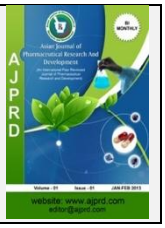
Available online on 15.12.2025 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Review Article

From Concept to Clinic: The Expanding Frontier of Transethosome-Based Drug Delivery Systems

Salunke Harshada*[1], Dr.Hangargekar Sachin[1], Dongare Dnyneshwar[2], Bamankar Akshay[3], Kharosekar Pooja[4]

Department of Pharmaceutics, Shivlingeshwar College of Pharmacy, Almala, Tq- Ausa, Dist.-Latur, Maharashtra (MH), India 413520.

A B S T R A C T

Transethosomes are an emerging class of ultra-deformable, lipid-based Nano carriers designed to overcome the limitations of conventional topical and transdermal drug delivery systems. As hybrid vesicles combining the characteristics of transferosomes and ethosomes, they incorporate phospholipids, ethanol, and edge activators to achieve exceptional flexibility, stability, and skin-penetration capability. This review highlights the fundamental principles, composition, and development of transethosomes, along with a detailed discussion of their various preparation techniques and evaluation parameters, including vesicle size, morphology, zeta potential, entrapment efficiency, elasticity, drug release behaviour, and stability. Their unique ability to enhance drug permeation through the stratum corneum enables the effective delivery of molecules ranging from small drugs to large biomacromolecules. Recent advancements demonstrate the broad therapeutic applicability of transethosomes in delivering antifungal, anti-inflammatory, anticancer, antibiotic, hormonal, ant arthritic, antihypertensive, ophthalmic, and cosmetic agents. With improved bioavailability, sustained release profiles, reduced systemic side effects, and high patient compliance, transethosomes represent a highly promising platform for innovative dermal and transdermal drug delivery.

Keywords: Transethosomes; Transdermal drug delivery; Ultra-deformable vesicles; Phospholipid Nano carriers; Skin permeation; Ethanol-based vesicles; Edge activators.

A R T I C L E I N F O: Received 10 sept. 2025; Review Complete26 Oct. 2025 ; Accepted 04 nov. 2025 ; Available online 15 Dec. 2025

Cite this article as:
Salunke H, Hangargekar S, Dongare D, Bamankar A , Kharosekar P, From Concept to Clinic: The Expanding Frontier of Transethosome-Based Drug Delivery Systems, Asian Journal of Pharmaceutical Research and Development. 2025; 13(6):214-222,
DOI: http://dx.doi.org/10.22270/ajprd.v13i6.1679

*Address for Correspondence:
Salunke Harshada, Department of Pharmaceutics, Shivlingeshwar college of pharmacy, Almala, Tq- Ausa, Dist.-Latur, Maharashtra (MH), India 413520.

INTRODUCTION

One of the most popular methods of medication administration is through the oral route. However, the oral route has a number of drawbacks, including first-pass metabolism. To solve this issue, scientists and researchers created topical medication administration, which can enhance patient compliance and localized effects while avoiding the effects of first-pass metabolism. (1) To overcome these difficulties, transdermal route has been tried having merits such as bypasses first pass metabolism. For medications with a high first pass metabolism, transdermal formulation can demonstrate superior bioavailability compared to oral administration, as well as increased efficacy, safety, convenience, and patient compliance.(3)New lipid vesicles known as highly deformable vesicles have been developed to improve medicine administration. This sort of vesicle comes in a variety of forms, including ethosomes, transferosomes, and transethosomes, and is used to deliver cosmetics and pharmaceuticals. (5)

Ultra deformable vesicles (UDV) have lately emerged as a viable technique for developing more effective and creative cutaneous and transdermal medicines. Deformable vesicles, such as transethosomes, have the benefit of being nontoxic and thermodynamically stable formulation. They have been employed for the cutaneous and transdermal distribution of a variety of compounds, including peptides and proteins. Furthermore, their production is quite straightforward and scalable. (8)

Transethosomes are novel lipid-based vesicular structures intended to increase drug administration through the skin.

These vesicles consist of four major components: phospholipids, ethanol, an edge activator, and water. Phospholipids serve as key carriers, helping to transfer medication molecules straight into the skin. (6) Transethosomes, a hybrid of transferosomes and ethosomes, are produced. It is very elastic and has a non-uniform spherical shape. It is easy to load medications with both low and large molecular masses. (7) Song et al. developed the name transethosomes and the underlying concept in 2012, and they are distinguished by their high ethanol content (up to 30%) and the presence of an edge activator. (8)Transethosomes also increase medication penetration across ocular barriers, allowing for tailored distribution to specific ocular tissues and improved bioavailability. They provide prolonged medication release, lowering the frequency of delivery and the likelihood of side effects in other regions of the body. They are patient-friendly, providing an easy and non-invasive approach for self-administration. (10)

For the most up-to-date and accurate information on "transethosomes" in pharmaceuticals, chemistry, and related sciences, please refer to the latest scientific literature, research papers, and reputable online sources. (12) Additionally, this article focuses solely on the numerous techniques to drug delivery via functionalization, photodynamic treatment, and diverse routes of administration.. Furthermore, the therapeutic applications of transethosome-based drug delivery systems are also discussed. (10)

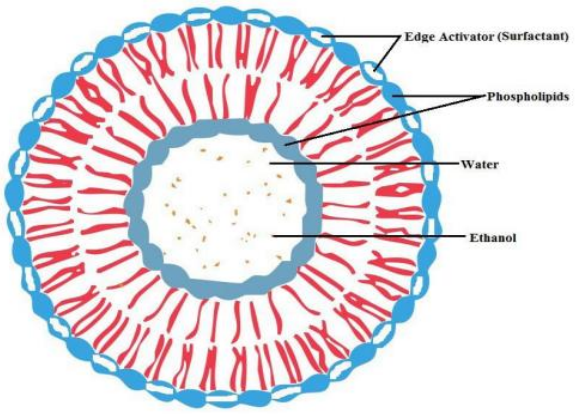


Figure 1: Structure of Transethosome

2. History

Table 1: History of Transethosome

Year	Milestone	Details
1990s	Emergence of Transferosomes	Transferosomes introduced as ultra-deformable vesicles to improve skin penetration.
Early 2000s	Ethosomes Developed	Ethanol-based vesicles (ethosomes) created to enhance drug delivery through the stratum corneum.
2010s	Concept of Transethosomes	Transethosomes emerged by combining features of transferosomes and ethosomes—ethanol, phospholipids, and edge activators.
2018	First Comprehensive Reviews	Studies began detailing transethosomes as a hybrid vesicular system for transdermal delivery.
2020s	Expanded Applications	Research expanded into using transethosomes for delivery of anti-inflammatory, antifungal, and anticancer drugs.
2025	Latest Advances	Reviews highlight their superior deformability, stability, and skin permeation compared to earlier systems.

1. Advantages of Transethosome

- Enhancement of drug penetration through the skin in transdermal drug delivery (TDD).(2)
- The transethosomal system is passive, non-invasive and is available for immediate commercialization.(8)
- It contains non-toxic raw materials in the formulation.(8)
- Can be used to deliver the drugs with larger molecular weight this phenomenon makes it an ideal candidate to deliver proteins and peptides through the skin.(11)
- It's an effective drug carrier to deliver different dosage form.(11)
- Transethosomal drug delivery has potential applications in animal medicine and aesthetics. (13)
- It has a high degree of patient compliance since it is administered as a semisolid gel or a cream.(13)
- This drug delivery technique is more stable than other standard vesicles. (13)
- This is a straightforward method of medication delivery compared to iontophoresis, laser surgery, cryosurgery, and other sophisticated procedures.(13)
- The preparation method of nanotransethosomes is easy and it has high penetration power.(19)

4. Disadvantages of Transethosome

- Product loss during transition between an alcoholic to water medium. (2)
- May cause skin irritation or allergic responses, not suited for people with sensitivedermatitis.(2)
- Agglomeration of nanotransethosomes takes place if it is not prepared in the proper method.(1)
- Adequate solubility of the drug in both lipophilic and aqueous environments to reach dermal microcirculation and gain access to the systemic circulation. (8)
- The molecular size of the drug should be reasonable that it should be absorbed percutaneously .(8)

5. Component of Transethosome

- Ethanol
- Phospholipid
- Cholesterol
- Edge activator

a. Ethanol

The characteristics of ethanol, such as stability, size, entrapment effectiveness, and skin permeability, contribute to its role as an effective penetration promoter.(2)Ethanol enhances the properties of transethosomes by increasing the softness and deformability of the vesicular membrane while also serving as a permeation enhancer.(5)Ethanol is a key ingredient that makes transethosomes work so well. It helps keep these tiny carriers stable, controls their size, improves howmuchmedication they can hold, and makes it easier for the drugs to pass through the skin. Transethosomes usually contain 10–20% ethanol, which is what gives them their soft and flexible texture.(6)A study found that TEs containing 10%–20% ethanol showed higher stability and deformability compared to those containing 30%–50% ethanol.(10) Increased ethanol concentration will improve entrapment efficiency. Increased ethanol concentrations beyond the ideal concentration cause leaky bilayers, increased vesicular size, and a significant drop in entrapment efficiency. (20)

b. Phospholipid

The selection of phospholipids is a crucial factor in the development of ethosomal systems, significantly affecting the size of the ethosomes. Both the type and concentration of phospholipids play a vital role in determining the size, entrapment efficiency, zeta potential, stability as well as the penetration and permeation properties of the vesicular system. (2) Phospholipids are essential for vesicular formation and may be synthesized naturally. Natural phosphoglycerides or phospholipids are obtained from natural sources such as soybeans, egg yolks, and sunflower seeds, enhancing skin permeation by fluidizing the stratum corneum layer.(5) For making transethosomes, the ideal phospholipid concentration usually ranges from 2% to 5%, as this helps ensure optimal stability and performance.The size, zeta potential, entrapment effectiveness, stability, penetration, and permeation properties of the TEs are all influenced by the kind and quantity of phospholipid used and thus selection of a suitable phospholipid is a significant factor in the formation of stable TEs.(6) Utilizing natural unsaturated phospholipids cause the SC to fluidize, allowing APIs to permeate deeper layers. However, using saturated (hydrogenated) phospholipids improves or restores the skin's barrier function, facilitating APIs to remain intact for longer.(10)The use of Lipoid E80 phospholipid resulted in production of stable vesicles due to higher concentration of phosphatidyl choline content.(20)

c. Cholesterol

Cholesterol in transethosomal formulations increases stability and improves drug entrapment efficiency. It has also been reported that adding cholesterol may increase the size of transethosome vesicles. Several studies have used a 3% concentration of cholesterol in formulations to stabilize the vesicular system and prevent particle agglomeration. (5) The integration of cholesterol into the ethosomal system increased stability and entrapment efficiency. It has been reported that cholesterol increases vesicular size. Cholesterol concentrations ranged from 3% in some formulations. At a cholesterol concentration of 0% to 0.15% w/w, vesicular size increased from 102±13 nm to 152±12 nm. (20) However, higher cholesterol concentration can reduce encapsulation efficiency due to its low solubility. (5)

d. Edge activator

Selecting a suitable edge activator is a vital step in transethosomal (TE) formation since it has a substantial impact on their features. Edge activators from all three surfactant types (anionic, cationic, and non-ionic) can be used in transethosomal systems. (2) Edge activators in transethosomal formulations improve phospholipid vesicles' deformability and flexibility. The type and quantity of edge activators significantly influence the drug's permeability profile. Excess edge activators may increase the zeta potential, indicating more stability and a threefold increase in encapsulation efficiency. (5) Surfactants used in the production of TEs include Tween 20, sodium cholate, dipotassium glycyrrhizinate, bile salts, Span 80, oleic acid, and Tween. (10)Polyethylene glycol is one surfactant option for TE preparation, while tweens and spans are most typically used as edge activators. Studies indicate that Tween 80, in particular, improves stability and lowers vesicular size in transethosomal systems. (2)

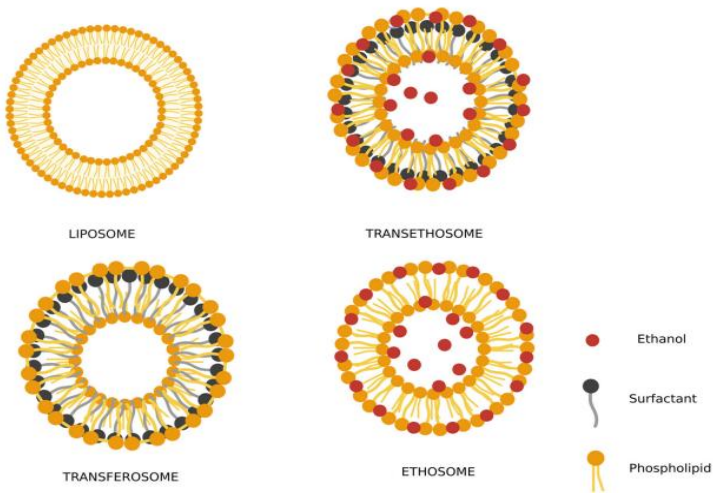


Figure 2: Schematic Illustration of Various Lipid-Based Nano carriers with Phospholipid, Ethanol, and Surfactant (Liposome, Transethosome, Transferosome, and Ethosome).

Table 2: Material Used in Transethosome

Component	Function	Examples	Typical Concentration Range
Phospholipids	Forms the bilayer structure of vesicles	Soy lecithin, Phosphatidylcholine (PC), Egg lecithin	2–5% w/v
Ethanol	Enhances skin permeability and vesicle flexibility	Ethanol (absolute or 95%)	20–40% v/v
Edge Activator	Improves deformability of vesicles	Sodium cholate, Tween 80, Span 80, Sodium deoxycholate	0.5–2% w/v
Drug (Active Agent)	Therapeutic compound to be delivered	Diclofenac, Ibuprofen, Acyclovir, Curcumin	Variable (based on formulation)
Water	Hydration medium for vesicle formation	Purified water, Milli-Q water	q.s. to 100%
Penetration Enhancer	Facilitates deeper skin absorption	Propylene glycol, Oleic acid, Dimethyl sulfoxide (DMSO)	1–5% w/v
Stabilizer/Antioxidant	Prevents oxidation and degradation	α-Tocopherol (Vitamin E), BHT, Ascorbic acid	0.01–0.1% w/v
Buffering Agent	Maintains pH stability	Phosphate buffer, Citrate buffer	pH 5.5–7.4
Preservative	Prevents microbial growth	Benzalkonium chloride, Methylparaben	0.1–0.2% w/v

1. Method of preparation of Transethosome

- Cold method
- Hot method
- Ethanol injection method
- Reverse phase evaporation method
- Thin film hydration technique

a) Cold Method

This method of preparation of transethosomes phospholipids was added in ethanol, properly mixed with each other, and heated to 30°C (Organic Phase). In a second step in a separate container, the edge activator, drug and water all combined together and heated up to 30°C (Aqueous phase). Then an aqueous phase is added to the alcoholic phase with constant stirring for 5 to 10 mins and the temperature is maintained to 30°C throughout the procedure. Now the above mixture is sonicated in a sonicator.(1)

b) Hot Method

Phospholipid, after being dispersed in water, is heated to 40°C. A mixture consists of glycol and ethanol and is heated to 40°C. The aqueous and organic phases are combined while stirring continuously. Based on the solubility of drugs, the solvent system is chosen (water or ethanol). Throughout the procedure, a constant temperature of 40°C is maintained. The vesicular size can be altered by probe sonication.(3)

c) Ethanol Injection Method

Using this procedure, phospholipid, surfactant, and medication are combined in ethanol and stirred continuously at 35 degrees Celsius to prepare the organic phase. To create a homogeneous mixture, the previously prepared organic phase was combined with the aqueous phase, which was made up of water and edge activator, while being constantly stirred. To stop ethanol from evaporating, the resultant solution is sealed with a glass bottle.(9)

d) Reverse phase evaporation method

The drug and edge activator are dissolved in an aqueous solvent, whereas the phospholipids are dissolved in an organic solvent. After that, the aqueous phase is added to the organic phase, and the mixture is placed in an ultrasonic bath set at 0°C until two-phase separation takes place. The organic phase is removed, and gel formation occurs under low pressure. The lipid layer is incorporated into the aqueous layer following constant agitation. The sample is filtered at the end.(3)

e) Thin-film hydration technique (TFH)

The thin film hydration technique is used to prepare multilamellar vesicles and this method is also called the Rotatory Evaporation Sonication method. In this method, Phospholipids, drugs, and edge activators are dissolved in the organic solvents of chloroform and ethanol in a 2:1 ratio. A thin film was formed upon the evaporation of solvents at a phase transition temperature under reduced pressure. The thin film was hydrated using a saline phosphate buffer of pH 6.5 by rotation of 60 rpm for 1 hour and kept overnight for complete hydration of the vesicles.(12)

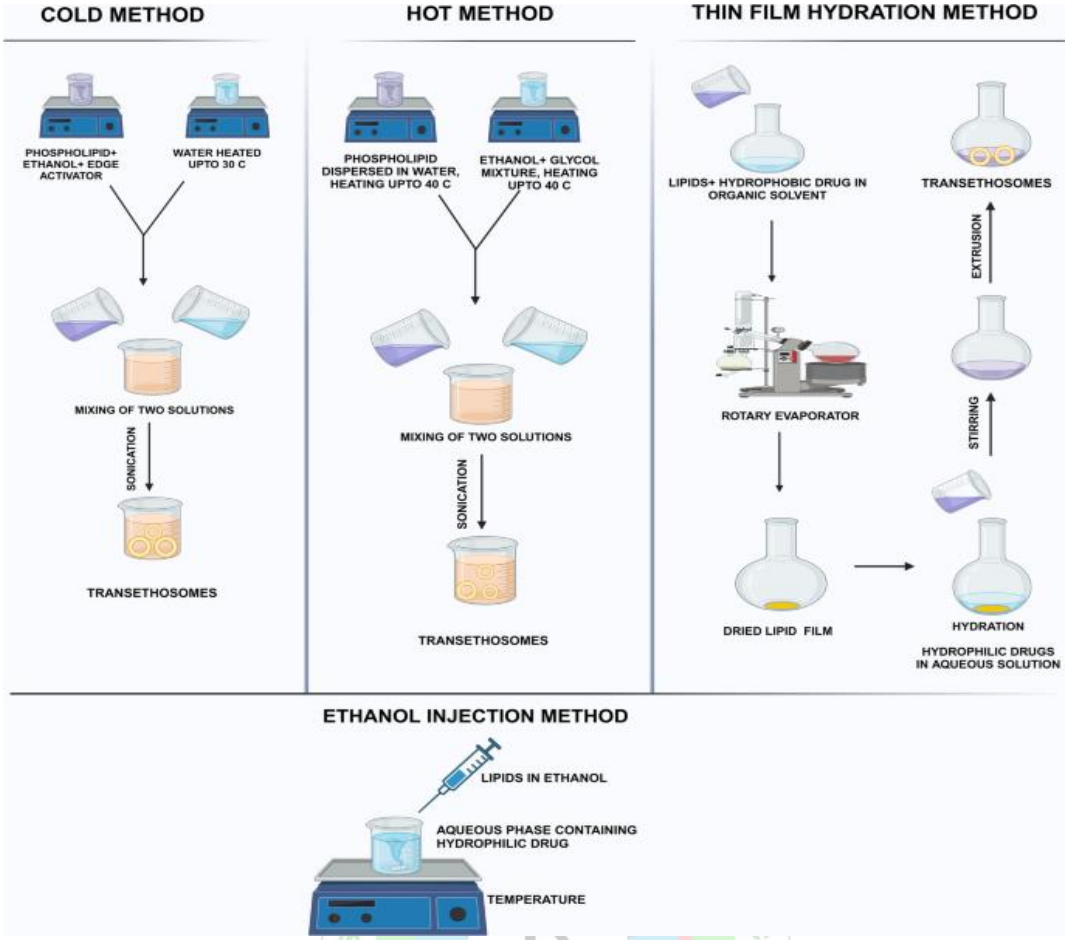


Figure 3: method of preparation of transethosome

2. Evaluation of transethosome

a) Morphology

Morphology is described as the study of the shape and size of vesicle carriers. Vesicular carriers have a consistent spherical shape, are soft and flexible, and their center is encapsulated. The vesicular carrier might be tiny, unilamellar, or multilamellar depending on its composition. The morphology of the vesicular carrier is evaluated using a microscope. Because the majority of the vesicles are Nano sized, the morphology is examined using scanning electron microscopy. In addition to identification studies, morphology explains the pattern of particle packing and aggregation. (3)

b) Shape

Shape of transethosome can be seen under transmission electron microscope.Six samples are inserted into a copper grid having carbon coating to create a thin film matrix. Phosphotungstic acid stains it negatively. Transethosomes were found to exist in an atypically spherical shape. (18)

c) Size Distribution and Vesicle Size

In transethosomal gels, the size and distribution of vesicles are crucial for skin penetration, release rate, and encapsulation. Dynamic Light Scattering (DLS) is a popular method for determining vesicle size since it uses light scattering analysis to quantify particle size distribution and gives features such as mean size and polydispersity index. Size determination from micrographs is facilitated by Transmission Electron Microscopy (TEM), which provides a direct view of vesicle morphology. Atomic Force Microscopy (AFM) allows for high-resolution analysis of vesicle size and surface topology. These procedures ensure that transethosomal gels are correctly designed and effective. (21)

d) Entrapment Efficiency

By calculating entrapment efficiency, we may simply quantify the amount of drug entrapped in nanotransethosomes. It can be accomplished using the ultracentrifugation technique, commonly known as column centrifugation. In this technique, the medication is first put into nanotransethosomes, which are then placed in a column and centrifuged. The ultracentrifugation process allows for easy control of both speed and temperature. After centrifugation, the top layer forms and separates from the vesicles. The vesicles are then lysed using solvents such as triton-X-2, propanol, and methanol. The drug content can then be determined using UV-visible spectrophotometry. The amount of drug entrapped in the vesicular system can be determined using formula (19).

% Drug Entrapment = Amount of entrapped drug/Total amount of drug

e) Zeta Potential

The Zeta potential is a physical attribute that determines a product's stability and can be tested with a Zeta size. The charge of the vesicular carriers is an important feature that depends on the formulation excipients and can influence vesicular characteristics. According to Salem et al., a positive charge on the vesicular surface reduces vesicle aggregation caused by electrostatic repulsions, increasing stability. It provides information about each element in the formulation, including interactions and surface chemistry. Furthermore, the presence of ethanol causes the surface of the Nano vesicles to be negatively charged, increasing their colloidal stability.The phosphate groups' negative charge altered the vesicles' negative zeta potential. A laser is required as a light source to highlight the sample's vesicles and quantify the zeta potential. The laser beam travels from the center of the sample cell being inspected at a specific angle. The charge of TE is inversely proportional to their rate of movement. (10)

f) Drug content

The drug concentration in transethosomal gel was evaluated using HPLC. The amount of medication in the gel was evaluated by properly measuring 5 gm. and dissolving it in 50 ml of transethosomal gel in purified water, followed by sonication with phosphate buffer at pH 7.4. Sonication for 15 minutes; heating for 5 minutes. The test was performed in triplicate, and the average percentage of drug content was calculated. The present drug content in transethosomal preparation was calculated using the following formula: (11).

% drug content equals sample absorbance divided by standard absorbance.

g) Elasticity Measurement

Lasticity measurement is an essential aspect in penetration into the skin. The extrusion method is used to determine the elastic characteristics of vesicles. The vesicles were extruded through the cellulose membrane filter holes at appropriate pressure. Extruded vesicle dispersion is computed by the following formula (12).

$E = J * (rv/rp)2.$

E represents the elasticity index of the vesicle membrane.

J = The rate of penetration through a membrane filter.

rv = represents the size of the vesicle after extrusion, while

rp = represents the membrane pore size.

h) Phase Transition Temperature

Phase transition temperature is studied to understand the release of the drug from the vesicles. The Differential Scanning Calorimeter (DSC) is used to identify it. Each sample is analysed at a specific temperature range under a constant nitrogen stream. The samples are compared using differential thermal curves.(3)

i) Determination of pH

It is critical to use a digital pH meter to determine the pH of transethosomes (TEs) in a gel. The pH of a transdermal delivery method can influence how well a medicine penetrates the skin. If the pH is too acidic or alkaline, it might induce skin irritation, reducing drug delivery effectiveness and patient compliance. (6) Standard buffer solutions with known pH values, typically pH 4, 7, and 10, are used to calibrate the pH meter. The pH value is then measured after immersing the electrode in a small amount of transethosomal gel or a diluted sample, which is frequently diluted with deionized water. To ensure skin compatibility, transethosomal gels should generally have a pH of 4.5 to 6.5 (21)

j) Stability Studies of TE

Chemical and physical stability are the two most important variables influencing TEs' eventual biological functions. TEs' physical stability is often assessed based on their size and appearance. This occurrence is related to the tendency to aggregate or agglomerate. Vesicular fusion and rupture during storage can cause medication leaking from TEs. Chemical stability refers to TEs' capacity to maintain EE levels in changing medium conditions, including pH, electrolyte composition, oxidizing agents, and surface-active components. Chemical deterioration can alter the permeability of lipid membranes.Furthermore, drug-phospholipid interactions may reduce the chemical stability of TEs. As a result, stability studies are critical during liposomal vesicle storage, particularly when hydrophilic compounds are present. Drug-loaded TE is maintained for three months at two temperatures: room temperature (25 ± 2°C) and refrigeration temperature (4 ± 2°C), with relative humidity (60 ± 5%). The formulation was stored in a borosilicate container to prevent interaction between the stability study formulation and the glass container. The formulation's physical changes and pharmacological content were assessed. (10)

k) Ex-vivo Skin Permeation Studies

Ex-vivo drug release and permeation of the drug were investigated by using a modified. Franz diffusion cell with rat abdomen skin as a barrier medium. The temperature of the receptor medium was maintained at 37±1º C. The receptor compartment contained 13.3 ml phosphate buffer solution (PBS) of pH 7.4 and was constantly stirred by a magnetic stirrer at 350 rpm. Skin samples were fixed over the diffusion cells in such a way that the dermis faced the receptor compartment while the stratum corneum side faced the donor compartment. An amount of 1gm prepared gel formulation was administered in the donor compartment.2 ml samples were withdrawn through

the sample port of the diffusion cells at 30, 60, 90, 120, 180, 240, and 360 minutes and analysed by validated UV method. To maintain a sink condition throughout the study period, the receptor phase, from which the sample was taken, was immediately replenished with an equal volume of dissolution medium. Once the permeation study is completed, the skin attached to the diffusion cell was removed to determine the amount of drug deposited in the skin layer. Skin samples were thoroughly washed with distilled water, and cleaned with cotton wetted in normal saline solution. The skin was homogenized with 5ml DMSO and 5ml acetonitrile to extract the drug which was retained in the skin sample.The suspension thus obtained was filtered with a 0.22-mm membrane filter. Then the processed sample, upon suitable dilution, was analysed by the developed UV method.(9)

l) In vitro drug release

In vitro drug release investigations of transethosomes are critical for determining the pace and amount of drug release from the vesicles. These experiments are often carried out utilizing membrane diffusion techniques, dialysis bag diffusion, or Franz diffusion cells. The dialysis bag technique is used to investigate medication release patterns. This procedure involves putting the transethosome formulation to the dialysis membrane, which is then placed in a conical flask filled with a buffer solution and incubated. Aliquots are withdrawn at predetermined intervals and centrifuged using the column centrifugation method. The released medication is assessed using the proper process. The drug discharge can last for 24 hours. This reduces the frequency of dosing, hence enhancing patient comfort. (3)

m) Spreadability

The Spreadability of the gel formulation was determined, by measuring the diameter of 1 g gel between horizontal plates (20×20 cm^2) after 5 minutes. The standardized weight tied on the upper plate was 500g. (9)

$S = M \times L/T$

Where, S = Spreadability,

M = Weight tied on the upper plate

L = Length (cm) of glass plate

T = Time taken (second)

n) Deformity Index

Deformity index studies are used to measure the flexibility of ultra-deformable liposomes, commonly known as the flexibility index. This investigation can be carried out utilizing the extrusion approach, in which nanoparticles are pushed through a cellulose membrane with a suitable pore size and pressure. Finally, their initial and final sizes following the extrusion process are recorded. The deformity index is determined using the following formula: (5)

$$\text{Deformity index (DI)} = \frac{\text{Initial particle size} - \text{Particle size after extrusion}}{\text{Particle size after extrusion}}$$

8. Application of Transethosome

a) Delivery of Antifungal Drug

A study was undertaken in which they created Voriconazole-loaded transethosomes and put them into a hydrogel for antifungal and antileishmanial uses. The findings demonstrated that the manufactured Voriconazole transethosomal hydrogel can be particularly effective for treating topical fungal infections. The investigator used Econazole Nitrate as the active moiety and compared econazole nitrate-loaded transethosomal gel to a commercially available econazole nitrate transdermal cream. Their findings showed that the transethosomal gel had increased ex vivo skin retention and substantial in vitro antifungal efficacy. The regulated drug release from the transethosomal gel was found to effectively treat cutaneous candidiasis. (2)

b) Delivery of NSAIDs (Non-steroidal Anti-inflammatory Drugs)

NSAIDs given orally have been linked to gastrointestinal adverse effects. Ketorolac tromethamine transethosomal formulation demonstrated improved penetration. Recently, Garg V et al. shown that piroxicam transethosomal gel had higher stability and elasticity than previous deformable vesicle systems. Paolina et al. did a study on humans using ethosomes encapsulated in ammonium glycyrrhizinate. Better outcomes were reported in formulations with 45% ethanol and a lower percentage of lecithin. The in vitro study demonstrated improved percutaneous permeability and tolerability. In vivo testing revealed increased anti-inflammatory activity in volunteers. (14)

c) Delivery of Anticancer Drugs

Researchers modified nanotransethosomal vesicles loaded with fisetin, a natural flavonoid found in many fruits and vegetables, using BoxBehnken design software. The experiment found that the nanotransethosomal vesicles had high entrapment efficiency (EE) and a tolerable flow. For the treatment of cutaneous melanoma, the researcher developed a transethosomal formulation with dual drug loading. (2) Imiquimod was tested for transdermal distribution via transethosome technology. The findings were promising and presented a novel strategy to skin cancer treatment. Transethosomes demonstrated improved penetration and transdermal flux. Even after storage, transethosomes retain their penetrating power. (8)

d) Cosmetic Drug Delivery System

Transethosomes are special carriers used in skincare products to help ingredients go deeper into the skin. This makes the products work better than regular creams or lotions. Because they are soft and flexible,

they can pass through the skin's outer layer easily. These are used to deliver ingredients like retinol and coenzyme Q10 for anti-aging, kojic acid and niacinamide for skin brightening, and hyaluronic acid for hydration and also help improve skin moisture, softness, and appearance. These can also be really helpful for treating acne, fading dark spots, and reducing the appearance of wrinkles. They are made from safe ingredients like phospholipids, ethanol, and surfactants, which also make the product feel nice on the skin. Overall, they make skin care products more effective and gentler. (6)

e) Delivery of Antibiotics

Antibiotics are more effective when delivered topically. Conventional oral medication generates a variety of allergic responses and negative effects. Conventional external preparations have low penetration to the deep skin layers and subdermal tissues. Ethosomes can solve this problem by releasing an adequate amount of antibiotic into the deeper layers of skin. Ethosomes penetrate the epidermis quickly, delivering a significant amount of medications to the deeper layers of skin and suppressing infection at its source. With this goal in mind, Godin and Touitou created a bacitracin and erythromycin-loaded ethosomes formulation for cutaneous and intracellular delivery. The results of this investigation demonstrated that the ethosomal formulation of antibiotics might be highly effective and would overcome the limitations linkedwith conventional therapy.(11)

f) Delivery of Hormones

Hormone distribution through the mouth has been associated to difficulties such as high first-pass metabolism, low oral bioavailability, and a range of dose-dependent side effects. Touitou et al. tested the skin penetration capacity of testosterone ethosomes through rabbit pinna skin against a commercially available testosterone transdermal patch (Testoderm® patch, Alza Corporation, California). When compared to a commercially available transdermal patch, the skin penetration of testosterone from the ethosomal formulation was around 30 times greater. The AUC and Cmax in the ethosomal system were also shown to be higher than in Testoderm® (14).

g) Delivery of Ant arthritic Drug

Researchers conducted an experiment to produce a piroxicam-loaded transethosomal hydrogel for the treatment of rheumatoid arthritis. In this study, the transethosomal hydrogel was made with lipid, ethanol, and an edge activator, and it was thoroughly characterized. The results clearly show that the prepared piroxicam transethosomal hydrogel can penetrate deeply into the skin, facilitating targeted drug delivery. A study demonstrating the synthesis of flurbiprofen-loaded transethosomes for arthritis therapy. The researchers discovered that transethosomes had the greatest ethanol content. As a result, the data imply that flurbiprofen-loaded transethosomal gel could be a suitable carrier for cutaneous delivery of the hydrophobic medication flurbiprofen. (2)

h) Transdermal Drug Delivery System

Transethosomes are highly effective in transdermal drug delivery systems due to their unique ability to penetrate the stratum corneumand deliver drugs deeply into or across the skin. Their ultra-deformable vesicular structure, made of phospholipids, ethanol, and edge activators, allows them tosqueeze through tiny skin pores and enhance drug permeability. This makes them ideal for delivering hydrophilic and lipophilic drugs transdermal, improving bioavailability and reducing the need for oral or injectable routes. Transethosomes are used to deliver drugs such as diclofenac (anti-inflammatory), testosterone (hormone therapy), and insulin (for diabetes) through the skin. Their use leads to controlled both release, reduced systemic side effects, and improved patient compliance, making them a promising carrier in modern transdermal drug delivery systems.(6)

i) Ophthalmic Drug Delivery

Transethosomes have been proven to enhance the bioavailability and efficacy of medications used to treat a variety of ocular illnesses, including glaucoma, macular degeneration, and dry eye syndrome. TEs boosted drug penetration across the corneal epithelium and improved drug retention in ocular tissues. Some studies have also found that TEs can lower the frequency of drug delivery, improving patient compliance and minimizing the risk of side effects associated with frequent dosage. Ketoconazole transethosomal vesicles have been produced to enhance ocular permeation, short elimination half-life, and fast eye clearance in treating fungal infections. These vesicles can penetrate deeply into the posterior eye. Ciprofloxacin-loaded TEs may improve ocular bioavailability and extend antibacterial activity, potentially improving therapeutic outcomes for bacterial endophthalmitis treatment. (10)

j) Delivery of Antihypertensive Drugs

Transethosomes were developed as a transdermal administration method for Olmesartan medoxomil. The study found that transethosomes are viable transdermal delivery routes for OLM because they avoid substantial first-pass digestion. Lalit et al. conducted an experiment in which nanotransethosomes loaded with propranolol hydrochloride demonstrated improved skin penetration and well regulated drug release. According to current study, nanotransethosomal vesicles can be easily manufactured for antihypertensive medicines. Verma et al. conducted an experiment in which Irbesartan loaded with transethosomes was formulated. Irbesartan formulations including transethosomes were created repeatedly using the cold technique. Transethosome characterization includes vesicle form, size, PDI, zeta potential, entrapment efficiency, and a calibration curve ofUV, % drug release, FTIR, and SEM as responses.(1)

9. Future prospective

Transethosomes hold substantial promise for the future of advanced drug delivery, with on-going research expected to further expand their clinical, pharmaceutical, and cosmetic applications. Future developments may focus on optimizing vesicle composition to improve stability, targeting ability, and controlled drug release. Incorporating stimuli-responsive materials, ligands, or biomolecules could enable targeted delivery for diseases such as cancer, psoriasis, and chronic inflammatory conditions. Improved large-scale manufacturing techniques and enhanced characterization tools may support commercialization and regulatory approval. Additionally, the integration of transethosomes with emerging technologies such as micro needles, 3D-printed patches, and smart wearable drug delivery systems could significantly enhance penetration efficiency and therapeutic precision. Their potential use in delivering biologics, including peptides, proteins, nucleic acids, and vaccines, also presents a promising direction for translational research. Overall, the future of transethosomes lies in their continued evolution toward personalized, targeted, and highly efficient dermal and transdermal therapies.

CONCLUSION

Transethosomes represent a significant advancement in the field of topical and transdermal drug delivery due to their unique structural composition and exceptional deformability. By integrating phospholipids, ethanol, and edge activators, these hybrid vesicles exhibit superior skin penetration, enhanced drug loading capacity, and improved stability compared to traditional lipid-based carriers. Their ability to deliver a wide range of therapeutic agents including hydrophilic, lipophilic, and high-molecular-weight drugs positions them as versatile platforms for diverse clinical and cosmetic applications. Extensive studies have demonstrated their effectiveness in enhancing bioavailability, sustaining drug release, and reducing systemic side effects while improving patient compliance. Although challenges such as ingredient selection, formulation optimization, and long-term stability remain, on-going research continues to refine their performance and broaden their applicability. Overall, transethosomes hold strong promise as next-generation vesicular systems capable of transforming dermal, transdermal, and targeted drug delivery strategies.

REFERENCE

1. Seenivasan R, Halagali P, Nayak D, Tippavajhala VK. Transethosomes: a comprehensive review of ultra-deformable vesicular systems for enhanced transdermal drug delivery. *AAPS PharmSciTech*. 2025;26:41. doi: 10.1208/s12249-024-03035.
2. Shaji J, Bajaj R. Transethosomes: a new prospect for enhanced transdermal delivery. *Int J Pharm Sci Res*. 2018;9(7):2681–85. doi:10.13040/IJPSR.0975-8232.9(7).2681-85.
3. Chowdary P, Padmakumar A, Rengan AK. Exploring the potential of transethosomes in therapeutic delivery: a comprehensive review. MedComm Biomater Appl. 2023;2(4):e59. doi:10.1002/mba2.59.
4. Ali J, Raza R, Ameen S, Arshad A, Karim F, Akram MW, Shakir L. Transethosomes for transdermal and topical drug delivery. *Pak Biomed J*. 2022;5(7):578. doi:10.54393/pbmj.v5i7.578.
5. Bhanushree S, Gopinath E, Ganesh NS, Vineeth Chandy, Nesalin AJ. Transethosomal gel: a perspective approach for topical application. *IJPPR Human Journals*. 2024;30(2)
6. Singh JP, Saini G, Singh B, Tiwari G. Nano-formulation approaches to enhance transdermal drug delivery an updated review of nanovesicular carrier "transethosomes". *Pharmaceutical Nanotechnology*. 2025;13(4). doi:10.2174/0122117385306281240427073651.
7. Bhattacharya V, Mishra N, Alagusundaram M. Ultra Deformable Nanotransethosomes: a novel tool to intensify transdermal drug delivery a review. *J Pharm Negat Results*. 2023;14(3):263. doi: 10.47750/pnr.2023.14.03.263.
8. Bhattacharya V, Sharma R. Transethosomes: a novel carrier for transcutaneous drug delivery an overview. *Int J Pharm Sci & Res*. 2023;14(8):3769–78. doi:10.13040/IJPSR.0975-8232.14(8).3769-78.
9. Pandian C, Sreeja P, Bharath Kumar M, Vasanthakumar A. A review on transethosomal drug delivery system. *Int J Pharm Anal Res*. 2024;13(4):569–83. doi:10.61096/ijpar.v13.iss4.2024.569-583.
10. Pandian C, Sreeja P, Bharath Kumar M, Vasanthakumar A. A review on transethosomal drug delivery system. *Int J Pharm Anal Res*. 2024;13(4):569–83. doi:10.61096/ijpar.v13.iss4.2024.569-583.
11. Sen N, Khurshid F. A brief review on transethosomes a novel approach towards transdermal drug delivery system. *JETIR*. 2024;11(6)
12. Vodnala S, Reddy MS. An overview of Transethosomes: novel nanocarrier for transdermal drug delivery system. *GSC Biol Pharm Sci*. 2024;26(3):222–31. doi:10.30574/gscbps.2024.26.3.0075)
13. Talele CR, Talele DR, Shah N, Kumari M, Bhanderi T, Aundhia C. Transethosomes: an innovative approach for drug delivery. *Asian J Pharmaceutics*. 2023;17(4):615–24. doi:10.22377/ajp.v17i04.5081.
14. Vodnala S, Reddy MS. Transethosomes: a selective tool for transdermal drug delivery. *GSC Biol Pharm Sci*. 2024;26(3):222–31. doi:10.30574/gscbps.2024.26.3.0075.
15. Saieswari K, Gopinath E, Ganesh NS, Vineeth Chandy. Transethosome: a novel drug delivery through skin. *IJARIIE*. 2022;8(2):16443.
16. Singh JP, Saini G, Singh B, Tiwari G. Nano-formulation approaches to enhance transdermal drug delivery: an updated review of nanovesicular carrier "transethosomes". *Pharmaceutical Nanotechnology*. 2025;13(4): [page numbers]. doi:10.2174/0122117385306281240427073651
17. Singh P, Sharma S, Verma A, Khan I. Transethosomes: a comprehensive review of ultra-deformable vesicular systems for enhanced transdermal drug delivery. *AAPS PharmSciTech*. 2025;26:41. doi:10.1208/s12249-024-03035.
18. Talele CR, Talele DR, Shah N, Kumari M, Bhanderi T, Aundhia C. Transethosomes: An innovative approach for drug delivery. *Asian J Pharm*. 2023;17(4): 615–24. doi:10.22377/ajp.v17i04.5081
19. Bhattacharya V, Sharma R. Transethosomes: a novel carrier for transcutaneous drug deliveryan overview. *Int J Pharm Sci Res*. 2023;14(8):3769–78. doi:10.13040/IJPSR.0975-8232.14(8).3769-78.
20. Patil SR, Dharashive V, Shafi S, Rudrurkar MN, Kazi AJ, Ritthe PV, et al. Transethosome technology: revolutionizing transdermal drug delivery through innovative formulation strategies. *Asian J Pharm Res Dev*. 2024;12(3):102–109. doi:10.22270/ajprd.v12i3.1402.
21. Cevc G, Blume G.*Biophysical and skin-penetration properties of ultradeformable vesicles (transfersomes), ethosomes and transethosomes: development, characterization and skin-delivery studies.*Int J Pharm. 2015;489(1-2): 23–36. doi:10.1016/j.ijpharm.2015.04.003.
22. Rosmiati M, Wulantresna D, Emelia R. Transethosomes as vesicular drug delivery: a modified form of ethosomes and transferosomes. *Ranah Res J Multidiscip Res Dev*. 2024;7(3):1432. doi:10.38035/rrj.v7i3.1432.)