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Review Article

AN OVERVIEW ON ULTRA DEFORMABLE VESICULAR DRUG DELIVERY SYSTEMS IN TRANSDERMAL DRUG DELIVERY

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ABSTRACT

Transfersomes are emerging carriersin transdermal applications owing to numerous benefits like ease of application, reduction in dose frequency, In this review, we will describe about the penetration mechanism of transfersomes, method to prepare the formulation and characterization of transferosomal formulation, like thin film hydration, vortexing sonication, modified handshaking, suspension homogenization, centrifugation, and ethanol injection apart from these characterizations include, vesicle size, shape zeta potential, *in vitro,* and *in vivo* to find out the optimized formulation charactering the transferosomal preparations chemical, physical and miscellaneous properties to meet the ideal requirements of formulation and achieve the grater bioavailability and to attain good stability. These formulations are gaining good importance as Novel Drug Delivery Systems because of their patient compliance, ultra deformable and flexible nature due to the presence of surfactants and other pharmaceutical excipients like cholesterol, phospholipids in the formulation; hence these are known as first-generation liposomes.

Keywords: Transfersomes, Homogenization, Thin film hydration. Sonication, Novel drug delivery systems. C, Cholesterol

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INTRODUCTION

In most of the cases, the effective and successful treatment may not possible because of many reasons, such as hepatic first-pass metabolism, adverse reactions denying of invasive procedure, poor patient compliance. Numerous drug delivery techniques have been found during the last few decades to address these problems. Among the drug delivery system, one of the promising approaches is the transdermal drug delivery system as they are painless and did not show first-pass effects. Given the increased patient convenience, longer duration of action, and less side effects, it is an intriguing choice. The usage of drug with short half-life improving pharmacological as well as physiological responses and avoid the changes in drug concentrations and differences in inter and intra patients. Thus, advances in drug delivery systems are being made in the pharmaceutical industry using a variety of physical and chemical methods, such as iontophoresis, sonophoresis, or colloidal carriers like liposomes, niosomes, and transferosomes [1-4]. This review aims to focus on the usage of the Tfs as a drug delivery system in the management of various diseases. A more detailed overview has been provided about the Tfs preparation, penetration mechanism, and therapeutic applications, including drug delivery. This literature survey was done in PubMed, google scholar, MDPI and the keywords were used to serach preparation methods, applications. The review has a collection of articles from the last 27 y (from 1996 to 2022).

Transfersomes

The vesicular carrier system is specifically developed to include an edge activator (surfactant) and at least one internal aqueous compartment that are surrounded by a lipid bilayer, as shown in fig. 1.

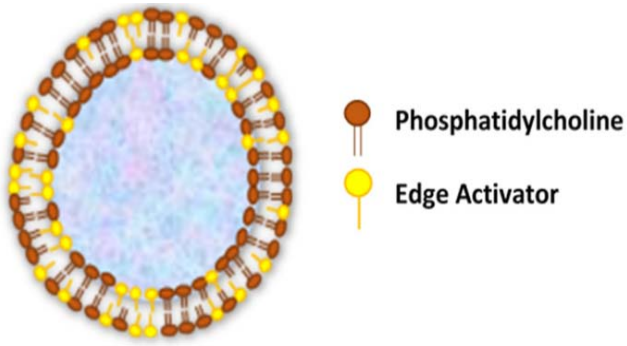

Fig. 1: Structure of transfersome [2]

The lipid bilayers which are surrounded the aqueous compartment promote the ultra-deformability of the vesicles having self-regulating and optimizing capacities along with that, the elastic nature, through small openings or skin constrictions, transfersomes (TFs) can deform and squeeze itself as entire vesicles without experiencing any noticeable loss. Transfersome is composed of edge activator (single chain surfactant) and phospholipid content; when combined with the suitable lipid in the right proportion, surfactants play an excellent role as membrane destabilizing agents to increase the deformability of vesicle membranes, switching the TFs to turn as deformable as well as ultra-flexible which results improved permeation competence. Hence major flaws of conventional liposome's can overcome by TFs. Additionally, even after entering through the minute pores, the TFs maintain their diameters despite fragmentation. The use of surfactants in transfersomal preparations led to improved performance over other vesicles, and surfactants in TFs can improve hydrophobic drugs more soluble, increasing the effectiveness of formulations' entrapment. Skin permeability is

improved even though surfactants have the capacity to fluidize and solubilize the dermal lipids. Many research publications revealed the fact that TFs are having the capacity to carry drugs of high and low molecular weights. It has been noticed that the vesicles with larger in size ≥600 nm are unable to penetrate into the deeper layers of the skin on the other hand vesicles with size ≤ 30 0 nm are able to penetrate the skin's deepest layers. Additionally, it has been stated that as compared to larger ones, with a 120 nm size showed statistically improved skin penetration [1] Novel transferosomal delivery technologies ensure optimal transfer, enhanced bioavailability, and promising stability of herbal compositions. Since TFs have a high capacity for skin penetration and can produce skin drug depots for sustained or prolonged drug delivery of medications into the skin's deepest layers, they offer a favorable overall outlook for the drug delivery concept [4].

Merits

Because of their high deformability and elasticity, transfersomes can allow them to squeeze through skin barriers constrictions that are incredibly tiny, such as 5 to 10 times less than the vesicle diameter.

High vesicle deformation is beneficial for topical and systemic treatments, as it allows drug delivery through the skin without noticeable loss of intact vesicles

As vesicles are composed of natural phospholipids and edge activators, these are biocompatible and biodegradable; proteins and peptides, insulin, corticosteroids, interferons, anesthetics, NSAIDs, anticancer drugs and herbal medications are just some of the active substances that can be delivered by transfersomes.

These are ideal for drugs with narrow therapeutic action promote superior bioavailability. Due to extended duration of action minimizes the dosing frequency is possible. Avoid intra-and inter patient variability, and increase therapeutic effectiveness. Nearly 90% of drug entrapment efficiency can be possible with transferosomes Easy to scale up becuase process is quick and easy [1-5].

Demerits

As the TFs leads to oxidative stress, they are said to be chemically unstable; synthetic phospholipids are encouragd rather than natural polymers due to their purity.

The main obstacle to the widespread implementation of TFs is its financial sustainability. The important factors that contribute to an increased cost of the finished product are the high production cost of TFs and the high cost of phospholipids, a crucial element in formulating [1-2]

Formulation considerations

In the formulation of TFs firstly, the phosphatidylcholine (amphipathic ingredient) encapsulates lipid vesicle, secondly, bilayer softening component like surfactant which improves the lipid bilayer flexibility and generally used components in the formation of transfer some vesicle is listed in table 1 [5].

Table 1: Various ingredients used in formulation of transfersome vesicles

S. No.	Type	Example	Function	References
1	Surfactantsor Edge activators	Sodium cholate, sodium deoxycholate, Tween and Span 80, Tween 20, Span 60	Vesicle forming agent	[5, 51]
2	Buffers	Saline phosphate buffer(pH6.4), Phosphate buffer (pH 7.4)	Hydrating medium	[5]
3	Phospholipids (PLs)	Dipalmitoylphophatidylcholine, egg and soya phophatidylcholine.	Vesicle forming agent	[5, 52]
4	Solvents	CH_3CH_2OH (ethanol), CH_3OH (methanol), C_3H_8O (isopropyl alcohol) and $CHCL_3$(chloroform)	As solvent	[5]

Penetration mechanism of transferosomes

The drug delivery systems which have ability to carry drug molecules through intact skin is known TFs. It is believed that carriers can pass through the skin without being restricted because of two factors: the considerable deformability (elastic nature) of the bilayered vesicle and the osmotic gradient exists over the skin. Due to their extreme flexibility, TFs create a transepidermal osmotic gradient with the help of surfactants, after that, squeeze themselves across the stratum corneum and transport drugs across the entirety of the skin. Hydro taxis is nothing more than the result of TFs penetration, and electromechanics principles govern the permeation. The hydrostatic transport difference is what allows intact TFs to penetrate across the stratum corneum. Once TFs enters the pore, it has the ability to change the function of the membrane in the opposite direction, which results in self-optimizing deformability. While low elastic mechanisms rise to dilution, which considerably reduces active membrane deformation rate and permit highly deformable particles to migrate throughout the pores, TFs transport method is susceptible for its deformability starting to collect at the location of tension. The flexibility of the membrane, which is made possible by adequate ratios of surfactants, has a role in determining whether or not TFs are able to go through the skin and epithelial issue. The elasticity of the TFs membrane lessen the chance of rupturing entire vesicle in the skin and makes it possible for ultra-deformable TFs to adjust the composition of the membrane in a localised and reversible manner when they are forced against or attracted into small pores. As a result, the energetic cost of membrane deformation is significantly reduced, enabling the extremely flexible particles to enter and pass through the pores quickly and effectively. Mechanism of action of TF sis given in fig. 2.

In accordance with the first mechanism, intact vesicles enter the stratum corneum, where they are surrounded by drug and are controlled by a naturally occurring *in vivo* transcutaneous hydration gradient [2, 6-8].

Methods

As there no patented methods to prepare TFs there is no specific procedure or protocol to prepare TFs and there are various methods to prepare and given them below

Thin film hydration technique

In a round-bottomed flask (RBF) with a proper (v/v) ratio of methanol and chloroform, the surfactant (vesicle formers) and PL sare placed. Drugs that are lipophilic can be added during this period. In order to obtain a thin layer, in a rotary vacuum evaporator, the organic solvent is evaporated above the lipid transition temperature while under reduced pressure. Following the incorporation of a hydrophilic drug, by rotating at the right temperature for the appropriate period of time, the hydration of obtained film carried out using buffer with a suitable pH. This phase results in swollen vesicles at room temperature, which is then followed by sonication (bath or probe). Extrusion across a sandwich of 200 nm to 100 nm polycarbonate membranes homogenizes the sonicated vesicles [9-10, 12-15].

Vortexing sonication method

The surfactant, drug and PL sare blended together in a phosphate buffer then vortexed for obtaining a milky suspension by this technique. The suspension is sonicated and then extruded using polycarbonate membranes after sonication process. In this procedure, cationic lipids like DOTMA must be combined with PBS to produce a concentration of 10 mg/ml, then counting sodium deoxycholate, has also been used to set cationic transfersomes. The mixture is extruded through a polycarbonate (100 nm) filter after being sonicated and vortexed [16-20].

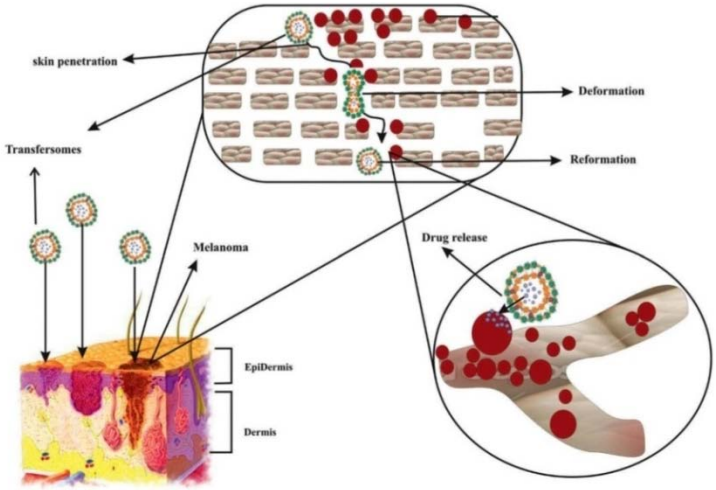

Fig. 2: Penetration mechanism of transferosomes [4]

Modified handshaking process

The basic principle of both the "modified handshaking method" and the rotating evaporation-sonication method is same. The process of modified handshaking includes the introduction of drug, organic solvent, hydrophobic drug, PLs into a RBF. The solvent should perfectly liquefy excipients for yielding a colorless solution. The organic solvent is then eliminated using handshaking evaporation rather than rotational vacuum evaporation. The RBF is only partially submerged in hot water (between 40 and 60 degrees Centigrade). A thin lipid film then begins to form on the flask wall. Overnight, the flask is left in order to let the solvent entirely evaporate. The formed film is then gently shaken while being hydrated with a suitable buffer solution at a temperature above its phase separation temperature. At this point assimilation of water-soluble drugs is possible [21-26].

Suspension homogenization method

To produce TFs, the ethanolic solution containing phospholipid was mixed with the specified amount of surfactant. After that, a total lipid concentration is created by combining the suspension that was formed and the buffer. The mixture is then two to three times sonicated, frozen, thawed [27-29].

Centrifugation process

The organic solvent was used to dissolve all the components of the formulations i.e. PLs, surfactant, and lipophilic drug. The mixture was then subjected to rotary evaporators under reduced pressure to remove the solvent. Under vacuum, any residual solvent is cleaned up. By centrifuging the formed lipid film at room temperature, the proper buffer solution is soaked into it. Drugs that are hydrophilic can be incorporated at this stage. The vesicle which are obtained swell at ambient temperature. The resulted multilamellar vesicles then sonicated at ambient temperature [30].

Ethanol injection method

During this process, a constant temperature is applied to the drug-containing aqueous solution while being continuously stirred. Aqueous solution is dropwise mixed with PLs and surfactantsethanolic solution. Lipid molecules precipitate out of the solution and generate bilayered structures as it reacts with aqueous media. This method has a number of benefits over alternative ones, such as ease, consistency, and scale-up [31].

Characterization of the TFs

The TFs are characterized by different techniques to obtain a optimized formulation and they are listed as: Size, shape, size distribution, polydispersity index, zeta potential number of vesicles per cubic mm, degree of deformability, entrapment efficiency and skin permeability. Each of the above-mentioned characterization methods is thoroughly explained below.

Zeta potential, morphology and vesicle size

One of the essential aspects when preparing TFs, comparing batches, and scaling up procedures is the vesicle size. Changes in vesicle size during storage are a significant factor in the formulation's physical stability. Fusion process is experienced by the vesicles size below 40 nm due to bilayer membrane curvature. In contrast, significantly bigger and electro-neutral TFs aggregate by vanderwaals interactions because of the relatively wider membrane contact areas. Vesicle size affects the ability of TFs to encapsulate drug molecules, preferentially high lipid to core is required in case of lipophilic and aphiphilic agents. While hydrophilic molecules are encapsulated in large aqueous core. The vesicle diameter can typically be determined using the dynamic light scattering (DLS) method or photon correlation spectroscopy (PCS). The suspension of the vesicle can be combined with the appropriate media, and three separate measurements of the vesicular size can be made. Additionally, distilled water can be used to prepare the sample and a 0.2 mm membrane filter can be used to filter it. To determine the vesicle sizes using DLS or PCS, the filtered sample is then diluted with filtered saline. Additionally, the size and size distribution of vesicle is determined by Malvern Zetasizer DLS method-associated computerised inspection system and to observe the structural alterations, transmission electron microscopy (TEM) is employed. When measuring the zeta potential, the Malvern Zetasizer employs the electrophoretic mobility approach. Phase contrast microscopy or transmission electron microscopy (TEM) can be used to viewtransfersome vesicles [32-36, 50].

Number of vesicles per cubic mm

This optimization of composition is vital factor. The TFs were diluted 5times with 0.9% Nacl solution before sonication. This sample is examined using an hemocytometer and optical microscope. Using an optical microscope, the transfersomes with vesicles larger than 100 nm can be seen [37-39]. We count and determine the number of transfersomes in small squares using the equation:

$$\text{Total no. of transfersosomes per cubic mm} = \frac{(\text{Total number of transfersomes} \times \text{dilution factor into } 4000)x^2}{\text{Total number of squares counted}}$$

Entrapment Efficiency (%EE)

%EE, which measures how much drug is entrapped within the formulation, is a scientific term. Several techniques, including mini-column centrifugation, are used to separate the free drug from the vesicles and measure the EE. One can use either direct or indirect ways to find the % EE in this procedure. The direct method might help to eliminate the supernatant after ultracentrifugation and then disrupting the vesicles sediment with a suitable solvent that has the ability to lyses the sediment. The resultant solution can then be

thinned out and filtered through syringe filter (0.22-0.45 m) to get rid of contaminants. Analytical techniques, such as modified high-performance liquid chromatography (HPLC) or spectrophotometry, are used to determine the drug content, This is based on the active pharmaceutical ingredient's analytical procedure (API) [40-43] The percentage drug entrapment efficiency is stated as:

$$\%\text{Entrapment efficiency} = \frac{\text{Amount of the drug to be entrapped}}{\text{Total amount drug added}} \times 100$$

Filtering the supernatant to eliminate impurities and diluting with a suitable solvent is the indirect method to calculate the %EE. The amount of the drug present in the supernatant as the free drug is calculated using the appropriate analytical technique [43-45]. Therefore the percentage entrapment efficiency is stated as:

$$\%\text{Entrapment efficiency} = \frac{\text{Total amount drug added} - \text{amount of free drug}}{\text{Total amount of drug added}} \times 100$$

Degree of deformability

This variable is significant since it influences how well the transfersomal formulation permeates. The benchmark for this investigation is pure water. Numerous microporous filters with known pore diameters between 50 and 400 nm are used to pass the preparation. DLS measurements are utilized to capture the particle size and size distribution after every run. The degree of deformability is written as:

$$D = J\,(rv/rp)$$

Where J = amount of suspension extruded during 5 min,

rv = size of the vesicle,

D= degree of deformability,

rp= pore size of the barrier [43-46].

***In vitro* drug release**

The drug release profile briefs about kinetics and release mechanism of drug which provide basic knowledge on formulation design, facilitating the use of scientific method to improve the transfersomal formulation. TFs *in vitro* drug release is normally assessed in contrast to the reference product or free drug. Numerous investigations have undoubtedly produced fruitful information about the drug release patterns of developed transfersomal formulations. In contrast to the later burst of drug release from the ketoconazole suspension (27.35%) after 6 h, the first burst of drug release from the ketoconazole-loaded transfersomal gel was higher at 40.67%. After 6 h about 80% drug was released from the transferosomal vesicles, according to the lidocaine release profile *in vitro*. In the process of evaluation, Franz diffusion cells are used. By using adhesive tape, the donor chamber is attached to the receptor chamber. A magnetic bar stirs the fluid in the receptor chamber continuously. The temperature of the receptor fluid should be maintained at 32±1 °C, which is the *in vivo* skin surface temperature, in the release study because the usually skin surface temperature is around 32 °C. A 0.45 µm average pore-sized mixed cellulose ester membranes are used. Membrane pores are immersed in phosphate buffer (release medium) overnight at ambient temperature to swell. Aliquots of 1 ml of receptor media are withdrawn at regular intervals (like 0, 0.5, 1, 2, 3, 4, 5 and 6 h). To maintain the sink conditions, an equal volume of fresh PBS is substituted for the receptor medium. The resulting samples may be examined using suitable techniques, such as UV [47].

***In vitro* skin permeation studies**

This test evaluates the efficacy of transdermal drug delivery systems and identifies the factors which influence transdermal drug flux, which is often expressed in units of µg/cm²/h. Before conducting expensive *in vivo* studies, this study's findings can be utilized to project *in vivo* behaviours from a range of transdermal delivery systems and to improve the formulation. In a perfect world, this type of formulation's permeation properties would be evaluated on human skin. However, the human skin is less desirable for the permeation study because to its restricted availability, ethical issues, and religious limitations. There have apparently been references to more widely accessible alternatives to human skin, including pig, rat, mouse, monkey, guinea pig, and snake skin. Additionally, it should be noted that investigations using human skin model may not always yield the same results as percutaneous absorption through different animal skins. Additionally, synthetic membranes such as (Strat M®) have been used in skin permeation studies as an additional choice. According to reports, artificial membranes closely resemble human skin. In contrast to human and animal skins, this method has the benefit of being highly sensitive and consistent in its permeability. Franz diffusion cells are known to study skin permeability. On the receptor compartments, the chosen membranes are placed horizontally with the stratum corneum facing the donor compartments on the other side. To agitate the solution of saline phosphate buffer in Franz diffusion cell receptor compartments magnetic bars are used. The receptor fluid temperature should be maintained 37±5 °C since it mimics blood flow beneath the skin. Each donor compartment is administered a suitable amount of the testing formulations as it is placed on the membrane, and in order to simulate non-occluded conditions, the diffusion cell's top is opened. At appropriate time intervals, the receptor media are taken in specified amounts as aliquots, and to maintain the sink conditions, an identical amount of fresh receptor medium is substituted for the receptor medium. The obtained samples may be examined using spectroscopic analysis or HPLC [47, 48].

Stability of TFs

Stability investigations of TFs lead aggregation on dispersion and leakage from the produced vesicles on storage was found. For three months, the prepared transfersomal dispersions were kept in 15 ml amber vials that were firmly sealed at three distinct temperatures (4±1 °C, 25±1 °C, and 37±1 °C). At predetermined intervals, aliquots (1 ml) from every transfersomal preparation were obtained in order to measure the size of particle, encapsulation level of of the transfersomal vesicles. The occurrence of any sedimentation or creaming was evaluated in relation to the physical properties of transfersomal dispersion [43, 47-49].

Formulation applications of TFs

Antioxidants delivery

Avadhani *et al.* (2017) successfully prepared epigallocatechin-3-gallate (EGCG) nano TFs with hyaluronic acid resulted in thin-film on hydration which was named as high-pressure homogenization technique. This was done to improve the potency of these substances as antioxidants, UV radiation protectors, and anti-aging agents.

Wu *et al.* (2019), using the high-pressure homogenization method, TFs were produced and mixed with resveratrol. It was found that the acquired transfersomes had the ability to improve the resveratrol's stability, bioavailability, and solubility, as well as its safety.

Anticancer drug delivery

Jiang et,. al.(2018) study focused on the topical treatment of melanoma using paclitaxel-containing oligopeptide hydrogels TFs-embedded via the thin-film dispersion method. It has been proven that transfersomes, which are composed of tween80, sodium deoxycholate and phosphatidylcholine are capable of penetrating into cancer tissues.

Delivery of corticosteroids

In 2003 and 2004, Cevc and Blume examined the biological characteristics and activity of TFs loaded with the halogenated corticosteroid triamcinolone acetonide. Based on the findings, TFs enhanced biological potency, increased the duriation of action, and minimized therapeutic dosage.

Delivery of anti-Inflammatory drugs

A number of research teams produced and investigated TFs containing diclofenac sodium, celecoxib, mefenamic acid, and curcumin for topical delivery. Transformers may ameliorate the stability and potency of anti-inflammatory drugs, according to

studies. As an extension to above information details of various preparations of potential TFs are enlisted in table 2.

Table 2: Applications of TFs as transdermal delivery systems

No.	Drug	Methodology and formulation details	Outcome	References
1	Raloxifene HCl	Phospholipon 90G, sorbitan80, chloroform, methanol and rotary evaporation method	The formulation of transferosmes developed with sorbitan 80 effective transdermal applications.	[22]
2	Mefenamic acid	SPC, SP60, 2:1 chloroform: ethanol, pH 7.4 PBS, orbital shaker, modified handshaking, thin-film hydration.	Good spread ability and drug release profile produced 12 h better outcomes.	[23]
3	Ketoconazole	Conventional solvent evaporation technique, phospholipon 90G, ethanol of lipoid S100, Tween 80	showed good potential for drug delivery and promising antibacterial action.	[24]
4	Itraconazole	Phosphate buffer (pH 6.8), Soya phosphatidylcholine, tween80, span80, chloroform, methanol (3:1), and 30 min of sonication, thin-film hydration process.	Promising outcome with targeted delivery and extended release	[25]
5	Ibuprofen	Rotary evaporation method for hydrating lipid films, Soya phosphatidylcholine, Span80, tween 80, ethanol, and PBS	Potent therapeutic delivery system with high stability and extended drug release	[26]
6	Repaglinide	Using a bath sonicator, sonicated the following ingredients (3:1), soy lecithin, span80, span60, span40, tween80, PBS (pH 6.8)	Site specificity, enhanced topical administration, and delayed antihyperglycemic agent release	[27]
7	Curcumin	Lecithin, TWEEN80 and SP80, 95:05 and 85:15 lecithin: surfactant ratio, ethanol, isopropyl alcohol, PBS(pH7.4), modified handshaking method	Possess strong anti-inflammatory effects and have improved penetration and bioavailability	[29, 30]
8	Embelin	Thin film hydration span 80 and tween 80	Potentially effective in treating skin cancer	[31]
9	Minoxidil and caffeine	Lecithin was combined with varying concentrations of edge activators using the modified thin-film hydration approach (SPC, TW20, TWEEN80), and then dissolved in chloroform.	The effectiveness of the minoxidil and caffeine entrapment was improved by increasing the polysorbate ratio. Compared to the commercial product, topical use of this composition significantly increased the effectiveness of promoting hair growth in rats.	[32]
10	Tizanidine HCl	Using a bath sonicator, L-α-Phosphatidycholine, cholesterol, span80, tween80, sodium deoxycholate, Brij 35, and PBS were sonicated.	With sustained drug release, there is an increase in the bioavailability in treatment of spasticity	[33]
11	Cannabidiol	Thin-film hydration method with chloroform, methanol, soyalecithin, cholesterol, polysorbate80	Synthesized cannabidiol transfersomes may be easily incorporated into a suppository base, and optimization is required further to control the onset of action, release	[34]
12	Tacrolimus	Soya phosphatidylcholine, sodium deoxycholate, chloroform: methanol (2:1), phosphate buffer, pH 7.2, thin lipid film hydration	Better skin permeations compared to liposomes result in better antipsoriatic activities	[35]
13	Miconazole	Soya lecithin, span80, tween80, carbopol 934. Solvent casting method.	Miconazole nitrate could reach the pilosebaceous unit through the skin in 24 h.	[36]
14	Imperatorin	Thin film hydration Phosphatidylcholine from soybean (90%), Cholesterol, dicetyl phosphate, Tween 20 and Tween 80	The greatest amount of Imperatorin was delivered by cationic-UDLs across the skin and into the deeper layers of the epidermis.	[37]
15	Clonazepam	Thin film hydration technique phospholipon90G, sodium deoxycholate and labrafil	The PTZ seizures challenge showed the optimized TFs' effectiveness in directly delivering the medication to the brain in an effective concentration.	[38]
16	Metronidazole	Soya phosphatidylcholine, carbopol 934, chloroform and ethanol	The transfersomal composition of the produced gel, which contains metronidazole, was improved and can be used for topical preparation	[39]
17	Insulin	Reverse phase hydration, soya lecithin, sodium deoxy cholate and tween 80	High permeation of optimized gel with iontophoresis	[40]
18	Econazole	Thin film hydration, Soya Lecithin, Sod cholate and span 80, brij 35	Improvement in drug release pattern and drug delivery	[41]
20	Cephlexin	Thin film hydration, Phospholipon 90H, sodium deoxy cholate,	Increased penetration and sustained drug delivery	[42]

CONCLUSION

The drug delivery via the transdermal route of administration is very preferable due its unique and versatile characteristics, mean while in complete delivery of drugs major concern due restriction of entry of the drugs through skin by stratum corneum. On the basis of literature survey it was understood that the transdermal flux of the therapeutic drugs is increased via TFs, specifically developed vesicles that can squeeze through skin pores that become considerably smaller than they are under stress. It is beyond dispute that therapeutic agents with both small and large molecular weights can be transported efficiently by TFs. Applications for enhanced delivery employing formulations of TFs are emerging. However, just two TFs-based formulations are available today, and the reported clinical studies mostly make use of insulin and ketoprofen. Additional transfersome research may lead to creative, prospective therapeutic approaches for a range of disease with its site specificity and deformable nature of vesicle is, attracting many research fellows in field of drug delivery.

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Nil

AUTHORS CONTRIBUTIONS

All authors have contributed equally.

CONFLICTS OF INTERESTS

Declare none

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