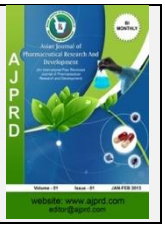
Available online on 15.06.2024 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

Open Access to Pharmaceutical and Medical Research



Open Access

Review Article

Transethosome Technology: Revolutionizing Transdermal Drug Delivery

Sneha R.Patil*, Vishveshwar Dharashive, Sameer Shafi, Muktai N. Rudrurkar, Anis J. Kazi, Punam V.Ritthe, Rohini U. Sante, Imran Shaikh

Shivlingeshwar College of Pharmacy, Almala Tq. Ausa Dist. Latur – 413520, Maharashtra [MH], India.

A B S T R A C T

In recent years, transdermal drug delivery has become increasingly popular as it overcomes issues with oral administration. The main challenge in this method is the complex stratum corneum barrier that prevents the transdermal administration of drugs. However, modern lipid-based nanosystems, particularly transethosomes, can effectively penetrate the dense network of the stratum corneum. Transethosomes are a promising and unique technique for improved transdermal medication administration via the skin, as compared to transferosomes and ethosomes. They are composed of phospholipid, ethanol, water, and edge activators or permeation enhancers. The combination of ethanol and edge activators allows the medication molecules to be delivered into circulation. There are various techniques used in the formulation of transethosomes, including the Cold method, Hot method, Thin film hydration method, and Mechanical dispersion method. Transethosomes have small particle sizes and can easily change the shape of vesicles, allowing them to pass through the layers of skin. The characterization of vesicles includes the size of the particle and surface charge, Transmission Electron microscopy, determination of entrapment efficiency, surface morphology study, interaction study by DSC and FTIR, drug content, and stability of vesicles. The transdermal route using UDV can administer various medication classes, including anti-arthritic, antibacterial, anticancer, antiviral, and analgesic.

Kewords: Transethosomes, Revolutionizing, Transdermal Drug Delivery,

A R T I C L E I N F O: Received 13 Feb. 2024; Review Complete 19 April 2024; Accepted 16 May 2024 ; Available online 15 June. 2024

Cite this article as:

Patil SR, Dharashive V, Shafi S, Rudrurkar MN, Kazi AJ, Ritthe PV, Sante RU, Shaikh I, Transethosome Technology: Revolutionizing Transdermal Drug Delivery, Asian Journal of Pharmaceutical Research and Development. 2024; 12(3):102-109

DOI: http://dx.doi.org/10.22270/ajprd.v12i3.1402

*Address for Correspondence:

Sneha R.Patil, Shivlingeshwar College of Pharmacy, Almala Tq. Ausa Dist. Latur – 413520, Maharashtra [MH], India.

INTRODUCTION:

There are various ways to administer drugs to the human body, and the most common method is through the mouth. However, this method has some limitations, such as the drug being eliminated before reaching the bloodstream, and interactions with other drugs. So, alternative drug administration methods have been developed. One such method is transdermal drug delivery, which has several advantages over other methods of drug administration. Transdermal drug delivery comprises a self-contained, discreet dosage form that is applied to the skin, allowing the drug to be delivered at a controlled rate into the bloodstream. This method has several benefits over injectable and oral methods, as it is more convenient for patients, avoids first-pass metabolism, and is more likely to be compliant with the patient's needs.[1]

ADVANTAGES OF TRANSDERMAL DRUG DELIVERY:[1]

The advantages of transdermal delivery over other delivery systems are as follows:

- Transdermal drug delivery system is a way of delivering drugs that allows them to bypass the first-pass metabolism.
- This method reduces the side effects that are commonly associated with traditional drug delivery systems.
- It also helps in achieving a constant plasma drug concentration, which can be beneficial for certain types of drugs with short half-life and low therapeutic index.

- The system has the added advantage of being easily removable in case of drug toxicity.
- Additionally, it reduces the dosing frequency and enhances patient compliance. It is possible to achieve the same therapeutic effect with a lower daily dose of the drug when using transdermal drug input.

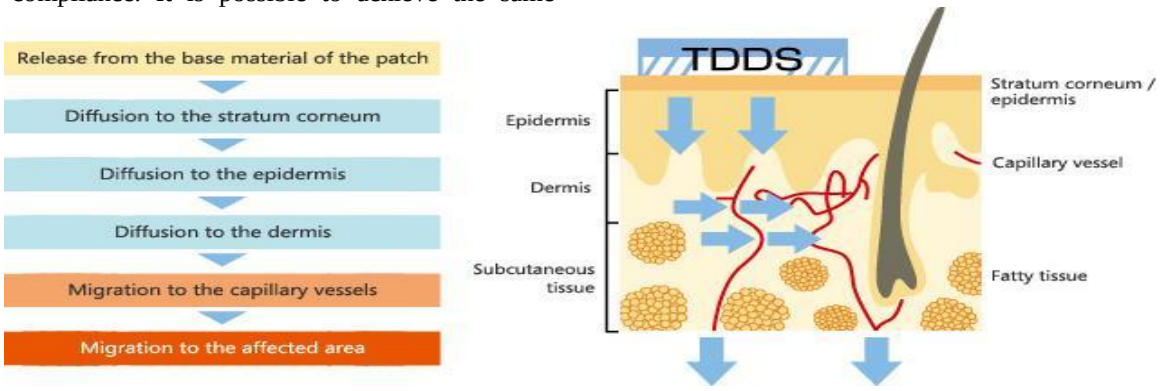


Figure 1: Mechanism Of Transdermal Drug Delivery.

Different Vesicular System and their Principalcomponents:

Transferosomes: phospholipid and edge activator.

Liposomes: phospholipid and cholesterol.

Niosomes: non-ionic surfactant and cholesterol.

Ethosomes: phospholipid and ethanol.

Phytosomes: phospholipid and phytoconstituents.

Pharmacosomes: phospholipid.

Similarities between Ethosomes, Transferosomes, and Transethosomes.

Table 1 , presents the differences between ethosomes, transferosomes, and transethosomes. Among these formulations, transethosomes have been found to be superior due to their high drug encapsulation efficiency and transdermal flux rate. They are capable of penetrating deep layers of skin and can change shape to deliver drugs more effectively.

Table 1: Similarities between ethosomes, transferosomes, and transethosomes

Variables	Ethosomes	Transferosomes	Transethosomes
Constitution	Phosphatides, ethyl alcohol and water.[8]	Phosphatides, edge stimulator, and water.[9]	Phosphatides, ethyl alcohol, edge stimulator and water.[10]
Encapsulation efficiency	High than liposomes.[11]	High than ethosomes.[12]	High than both ethosome and transferosomes.[5]
Transdermal flux rate	Greater than liposomes.[13]	High or equal to ethosomes.[14]	Highest flux rate.[15]
Permeation mechanism	Fat perturbation[16]	Distortion of vesicles.[17]	Transformation in structure of vesicles.[10]

Structure of Transethosomes :[1,2,3,4,5]

As seen in Figure 1, Transethosomes are a type of vesicle based on phosphatidylcholine that contains phosphatides, ethanol, edge stimulator, and water. Phosphatides act as a vehicle for delivering medication molecules to the surface. Transethosomes can easily combine with the horny layer, which enhances tissue moistening, and can combine with fats of stratum corneum. They have both hydrophilic and hydrophobic components.

Edge stimulator is an effective dual-layer softening agent that is often included to increase permeation and mobility. Ethanol is the primary component of the transethosomal system, which gives it a unique identity as a vesicle. Ethanol disrupts the topmost layer of the skin and makes these tiny structures flexible and versatile through fluidization, allowing them to enter the stratum corneum through extremely small openings. Water is a crucial component because it aids in the formation of a bilayer when phospholipids are introduced and promotes system flexibility.

The lipid bilayer is altered and made flexible as ethanol and edge stimulator are combined, allowing for deeper penetration into the dermis.

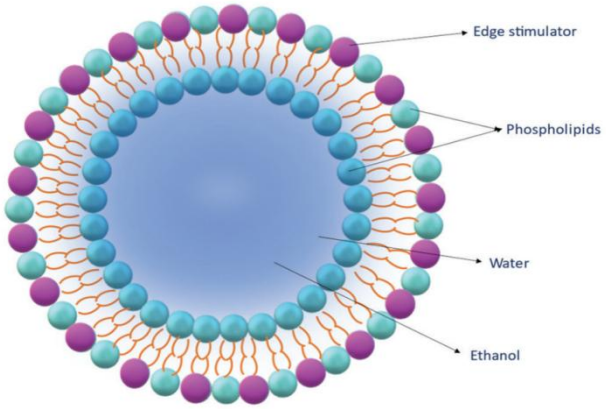


Figure 2: Structure of transethosomes

MECHANOSM OF ACTION:[6]

The vesicular system plays an important role in the transdermal delivery of drugs. It enhances the permeation of active drug components through the skin. The vesicles penetrate the skin and the drug is able to pass through it. Permeation enhancers such as Ethanol, Propylene glycol, and Isopropyl myristate increase the fluid content in the lipid bilayer along with the lipid content present in the stratum corneum, resulting in improved drug delivery.

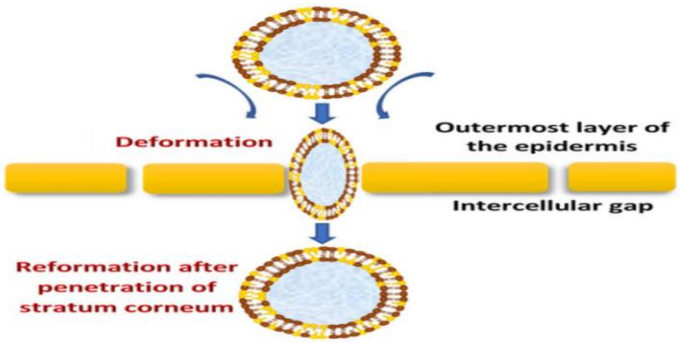


Figure 3: Mechanism of action of Transethosomes.

STRUCTURE OF SKIN :[7,8,9]

The three layers of skin are epidermis, dermis, and hypodermis.

Epidermis

The epidermis is the top layer of skin made up of keratinocytes. It comprises of two layers: non-viable and viable epidermis. The non-viable epidermis layer is also called the stratum corneum or horny layer. It is the outermost layer of the skin and is made up of tightly packed lipid bilayers that are found in the spaces between corneocytes. The stratum corneum serves as a crucial barrier that prevents the entry of outside materials into the body, including medication absorption.

Dermis

The medication is absorbed from the connective tissue matrix in this layer. Hair cavities, sebum glands, and sweat glands ascend to the epidermis, which also participates in drug transport.

Hypodermis

It is composed of a layer of subcutaneous fat tissue, which functions to cushion nerve endings and blood capillaries from shock while also providing nourishment and protection.

Layers of Epidermis :[10]

The layers of the epidermis include the stratum basale (the deepest portion of the epidermis), stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum (the most superficial portion of the epidermis).

Stratum basale, also known as stratum germinativum, is the deepest layer, separated from the dermis by the basement membrane (basal lamina) and attached to the basement membrane by hemidesmosomes. The cells found in this layer are cuboidal to columnar mitotically active stem cells that are constantly producing keratinocytes. This layer also contains melanocytes.

Stratum spinosum, 8-10 cell layers, also known as the prickle cell layer contains irregular, polyhedral cells with cytoplasmic processes, sometimes called “spines”, that extend outward and contact neighboring cells by desmosomes. Dendritic cells can be found in this layer.

Stratum granulosum, 3-5 cell layers, contains diamond shaped cells with keratohyalin granules and lamellar granules. Keratohyalin granules contain keratin precursors that eventually aggregate, crosslink, and form bundles. The lamellar granules contain the glycolipids that get secreted to the surface of the cells and function as a glue, keeping the cells stuck together.

Stratum lucidum, 2-3 cell layers, present in thicker skin found in the palms and soles, is a thin clear layer consisting of eleidin which is a transformation product of keratohyalin.

Stratum corneum, 20-30 cell layers, is the uppermost layer, made up of keratin and horny scales made up of dead keratinocytes, known as anucleate squamous cells. This is the layer which varies most in thickness, especially in callused skin. Within this layer, the dead keratinocytes secrete defensins which are part of our first immune defense.[i]

COMPOSITION AND FUNCTION OF TRANSETHOSOME :

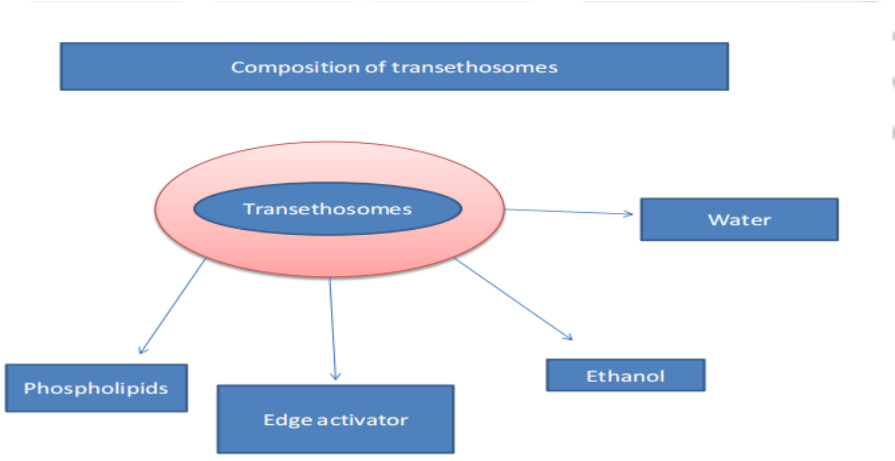


Figure 4: Composition of Transethosomes.

Transethosome components are under the category of "Generally Recognized as Safe" (GRAS)listed compounds22. Table 2 lists excipients that are often used and have GRAS Approval.

Table 2: GRAS approved list of excipients

Architecture	Excipients	Function
Phosphatides (2–5%)[23]	L-α-Lecithin, Phospholipon, and Phospholipon 90NG[24]	Vesicle formation
Edge stimulator[25]	Oleic acid, cholalic acid sodium salt, Tween 80, Tween 20, desoxycholic acid sodium salt, and Span 80[12]	It gives the vesicle flexibility and improves penetration.
Alcohol (40%)[11]	Ethanol, isopropanol, methyl glycol, and carbitol[24]	It makes the vesicle envelope supple.
Water (qs)	Water	Vesicle synthesizing agent

MERITS OF TRANSETHOSOMES :[11,12]

Transethosomes are a drug delivery system that does not require invasive procedures. They are designed to bypass the first-pass metabolism of the liver, which can cause side effects like vomiting or stomach irritation. Compared to other vesicular systems, transethosomes are more stable and can penetrate the skin more effectively. They can be used to encapsulate drugs, which allows for the controlled and sustained release of medication. To ensure patient compliance with their medication regimen, transethosomes can be administered in a semi-solid form, such as a topical gel or cream.

DEMERITS OF TRANSETHOSOMES :[12,13,3]

Due to the presence of ethanol in the formula, it may cause skin irritation, dermatitis and allergic reactions. Insufficient vesicle production can lead to the fusion of transethosomes.

METHODOLOGY:[14]

Vesicular nano-transethosomal systems can be easily prepared without the use of high-tech machines. These systems can be incorporated into gels, creams, or patches to increase their penetrability into the skin. There are various methods available for preparing the vesicular system, which are commonly used.

Different techniques of transethosomes formulation:

- Cold method
- Hot method
- Reverse phase evaporation method
- Direct method
- Mechanical dispersion method
- Ethanol injection

Cold method:[15]

To create vesicles, the phospholipid is mixed with ethanol by shaking it vigorously. This mixture is then heated to 30°C in a water bath. In another vessel, water is heated to the same temperature and added slowly to the ethanolic mixture. A magnetic stirrer is used at 700rpm to ensure uniform mixing during the process. If needed, a probe sonicator can be used to adjust the size of the vesicles.

Hot method:[16]

The process of creating phospholipid involves dispersing it in water and heating it up to 40°C. Similarly, a combination of ethanol and glycol is heated up to the same temperature. Next, the organic phase is mixed with the aqueous phase while stirring uniformly. Depending on the solubility of the drugs, either water or ethanol is chosen as the solvent system. The temperature is kept constant at 40°C throughout the process. To regulate the vesicular size, probe sonication can be employed.

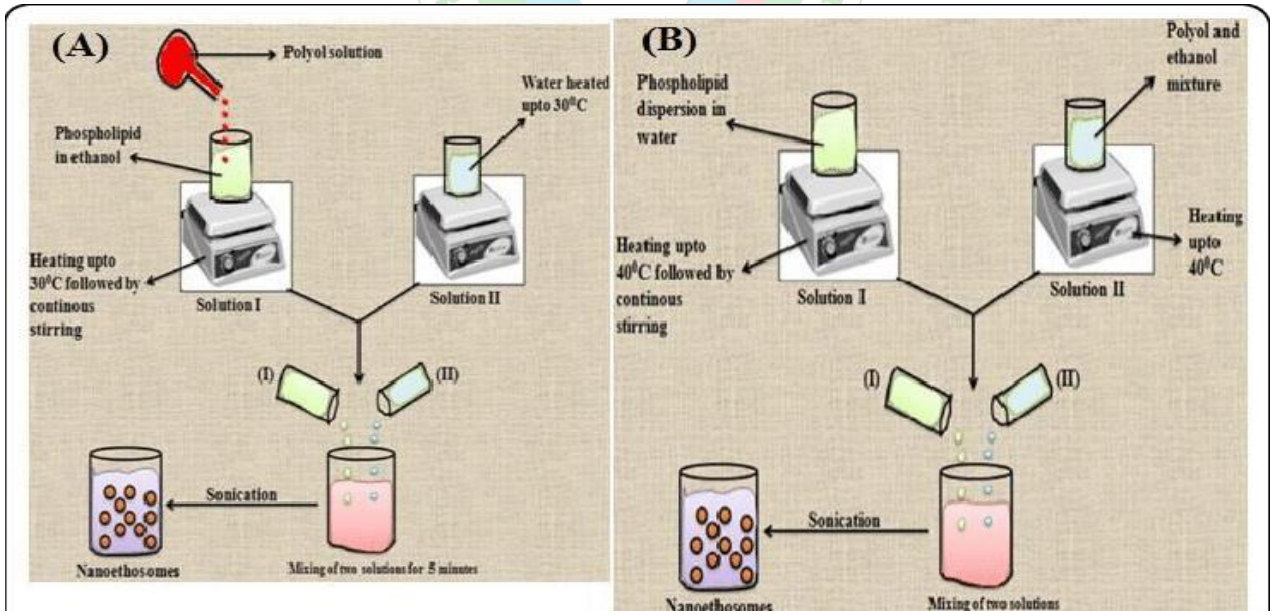


Figure 5: (A) Cold technique (B) Hot technique

Mechanical dispersion technique: [17]

In this technique, we use a round bottom flask and dissolve a mixture of liquid and surfactant in ethanol. To improve the efficiency of the process, we can combine hydrated thin film and ultrasound homogenization. We can produce a thin lipid film using a rotary evaporator, and remove the excess organic solvent by leaving it overnight under vacuum. For the hydration process, we use 10% v/v ethanol in phosphate buffer (pH 6.5) at 60 rpm. If we want to modify the vesicular size, we can use sonication technique.

Direct method:

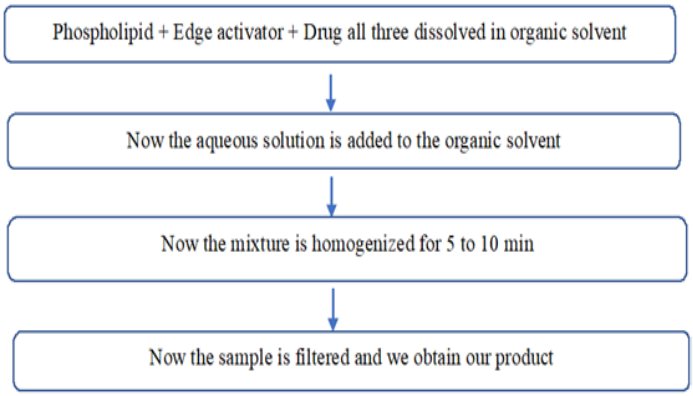


Figure 6: Direct method of transethosomes formulation

Reverse phase evaporation: [18,3]

Nanotransethosomes can be prepared using a specific method. First, dissolve the phospholipids in an organic solvent, and dissolve the drug and edge activator in an aqueous solvent. Next, add the aqueous phase to the organic phase and place the mixture in an ultrasonic bath at 0°C until two-phase separation occurs. Remove the organic phase and allow gel formation to occur under low pressure. After continuous agitation, the lipid layer is incorporated in the aqueous layer. Finally, filter the sample to complete the process.

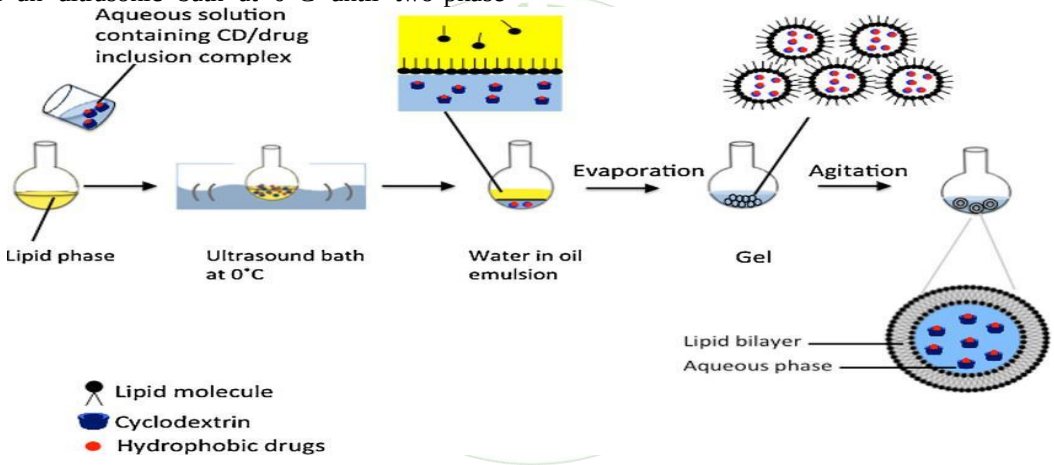


Figure 7: Formulation of Transethosomes by Reverse Phase Evaporation.

Ethanol injection method :

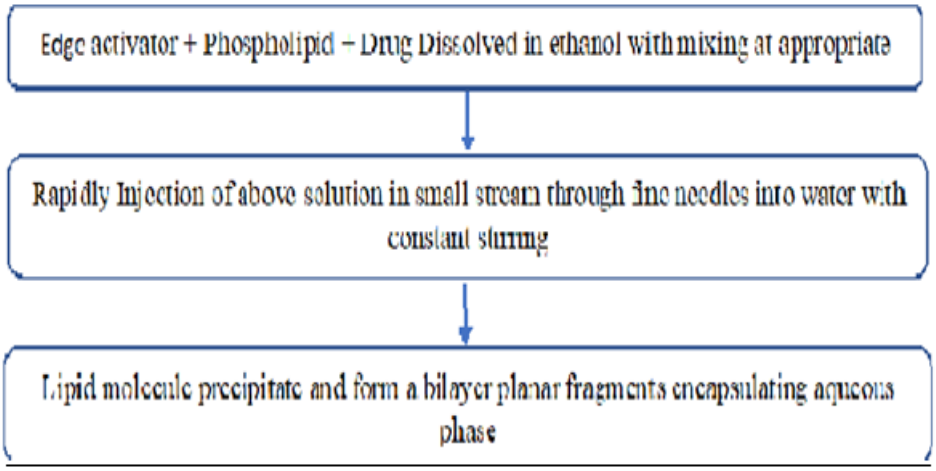


Figure 8: Ethanol injection system.

EVALUATION OF TRANSETHOSOMES:

Size of particle and surface charge[19]

Particle size and surface charge can be determined using specialized equipment. A laser scattering particle size distribution analyzer can be used to measure the size of the particle, while a zeta potential analyzer can measure the surface charge.

Transmission electron microscopy (TEM)[20]

To visualize the vesicles, transmission electron microscopy (TEM) can be used. The conventional negative staining method requires the use of 1% Phosphotungistic acid (PTA), and once dried, can be visualized.

Determination of entrapment efficiency[21]

The technique of ultracentrifugation is utilized to determine the entrapment efficiency of transethosomes. The process of ultracentrifugation is conducted at a speed of 1500 rotations per minute for 60 minutes at a temperature of 4°C. The sediment and supernatant liquid are separated, and the amount of sediment is measured to determine the drug entrapment efficiency. The entrapment efficiency is calculated using the following formula:

% Entrapment efficiency = Amount of API entrapped x 100.

Surface morphology study:[22]

Transethosomes consist of lipids which influence their surface morphology. The surface morphology can be determined through SEM analysis

Interaction study by using DSC and FTIR:[20]

Differential Scanning Calorimetry (DSC) is a method used to study how drugs interact with lipids. The Mettler DSC can determine the transition temperature (Tm) of the vesicular lipid system. To measure the Tm, aluminum crucibles are used at a heating rate of 10°/min within a temperature range of 200-300°C. Additionally, the Fourier Transform Infrared (FTIR) technique can also be used to study the interaction between drugs and lipids.

Drug content:[23]

To determine the drug content in transethosomes, a UV spectrophotometer can be used. For quantification, High-Performance Liquid Chromatography (HPLC) is the preferred method.

Stability of Ethosome: [23]

To assess the drug retention ability of transethosomal formulations, the preparations are subjected to different temperatures for varying periods of time. These temperatures include 25±2°C (room temperature), 37±2°C, and 45±2°C. In addition, the stability of ethosomes can be quantitatively determined by monitoring the size and morphology of the vesicles using DLS and TEM.

In vivo permeation study[24,2]

Skin distribution studies are conducted in rodents like rats and mice to evaluate the permeation of medication through various sections of skin, following transethosomal injection. The amount of medication accumulated in the horny layer is measured using a fluorospectrophotometer, after 24 hours. To visualize medication distribution across multiple layers of skin, wide-field fluorescence microscopy is used. It has been found that transethosomes penetrate deeper into the epidermal layers and overcome the barrier of the stratum corneum.

Ex vivo skin permeation [27,25,26]

Animal skin, such as goat or rat skin, is used in research to study skin permeation. A mucosal sample is placed on a diffusion cell containing phosphate-buffered saline in the receptor medium. The formulation is applied to the Franz diffusion cell's donor compartment, which is situated on the side of the horny layer. At regular intervals and a steady temperature, the sample is withdrawn from the cell's receiver compartment. The sink condition is maintained, and the sample is evaluated using High-performance liquid chromatography. It was observed that drug penetration through the surface is greater in transethosomal form when compared to other vesicular systems. Transethosomes were found to have higher flux rates. The total amount of drug penetration through an animal's membrane is determined by ,

$$Q_A = \left[C_T V_R + \sum C_i V_S \right]$$

C_T= Concentration of drug at particular time

V_R= Volume of receptor compartment of diffusion cell

Cn= Drug Concentration at the *n*th sample

V_S = Volume of sample

Q_A= Total amount of drug per unit area.

APPLICATION OF NANOTRANSETHOSOMAL VESICULARSYSTEM:

Delivery of Anticancer Drugs :[25]

An experiment was conducted to optimize nanotransethosomes vesicles loaded with fisetin using Box Behnken design software. Fisetin is a natural flavonoid that is found in various fruits and vegetables in ample amounts. The results of the experiment showed that the Nanotransethosomal vesicles had good EE (encapsulation efficiency) and reasonable flux was observed.

Delivery of Antiarthritic Drug :[30,28,29,3]

An experiment was conducted to develop and evaluate Naproxen Sulphapyridine transethosomal vesicle for transdermal delivery of drugs in the management of Rheumatoid Arthritis. The study combined and loaded the ethosomal hydrogel with NAP-SULF, an NSAID and DMARD that could reduce inflammation and pain. The researchers modified the thin film hydration technique to develop NAPSULF EH.

In Another study, they loaded Sinomenine hydrochloride, a drug for treating inflammation, onto ascorbic acid (an antioxidant) transethosomes. Ascorbyl palmitate was used as an antioxidant and transethosomes were used as a basic transdermal carrier. The study found that ASTE can be transdermally delivered to inflamed joints of CFA rats with

similar therapeutic efficacy to gastric administration of Sinomenine hydrochloride.

experimented with piroxicam-loaded transethosomal hydrogel to treat Rheumatoid Arthritis. They prepared nanotransethosomal hydrogel using lipid, ethanol, and edge activator and characterized them. The study found that the formulated piroxicam nanotransethosomal hydrogel can penetrate deeper into the skin with targeted drug delivery.

In another research work, formulated flurbiprofen-loaded transethosomes for the treatment of arthritis. The study found that TE contains the highest percentage of ethanol. Thus, from the result, it can be concluded that FLU-TELS gel could be a potential carrier for the dermal delivery of the hydrophobic drug Flurbiprofen.

Delivery of Antihypertensive Drugs: [32,31,11]

Recently, experiments were conducted to formulate transethosomes as a transdermal delivery system for Olmesartan medoxomil and Propranolol hydrochloride. The results have concluded that transethosomes could be considered as promising transdermal delivery systems for these drugs. They can avoid extensive first-pass metabolism and show better skin in vitro permeation with highly controlled drug release. Based on recent research, it can be concluded that nanotransethosomal vesicles can be easily prepared for antihypertensive drugs. Another experiment was conducted to formulate Irbesartan loaded with transethosomes. The formulations were prepared using the cold method and characterized for vesicle shape, size, PDI, zeta potential, entrapment efficiency, calibration curve of UV, % drug release, FTIR, and SEM.

Delivery of Antifungal Drug :[33]

An experiment was conducted to observe the formulation of Voriconazole-loaded transethosomes and their incorporation into a hydrogel for antifungal and antileishmanial application. The results of the experiment showed that the developed Voriconazole transethosomal hydrogel can be highly effective in treating fungal infections that occur on the skin surface.

Delivery of NSAIDs (Non-steroidal Anti-inflammatory Drugs): [17,18]

NSAIDs, when taken orally, have been associated with gastrointestinal side effects. However, a transethosomal formulation of ketorolac tromethamine has been found to have better penetration. Recent studies suggest that piroxicam transethosomal gel is more stable and elastic than other deformable vesicle systems. In an experiment, humans were given ethosomes containing ammonium glycyrrhizinate. The formulation with 45% ethanol and a lower proportion of lecithin produced better results. The in vitro study showed improved tolerability and percutaneous permeability, while the in vivo trial showed increased anti-inflammatory activity in volunteers.

Delivery of hormones: [34]

When administering hormones orally, there are several issues that can affect their effectiveness, such as high first-pass metabolism, poor oral bioavailability, and various dosage-dependent side effects. A study was conducted to compare the skin penetration capacity of a commercially available testosterone transdermal patch (Testoderm® patch, Alza Corporation, California) with a testosterone ethosomal formulation. The study used rabbit pinna skin to test the skin penetration of the two formulations. The results showed that the ethosomal formulation had about 30 times greater testosterone skin penetration than the commercially available transdermal patch. Additionally, the ethosomal system's AUC (area under the curve) and Cmax (maximum concentration) were found to be larger than those of Testoderm®.

FUTURE PROSPECT:

Transethosomal vesicular carriers are a type of innovative medication delivery technology currently being studied by researchers. The creation, production, importation, exportation, and distribution of drugs should be regulated to ensure adherence to established standards, which bodes well for the future. The manufacturer should verify that the transethosomal formulation meets the required standards. Excipients used by researchers are considered "Generally Regarded as Safe" and clinically non-toxic (GRAS). It provides an excellent carrier system that guarantees the stability of various proteins and medications, with the ability to load both hydrophilic and hydrophobic drugs. Transethosomes are capable of delivering many types of drugs, including antivirals, anti-diabetics, and anticoagulants. It is possible to administer an anticancer medication combination as transethosomes with minimal cytotoxicity. To enhance the effectiveness of a drug, combinations of different medications can be given as transethosomes. There is not much clinical trial literature available because it is not yet commercially available, but transethosomes have a lot of potential for use as a delivery system for topical or transdermal drugs.

CONCLUSION :

Certain active ingredients are unable to penetrate the skin's protective barrier. However, when drugs are encapsulated in transethosomal formulations, they are able to pass through the skin's outermost horny layer using both inter- and intracellular channels. Transethosomes consist of ethanol and an edge stimulator. Ethanol enhances the flexibility of the lipid layer, while also reducing the size of the vesicles. The edge stimulator aids in skin pore distortion and permeation. Due to their small size and fluidity, transethosomes can penetrate several sections of skin. This makes them a promising candidate for the treatment of skin cancer. Biomolecules enclosed in transethosomal formulations can penetrate deeper into the skin. This makes the concept of transethosome vesicular carriers an effective tool in pharmaceutical nanotechnology and medicinal products. However, further research is needed to fully understand and develop this vesicular system for use in the market.

REFERENCES:

1. Hani Yousef; Mandy Alhajj; Sandeep Sharma.Anatomy, Skin (Integument), EpidermisNCBI Bookshelf November 14, 2022.
2. Albash R, Abdelbary AA, Refai H, El-Nabarawi MA. Use of transethosomes for enhancing the transdermal delivery of olmesartan medoxomil: in vitro, ex vivo, and in vivo evaluation. International journal of nanomedicine. 2019 Mar 15:1953-68.
3. Mishra KK, Kaur CD, Verma S, Sahu AK, Dash DK, Kashyap P, Mishra SP. Transethosomes and nanoethosomes: Recent approach on transdermal drug delivery system. Nanomedicine. 2019 Feb 13;2:33-54.

4. Bragagni M, Mennini N, Maestrelli F, Cirri M, Mura P. Comparative study of liposomes, transfersomes and ethosomes as carriers for improving topical delivery of celecoxib. Drug delivery. 2012 Oct 1;19(7):354-61.
5. Rai S, Pandey V, Rai G. Transfersomes as versatile and flexible nano-vesicular carriers in skin cancer therapy: The state of the art. Nano reviews & experiments. 2017 Jan 1;8(1):1325708.
6. Gondkar SB, Patil NR, Saudagar RB. Formulation development andcharacterization of drug loaded transethosomes for transdermal delivery. Int J Chemtech Res.2017;10(6):535-44.
7. Cevc G. Transfersomes, liposomes and other lipid suspensions on the skin: Permeation enhancement, vesicle penetration, and transdermal drug delivery. Crit Rev Ther Drug Carrier Syst 1996;13:257-388.
8. Benson HA. Transdermal drug delivery: Penetration enhancement techniques. Curr Drug Deliv 2005;2:23-33.
9. Godin B, Touitou E. Ethosomes: New prospects in transdermal delivery. Crit Rev Ther Drug Carrier Syst 2003;20:63-102.
10. Hani Yousef; Mandy Alhajj; Sandeep Sharma. Anatomy, Skin (Integument), Epidermis NCBI Bookshelf November 14, 2022.
11. Kesharwani R, Patel DK, Sachan A, Kumar V, Mazumdar B. Ethosomes: A novel approach fortransdermal and topical drug delivery. Res J Top Cosmet Sci 2015;6:15-20.
12. Verma P, Pathak K. Therapeutic and cosmeceutical potential of ethosomes: An overview. J Adv Pharm Technol Res 2010;1:274-82.
13. Modi CD, Bharadia PD. Transfersomes: New dominants for transdermal drug delivery. Am J Pharm Tech Res 2012;2:71-91
14. Bajaj Kajal, Parab Bhagyashri and Shidhaye Supriya: Nano-transethosomes: A novel tool for drug deliverythrough skin. Indian Journal of Pharmaceutical Education and Research 2021: 1-10.
15. Sravani A, Shyamala SJ. An updated review on transethosomes. World J Pharm Res. 2019;8(13):629-37.
16. Dehaghani MZ, Mahapatra D, Joseph T. Novel vesicular system: an overview.Journal of applied pharmaceutical science. IntJ Med Phar Sci. 2021;11(08).
17. Shaji J, Bajaj R. Transethosomes: A new prospect for enhanced transdermal delivery. International Journal of Pharmaceutical Sciences and Research. 2018 ;9(7):2681-5.
18. Saieshwari K, Gopinath E, Ganesh N.S, Vineeth Chandy. Transethosome: A noveldrug delivery through skin.IJARIIE. 2022;8(2):1736-1746.
19. Song CK, Balakrishnan P, Shim CK, Chung SJ, Chong S, Kim DD. A novel vesicular carrier, transethosome for enhanced skin delivery of voriconazole: Characterization and in vitro/in vivo evaluation. Colloids Surf B. 2012;92:299-304.
20. Roshini R, Saraswathi T, Damodharan M. Ethosomes: Novel lipid vesicular Andnon-invasive delivery carrier–A review. Journal of Positive School Psychology http://journalppw.com. 2022;6(8):4099-111.
21. Nandure HP, Puranik P, Giram P, Lone V. Ethosome: A Novel Drug Carrier.International Journal of Pharmaceutical Research and Allied Sciences. 2013; 2(3):18–30.
22. Touitou E, Dayan N, Bergelson L, Godin B, Eliaz M. Ethosomes – novel vesicular carriers for enhanced delivery: characterization and skin penetration properties. J Control Release. 2000; 65(3):403–418.
23. Pandey V, Golhani D, Shukla R. Ethosomes: Versatile vesicular carriers for efficient transdermal delivery of therapeutic agents. Drug Deliv. 2015;22(8):988-1002.
24. Salem HF, Nafady MM, Kharshoum RM, Abd El-Ghafar OA, Farouk HO. Mitigation of rheumatic
25. arthritis in a rat model via transdermal delivery of dapoxetine HCl amalgamated as a nanoplatform: In vitro and in vivo assessment. Int J Nanomedicine 2020;15:1517-35.
26. Moolakkadath T, Aqil M, Ahad A, Imam SS, Iqbal B, Sultana Y, et al. Development oftransethosomes formulation for dermal fisetin delivery: Box-Behnken design, optimization, in vitro skin penetration, vesiclesskin interaction and dermatokinetic studies. Artif Cells Nanomed Biotechnol 2018;46:755-65.
27. Kaur P, Garg V, Bawa P, Sharma R, Singh SK, Kumar B, et al. Formulation, systematic optimization, in vitro, ex vivo and stability assessment of transethosome based gel of curcumin. Asian J Pharm Clin Res 2018;11:41-7.
28. Abdulbaqi IM, Darwis Y, Assi RA, Khan NA. Transethosomal gels as carriers for the transdermal delivery of colchicine: Statistical optimization, characterization, and ex vivo evaluation. Drug Des Devel Ther 2018;12:795-813.
29. Sajeev Kumar Babasahib, Roaddy Well Born and Nulgumnalli Manjunathaiah RaghavendraTransethosomal hybrid composites of naproxensulphapyridine in hydrogel carrier: anti-inflammatory response in completefreund's adjuvant induced arthritis rats, Artificial cells. Nanomedicine and Biotechnology 2022; 50: 59-70.
30. Song H, Wen J, Li H, Meng Y, Zhang Y and Zhang N: Enhanced transdermal permeability and drug deposition of rheumatoid arthritis via sinomeninehydrochloride-loaded antioxidant surface transethosome. Int J Nanomedicine 2019; 14: 3177-3188.
31. Bragagni M, Mennini N, Maestrelli F, Cirri M and Mura P: Comparative study of liposomes, transfersomes and ethosomes as carriers for improving topical delivery of celecoxib. Drug Deliv 2012; 19(7): 354-361.
32. Gadad AP, Patil AS, Singh Y, Dandagi PM, Bolmal UB and Basu A: Development and evaluation of flurbiprofen loaded transethosomes to improve transdermal delivery. Indian J of Pharmaceutical Education and Research 2020; 54(4): 954-62.
33. Akhtar N, Varma A and Pathak K: Ethosomes as vesicles for effective transdermal delivery: from bench to clinical implementation. Curr Clin Pharmacol 2016; 11(3): 168- 190.
34. Lalit Kumar and Puneet Utreja; Formulation and characterization of Transethosomes for Enhanced Transdermal Delivery of Propranolol Hydrochloride, Micro and Nanosystems 2020; 12: 38-47.
35. Aggarwal R, Sahoo PK. Ethosome: The novel drug delivery carriers. Sch Acad J Pharm. 2018;7(6):266-273.