TRANSETHOSOME: A NOVEL DRUG DELIVERY THROUGH SKIN

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ABSTRACT

Transdermal route is one of the promising routes for delivery of drugs. The delivery of drugs through skin is still a challenge as some bioactive molecules does not pass easily through stratum corneum. The development of ultradeformable vesicles (UDV) is an improved tool for dermal and transdermal therapies. The UDV includes ethosomes, transferosomes and transethosomes. Transethosome vesicular system provides enhanced permeation of drug through stratum corneum of skin due to the presence of increased concentration of ethanol, edge activators and phospholipids. Various methods are involved in the formulation of transethosomes such as hot method, cold method, thin film hydration method, reverse phase evaporation, transmembrane pH gradient method, ethanol injection method. Due to deformable characteristics of vesicular system results in increased drug entrapment efficiency, permeation and penetration of drug into the deeper layer of skin. The characterization of the vesicles include morphology of transethosomes, particle size and zeta potential, entrapment efficiency, transition temperature, drug content, vesicle stability, skin permeation studies, measurement of elasticity. These vesicular systems can be used for transdermal delivery of various drugs like antiviral, antibiotics, analgesic, anticancer, anti-arthritis etc.,

Keywords: *transdermal delivery, ultradeformable vesicles, edge activators, transethosomes, entrapment efficiency.*

1.INTRODUCTION:

The topical delivery of drug is considered as the one of the promising approaches. One of the promising substitutes for topical delivery is the transdermal delivery system. The main advantage of transdermal delivery system is to bypass first pass metabolism, localized effect, better patient compliance, increased efficacy by delivering the drugs to underlying percutaneous layer of skin[1]**.** The permeation of drugs through this system can be enhanced by various mechanism which includes chemical or physical enhancers like iontophoresis, sonophoresis etc**.,**[2]**.** The physicochemical properties such as lamellarity, size, surface charge, thermodynamic phase can be used to describe the effectiveness of a vesicular system. It has the capability to encapsulate large variety of drugs like hydrophilic, lipophilic and charged hydrophilic and amphiphilic drugs[3]**.**

Drugs with low or high partition coefficient has difficulty in reaching systemic circulation. To overcome this disadvantage novel drug delivery vesicles such as ultradeformable vesicles (UDV) have been developed. The UDV includes ethosomes, transferosomes and transethosomes are developed for administration of pharmaceuticals. Due to the presence of edge activators these deformable vesicles have higher penetration of drug through skin and higher entrapment efficiency. The fusion and aggregation can be avoided due to high elasticity and decreased vesicle size[4]. Many compounds, such as peptides and proteins, have been delivered dermally and transdermally using deformable vesicles. Furthermore, its manufacturing is straight forward and easy to scale up[5].

Ethosomes are novel lipid carriers which is composed of phospholipids, water and high concentration of ethanol. Ethanol act as permeation enhancer that affects the intercellular region of stratum corneum[6]. They contain 20-50% of ethanol in ethosomal formulation disturb the skin lipid bilayer. In this system modification of negative charge is caused by the ethanol that leads to some degree of stabilization[7].

The transethosomal system improves the physical and chemical qualities of therapeutic drug that is enclosed in transdermal and dermal delivery**.** The presence of higher concentration of ethanol releases the drug to targeted area by widening the pores of outer layer by inducing hydration[7]. The preparation of transethosomal system is not a complicated process and it does not require any pharmaceutical additives. The bioactive agent can be released in a gradual and slow manner. The entrapment of low to high molecular weight drugs can be done easy[8].

ADVANTAGES OF ETHOSOMAL SYSTEM[4,5]:

- The permeation of drug through skin is high for transdermal drug delivery.
- Avoidance of first pass metabolism
- The stability of formulation is high
- The delivery of sustain release and control release drug is possible
- Reduced side effects like gastric irritation, vomiting.
- Can be administered in the form of semisolid dosage form.
- It is suitable for the drugs with short half-life and narrow therapeutic range
- Controlled plasma level can be maintained.

TYPES OF ETHOSOMAL SYSTEM:

- Classical ethosomes
- Binary ethosomes
- Transethosomes

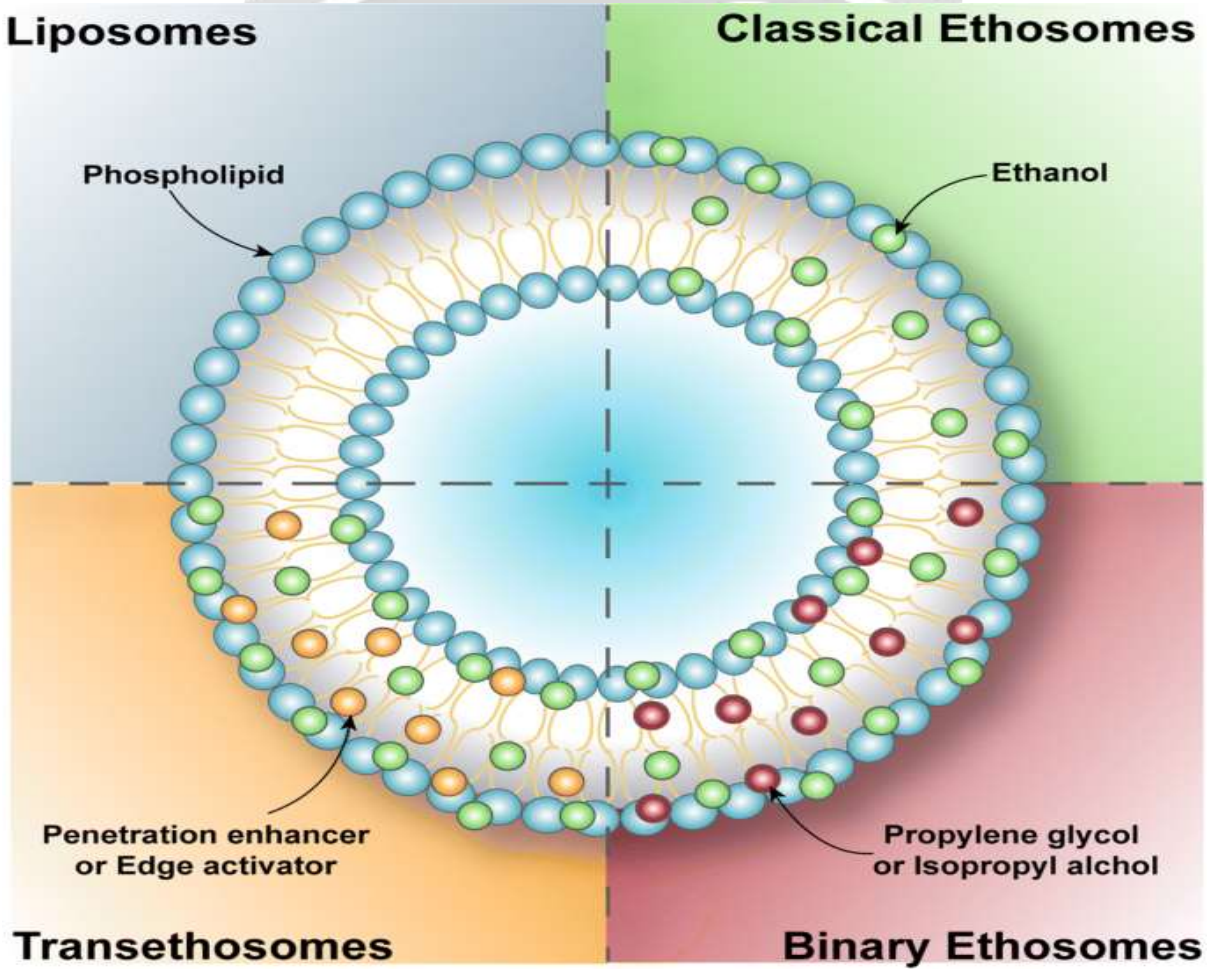


Fig 1: Types of Ethosomal system

Classical ethosomes

These are classical liposomes composed of phospholipids, ethanol concentration up to 45% w/w and water. These are smaller in size, negative potential and has higher entrapment efficiency. The molecular weight ranges from 130.007 Da to 24k Da[2].

Binary ethosomes

These are produced by adding alcohols to the classical ethosomes. Alcohols like Propylene Glycol (PG) and Isopropyl Alcohol (IPA)[2].

Transethosomes

These are lipid vesicles composed of transferosomes and ethosomes. Transethosomes contain upto 30% of ethanol which is a good penetration enhancer. They are irregular in shape. They contain advantages of both ethosomes and transferosomes. Rearrangement of lipid bilayers occurs in combination of ethanol and edge activator resulting in higher values in vesicles elasticity and skin penetration studies. They have a tendency to cross the intact skin by transcutaneous hydration gradient[9].

MECHANISM OF ACTION

The transethosome mechanism involves in two phases:

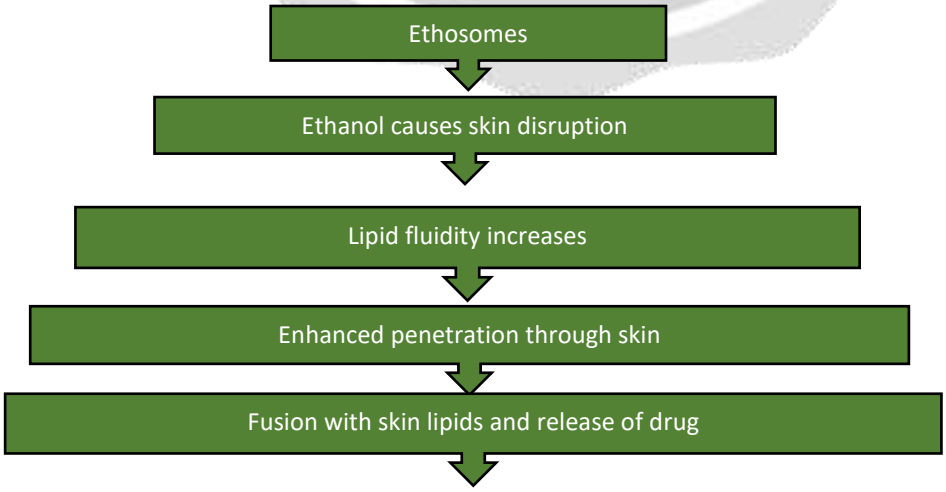
- Ethanol effect
- Ethosome effect

Ethanol effect:

Ethanol effect is considered to be the first mechanism for distribution of drug deeper into the skin layers. This results in reduced transition temperature of lipids in the stratum corneum and increased fluidity in transethosome which penetrates into the lipid layer of the skin by decreasing the density[2]. The presence of alcohol at the surface results in change in membrane shape. It is proved that alcohol breaks the single layer continuity by enhancing the fusion of discontinuous membrane[8].

Ethosome effect:

Transethosome effect is the second mechanism involved. The ethosomal system permeates and penetrates into the lipid layer. The movement of transethosomes through stratum corneum is facilitated by hydration force and bypasses the skin by osmotic theory[5]. Some of the penetration enhancers like (tween 20, tween 60, span 60, span 65, span 80 etc.,) disrupts the intracellular lipid in the stratum corneum layer which facilitates the permeation of drug across the skin[10]



SALIENT FEATURES OF TRANSETHOSOMES:

- Due to enhanced biocompatibility and biodegradable nature, their entrapment efficiency is higher
- They have higher flux rate due to increased flexibility
- Drugs with low and high molecular weight can be entrapped
- Transethosome system can be used for both systemic and topical delivery.
- Higher rate of penetration through skin when compared to other vesicular system[3].

COMPOSITION OF TRANSETHOSOMES:

- High concentration of ethanol
- Phospholipids
- Cholesterol
- Edge activators or penetration enhancer (tween 20, tween 60, tween 80, span 60, span 65, span 80, sodium deoxycholate, propylene glycol).
- Drug/active compound[11].

Ethanol

Ethanol is considered as an efficient penetration enhancer which is characterized in terms of size, stability, entrapment efficiency and skin permeability. The concentration of ethanol in transethosome is up to 10%-20% and also provides softness to the vesicles containing transethosomes[2].

Increased concentration of ethanol results in decrease in size of ethosomes and shifting of vesicular charge from positive to negative which is an important parameter that produces impact on vesicular properties such as stability and vesicle skin interaction. Increase in ethanol concentration will increase the entrapment efficiency. Increase in ethanol beyond the optimal concentration results in leaky bilayer, increased vesicular size and critical decrease in entrapment efficiency**.** The solubility of hydrophilic and lipophilic drug is increased by ethanol which results in increased drug loading[11].

Phospholipids

The phospholipid selection is an important parameter to develop an ethosomal system. It has a significant impact on the size of ethosome. The type and the concentration of phospholipid is an important factor which influences the size, entrapment efficiency, zeta potential, stability and penetration and permeation properties of the vesicular system[2].

This helps in formation of vesicles in which the concentration of phospholipids ranges from 0.5% to 5%. Increase in phospholipid concentration results in slight or moderate increase in size of the vesicle[2].

Shen *et al.,* found that the use of Lipoid S100 or SPC50 in preparation of transethosome resulted in smaller size when compared to those produced by Lipoid E80. The use of Lipoid E80 phospholipid resulted in production of stable vesicles due to higher concentration of phophotidylcholine content. Thereby further increase in phospholipid concentration will have no effect on entrapment efficiency**.**

Cholesterol:

The incorporation of cholesterol into ethosomal system resulted in enhanced stability and entrapment efficiency. It is reported that cholesterol increases the vesicular size. The concentration range of cholesterol used were found to be <3% in some formulation. Increased concentration of cholesterol at the range of 0% to 0.15% w/w resulted in increased vesicular size from 102± 13 nm to 152± 12 nm. It is found that cholesterol stabilizes into the ethosomal system and prevents the aggregation of the particles[12].

Edge activators or penetration enhancer:

The proper selection of edge activator is a critical step in the formulation of transethosomes as they influence the properties of the ethosomal system. The most commonly used edge activators are tweens and spans[10].

Surfactants[10]:

The most commonly used surfactants for the transethosomal system include the anionic and non-ionic surfactants. The non-ionic surfactants include Cremophor EL-35, Cremophor RH-40 etc., and some of the anionic surfactants used are Sodium cholate, Deoxycholic acid, Sodium stearate. The surfactant like Polyethylene glycol can be used in the preparation of transethosomes.

Tweens and Spans

Tweens and Spans like Tween 80, Tween 60, Tween 20, Span 20 Span 40, and Span 60 are used in the formulation of transethosomal system. It is reported that Tween 80 in ethosomal system resulted in increased stability and reduction in vesicular size. This resulted in enhanced skin permeation property.

Formulation containing Tween 20 was established by Bragagni *et al.*, This resulted in smaller vesicle size (258.4±3.3 nm), enhanced *Ex vivo* skin penetration through the human skin and enhanced entrapment efficiency compared to ethosomal system containing Tween 80.

The addition of Tween 60 to the transethosomal formulation of artesunate and febrifugine resulted in unstable formulation due to formulation of crystals after 5 days.

Another study resulted that use of Span 20 in transethosome formulation containing caffeine and vitamin E was successful.

Cremophor:

Cremophor is an ethoxylated detergent. Shu Meng *et al*., used cremophor EL-35 in the preparation of testosterone propionate ethosomal system at the concentration range of 0.5%-1.5%. The use of cremophor EL-35 resulted in increased solubility of drug which further resulted in enhanced entrapment efficiency and reduction in vesicular size.

Cremophor RH-40 was used by Shen *et al.*, in the formulation of artesunate and febrifugine transethosome, it was found that the vesicles were unstable due to formation of needle crystals after 5 days[10].

Propylene glycol:

Edge activator/penetration enhancer	**Concentration in ethosomal system**	**Type**
Tween 80	10%-50%	Nonionic surfactants
Tween 60	1%-50%	Nonionic surfactants
Tween 20	15%-50%	Nonionic surfactants
Span 20,40,60,80	1%-50%	Nonionic surfactants
Cremophor EL-35	0.5%-1.5%	Nonionic surfactants
Cremophor RH-40	1%-50%	Nonionic surfactants
Polyethylene glycol 4000	1%, Molar ratio- Phosphatidylcholine: cholesterol: polyethylene glycol 4000- (2:1:1 and 6:2:1)	Surfactants
Sodium stearate	Molar ratio- Phosphatidylethanolamine: cholesterol: sodium stearate (2:1:2.5)	Anionic surfactants
Sodium deoxycholate	0.8%w/v	Bile acid/anionic surfactant

Table 1: *Edge activator or penetration enhancers used in preparation of transethosomes*[10]

Propylene glycol is an extensively used penetration enhancer in the preparation of ethosomal system.

Transethosome formulation containing propylene glycol provides enhanced distribution of the drug through the vesicles. This resulted in increased drug solubility and higher entrapment efficiency of drugs. The propylene glycol is most used in the preparation of binary ethosomes. It is used in concentration range of 5%-20%. The Bhalaria used PG in a novel delivery antifungal drug of ethosomal system and the DSC studies resulted that use of PG in this ethosomal system resulted in increased fluidity of ethosomes than liposomes and the *In vitro* diffusion of drug from ethosomes was twice than the liposome[13].

METHOD OF PREPARATION OF TRANSETHOSOMES

- Hot method
- Cold method
- The Ethanol injection -Sonication method
- The Reverse phase evaporation method
- Transmembrane pH gradient method
- Thin film hydration method

Hot method:

The hot method was first established by Touitou in 1996. The dispersion of phospholipid in a beaker containing water by heating in a water bath at 40ºC. Ethanol and propylene glycol are mixed and heated in a water bath to 40ºC in a separate water bath. The organic phase is then added to the aqueous phase. Depending on the hydrophobic/hydrophilic properties, the drug is dissolved in ethanol or water. The probe sonication or extrusion method can be used to reduce the vesicle size of the ethosomal formulation to the desired extent[11].

Cold method:

It is the most widely used method for the preparation of ethosomal formulation. In this method either normal saline solution or water is used as aqueous phase. The organic phase consists of phospholipids in ethanol. This method is widely used for the preparation of binary ethosomes. By using a syringe pump aqueous phase is added dropwise to the organic phase and stirred continuously using a magnetic stirrer at a speed of 700-2,000 rpm for 30minutes. Depending upon its physicochemical properties drug is dissolved in either organic or aqueous phase and then incorporated into the ethosomal system[10].

Ethanol injection sonication method:

This method was described by Touitou *et al.,* In this method the drug is dissolved in water and filled in a syringe. Another glass bottle was used in which lipids are dissolved in ethanol. With continous stirring aqueous phase is added to the organic phase in a fine stream[7].

Mechanical dispersion method:

Round bottom flask is used in this method. Soya phosphotidylcholine is dissolved in a round bottom flask containing suitable organic mixture. The organic solvent is evaporated using a rotary vacuum evaporator under a temperature that is above lipid transition temperature. The flak is then left overnight, where the lipid film gets deposited on the flask from which the trace of solvents can be obtained. Simple rotation of round bottom flask is done for the hydration for different concentration of drug mixture[8].

Reverse phase evaporation method:

Ethanol is used as organic solvent in which lipids are dissolved. Edge activators is added to the aqueous phase. The aqueous phase is then introduced into the organic phase. The separation of two phases is done by placing the mixture in ultrasonic bath 0ºC. Under low pressure the formation of gel occurs by removal of organic solvent. The mixture is then agitated and the lipid layer is encapsulated then subjected to filtration[4].

Transmembrane pH gradient method:

This method was first used for the formulation of liposomes. Zhou *et al.,* 44 and Fan *et al.,* 55 used this method for the preparation of alkaloid ethosomal system of Sophora alopecuroides and terandrine. In this method drug is loaded actively based on pH-gradient difference between the internal acidic phase and the external basic phase of the ethosomal formulation. This method involves three steps for the formulation of ethosomal system: First

stage involves the preparation of blank ethosomal system, the second stage involves loading of drug actively followed by final stage of incubation at specified temperature and time for the active passage of unionized drug to the bilayer of ethosomal vesicle[7].

Thin film hydration method:

In this method accurately weighed drug, lipid and edge activator are dissolved in a mixture containing organic mixture. A rotary evaporator can be used which forms a thin film on evaporation under reduced pressure. The film is then hydrated using pH 7.4 buffer with different concentration of ethanol. The mixture is then left overnight for hydration[9].

CHARACTERIZATION OF TRANSETHOSOMES:

Various characterization methods of transethosomes

- Morphology of Transethosomes
- Particle Size and Zeta Potential
- Entrapment Efficiency
- Transition Temperature
- Drug content
- Vesicle stability
- Skin Permeation studies
- Measurement of elasticity

Morphology of Transethosomes[10]

Vesicle shape of transethosomes can be identified. The visual imaging can be done by using

- ✓ Transmission electron microscopy (TEM)
- ✓ Scanning electron microscopy (SEM)

Particle size and Zetapotential[3,5]

Particle size of the transethosomes can be studied by using

- ✓ Dynamic light Scattering (DLS)
- ✓ Photon correlation spectroscopy (PCS)

The size of transethosomes ranges from tens of nanometers to microns.

The surface charge of the particle can be studied using Zeta potential.

The Stability of the particle can also be predicted by this method.

Entrapment Efficiency[7]:

The entrapment efficiency is an essential characterization of transethosomes. It is carried out by ultracentrifugation technique. This method describes the efficiency of ethosomes to entrap both hydrophilic drug and lipophilic drug by high degree lamellarity and the presence of ethosomes in vesicles.

Entrapment efficiency= DE/DT*100

DE-Amount of drug in ethosomal sediment

DT-Amount of drug used for the preparation of system

Transition Temperature[4]:

The release of drug from the vesicle can be studied using this method. The samples are identified by comparing the differential thermal curves obtained from the Differential Scanning Calorimeter (DSC**)** under a constant nitrogen stream.

Drug content[14,15]:

The amount of drug present in transethosome formulation can be determined by using methods such as

- ✓ U.V. spectrometer

- ✓ High Performance Liquid Chromatography.

Vesicle stability[16]:

The vesicle stability of transethosomal formulation were studied by placing them at different temperatures, i.e., 25±2ºC, 37±2ºC, 45±2ºC. DLS and TEM can be used to monitor the size and morphology of transethosomes.

Skin permeation studies[17]:

The skin permeation studies of transethosomes can be studied using an *in-vitro* method by using a Franz diffusion cell. In this method the ability of ethosomal preparation to penetrate through the skin can be determined using Confocal Laser Scanning Microscopy (CLSM). The temperature is maintained at 32ºC±1ºC. The area of the receptor compartment call is 10 ml `which contains PBS (10ml of pH 6.5). The skin is placed between the donor and the receptor compartment. The prepared formulation of transethosomes is then applied to the epidermal surface of skin. Samples are withdrawn at different time intervals such as 1, 2, 3, 4, 8, 12, 16, 20, 24 hours. The withdrawn samples are analyzed and assayed by high-performance liquid chromatography (HPLC)

Measurement of elasticity[4]:

The measurement of elasticity of ethosomes can be performed by using extrusion method. In this method an extruder is used through which the ethosomal formulation are passed through filter membrane of diameter 50nm. Stainless steel filter of diameter 25 mm can be used under the pressure of 2.5 bar. The quantity of vesicle suspension extruded in 5minutes are measured. The elasticity of vesicle membrane can be calculated by using the following formula: $\mathbf{E = J*(r_v / r_p). ()}$

Determination of pH[18]:

The pH of the transethosomal formulation can be estimated by using digital pH meter.

Degree of degradability and turbidity[19]:

Degree of deformablility of ethosomal formulation can be determined by using extrusion method. Nephalometer is used for determining the turbidity of transethosomal formulation.

APPLICATIONS OF ETHOSOMAL SYSTEM:

Ethosomes are typically used to replace liposomes. The transdermal mode of medication delivery is the most popular. Ethosomes can be used to transfer hydrophilic and impermeable medicines to the skin via transdermal administration. The ethosomal carrier has been employed with a variety of medicines[7].

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

NSAID's administered through oral routes are associated with GI side effects. Ketorolac tromethamine transethosomal formulation showed enhanced penetration. Recently Garg V *et al.,* proved piroxicam transethosomal gel shows enhanced stability and highest elasticity as compared to other deformable vesicle system[10].

Paolina *et al.,* conducted experiment on humans taking ethosomes entrapped with ammonium glycyrrhizinate. The better results found in formulation containing 45% of ethanol and lesser concentration of lecithin. The *in vitro* study resulted in enhanced percutaneous permeation and better tolerability. The *In vivo* study resulted in enhanced anti-inflammatory activity in volunteers[20].

Delivery of hormones:

Hormone delivery via mouth has been linked to issues such as high first-pass metabolism, low oral bioavailability, and a variety of dose-dependent adverse effects. Touitou *et al.,* compared the skin penetration potential of testosterone ethosomes through rabbit pinna skin to 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 roughly 30 times higher. The AUC and Cmax in the ethosomal system were likewise found to be higher than in Testoderm®[21].

Delivery of Antibiotics:

Antibiotics used topically are a better option for boosting their therapeutic efficacy. Oral therapy used in the past has resulted in a number of allergic responses as well as a number of negative effects. Ethosomes can avoid concerns like limited permeability to deep skin layers and subdermal tissues that are common with standard external preparations. Ethosomes penetrate the epidermis quickly, delivering a large quantity of medicines to the deeper layers of the skin and suppressing infection at its source. Godin and Touitou produced a bacitracin and erythromycin-loaded ethosomal formulation for cutaneous and intracellular delivery with this purpose in mind. The findings of this investigation demonstrated that an ethosomal antibiotic formulation could be highly effective and overcome the drawbacks of traditional therapy[21].

Delivery of Antifungal Drugs:

The penetration of transethosomes containing terbinafine, amphotericin B, and ketoconazole was improved. In comparison to normal liposomes, deformable liposomes, and ethosomes, voriconazole transethosomes displayed skin penetration and deposition[10].

Delivery of Anti-parkinsonism agent:

Dayan and Touitou created an ethosomal formulation of the psychoactive substance trihexyphenidyl hydrochloride (THP) and compared it to traditional liposomal formulations. THP is an antagonist of M1 muscarinic receptors that is used to treat Parkinson's disease. The findings suggested that the ethosomal-THP formulation had a higher skin penetration capacity and might be used to better control Parkinson's disease[21].

Delivery of Anti-Viral Drugs:

Zidovudine is a powerful antiviral medication that targets the AIDS virus. Zidovudine has a lot of negative side effects when used orally. An adequate zidovudine zero-order delivery is desired to maintain the projected anti-AIDS impact (Kim, S., & Chien, Y.W. 1996). According to Jain *et al.,* (2004), ethosomes can improve transdermal flow, extend release, and provide an appealing route for zidovudine distribution. Another antiviral medicine that is commonly used topically to treat Herpes labialis is acyclovir (Spruance, S. L. 1992, September). The current marketed acyclovir external formulation has been linked to inadequate skin penetration of hydrophilic acyclovir into the dermal layer, resulting in low therapeutic efficacy[21].

Transcellular Delivery:

Touitou *et al.,* used CLSM and FACS techniques in different cell lines to demonstrate greater intracellular uptake of bacitracin, DNA, and erythromycin. In comparison to the commercial formulation, ethosomes showed better cellular uptake of anti-HIV drugs zidovudine and lamivudine in the MT-2 cell line, suggesting that ethosomes could be a promising therapeutic option for anti-HIV therapy[21].

Cosmeceutical application of ethosomes:

Ethosomes have been successfully used in cosmetic formulations for a variety of benefits, including greater stability, reduced skin irritation from irritating cosmetic chemicals, and improved transdermal penetration, particularly in elastic forms. Curcuma longa extract-based ethosomal creams have also been developed and tested for photoprotective and antiwrinkle effects. When administered to human volunteers as a photoprotective and antiwrinkle agent in both investigations, C. longa extract loaded ethosomal creams exhibited encouraging outcomes. Yeh *et al.,* created a transethosome-based hair dye that was proven to be more successful than a hydroethanolic solution in delivering and boosting the absorption of black tea extracts to the hair surface[7].

Delivery of Anticancer drugs:

To treat cutaneous melanoma, Lei *et al.,* conducted trials using a transethosomal formulation with dual drug loading. They chose two medicines, dacarbazine and tretinoin, that exhibited a synergistic impact and reduced cytotoxicity when compared to the other formulations.

When compared to a single loaded medication, dual loaded transethosomes demonstrated increased anticancer activity. They discovered that skin penetration can be improved. When compared to ethosomes, Shaji *et al.,* found that encapsulating 5-fluorouracil into a transethosomal gel resulted in enhanced deformability, increased skin penetration, and deeper skin targeting[4].

FUTURE PROSPECTS:

The majority of active chemicals do not make it past the stratum corneum barrier. Because they have the capacity to fluidize and destabilise the stratum corneum's hard lipid layer, ethanol-based nanocarriers have created a new window for delivering diverse bioactive compounds transdermally. Clinical investigation of the ethanol-based nanocarrier technology is still difficult. To determine their potency, they must be evaluated clinically. Because ethanol has an irritating effect on skin, ethanol-based nanocarriers need to be tested in particular specific clinical situations, such as their application to open regions of eczema[22].

Transethosomal vesicular carriers have piqued researcher interest among the current innovative drug delivery technologies. It ensures a bright future by requiring drug development, manufacture, importation, exportation, and distribution to adhere to strict guidelines. It has a superior carrier system, which ensures the stability of various proteins and medications. It can be used to load both hydrophilic and hydrophobic medications. Transethosomes can be used to test a variety of drugs, including antivirals, anti-diabetics, and anticoagulants. Transethosomal administration of an anticancer medication combination with low cytotoxicity and good skin penetration is possible[4].

CONCLUSION:

The permeation of some bioactive molecules through skin has barriers. The development of ethanol based ultradeformable vesicular (UDV) systems provides greater penetrability through skin. The novel vesicular system includes ethosomes, transferosomes, transethosomes. Among this transethosomal vesicular system has the ability to provide better solubility, penetration, flexibility due to its greater compatibility to both hydrophilic as well as hydrophobic drug molecules. The transethosomal system is composed of ethanol and edge activators that helps in enhanced topical delivery of drug to the targeted site. Due to high carrier facility transethosomal system has the capability to deliver drugs with large molecular weight like peptides and protein molecules. The topical application of transethosomal gel or cream has high patient compliance. This ethosomal system are also used in delivery of antifungal, antiviral, anticancer, antiparkinsonian drugs and cosmeceuticals. The transethosome vesicular system offers safety, efficacy, patient compliance hence is more superior to other conventional transdermal permeation techniques.

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