ISSN: 2456-4508

JPRE

Review Article

SGVU Journal of Pharmaceutical Research & Education

Journal homepage: http://www.gyanvihar.org/researchjournals/

Ethosomes and Pharmacosomes: A Comparative Study of Drug Delivery

Priyanka Maurya [1*], Dr. Tapasvi Gupta [1], Dr. Prashant Kumar Dhakad[1], Dr. Ritu M Gilhotra[1]

[1]Gyan Vihar School of Pharmacy, Suresh Gyan Vihar University, Jaipur, Rajasthan, India.

*Corresponding Author: Priyanka Maurya

E-mail: priyankamauryapharma@gmail.com

ABSTRACT

The field of drug delivery has witnessed significant advancements with the development of novel vesicular systems, among which ethosomes and pharmacosomes have garnered considerable attention. Ethosomes are lipid-based vesicular carriers comprising high concentrations of ethanol, facilitating enhanced drug permeation through the skin. On the other hand, pharmacosomes are self-assembling systems formed by the complexation of drugs with lipids or surfactants, exhibiting improved solubility and stability profiles.

This comparative analysis aims to evaluate the key characteristics, advantages, and limitations of ethosomes and pharmacosomes in drug delivery. Ethosomes, owing to their high ethanol content, possess superior skin permeation capabilities, making them suitable for transdermal and topical delivery applications. Conversely, pharmacosomes demonstrate versatility in accommodating a wide range of hydrophobic and hydrophilic drugs, addressing solubility challenges associated with conventional drug delivery systems. Furthermore, this analysis examines the influence of formulation parameters, such as lipid composition, drug-to-lipid ratio, and preparation methods, on the performance of ethosomes and pharmacosomes. Additionally, factors such as stability, biocompatibility, and scalability are discussed to provide insights into the translational potential of these vesicular systems for clinical applications.

Overall, this comparative analysis underscores the importance of understanding the distinct attributes of ethosomes and pharmacosomes to tailor their formulations for specific therapeutic objectives. By elucidating their mechanisms of action and performance characteristics, this study contributes to the rational design and optimization of vesicular-based drug delivery systems, ultimately enhancing therapeutic efficacy and patient outcomes.

Key Words: Ethosomes, Pharmacosomes, Mechanism, Additives, Vesicular Formulation

INTRODUCTION: Conventional drug delivery systems often face challenges related to poor bioavailability, limited tissue penetration, and systemic toxicity. To address these challenges, researchers have developed innovative drug delivery systems that can improve the pharmacokinetic and pharmacodynamic properties of therapeutic agents. Ethosomes and pharmacosomes represent two such systems that offer unique advantages over traditional formulations.[1]

ETHOSOMES: Ethosomes are lipid-based vesicular carriers that contain high concentrations of ethanol (typically 20-45%) along with phospholipids and water. The presence of ethanol imparts fluidity to the lipid bilayers, enhancing the penetration of drugs through the skin or mucous membranes. Ethosomes can encapsulate both hydrophilic and lipophilic drugs, making them versatile delivery vehicles for a wide range of pharmaceutical compounds.[2]

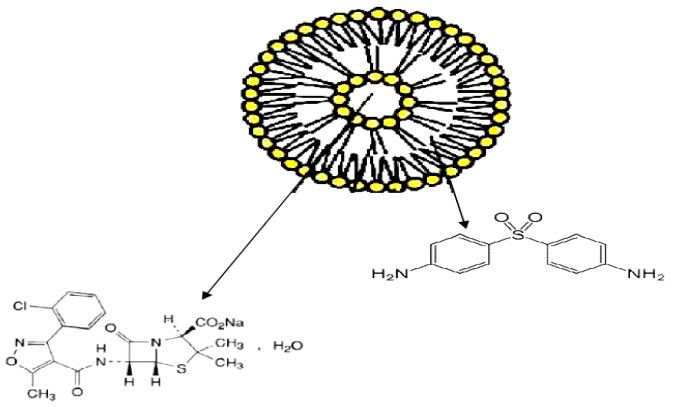

Figure 1: Structure of ethosome

MECHANISM OF ACTION: Ethosomes exert their effects through several mechanisms, including penetration enhancement, hydration, and disruption of the stratum corneum.

Ethanol increases the fluidity of the lipid bilayers in the stratum corneum, facilitating the diffusion of drugs into the underlying layers of the skin. Additionally, the hydration properties of ethosomal formulations help to maintain skin hydration, which can further promote drug permeation. Moreover, the presence of ethanol can disrupt the intercellular lipid matrix, allowing for deeper penetration of drugs into the skin.[3-5]

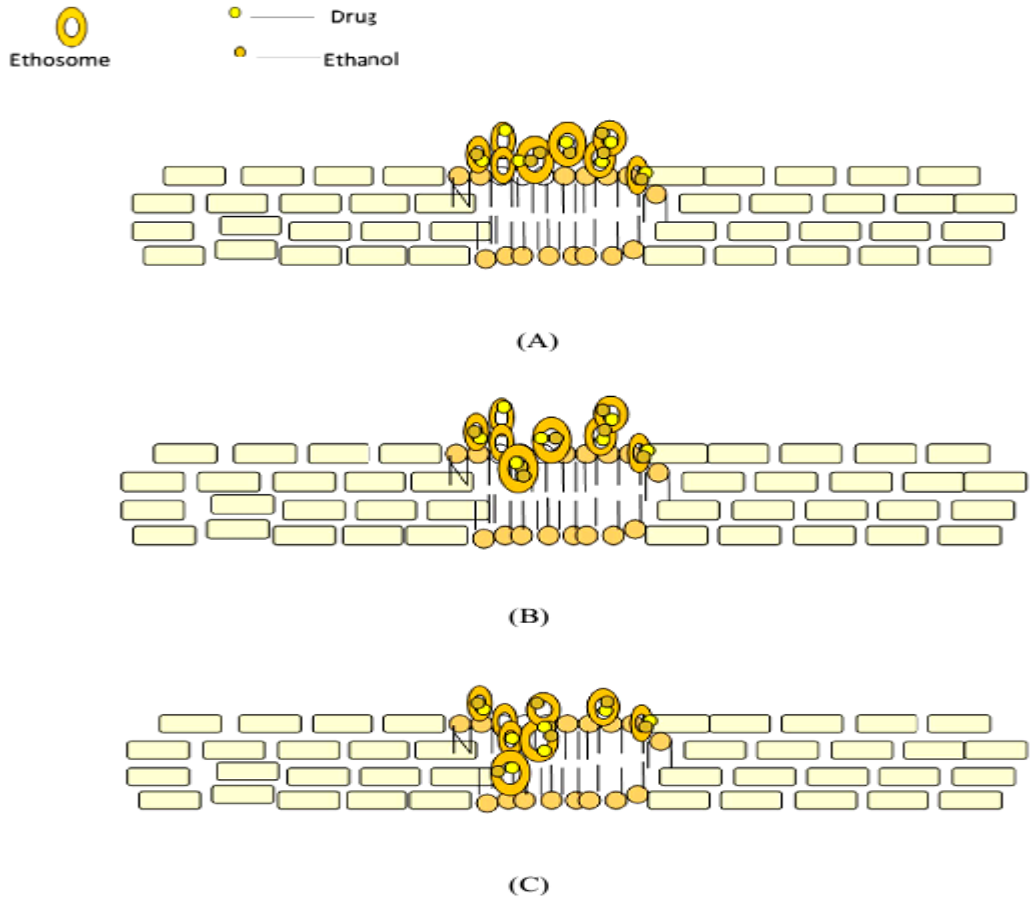

Figure 2: Release mechanism of drug from ethosomes (A) release of ethanol from the ethosomes (solid circles) and fluidizes the skin lipids to increases skin permeation, (B) release of lipids (open circles) from ethosomes and interaction of ethosomes with skin lipid bilayer, (C) ethosomes squeeze through the skin lipid bilayer. Drug molecules are shown as asterisks inside the vesicles

ADVANTAGES OF ETHOSOMES:

1. Enhanced drug penetration: Ethosomes can improve the penetration of drugs through the skin or mucous membranes, leading to higher bioavailability.

2. Versatility: Ethosomes can encapsulate both hydrophilic and lipophilic drugs, making them suitable for various therapeutic applications.
3. Stability: Ethosomes exhibit good stability under ambient conditions, allowing for long-term storage without significant degradation.
4. Noninvasive administration: Ethosomal formulations can be administered topically or transdermally, offering a convenient and noninvasive route of drug delivery.[6]

LIMITATIONS OF ETHOSOMES:

1. Ethanol content: The high ethanol content in ethosomal formulations may cause skin irritation or sensitivity in some individuals.
2. Drug compatibility: Not all drugs are compatible with ethosomal formulations, and compatibility testing is necessary to ensure efficacy and stability.
3. Cost: The production of ethosomal formulations may involve additional costs compared to conventional formulations, primarily due to the use of specialized ingredients.[7]

APPLICATIONS OF ETHOSOMES:

Ethosomes have found applications in various therapeutic areas, including dermatology, cosmeceuticals, and transdermal drug delivery.

They have been used to deliver drugs for the treatment of skin disorders such as psoriasis, acne, and fungal infections.

Additionally, ethosomal formulations have been explored for the delivery of anti-inflammatory agents, antioxidants, and vitamins for skincare purposes.[8]

ADDITIVES USED IN ETHOSOMES:[9]

Table 1: Additives used in Ethosomes

Additive	**Function**
Ethanol	Enhances permeation through skin
Phospholipids	Forms vesicular structure, improves stability
Surfactants	Enhances vesicle formation and stability
Cholesterol	Modulates membrane fluidity

Additive	Function
Penetration enhancers	Augments skin permeation
Antioxidants	Protects formulation from oxidation
Preservatives	Prevents microbial growth
Hyaluronic acid	Provides hydration to skin
Antimicrobial agents	Ensures sterility of formulation
Propylene glycol	Enhances solubility and permeation of drugs

These additives play crucial roles in formulating ethosomes, contributing to their stability, permeation enhancement, and overall efficacy in drug delivery applications.

METHOD OF PREPARATION OF ETHOSOMES

Ethosomal formulation may be prepared by hot or cold method as described below. Both the methods are convenient, do not require any sophisticated equipment and are easy to scale up at industrial level. [10-12]

COLD METHOD:

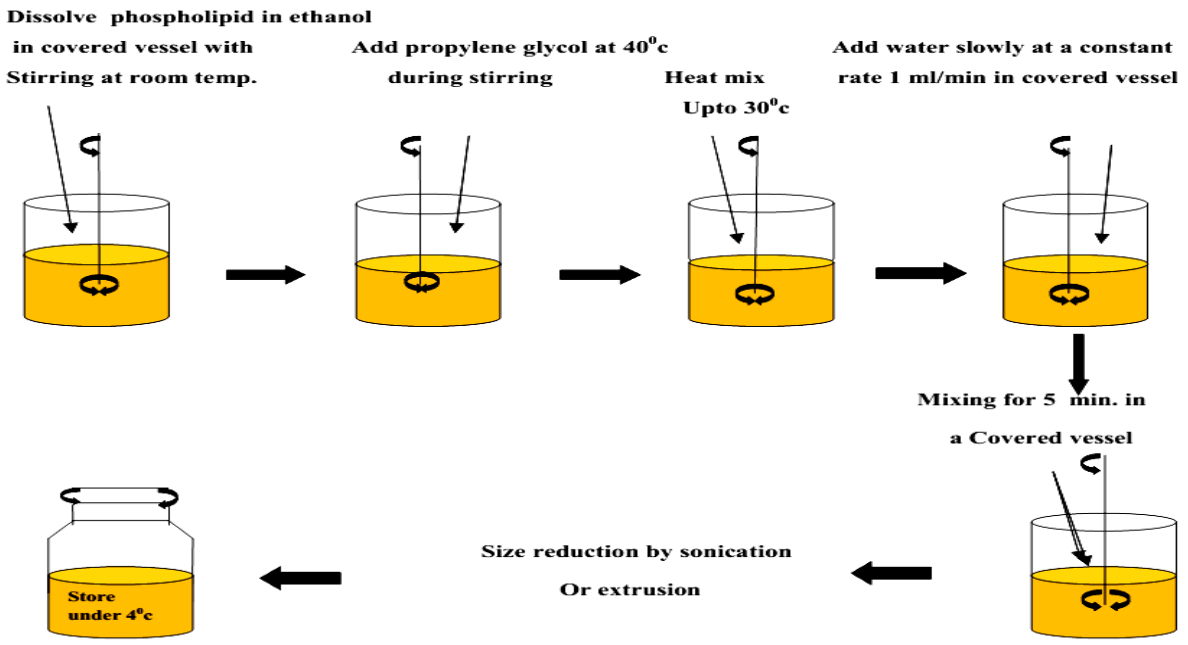

Figure 3: Preparation of ethosome by cold method

HOT METHOD:

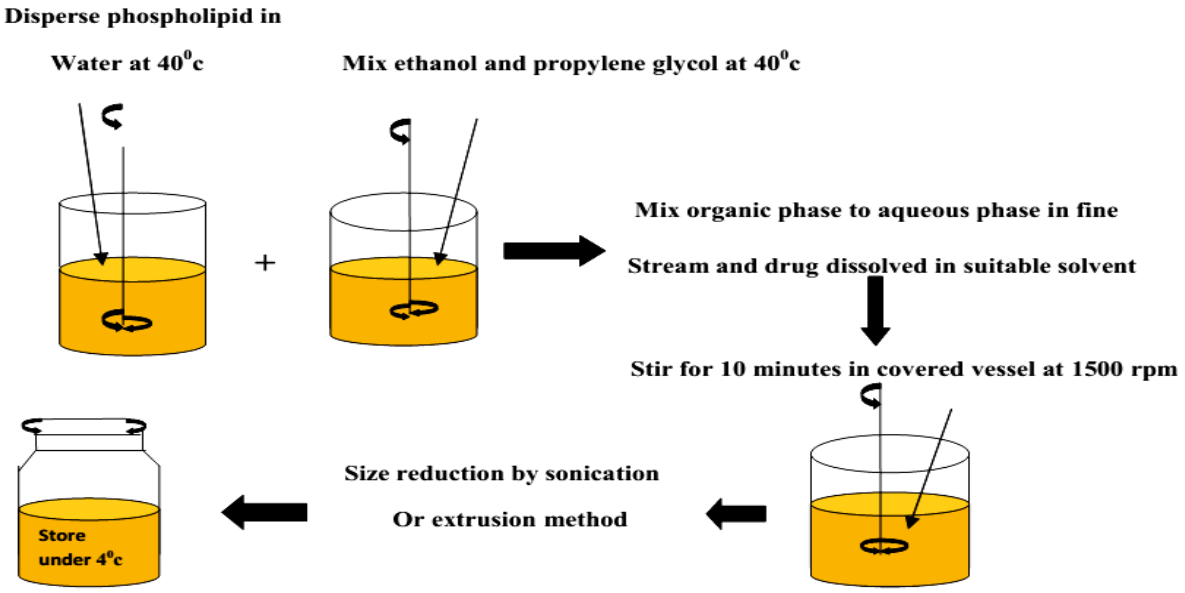

Figure 4: Preparation of ethosome by Hot method

PHARMACOSOMES

DEFINITION: Pharmacosomes are lipid-based nanoparticles that consist of a phospholipid bilayer encapsulating drug molecules. Unlike traditional liposomes, pharmacosomes contain drugs covalently attached to the lipid bilayer or encapsulated within the bilayer structure. This unique design provides several advantages, including improved drug stability, controlled release kinetics, and targeted delivery to specific tissues or cells.[13]

MECHANISM OF ACTION: Pharmacosomes deliver drugs through a combination of passive and active targeting mechanisms. The phospholipid bilayer of pharmacosomes can shield encapsulated drugs from enzymatic degradation, enhancing their stability in biological fluids. Moreover, the surface of pharmacosomes can be modified with targeting ligands such as antibodies or peptides, allowing for specific binding to target cells or tissues. Once bound to the target, pharmacosomes can release their payload either through passive diffusion or active mechanisms such as receptor-mediated endocytosis.[13,14]

ADVANTAGES OF PHARMACOSOMES:

1. Enhanced drug stability: Pharmacosomes protect encapsulated drugs from degradation in biological fluids, improving their stability and shelf life.
2. Controlled release: The lipid bilayer structure of pharmacosomes enables controlled release of drugs, leading to sustained therapeutic effects.
3. Targeted delivery: Pharmacosomes can be surface-modified to target specific cells or tissues, minimizing off-target effects and enhancing therapeutic efficacy.
4. Biocompatibility: Pharmacosomes are biocompatible and biodegradable, minimizing the risk of adverse reactions or toxicity.[15]

LIMITATIONS OF PHARMACOSOMES:

1. Complexity of formulation: The preparation of pharmacosomes can be more complex compared to conventional liposomal formulations, requiring specialized equipment and expertise.
2. Cost: The production of pharmacosomes may involve higher costs due to the use of sophisticated techniques and materials.
3. Immunogenicity: Surface modifications of pharmacosomes for targeted delivery may increase their immunogenicity, potentially eliciting an immune response in some individuals.[16]

APPLICATIONS OF PHARMACOSOMES: Pharmacosomes have diverse applications in drug delivery, including cancer therapy, gene delivery, and vaccine development. In oncology, pharmacosomes can deliver chemotherapeutic agents to tumor tissues while minimizing systemic toxicity. Moreover, pharmacosomes have been investigated for the delivery of nucleic acid-based therapeutics such as siRNA and mRNA for gene silencing or gene expression modulation. Additionally, pharmacosomes hold promise as carriers for vaccine antigens, enhancing immune responses and vaccine efficacy.[17]

ADDITIVES OF PHARMACOSOMES:[18]

Table 2: Additives of Pharmacosomes

Additive	**Function**
Phospholipids	Forms vesicular structure, stabilizes drug complexation
Surfactants	Aids in self-assembly of pharmacosomes
Chelating agents	Enhances drug encapsulation efficiency

Additive	Function
Solubilizers	Improves drug solubility in lipid bilayers
Co-solvents	Facilitates drug incorporation into lipid matrix
Stabilizers	Maintains pharmacosome integrity during storage
Cholesterol	Modulates pharmacosome membrane properties
pH adjusters	Optimizes drug release kinetics
Antioxidants	Prevents oxidation of lipid components
Cryoprotectants	Protects pharmacosomes during freeze-drying process
Ion-pairing agents	Enhances drug loading efficiency

These additives play crucial roles in formulating pharmacosomes, contributing to their stability, drug encapsulation efficiency, and overall performance in drug delivery applications.

METHOD OF PREPARATION OF PHARMACOSOMES:[19]

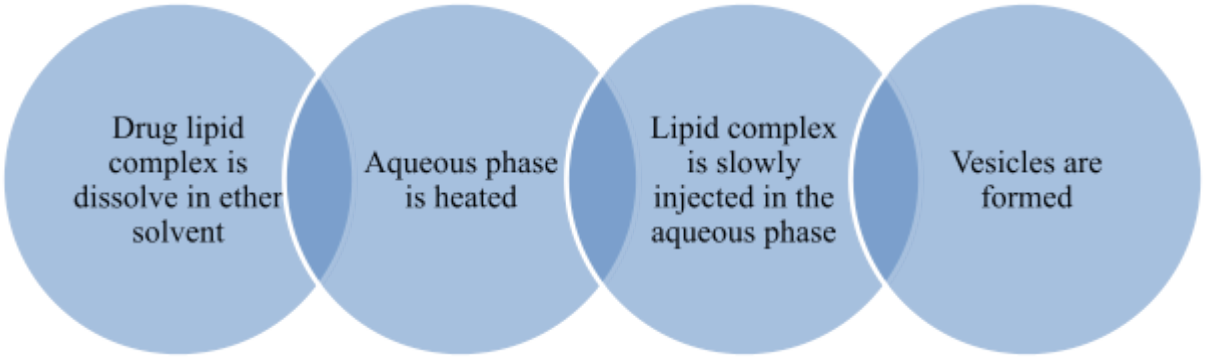

Figure 5: Method of preparation of Pharmacosomes

DIFFERENCE BETWEEN THESE VESICLE: Ethosomes and pharmacosomes are specialized vesicular systems used in pharmaceutical and cosmetic formulations. They differ from other vesicles like liposomes and pharmacosomes in several aspects. [20-22]

COMPOSITION: Ethosomes contain high concentrations of ethanol (usually between 20-45%), which helps in increasing the fluidity and flexibility of the lipid bilayers. On the

other hand, pharmacosomes are vesicular systems where drugs are covalently bound to phospholipids. This covalent bonding alters the pharmacokinetics and pharmacodynamics of the drug.

ENHANCED PENETRATION: Ethosomes have the ability to penetrate the skin more effectively compared to conventional liposomes due to the presence of ethanol. Ethanol disrupts the lipid matrix of the stratum corneum, the outermost layer of the skin, thereby enhancing drug permeation. Pharmacosomes, by virtue of their covalent attachment to drugs, also offer improved penetration and sustained release characteristics.

SIZE AND STABILITY: Ethosomes and pharmacosomes typically have smaller vesicle sizes compared to conventional liposomes, which can enhance their stability and penetration ability. The smaller size facilitates deeper penetration into the skin layers.

APPLICATIONS: Ethosomes are primarily used in transdermal drug delivery systems to improve the delivery of drugs across the skin barrier. They are particularly useful for delivering drugs that have poor skin permeability. Pharmacosomes, on the other hand, are used for targeted drug delivery and controlled release applications, especially for drugs that undergo rapid metabolism or have low bioavailability.

FLEXIBILITY: The presence of ethanol in ethosomes imparts flexibility to the vesicular membrane, allowing them to squeeze through the pores of the skin and facilitating deeper penetration. This flexibility is not typically found in conventional liposomes or niosomes.

Overall, ethosomes and pharmacosomes offer advantages over conventional vesicular systems in terms of enhanced penetration, stability, and targeted drug delivery, making them valuable tools in pharmaceutical and cosmetic formulations.

Table 3: Here's a table summarizing some research articles related to ethosomes and pharmacosomes [14-22]

Research Article Title	Authors	Journal	Year
"Ethosomes: A Novel Drug Delivery System"	Touitou E, Dayan N, Bergelson L	Journal of Drug Targeting	2000
"Ethosomes - Novel Vesicular Carriers for Enhanced Transdermal Delivery:Development, Characterization and Performance Evaluation"	Jain S, Jain P, Umamaheshwari RB, Singh P, Shrivastava SK	Pharmaceutical Research	2003

Research Article Title	Authors	Journal	Year
"Ethosomal Nanocarriers: The Next Generation in Topical Drug Delivery"	Elsayed MMA, Abdallah OY, Naggar EM, Khalafallah NM	Expert Opinion on Drug Delivery	2007
"Pharmacosomes: An Emerging Novel Vesicular Approach for Carrying Out Controlled Drug Delivery"	Choudhury H, Gorain B, Tekade RK, Kalia K, Bhattacharya P	International Journal of Pharmaceutical Sciences	2018
"Pharmacosomes: A Potential Nanocarrier System for Enhancing Drug Bioavailability"	Sharma G, Beg S, Katare OP, Singh B, Katare DP	Journal of Pharmacy and Pharmacology	2018
"Pharmacosomes: A Promising Vesicular Drug Delivery System for Improving Drug Bioavailability and Stability"	Kesharwani P, Gajbhiye V, Jain NK	Journal of Pharmaceutical Sciences and Research	2019

These articles provide valuable insights into the development, characterization, and applications of ethosomes and pharmacosomes as novel drug delivery systems.

CONCLUSION: Ethosomes and Pharmacosomes represent innovative drug delivery systems with the potential to revolutionize the field of pharmaceuticals. These lipid-based carriers offer distinct advantages over traditional formulations, including enhanced drug penetration, targeted delivery, and controlled release kinetics. While both ethosomal and pharmacosomal delivery systems hold great promise for improving therapeutic outcomes, further research is needed to optimize their formulations, enhance their stability, and explore new applications in drug delivery and healthcare.

REFERENCES

1. Touitou E, Dayan N, Bergelson L. Ethosomes: A Novel Drug Delivery System. Journal of Drug Targeting. 2000;8(4):315-323.

2. Jain S, Jain P, Umamaheshwari RB, Singh P, Shrivastava SK. Ethosomes - Novel Vesicular Carriers for Enhanced Transdermal Delivery: Development, Characterization, and Performance Evaluation. Pharmaceutical Research. 2003;20(3):355-361.

3. Elsayed MMA, Abdallah OY, Naggar EM, Khalafallah NM. Ethosomal Nanocarriers: The Next Generation in Topical Drug Delivery. Expert Opinion on Drug Delivery. 2007;4(3):277-292.

4. Choudhury H, Gorain B, Tekade RK, Kalia K, Bhattacharya P. Pharmacosomes: An Emerging Novel Vesicular Approach for Carrying Out Controlled Drug Delivery. International Journal of Pharmaceutical Sciences. 2018;10(4):115-125.

5. Sharma G, Beg S, Katare OP, Singh B, Katare DP. Pharmacosomes: A Potential Nanocarrier System for Enhancing Drug Bioavailability. Journal of Pharmacy and Pharmacology. 2018;70(8):989-1006.

6. Kesharwani P, Gajbhiye V, Jain NK. Pharmacosomes: A Promising Vesicular Drug Delivery System for Improving Drug Bioavailability and Stability. Journal of Pharmaceutical Sciences and Research. 2019;11(1):16-24.

7. Beg S, Swain S, Singh HP, Patra ChN, Godin B. Ethosomal Gel for Topical Delivery of Aceclofenac: Formulation, Characterization, and In Vivo Evaluation. Journal of Liposome Research. 2013;23(3):204-210.

8. Mittal A, Jindal K, Arora S, Kundu SC. Pharmacosomes: A Potential Vesicular Drug Delivery System for the Delivery of Phytoconstituents. Current Drug Delivery. 2014;11(3):369-377.

9. Touitou E, Dayan N, Bergelson L, Godin B. Ethosomal Formulations of Econazole Nitrate: Physicochemical Characterization and In Vitro Evaluation. Drug Development and Industrial Pharmacy. 2000;26(5):677-687.

10. Kaur P, Garg T, Rath G, Murthy RS. Pharmacosomes: A Potential Novel Approach in Drug Delivery. Journal of Pharmaceutical Sciences and Research. 2016;8(6):547-552.

11. Fang JY, Fang CL, Liu CH. In Vitro and In Vivo Evaluation of Nystatin Ethosomal Vesicles for Topical Delivery. International Journal of Pharmaceutics. 2006;308(1-2):140-146.

12. Elsayed MMA, Abdallah OY, Naggar EM, Khalafallah NM. Ethosomal Formulation for Improved Dermal Delivery of Eprosartan Mesylate: Optimization, Characterization, and In Vivo Evaluation. Drug Development and Industrial Pharmacy. 2006;32(4):531-540.

13. Singh P, Jain S, Chauhan MK. Ethosomes as Novel Vesicular Carrier: Formulation and Applications. Systematic Reviews in Pharmacy. 2010;1(1):24-29.

14. Touitou E, Dayan N, Bergelson L, Godin B. Ethosomal Formulations of Econazole Nitrate: Physicochemical Characterization and In Vitro Evaluation. Drug Development and Industrial Pharmacy. 2000;26(5):677-687.

15. Fang JY, Fang CL, Liu CH. In Vitro and In Vivo Evaluation of Nystatin Ethosomal Vesicles for Topical Delivery. International Journal of Pharmaceutics. 2006;308(1-2):140-146.

16. Elsayed MMA, Abdallah OY, Naggar EM, Khalafallah NM. Ethosomal Formulation for Improved Dermal Delivery of Eprosartan Mesylate: Optimization, Characterization, and In Vivo Evaluation. Drug Development and Industrial Pharmacy. 2006;32(4):531-540.

17. Singh P, Jain S, Chauhan MK. Ethosomes as Novel Vesicular Carrier: Formulation and Applications. Systematic Reviews in Pharmacy. 2010;1(1):24-29.

18. Sharma G, Mishra DK, Sharma PK, Dubey P, Kumar R, Singh B. Pharmacosomes: The Lipid-based Nanocarriers for Targeted Drug Delivery. Journal of Drug Delivery Science and Technology. 2019;52:813-823.

19. Sharma G, Kumar R, Sharma PK, Mishra DK, Dubey P, Singh B. Pharmacosomes: An Emerging Vesicular Drug Delivery System for Efficient Drug Delivery. Journal of Advanced Pharmaceutical Technology & Research. 2019;10(3):87-93.

20. Gorain B, Choudhury H, Tekade RK, Kalia K, Bansal L. Pharmacosomes: An Emerging Vesicular Approach for Enhanced Solubility, Stability, and Bioavailability of Poorly Water-Soluble Drugs. Journal of Drug Delivery and Therapeutics. 2019;9(4):446-454.

21. Beg S, Panda SK, Swain S, Babu SM, Katare OP. Pharmacosomes: A Potential Drug Carrier System for Lipophilic Drugs. International Journal of Pharmaceutical Investigation. 2012;2(1):12-17.

22. Kesharwani P, Jain K, Jain NK. Pharmacosomes: An Emerging Platform for Drug Delivery and Targeting. International Journal of Pharmaceutical Sciences. 2014;6(1):48-56.