparation:

Ethosomal formulations can be prepared using various methods, including the cold method, hot method, classic mechanical dispersion method, and classic method. These techniques are simple, cost-effective, and adaptable for both laboratory-scale preparations and industrial production, making them a practical option for large-scale pharmaceutical manufacturing.

a) Cold Method

The cold method is the most widely used approach for preparing ethosomal formulations. In this method, phospholipids, the drug, and other lipid components are dissolved in ethanol in a covered vessel at room temperature while being stirred vigorously using a mixer. Propylene glycol or another polyol is added during the stirring process. The mixture is heated to 30°C in a water bath. Separately, water is heated to the same temperature and added to the mixture with continued stirring for 5 minutes. The size of the ethosomal vesicles can be reduced to the desired level using sonication or extrusion techniques. The final ethosomal formulation is stored under refrigeration to maintain stability.[23]

b) Hot Method

In the hot method, phospholipids are dispersed in water by heating in a water bath at 40°C until a colloidal solution is formed. Separately, ethanol and propylene glycol are mixed and heated to the same temperature. Once both mixtures reach 40°C, the organic phase is added to the aqueous phase. Depending on the hydrophilic or hydrophobic nature of the drug, it is dissolved in water or ethanol before being added. The size of the ethosomal vesicles can be adjusted using probe sonication or extrusion techniques[24].

c) Classic Mechanical Dispersion Method

In this method, soya phosphatidylcholine is dissolved in a mixture of chloroform and methanol (3:1 ratio) in a round-bottom flask. The organic solvents are removed using a rotary vacuum evaporator at a temperature above the lipid transition temperature, resulting in the formation of a thin lipid film on the walls of the flask. Residual solvents are further removed by leaving the flask under vacuum overnight. The lipid film is then

hydrated by adding a hydroethanolic mixture containing the drug at various concentrations, with the flask rotated at an appropriate temperature to facilitate the formation of ethosomes[25].

d) Classic Method

In the classic method, the phospholipid and drug are dissolved in ethanol and heated to 30°C ± 1°C in a water bath. Double-distilled water is added in a fine stream to the lipid mixture under constant stirring at 700 rpm in a closed vessel. The resulting vesicle suspension is homogenized by passing it through a polycarbonate membrane using a hand extruder for three cycles, resulting in a stable ethosomal formulation[26].

Mechanism of Action

The enhanced permeability of ethosomes can be attributed to their unique mechanism of action:

a. **Ethanol Effect:** Ethanol disrupts the lipid bilayer of the skin's stratum corneum, increasing its fluidity and permeability.

b. **Vesicle Deformability:** Ethosomes' flexible structure enables them to pass through narrow intercellular spaces without breaking.

c. **Sustained Release:** The drug is gradually released from the vesicles, maintaining Mechanism of Drug Delivery Through Ethosomes[27].

Although the precise mechanism of drug delivery via ethosomes remains speculative, their enhanced efficacy is largely attributed to the interactions between ethosomes and the lipids within the skin. At physiological temperatures, the lipid multilayers of the stratum corneum are densely packed, presenting a significant barrier to permeation. Ethosomes overcome this barrier through two primary mechanisms: the "ethanol effect" and the "ethosome effect."[28]

a. The Ethanol Effect

Ethosomes contain a high concentration of ethanol, which plays a crucial role in disrupting the tightly packed lipid bilayers of the skin. Ethanol, when integrated into the vesicle membrane, enhances the fluidity and deformability of the ethosomes, enabling them to penetrate the stratum corneum more effectively.[29]

Ethanol interacts with the polar head groups of the lipids in the stratum corneum, reducing the rigidity of the lipid structure and increasing its fluidity. This interaction disrupts the skin's barrier function, creating small openings in the lipid matrix that ethosomes can exploit to deliver drugs into deeper skin layers. The high ethanol content also imparts a less tightly packed lipid membrane in the ethosomes themselves, maintaining stability while allowing for efficient penetration through the skin[30].

b. The Ethosome Effect

Beyond the ethanol-induced disruption, the ethosomes themselves actively participate in enhancing drug delivery. The malleable and interdigitated vesicles can fuse with the skin lipids, creating new pathways for drug permeation. This process facilitates the delivery of the encapsulated drug to deeper skin layers and, potentially, into systemic circulation.[31]

Ethosomes' flexible vesicle structure allows them to navigate the disrupted stratum corneum, releasing their drug payload efficiently. Drugs encapsulated in ethosomes exhibit improved attachment to the skin due to the positive zeta potential imparted by the vesicles[32]. This enhances the retention of the drug at the target site, promoting sustained delivery and improved therapeutic outcomes.[33]

Applications of Ethosomes

Ethosomes have been successfully employed in a variety of therapeutic areas:

a. Dermatological Disorders:

- **Psoriasis and Eczema:** Ethosomes enhance the delivery of corticosteroids and immunomodulators, providing rapid relief and reducing systemic side effects.
- **Acne Treatment:** Ethosomal formulations of antibiotics like clindamycin improve skin penetration and reduce bacterial resistance.[34]

b. Fungal Infections:

- **Clotrimazole and Ketoconazole:** Ethosomal gels show superior efficacy in treating tinea and candidiasis by delivering antifungal agents to deeper skin layers.
- **Terbinafine:** Enhanced bioavailability and reduced recurrence rates have been observed with ethosomal delivery.[35]

c. Transdermal Drug Delivery:

- **Hormone Replacement Therapy:** Ethosomes effectively deliver estradiol and testosterone, ensuring steady plasma levels.
- **Pain Management:** Drugs like diclofenac and lidocaine exhibit prolonged analgesic effects when delivered via ethosomes.[36]

d. Vaccination:

- Ethosomes are being explored as carriers for transdermal vaccines, enhancing immunogenicity and patient compliance.

e. Cosmeceuticals:

- Ethosomes are increasingly used in anti-aging, skin whitening, and moisturizing formulations, leveraging their ability to deliver active ingredients effectively.[37]

Limitations and Challenges

Despite their numerous advantages, ethosomes face certain limitations:

Stability Issues: Ethosomal formulations are prone to aggregation and leakage during storage.[38]

High Ethanol Content: May cause irritation or dryness in sensitive skin types.

Manufacturing Challenges: Scaling up production while maintaining uniformity is complex.[39]

Cost of Production: The use of high-purity phospholipids and ethanol increases manufacturing costs.

Recent Advances and Applications

Ethosomes have demonstrated promising results in treating various conditions, including:

Fungal infections: Terbinafine hydrochloride ethosomal gels have shown improved antifungal activity in onychomycosis and athlete's foot[40,41].

Dermatological disorders: Kaempferol-loaded ethosomes for antioxidant and anti-inflammatory effects[42].

Systemic drug delivery: Naftifine-loaded transethosomes enhance drug deposition into deeper skin layers[43].

Future Directions

Recent advancements in nano-formulations and quality-by-design approaches have improved the efficiency and stability of ethosomes[44]. Ongoing research focuses on targeted delivery, combinational therapies, and smart ethosomal systems, ensuring optimized therapeutic outcomes with minimal side effects.

To maximize the potential of ethosomes, future research should focus on:

Optimization of Formulations: Exploring novel excipients and stabilizers to enhance vesicle stability.[45]

Green Synthesis Methods: Developing eco-friendly processes to reduce environmental impact.[46]

Advanced Delivery Systems: Combining ethosomes with other nanocarriers like nanoparticles and micelles for synergistic effects.

Clinical Studies: Conducting large-scale trials to establish efficacy and safety across diverse patient populations.[47]

Conclusion

Ethosomes represent a promising and innovative approach in the field of transdermal drug delivery. Their unique composition, including phospholipids, ethanol, and water, enables the delivery of both hydrophilic and lipophilic drugs through the skin, offering significant advantages over traditional drug delivery systems. These include enhanced skin penetration, improved bioavailability by bypassing first-pass metabolism, high encapsulation efficiency, non-invasive delivery, and controlled drug release. Ethosomes hold great potential for treating a wide range of conditions, from dermatological disorders and fungal infections to systemic diseases and cosmeceuticals.

Despite their numerous benefits, there are still challenges to overcome, such as stability issues, high ethanol content, and manufacturing complexities. Future research should focus on optimizing formulations, improving stability, and exploring greener synthesis methods to make ethosomes a viable option for large-scale production. Furthermore, clinical studies are necessary to validate their safety and efficacy across diverse patient populations.

With continuous advancements and research, ethosomes have the potential to revolutionize drug delivery, offering more effective, patient-friendly, and cost-efficient treatments for a variety of medical conditions.

Acknowledgements: We thank Dr. Amandeep Singh sir for his advice and immense insights while writing this review article.

Authors contribution: All the authors have equal contribution.

Funding source: There is no funding source.

Conflict of interest: The authors reported no conflict of interest.

Ethical Approval: Not applicable

References

1. Ali S, Shabbir M, Shahid N. The structure of skin and transdermal drug delivery system-a review. Research journal of pharmacy and technology. 2015;8(2):103-9. https://doi.org/10.5958/0974-360X.2015.00019.0

2. Puri V, Froelich A, Shah P, Pringle S, Chen K, Michniak-Kohn B. Quality by design guided development of polymeric nanospheres of terbinafine hydrochloride for topical treatment of onychomycosis using a nano-gel formulation. Pharmaceutics. 2022 12;14(10):2170. https://doi.org/10.3390/pharmaceutics14102170 PMid:36297605 PMCid:PMC9611585

3. Guzel I, Gungor S, Erdal M. Improved skin penetration and deposition of naftifine from transethosomes and transethosomal gel formulations. Farmacia. 2022;70(3). https://doi.org/10.31925/farmacia.2022.3.18

4. Hajare A, Dol H, Patil K. Design and development of terbinafine hydrochloride ethosomal gel for enhancement of transdermal delivery: in vitro, in vivo, molecular docking, and stability study. J Drug Deliv Sci Technol. 2021 Feb 1;61:102280. https://doi.org/10.1016/j.jddst.2020.102280

5. Wokovich AM, Prodduturi S, Doub WH, Hussain AS, Buhse LF. Transdermal drug delivery system (TDDS) adhesion as a critical safety, efficacy and quality attribute. European Journal of Pharmaceutics and Biopharmaceutics. 2006 Aug 1;64(1):1-8. https://doi.org/10.1016/j.ejpb.2006.03.009 PMid:16797171

6. Bala P, Jathar S, Kale S, Pal K. Transdermal drug delivery system (TDDS)-a multifaceted approach for drug delivery. J Pharm Res. 2014 Dec;8(12):1805-35.

7. Arunachalam A, Karthikeyan M, Kumar DV, Prathap M, Sethuraman S, Ashutoshkumar S, Manidipa S. Transdermal drug delivery system: a review. Journal of Current Pharma Research. 2010 Oct 1;1(1):70. https://doi.org/10.33786/JCPR.2010.v01i01.015

8. Kumar N, Dubey A, Mishra A, Tiwari P. Ethosomes: A Novel Approach in Transdermal Drug Delivery System. International journal of pharmacy & life sciences. 2020 May 1;11(5).

9. Bhosale SS, Avachat AM. Design and development of ethosomal transdermal drug delivery system of valsartan with preclinical assessment in Wistar albino rats. Journal of liposome research. 2013 Jun 1;23(2):119-25. https://doi.org/10.3109/08982104.2012.753457 PMid:23324030

10. Patrekar PV, Inamdar SJ, Mali SS, Mujib MT, Ahir AA, Hosmani AH. Ethosomes as novel drug delivery system: A review. The pharma innovation. 2015 Nov 1;4(9, Part A):10.

11. Raghav SS, Kumar B, Sethiya NK, Pahwa S. Development and optimization of kaempferol loaded ethosomes using Box-Behnken statistical design: In vitro and ex-vivo assessments. Journal of Biomedical Materials Research Part B: Applied Biomaterials. 2024 Mar;112(3):e35394. https://doi.org/10.1002/jbm.b.35394 PMid:38433621

12. Mohanty, D., Mounika, A., Bakshi, V., Haque, M.A. and Sahoo, C.K., 2018. Ethosomes: a novel approach for transdermal drug delivery. Int. J. ChemTech Res, 11(8), pp.219-226. https://doi.org/10.20902/IJCTR.2018.110826

13. Maxwell, A. and Priya, S., 2024. Nanosized ethosomes-a promising vesicular drug carrier for transdermal drug delivery. Research Journal of pharmacy and technology, 12(2), pp.876-880. https://doi.org/10.5958/0974-360X.2019.00150.1

14. Priya S, Shridhar P, Shekhara K, Shenthar S, Kudva SK. Tolnaftate-Loaded Ethosomal Gel for Topical Delivery: Formulation and In Vitro Evaluation. Journal of Health and Allied Sciences NU. 2024 Jun 18. https://doi.org/10.1055/s-0044-1787293

15. Divya A, Ujjwal N. Ethosomes A review. International Journal of Pharmaceutical and Medicinal Research. 2016;4(4).

16. Bajwa M, Tabassam N, Hameed H, Irfan A, Zaman M, Khan MA, Shazly GA, Mehboob T, Riaz T, Jardan YA. Thermo-responsive sol-gel-based nano-carriers containing terbinafine HCl: formulation, in vitro and ex vivo characterization, and antifungal activity. Gels. 2023 Oct 20;9(10):830. https://doi.org/10.3390/gels9100830 PMid:37888403 PMCid:PMC10606830

17. Manjanna KM, Krishna GS, Keerthana PH. Studies on Development and Evaluation of Topical Ethosomal Gel Embedded Antifungal Agent for Athlete's Foot. RGUHS Journal of Pharmaceutical Sciences. 2023;13(2). https://doi.org/10.26463/rjps.13_2_3

18. Maurya SD, Prajapati S, Gupta A, Saxena G, Dhakar RC, Formulation Development and Evaluation of Ethosome of Stavudine, Indian J.Pharm. Educ. Res. 2010;44(1)

19. Guzel I, Gungor S, Erdal M. Improved skin penetration and deposition of naftifine from transethosomes and transethosomal gel formulations. Farmacia. 2022;70(3). https://doi.org/10.31925/farmacia.2022.3.18

20. Hajare A, Dol H, Patil K. Design and development of terbinafine hydrochloride ethosomal gel for enhancement of transdermal delivery: In vitro, in vivo, molecular docking, and stability study. Journal of drug delivery science and technology. 2021 Feb 1;61:102280. https://doi.org/10.1016/j.jddst.2020.102280

21. Zhan B, Wang J, Li H, Xiao K, Fang X, Shi Y, et al. Ethosomes: A promising drug delivery platform for transdermal application. Chemistry [Internet]. 2024 [cited 2025 Feb 4];6(5):993-1019. https://doi.org/10.3390/chemistry6050058

22. Aggarwal D, Nautiyal U. Ethosomes: A review. Int J pharm med res. 2016 Aug 10;4(4):354-63.

23. Bahe VG, Sutarkar AP, Khan SA. Ethosomes: A potential carrier for enhancing transdermal drug delivery.

24. Chauhan AS, Pandey K, Girijesh AJ, Dubey B, Jain P. A review on Ethosome: a novel drug delivery system for topical fungal disease. The pharma innovation journal. 2018;7(12):355-62.

25. Kumar GA, Wadood SA, Maurya SD, Ramchand D, Interpenetrating polymeric network hydrogel for stomach-specific drug delivery of clarithromycin: Preparation and evaluation, Asian Journal of Pharmaceutics-October-December 2010; 179-184. https://doi.org/10.4103/0973-8398.76738

26. Chauhan N, Vasava P, Khan SL, Siddiqui FA, Islam F, Chopra H, Emran TB. Ethosomes: A novel drug carrier. Annals of Medicine and Surgery. 2022 Oct 1;82. https://doi.org/10.1016/j.amsu.2022.104595

27. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. Journal of advanced pharmaceutical technology & research. 2010 Jul 1;1(3):274-82 https://doi.org/10.4103/0110-5558.72415 PMid:22247858 PMCid:PMC3255417

28. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes-novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. Journal of controlled release. 2000 Apr 3;65(3):403-18. https://doi.org/10.1016/S0168-3659(99)00222-9 PMid:10699298

29. Satyam G, Shivani S, Garima G. Ethosomes: A novel tool for drug delivery through the skin. J Pharm Res. 2010 Apr;3(4):688-91.

30. Jain S, Tiwary AK, Sapra B, Jain NK. Formulation and evaluation of ethosomes for transdermal delivery of lamivudine. Aaps Pharmscitech. 2007 Oct;8:249-57. https://doi.org/10.1208/pt0804111 PMid:18181532 PMCid:PMC2750697

31. Ainbinder D, Paolino D, Fresia M, Touitou E. Drug delivery applications with ethosomes. Journal of biomedical nanotechnology. 2010 Oct 1;6(5):558. https://doi.org/10.1166/jbn.2010.1152 PMid:21329048

32. Garg V, Singh H, Bimbrawh S, Kumar Singh S, Gulati M, Vaidya Y, Kaur P. Ethosomes and transfersomes: Principles, perspectives and practices. Current drug delivery. 2017 Aug 1;14(5):613-33. https://doi.org/10.2174/1567201813666160520114436

33. Nainwal N, Jawla S, Singh R, Saharan VA. Transdermal applications of ethosomes-a detailed review. Journal of liposome research. 2019 Apr 3;29(2):103-13. https://doi.org/10.1080/08982104.2018.1517160 PMid:30156120

34. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. Journal of advanced pharmaceutical technology & research. 2010 Jul 1;1(3):274-82. https://doi.org/10.4103/0110-5558.72415 PMid:22247858 PMCid:PMC3255417

35. Paiva-Santos AC, Silva AL, Guerra C, Peixoto D, Pereira-Silva M, Zeinali M, Mascarenhas-Melo F, Castro R, Veiga F. Ethosomes as nanocarriers for the development of skin delivery formulations. Pharmaceutical research. 2021 Jun;38(6):947-70. https://doi.org/10.1007/s11095-021-03053-5 PMid:34036520

36. Volkwyn M. In vitro biocompatibility of transferosomes, ethosomes and transethosomes (Doctoral dissertation, North-West University (South-Africa)).

37. Nainwal N, Jawla S, Singh R, Saharan VA. Transdermal applications of ethosomes-a detailed review. Journal of liposome research. 2019 Apr 3;29(2):103-13. https://doi.org/10.1080/08982104.2018.1517160 PMid:30156120

38. Maurya SD, Aggarwal S, Tilak VK, Dhakar RC, Singh A, Maurya G, Enhanced Transdermal Delivery of Indinavir Sulfate via Transfersomes, Pharmacie Globale (IJCP) 2010;1(06):1-7

39. Abdulbaqi IM, Darwis Y, Khan NA, Assi RA, Khan AA. Ethosomal nanocarriers: the impact of constituents and formulation techniques on ethosomal properties, in vivo studies, and clinical trials. International journal of nanomedicine. 2016 May 25:2279-304. https://doi.org/10.2147/IJN.S105016 PMid:27307730 PMCid:PMC4887071

40. Ita K. Current Status of Ethosomes and Elastic Liposomes in Dermal and Transdermal Drug Delivery. Curr Pharm Des. 2016;22(33):5120-5126. doi: 10.2174/1381612822666160511150228. PMID: 27165164. https://doi.org/10.2174/1381612822666160511150228 PMid:27165164

41. Musielak, E.; Krajka-Ku'zniak, V. Liposomes andEthosomes: Comparative Potential inEnhancing Skin Permeability for Therapeutic and Cosmetic Applications. Cosmetics 2024;11:191. https://doi.org/10.3390/cosmetics11060191

42. Kang, Y.; Zhang, S.; Wang, G.; Yan, Z.; Wu, G.; Tang, L.; Wang, W. Nanocarrier-Based Transdermal Drug Delivery Systems for Dermatological Therapy. Pharmaceutics 2024, 16, 1384. https://doi.org/10.3390/pharmaceutics16111384 PMid:39598508 PMCid:PMC11597219

43. Paiva-Santos AC, Silva AL, Guerra C, Peixoto D, Pereira-Silva M, Zeinali M, Mascarenhas-Melo F, Castro R, Veiga F. Ethosomes as Nanocarriers for the Development of Skin Delivery Formulations. Pharm Res. 2021 Jun;38(6):947-970. https://doi.org/10.1007/s11095-021-03053-5 PMid:34036520

44. Sivadasan, D.; Madkhali, O.A. The Design Features, Quality by Design Approach, Characterization, Therapeutic Applications, and Clinical Considerations of Transdermal Drug Delivery Systems-A Comprehensive Review. Pharmaceuticals 2024, 17, 1346. https://doi.org/10.3390/ph17101346 PMid:39458987 PMCid:PMC11510585

45. Monisha C, Ganesh GN, Mythili L, Radhakrishnan K. A review on ethosomes for transdermal application. Research journal of pharmacy and technology. 2019;12(7):3133-43. https://doi.org/10.5958/0974-360X.2019.00529.8

46. Roge AB, Sakhare RS, Bakal RL, Channawar MA, Bakde BV, Gawande SR, Chandewar AV. Ethosomes: Novel approach in transdermal drug delivery system. Research Journal of Pharmaceutical Dosage Forms and Technology. 2010;2(1):23-7.

47. Paiva-Santos AC, Silva AL, Guerra C, Peixoto D, Pereira-Silva M, Zeinali M, Mascarenhas-Melo F, Castro R, Veiga F. Ethosomes as nanocarriers for the development of skin delivery formulations. Pharmaceutical research. 2021;38(6):947-970. https://doi.org/10.1007/s11095-021-03053-5 PMid:34036520

48. Livia Nascimento Grossi, Wilson Rodrigues Braz, Natália Prado da Silva, Estael Luzia Coelho Cruz Cazarim, Miguel Gontijo Siqueira Palmieri, Guilherme Diniz Tavares, Frederico Pittella, Ethosomes as delivery system for treatment of melanoma: a mini-review, Oncologie, Volume 25, Issue 5,2023,Pages 455-459,ISSN 1765-2839 https://doi.org/10.1515/oncologie-2023-0177

49. Bangham, A. D., & Horne, R. W. "Negative staining of phospholipids and their structural modification by surface-active agents as observed in the electron microscope." Journal of Molecular Biology, 1964;8(5):660-668. https://doi.org/10.1016/S0022-2836(64)80115-7 PMid:14187392

50. Barry, B. W. "Mode of action of penetration enhancers in human skin." Journal of Controlled Release, 1987;6(1):85-97. https://doi.org/10.1016/0168-3659(87)90066-6

51. Williams, A. C., & Barry, B. W. "Penetration enhancers." Advanced Drug Delivery Reviews, 2012;64:128-137. https://doi.org/10.1016/j.addr.2012.09.032

52. Torchilin, V. P. "Recent advances with liposomes as pharmaceutical carriers." Nature Reviews Drug Discovery, 2005;4:145-160. https://doi.org/10.1038/nrd1632 PMid:15688077

53. Sahoo, S. K., & Labhasetwar, V. "Nanotech approaches to drug delivery and imaging." Drug Discovery Today, 2003;8(24):1112-1120. https://doi.org/10.1016/S1359-6446(03)02903-9 PMid:14678737

54. Gupta, G. D., & Gaud, R. S. "Release rate of nimesulide from different gellants." Indian Journal of Pharmaceutical Sciences, 2005;67(2):234-236.

55. Rathod, S., & Mehta, D. "Carbopol and its applications: A review." International Journal of Current Pharmaceutical Research, 2015;7(2):29-34.