SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

ETHOSOMES: AN AUGMENTED VESICULAR CARRIER FOR TRANSDERMAL DRUG DELIVERY

Raslamol . K[1]*, Abdu Rahim A M[2], Alwy Jose[2], Amrutha Surendran[2], Anitta Joy[2], Fathima M.U[2]

**Corresponding Author: [1]* Raslamol K, Professor and HOD, Department of pharmaceutics, Nirmala college of Health Science, Chalakudy*

[2]Department of pharmaceutics, Nirmala college of Health Science, Chalakudy

ABSTRACT

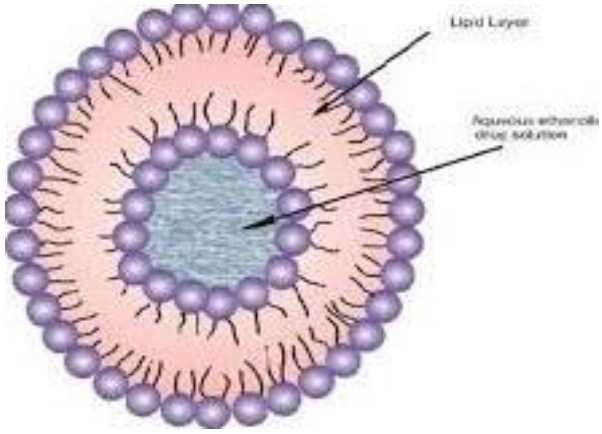
Ethosomes are innovative lipid vesicular carriers containing a high percentage of ethanol. These nanocarriers are specifically designed for the efficient delivery of therapeutic agents with varying physicochemical properties into deep skin layers and across the skin barrier. The initial ethosomes formula has been modified by adding new compounds, resulting in the development of new types of ethosomes. Various preparation techniques are employed to create these novel carriers. For ease of application and stability, ethosome dispersions are incorporated into gels, patches, and creams. A wide range of in vivo models and clinical trials are used to evaluate their efficacy in transdermal delivery. Ethosomes are categorized into classical ethosomes, binary ethosomes, and transferosomes based on their constituents. The differences among these systems are discussed from several perspectives, including formulation, size, zeta potential, entrapment efficiency, skin-permeation properties, and stability. Ethosome formulations have demonstrated good physical and chemical stability when stored in a well-closed container at ambient temperature. This study provides a comprehensive review of the effects of ethosome constituents and preparation methods on the final properties of these nanocarriers. Additionally, recent advancements and future prospects of ethosomes are highlighted, along with detailed information on the evaluation studies conducted on ethosomes.

KEYWORDS: *Ethosomes, Vesicular Carrier, Stability, Nanocarrier, Noval Carrier, Transdermal Delivery, Transferosomes.*

INTRODUCTION

Ethosomes are small structures with a bilayer arrangement similar to the natural lipid bilayers of body membranes. They are highly efficient in encapsulating drugs with various physicochemical properties. The stratum corneum is a significant barrier to effective transdermal drug penetration. The amphiphilic nature of ethosome vesicles enables the delivery of both hydrophilic and lipophilic drugs to their respective targets. Initially, liposomes were developed as the pioneering model in vesicular delivery systems. Vesicles play a crucial role in cellular communication and particle transport. Researchers have concluded that vesicular morphology facilitates efficient drug delivery and allows for cell-specific targeting, resulting in targeted action.The development of ethosomes stemmed from the need to improve upon the features of liposomes. Ethosomes were first developed by Touitou and her colleagues in 1997. These highly malleable, soft lipid vesicles have an enhanced ability to penetrate deeper into the skin and reach systemic circulation. Ethosomes typically range in size from 214 to 890 nm and contain ethanol concentrations of 20-45%, along with suitable phospholipids (0.5-10%) and water. They are considered modified successors to classical liposomes due to their increased ethanol content. The mechanism of ethosome permeation primarily involves disruption of the skin's lipid bilayer by ethanol, which enhances penetrability. The fluidized lipids in the membrane and the high flexibility of the vesicular membrane allow ethosomes to squeeze through pores in the stratum corneum that are smaller than the vesicles themselves. Further developments and modifications have been made to ethosome structure and composition to enhance their properties and effectiveness.

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal



ADVANTAGES

- Enhanced Penetration: Ethosomes are designed to improve drug penetration through the skin barrier.
- Increased Drug Loading: Ethosomes have a high capacity for drug encapsulation due to their flexible lipid bilayers.
- Versatility: Ethosomes can encapsulate a wide range of drugs with diverse physicochemical properties, making them suitable for delivering various types of therapeutic agents, including small molecules, peptides, and proteins.
- Targeted Delivery: Ethosomes can be modified to achieve targeted drug delivery by attaching ligands or targeting moieties to their surface.
- Improved Stability: Ethosomes formulations exhibit good physical and chemical stability, which is essential for the long-term storage and shelf-life of pharmaceutical products.
- Non-Invasive Route of Administration: Ethosomes offer a non-invasive route of drug administration, particularly for transdermal delivery.
- Potential for Combination Therapy: Ethosomes can be used to deliver multiple drugs simultaneously, allowing for combination therapy.

DISADVANTAGES

- Skin Irritation: The use of ethanol in Ethosomes formulations may cause skin irritation or sensitization in some individuals, particularly those with sensitive skin or allergies to alcohol-based products.
- Ethanol Content: The high concentration of ethanol in Ethosomes formulations may limit their use in certain applications or patient populations, such as pediatric or geriatric patients, due to concerns about ethanol toxicity or irritation.
- Stability Issues: Ethosomes formulations may exhibit instability over time, particularly with prolonged storage or exposure to certain environmental conditions. This can lead to changes in drug encapsulation efficiency, particle size distribution, or physical properties, affecting the efficacy and safety of the formulation.
- Limited Drug Compatibility: Some drugs may not be compatible with Ethosomes formulations due to their physicochemical properties or interactions with the lipid bilayers.
- Complexity of Formulation: Formulating Ethosomes can be complex and require specialized equipment and expertise.
- Regulatory Considerations: The use of Ethosomes formulations may be subject to regulatory restrictions or requirements, particularly regarding safety and efficacy assessments, labeling, and marketing claims. Meeting regulatory standards can add complexity and cost to the development and commercialization of Ethosomes-based products.
- Cost: The production of Ethosomes formulations may be more expensive compared to conventional drug delivery systems, due to the need for specialized materials, equipment, and manufacturing processes.

IDEAL PROPERTIES

- Enhance the permeation of the drug.
- Delivery of peptides, proteins, molecules.
- Smaller size than Liposomes.
- High drug entrapment, efficiency for both hydrophilic and lipophilic drugs.
- Good physical stability.

APPLICATIONS

Ethosomes offer a plethora of applications across various biomedical and pharmaceutical fields. Their ability to enhance drug penetration through the skin barrier makes them particularly suitable for transdermal drug delivery, enabling the effective delivery of therapeutic agents such as small molecules, peptides, and proteins. Additionally, Ethosomes find applications in topical drug delivery, facilitating targeted delivery to the site of action for dermatological conditions like psoriasis and acne. In cosmetics, Ethosomes are utilized for delivering active ingredients, improving skin hydration, elasticity, and appearance. Moreover, they hold promise in ophthalmic drug delivery, enhancing corneal penetration and bioavailability of drugs for treating ocular diseases.

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

Ethosomes are also explored for vaccine delivery, gene therapy, and theranostics, showcasing their versatility and potential for advancing healthcare through innovative drug delivery solutions.

FORMULATION TECHNIQES

CLASSICAL COLD METHOD

This method represents the simplest and most commonly employed approach for preparing Ethosomes systems. In this method, the organic phase is prepared by dissolving phospholipids (along with surfactants or penetration enhancers for transethosomes) in ethanol or a mixture of solvents (such as ethanol/PG for binary Ethosomes) at either room temperature or 30°C. The aqueous phase, comprising water, buffer solution, or normal saline solution, is then added to the organic phase in a fine stream dropwise or via a syringe pump, maintaining a constant rate of 175 or 200 µl/min. The resulting mixture is stirred vigorously at a speed ranging from 700 to 2,000 rpm using an overhead or magnetic stirrer. Depending on the physicochemical properties of the intended drug, it is dissolved either in the aqueous or the organic phase before incorporation into the Ethosomes system.

ETHANOLIC INJECTION METHOD

In this technique, the drug and phosphatidylcholine are dissolved in ethanol within a sealed glass container. Double or triple distilled water, heated to 30°C, is gradually added to the lipid solution in a fine stream under constant stirring at 700 rpm using a mechanical or magnetic stirrer. Mixing continues for an additional 5 minutes. The temperature is maintained at 30°C throughout the process, after which the system is allowed to cool to room temperature for 30 minutes. The resulting suspension of vesicles is homogenized either by passing it through a polycarbonate membrane using an extruder or by sonication using a probe sonicator.

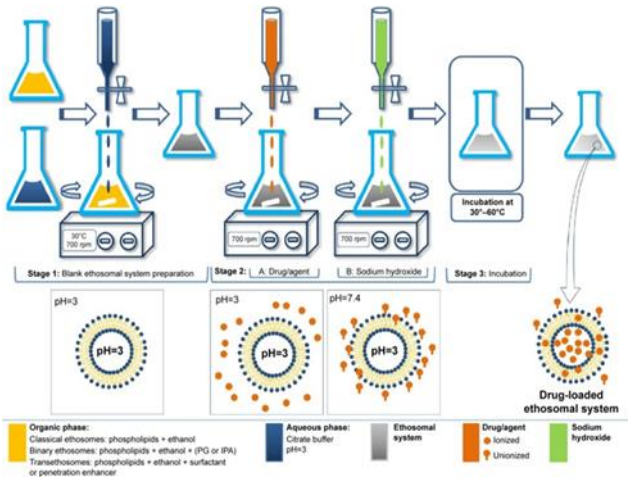
HOT METHOD

In a single vessel, phospholipids are dispersed in water and placed in a water bath at 40°C until a colloidal suspension forms. Simultaneously, in another vessel, ethanol is heated to 40°C and then slowly added dropwise to the phospholipid dispersion, while continuously stirring using a mechanical or magnetic stirrer. Depending on its hydrophilic or hydrophobic properties, the drug is dissolved either in the organic or the aqueous phase.

TRANSMEMBRANE PH GRADIENT METHOD

In this approach, the drug is actively loaded into the Ethosomes system based on the pH-gradient difference between the acidic interior of the internal phase and the basic exterior of the external phase. Initially, an empty Ethosomes suspension is prepared using any of the aforementioned methods, with the hydration process utilizing an acidic buffer, typically a citrate buffer with a pH of 3. Subsequently, the active drug is loaded into the empty Ethosomes suspension while continuously stirring. To create a pH gradient between the acidic internal (pH 3) and basic external phases of the Ethosomes system, an alkali, typically a 0.5 M sodium hydroxide solution, is added to raise the external pH to 7.4. In the final stage, the Ethosomes system is incubated at specified time and temperature conditions (typically 30–60°C), allowing the unionized drug to actively pass through the bilayer of the Ethosomes vesicles and become entrapped within.

REVERSE PHASE EVAPORATION METHOD



This is the least used method and specially designed to produce large unilamellar vesicles. The organic phase is prepared by dissolving the phospholipid in diethyl ether and then mixing it with the aqueous phase at a ratio of 3:1 v/v in an ultrasonic bath at 0°C for 5 min to form a water-in-oil emulsion. The organic solvent is removed under reduced pressure to produce a gel, which turns into a colloidal dispersion upon vigorous mechanical agitation.

SONICATION METHOD

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

In this method, phospholipids are dissolved in ethanol within a glass bottle. The drug is dissolved in double-distilled water and stirred using a magnetic stirrer. A syringe, connected hermetically to the glass bottle, allows the addition of ethanol while preventing evaporation. After the drug dissolves, the phospholipid-ethanol solution is added to the drug solution at a flow rate of 200 µl/min. The mixture is then finely homogenized at 50°C through sonication for 5 minutes (300 watts) using a probe-type ultrasonic instrument. The resulting colloidal solution is filtered through 0.22 µm disposable filters, yielding the Ethosomes formulation in the filtrate, which contains ethanol and water. All processes are conducted under nitrogen protection at room temperature.

MECHANICAL DISPERSTION TECHNIQUE

In this method, phosphatidylcholine is dissolved in a 3:1 chloroform:methanol mixture in a clean round-bottom flask. The organic solvents are then removed using a rotary flash evaporator above the lipid transition temperature, forming a thin lipid film under vacuum overnight. This film is then hydrated with varying concentrations of a hydroethanolic mixture containing the drug, stirred at 60 rpm for 1 hour at the corresponding temperature. The preparation is followed by sonication at 4°C using a probe sonicator. Tadros et al. followed a similar method, starting with lipid dissolution in a small volume of a 1:1 diethyl ether: chloroform mixture in a round-bottom flask. An aqueous phase containing a water-soluble drug is added to the organic phase at a 5:1 organic-to-aqueous phase ratio. The mixture is sonicated for 10 minutes, producing a stable white emulsion. The water and organic solvent mixture is then slowly evaporated at 55°C using a rotary flash evaporator until a thin film form on the flask wall. This film is kept under vacuum to remove any traces of organic solvent. The film is then hydrated with different concentrations of a hydroethanolic mixture for 1 hour with rotation. The resulting formulation is left at room temperature for 1 hour and then sonicated for 20 minutes at 4°C.

THIN FILM HYDRATION TECHNIQUE

In this technique, the phospholipid is initially dissolved in chloroform alone or a chloroform–methanol mixture, with ratios typically ranging from 3:1 to 2:1, in a clean, dry, round-bottom flask. Subsequently, the organic solvents are eliminated using a rotary vacuum evaporator at a temperature exceeding the lipid-phase transition temperature. Any remaining traces of solvents are removed from the lipid film deposited under vacuum overnight. Finally, the lipid film is hydrated with either a water–ethanol solution or a phosphate-buffered saline–ethanol solution.

MECHANISM OF PENETRATION

Ethanol and phospholipids synergistically enhance drug permeation through the skin in Ethosome formulations. Ethanol fluidizes the lipid bilayers of both Ethosome vesicles and the stratum corneum, altering their arrangement and decreasing the density of skin lipids. This allows the highly malleable and soft vesicles of the Ethosome system to penetrate the modified stratum corneum and create a pathway through the skin. The therapeutic agent is then released as these vesicles fuse with cell membranes in the deeper skin layers. While the exact mechanism of Ethosome skin penetration is not fully understood, drug absorption is suggested to occur in two phases:

Ethanol Effect:Ethosomes contain ethanol, which interacts with intercellular lipid molecules in the polar head group region, increasing their fluidity and decreasing the density of the lipid multilayer, thus enhancing membrane permeability.

Ethosome Effect:The high alcohol content increases skin permeability, allowing Ethosomes to easily penetrate deep skin layers. Here, they combine with skin lipids and release the drug into the deeper layers of the skin.

TYPES OF ETHOSOMES

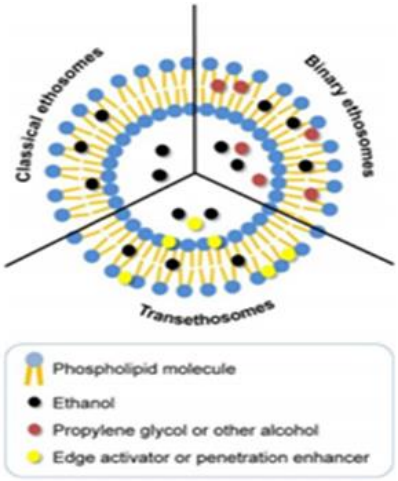
Ethosomes are classified into three main types based on their composition and structure:

Classic Ethosomes:These are the traditional form, composed of phospholipids, a high concentration of ethanol (20-45%), and water. They effectively enhance the permeation of drugs through the skin due to their fluidic and malleable nature.

Binary Ethosomes: This type includes an additional penetration enhancer, such as propylene glycol or isopropyl alcohol, alongside ethanol. The combination further improves skin permeation by enhancing the fluidity of the lipid bilayers and the stratum corneum.

Transethosomes:These are advanced Ethosomes that incorporate a combination of phospholipids, ethanol, and an edge activator like surfactants (e.g., Tween 80 or Span 80). The edge activators increase the elasticity of the vesicles, allowing them to deform and squeeze through narrow skin pores, thereby enhancing deeper drug delivery.

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

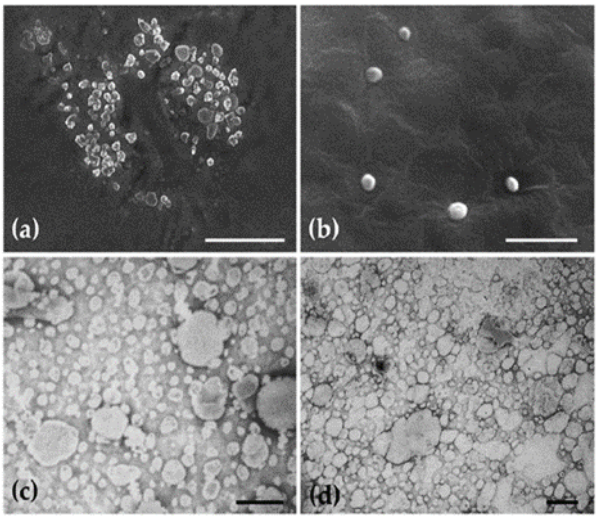


EVALUATION

Patients were monitored clinically and through digital photography before and after treatment for up to 8 weeks to evaluate the treatment response. Following the conclusion of treatment, monthly follow-ups were conducted for up to 3 months to detect any recurrence. Lesion severity scores were calculated and recorded at each visit, and these scores were compared to the baseline value registered at the first visit. Safety was assessed by recording adverse events such as itching, burning sensation, skin or clothing staining, and erythema. Histopathological examinations of psoriatic lesions were performed before and after treatment for both groups. All biopsy tissues were fixed in 10% formalin, routinely processed, and embedded in paraffin. Five-micron thick sections were cut from the paraffin blocks and stained with hematoxylin and eosin for routine histopathological evaluation. The tissue sections were observed under a light microscope to detect histopathological changes in both pre- and post-treatment specimens.

***IN-VITRO* STUDY**

Size and Morphology: In vitro studies often involve characterizing the size and morphology of invasomes using techniques such as Dynamic Light Scattering (DLS) and Transmission Electron Microscopy (TEM). These techniques help in understanding the physical characteristics and uniformity of the vesicles.



Encapsulation Efficiency:This involves determining the amount of drug encapsulated within the vesicles using High Performance Liquid Chromatography (HPLC).

Drug Release Kinetics: In vitro release studies calculate the controlled release properties of the vesicles using methods like dynamic dialysis and fluorescence spectroscopy.

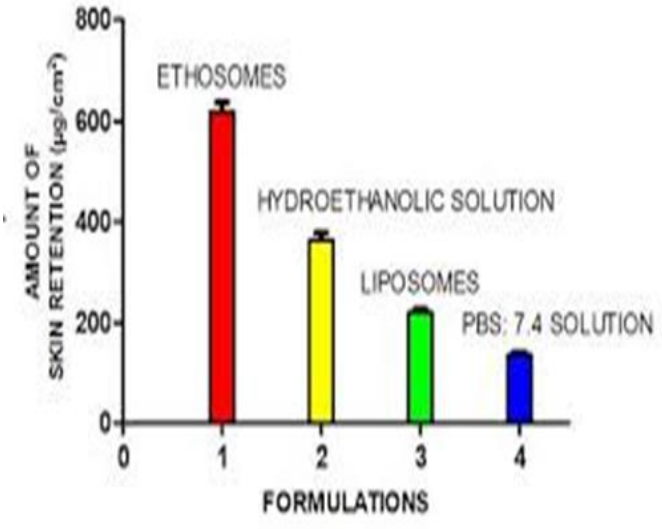
Stability Studies:Stability is a crucial factor studied under various storage conditions, including temperature and humidity variations. Techniques such as Dynamic Light Scattering (DLS) or Laser Diffraction are often used.

Cellular Uptake Studies: These studies help in understanding the interaction with skin cells and provide insights into the potential mechanisms of drug delivery. Confocal Laser Scanning Microscopy (CLSM) provides high-resolution images and allows visualization of cellular uptake in different layers of cells.

Skin Retention Study: The amount of drug retained in the skin is determined at the end of 12-hour in vitro permeation studies. The formulation remaining from the in vitro permeation experiment is removed by washing with distilled water. The receptor content is

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

replaced with 50% v/v ethanol and kept for an additional 12 hours with stirring, after which the drug content is estimated. This receiver solution diffuses through the skin, disrupting any liposome and Ethosome structures and extracting the deposited drug from the skin.



Vesicular stability. The abilities of the formulations to retain the drug content and shape are analysed at different temperatures I.E., 25 ± 2°C (Room Temperature, Rt), 37 ± 2°C And 45 ± 2°C For Different Periods of Time (1, 20, 40, 60, 80 And 120 Days). Nitrogen gas was flushed and was kept in sealed vials. Stability can be found by analysing the size and structure of vesicles over time and the mean size is measured by DLS while structural changes are estimated by making use of transmission electron microscopy.

Percent entrapment efficiency: The %EE of vesicles was determined by ultracentrifugation method. Required volume of the vesicular dispersion was centrifuged at 20,000 rpm for 3 h at a temperature of 4 °C (Remi cooling centrifuge CPR-30). The supernatant solution containing unentrapped drug was withdrawn and measured the concentration by UV spectrophotometer at 226 nm against the pH 7.4 phosphate buffer. The amount of drug unentrapped in liposomes and Ethosomes were determined by the Ex: %Entrapment Efficacy(%EE) = (Cd−C)Cd×100

Where Cd is total drug concentration and C is unentrapped drug concentration. The % EE of test gels was determined by ultra dialysis method. The free drug was removed from the gels by ultra dialysis using dialysis membrane. The dialyzed formulation was lysised with required quantity of methanol and it was further diluted with pH 7.4 phosphate buffer. The samples were analysed spectrophotometrically at 226 nm.

***IN- VIVO* STUDY**

In vivo studies of Ethosomes are conducted to evaluate their efficacy, safety, and pharmacokinetic properties when used for drug delivery through the skin. These studies typically involve the following steps:

Animal Selection: Appropriate animal models, such as rats or mice, are selected based on the intended use and ethical considerations.

Application: The Ethosome formulation is applied to the skin of the test animals. The site of application is often shaved and cleaned to ensure proper contact with the skin.

Monitoring:The animals are monitored for any immediate adverse reactions, such as irritation or inflammation, following the application of the Ethosome formulation.

Pharmacokinetic Studies: Blood samples are collected at various time intervals to analyze the concentration of the drug in the bloodstream. This helps in understanding the absorption, distribution, metabolism, and excretion (ADME) profile of the drug delivered via Ethosomes. Mice were anesthetized and confirmed to have intact skin after 24 hours. A deep second-degree burn model was created by applying sodium hydroxide to their back skin. Each mouse received daily treatments on three burn sites with Tβ-4 Ethosome gel, Tβ-4 gel, and blank gel. Wound area, inflammatory reaction, scarring time, healing time, and scar formation rate were recorded. After treatments, mice were sacrificed, and their skin was fixed in formaldehyde, dehydrated, embedded in paraffin, and stained with H&E for analysis.

Efficacy Evaluation:The therapeutic efficacy of the Ethosome formulation is assessed by measuring relevant biomarkers or through clinical observation of the disease or condition being treated.

Histopathological Examination: Skin biopsies are taken from the site of application to study any histological changes and to verify the penetration and distribution of the Ethosome vesicles within the skin layers.

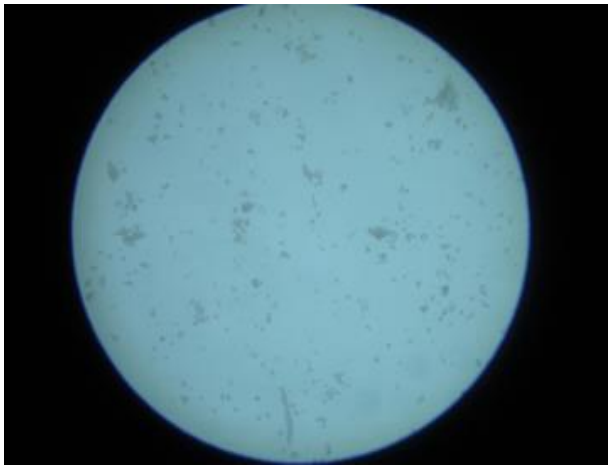
Safety Assessment: Any adverse effects, such as toxicity or allergic reactions, are recorded. This includes both local effects at the application site and systemic effects observed in the test animals.

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

Data Analysis:The data collected from the in vivo study is analyzed to determine the overall effectiveness and safety of the Ethosome formulation. Comparisons are often made with control groups or with traditional drug delivery methods to highlight the benefits of Ethosomes.

Skin Irritation Test: To evaluate and compare skin irritation from Tβ-4 Ethosome gel and blank Tβ-4 gel, a study was conducted on New Zealand rabbits. The rabbits were anesthetized, and their back hair was removed 24 hours before applying the formulations. The exposed back skin was cleaned with saline to ensure no damage. The skin was scratched to ooze blood and divided into three groups: Tβ-4 Ethosome gel, Tβ-4 gel, and blank gel (control). Both intact and damaged skin areas were treated with 0.5 g of each gel. Irritation and redness were observed at 1, 24, 48, and 72 hours post-application, using the Draize scale to grade irritation from 0 (no response) to 4 (severe response).

Physical Examination:All prepared formulations were visually inspected and assessed for color, homogeneity, consistency, spreadability, and phase separation.



Optical Microscopy Observation: The morphological aspects of the Ethosome vesicles prepared using the hot method were assessed through visual inspection and observation under an optical light microscope. Small quantities of the prepared formulations were placed on a clean glass slide with a coverslip and observed at 40x magnification under room temperature conditions.

Zeta Potential Determination and Particle Size Analysis:The zeta potential of the selected formula was determined using a Malvern Zetasizer. The formula was diluted with distilled water to obtain a clear specimen for analysis. Zeta potential measurements were conducted at ±25°C using a clear disposable zeta cell, with measurements taken in duplicates. The vesicle size of the formula was also analyzed using the Zetasizer. For this, three drops of the formula were diluted in distilled water and placed in a Zetasizer cuvette, followed by a blank cuvette for particle size analysis. Both zeta potential and particle size measurements were performed in duplicates.

CONCLUSION

The Ethosome formulation was prepared easily, economically, and successfully. The vesicles were characterized as spherical, homogeneous, spreadable, transparent, and washable. The formulation exhibited excellent stability, with a high zeta potential score indicating no clumping. It achieved the goal of sustained drug release and enhanced penetration. Overall, Ethosome nanoparticles are highly promising as a novel drug delivery system, enhancing penetration while sustaining drug release. Nearly two decades have passed since the invention of Ethosomes, during which these nanocarriers have demonstrated their unique ability to deliver therapeutic agents with various physicochemical properties through the skin for both local and systemic applications. Ongoing extensive research has led to the development of a new generation of Ethosome systems, called transethosomes, which offer superior vesicular properties and skin permeation abilities compared to classical Ethosomes. Transethosomes provide formulators with the flexibility to modify Ethosome properties by adjusting edge activators and penetration enhancers to meet specific research criteria. Incorporating Ethosome systems into vehicles such as gels, patches, and creams is a significant step toward achieving better skin permeation and therapeutic outcomes. However, further studies are needed to enhance the stability of Ethosome systems. Results from in vivo studies and clinical trials reflect the potential of Ethosome systems for the dermal and transdermal delivery of therapeutic and cosmetic agents.

REFERENCES

1. *Tsuruta et al: keratinocytes and lymphocytes in the pathogenesis of psoriasis. Recent Pat. Inflame. Allergy Drug Discovery. 2018, 3, 40–48.*
2. *Pradhan, M.; Singh, D.; Singh, M.R. Novel colloidal carriers for psoriasis: Current issues, mechanistic insight and novel delivery approaches. J. Control. Release 2013, 170, 380–395.*
3. *Krueger, J.G.; Bowcock, A. Psoriasis pathophysiology: Current concepts of pathogenesis. Ann. Rheum. Dis. 2022, 64 (Suppl. 2), ii30–ii36.*
4. *Koo, J. Population-based epidemiologic study of psoriasis with emphasis on quality-of-life assessment. Dermatol. Clin. 1996, 14, 485–496.*
5. *Peters, B.P.; Weissman, F.G.; Gill, M.A. Pathophysiology and treatment of psoriasis. Am. J. Health Syst. Pharm. 2020, 57, 645–659.*

SJIF Impact Factor (2024): 8.675| ISI I.F. Value: 1.241| Journal DOI: 10.36713/epra2016 ISSN: 2455-7838(Online)
EPRA International Journal of Research and Development (IJRD)
Volume: 9 | Issue: 5 | May 2024 - Peer Reviewed Journal

6. *Ryan, S. Psoriasis: Characteristics, psychosocial effects and treatment options. Br. J. Nur's. 2018, 17, 284–290.*
7. *Traub, M.; Marshall, K. Psoriasis-pathophysiology, conventional, and alternative approaches to treatment. Altern. Med. Rev. 2012, 12, 319–330.*
8. *Feely, M.A.; Smith, B.L.; Weinberg, J.M. Novel psoriasis therapies and patient outcomes, part 1: Topical medications. Cutis 2015, 95, 164–168, 170.*
9. *Griffiths, C.E.; Taylor, H.; Collins, S.I.; Hobson, J.E.; Collier, P.A.; Chalmers, R.J.; Stewart, E.J.; Dey. The impact of psoriasis guidelines on appropriateness of referral from primary to secondary care: A randomized controlled trial. Br. J. Dermatol. 2016, 155, 393–400.*
10. *Feely, M.A.; Smith, B.L.; Weinberg, J.M. Novel psoriasis therapies and patient outcomes, part 2: Biologic treatments. Cutis 2015, 95, 282–290.*
11. *Parish, L.C.; Millikan, L.E.; Witkowski, J.A. The modern story of anthralin. Int. J. Dermatol. 2019, 28, 373–374.*
12. *Saraswat, A.; Agarwal, R.; Katari, O.P.; Kaur, I.; Kumar, B. A randomized, double-blind, vehicle-controlled study of a novel liposomal dithranol formulation in psoriasis. J. Dermatol. Treat. 2018, 18, 40–45.*
13. *Agarwal, R.; Katara, O.P.; Vyas, S.P. Preparation and in vitro evaluation of liposomal/noisome delivery systems for ant psoriatic drug dithranol. Int. J. Pharm. 2010, 228, 43–52.*
14. *Shawal, V.K. Preformulating studies and preparation of dithranol loaded solid lipid nanoparticles. Int. J. Biomed. Res. 2012, 3, 343–350.*
15. *McGill, A.; Frank, A.; Emmett, N.; Turnbull, D.M.; Birch-Machin, M.A.; Reynolds, N.J. The anti-psoriatic drug anthralin accumulates in keratinocyte mitochondria, dissipates mitochondrial membrane potential, and induces apoptosis through a pathway dependent on respiratory competent mitochondria. FASEB J.2017, 19, 1012–1014.*
16. *Mendonca, C.O.; Burden, A.D. Current concepts in psoriasis and its treatment. Pharmacal. Ther. 2013, 99, 133–147.*
17. *Sehgal, V.N.; Verma, P.; Khurana, A. Anthralin/dithranol in dermatology. Int. J. Dermatol.2016, 53, e449–e46.*