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Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery System

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Abstract: *Transdermal delivery systems have gained a lot of interest in recent years due to their benefits compared to conventional oral and parenteral delivery system. It is the controlled and self-regulatory delivery systems that can improve patient compliance and provide a controlled release of therapeutic agents. The biggest challenge for transdermal delivery systems is the task of preventing the outer layer of the skin. Molecules weighing more than 500 Da and ionized compounds usually do not pass through the skin. Therefore, only a limited number of drugs can be administered by this route. The combination of drugs in transfersomes is one of the most effective ways to overcome this problem. Transferosomes combine the characteristics of liposomes with niosomes because Contain both liposomes (phospholipids and cholesterols) and niosomes as substances (nonionic surfactants; activists on edge). They have a two-dimensional structure that facilitates the encapsulation of lipophilic and hydrophilic, as well as amphiphilic, drugs with relatively high efficacy compared to conventional liposomes. Transfersomes are elastic in nature, can be deformed and squeeze like a solid fabric into holes that are much smaller than their size. This review aims to explain the concept of transfersomes, methodology, various methods of preparation and manufacture of materials and properties affecting transfersomes, as well as their latest applications in the administration of commercial drugs.*

Keywords: Transfersomes; Nano-encapsulation; Transdermal drug delivery system, Phospholipid.

I. INTRODUCTION

An efficacious, successful therapeutic treatment cannot be achieved in most cases, usually for a number of reasons, such as the emergence of early hepatic metabolism, side effects, drug rejection and follow-up of patients[1]. Therefore, many drug delivery programs have been developed and studied in recent decades to overcome these problems. Another promising approach is the use of transdermal delivery systems, as they are small invasive methods that do not have the first pass results. However, the skin-protective function that prevents or reduces the delivery of chemical transfer of treatment should be addressed [2,3]. Nanoencapsulation using a lipid-based vesicular system similar to liposomes has been used to overcome the above-mentioned challenge [4]. Liposomes facilitate the transport of drugs through the skin in three possible ways: exposure to the skin through the transfer of the drug directly from the vesicles to the skin, mixing with the lipid matrix of the stratum corneum, thereby increasing drug separation in the skin, and lipid exchange between membranes liposomal and cell membranes, facilitate the spread of the drug throughout the membrane [5,6]. However, the problem with liposomes is that they do not penetrate deeply into the active skin and blood circulation [7-9]. Flexibility of skin transfer It can be changed by mixing the appropriate active area They don't do it in the right amount. Providers like Sodium cholate, sodium deoxycholate, span 80, In the mid-80s, it has been used as an edge tool. Vesicular system used for the delivery of transdermal drugs Like liposomes, niosomes, or microemulsions. It is usually kept on the skin as well So do not pass drugs properly Skin. Transdermal drug delivery systems (TDDS) are designed to attract Approach to drug management in clinical dermatology [10]. Compared to normal Oral route, intravenous injection, or subcutaneous injection, TDDS provides a simple application Apart from the initial effect of passing and the adverse effects of the system [11].

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These days, TDDS is widespread Is used to treat many skin diseases, such as psoriasis, contact dermatitis, And skin cancer. In addition, TDDS is also suitable for long-term management, in particular Insulin delivery and other analgesic agents [12]. However, TDDS needs to win the file Skin barriers, including stratum corneum (SC), surrounding lipid bilayer, and dermal Tissue [13]. Risk-benefit ratio of topical triamcinolone acetonide In transfersomes compared to a cream containing triamcinolone acetonide for sale And the oil has already been tested under a randomized controlled trial. It turns out that Transfersomes can significantly improve the risk-benefit ratio of topical triamcinolone acetonide [14]. Therefore, transfersomes are known to be the most outstanding innovative transdermal drug carrier to this date [15].

1.1 Transfersomes

Transfersomes are vesicular carrier systems that are specially designed to have at least one inner aqueous compartment that is enclosed by a lipid bilayer, together with an edge activator[16]. Transfersomes, also called ultra deformable vesicles for applying to skin holding a lipid bilayer with phospholipids and edge activator along with aqueous layer. Depending on the lipophilicity the active object is closed with a core or between the seller. Compared to liposomes, transfersomes have a great potential for this touch the deeper areas of the skin once applied By topically application.

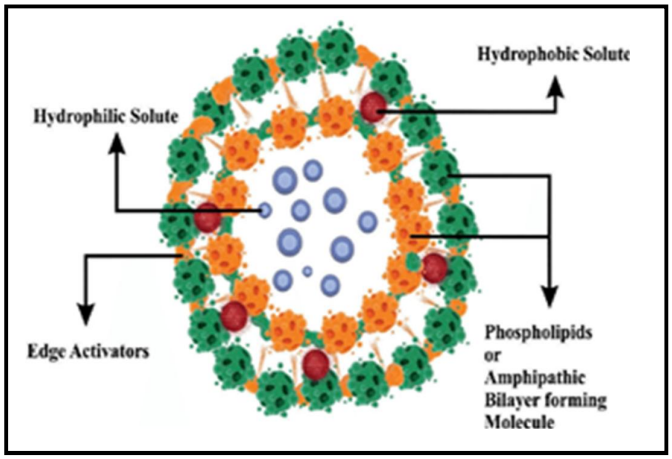

Fig. 1. Structure of transfersomes[17]

This aqueous core surrounded by a lipid bilayer makes ultra-deformable vesicles having both Self-optimizing and self-regulating capabilities [18]. In accordance with that, transferosomes are elastic In nature and can thereby deform and squeeze themselves as intact vesicles without a measurable loss through narrow pores or constrictions of the skin that are significantly smaller than the vesicle Size [19,20]. In contrast to conventional liposomes, they contain natural (such as such as egg phosphatidylcholine-EPC and soybean phosphatidylcholine-SPC) or synthetic (such as dimyristoyl phosphatidylcholine-DMPC, dipalmitoyl phosphatidylcholine-DPPC and dipalmitoyl phosphatidyl glycerol-DPPG) phospholipids [21], modified liposomal vesicular system (transfersomes) composed of phospholipid component and single-chain surfactant as edge activist [22]. Edge activators (EAs) operate differently as a membrane-substances that prevent the increase in vascular membrane degeneration also, when incorporated into proper dosage with the right lipid, gives the perfect blend, enables transfer to they are deformed, as well as ultra-dynamic variables, resulting in high saturation [23,24]. Thus, transfersomes overcome the major barriers to normal liposomes and penetration pores much smaller than their diameters. In addition, transfersomes are stored its size against cracking, even if it penetrates into small pores. Because in the use of EA in the formation of transfersomal, resulting in improved performance compared with normal liposomes [23,24]. The EAs used in the construction of the transfer can also facilitate the lubrication of hydrophobic drugs, thereby increasing the drug entrapment efficiency of the formulations [25–27]. The commonly used edge activator in this type of drug delivery system to increase flexibility are Tween80, span80, sodium cholate, sodium deoxycholate etc. and the commonly employed phospholipids used for vesicle forming are soya phosphatidylcholine, Egg lecithin's and cholesterol etc. Examples of components of transferosomes are tabulated.

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Table 1. List of Transferosome

S. No.	Example	Class	Use
1	Egg Phosphatidyl CholineSoya Phosphatidyl choline, , dipalamitoylphosphatidyl choline	Phospholipids	Vesicles forming component
2	Ethanol, methanol, isopropyl alcohol, chloroform	Solvents	As a solvent
3	Sod. Cholate, Sod. Deoxycholate, Tween-80, Span 80, Tween 20	Surfactants	Vesicles forming component (Edge Activators)
4	Saline phosphate buffer (pH 6.4), Phosphate buffer pH 7.4	Buffering agent	As a hydrating medium
5	Rhodamine-123 Rhodamine –DHPE Fluorescein –DHPE Nile-red	Dye	For CSLM study

Table 1: LIST OF TRANSFEROSOMES [28]

Advantages of Transfersomes as Vesicle-based Transdermal Drug Delivery Systems: [2,21,29,30]

- Transfersomes carriers are composed of hydrophilic and hydrophobic moieties, which result in becoming a unique drug carrier system that can deliver therapeutic agents with wide range of solubility.
- Transfersomes are able to squeeze themselves through constrictions of the skin barrier that are very narrow, such as 5 to 10 times less than the vesicle diameter, owing to their ultra-deformability and elastic properties.
- High vesicle deformability facilitates the transport of drugs across the skin without any measurable loss in intact vesicles and can be used for both topical, as well as systemic, treatments.
- Transfersomes carriers are very versatile and efficient in accommodating a variety of agents nearly independent of their size, structure, molecular weight or polarity.
- They are made up of natural phospholipids and EAs, therefore promisingly biocompatible and biodegradable.
- Transfersomes can be used for the delivery of various active compounds, including proteins and peptides, insulin, corticosteroids, interferons, anesthetics, NSAIDs, anticancer drugs and herbal drugs.
- Transfersomes are an obvious choice for achieving a sustained drug release, as well as a predictable and extended duration of activity.
- They are capable of increasing the transdermal flux and improving the site specificity of bioactive agents.
- Avoiding the first-pass metabolism, which is a major drawback in oral drug administration and result in optimized bioavailability of the drug.
- Minimize the undesirable side effects of the drug, as well as protect the drug from metabolic degradation; moreover, the utility of short half-life drugs.
- They protect the encapsulated drug from metabolic degradation. Easy to scale up and simple.

Limitations of transfersomes:

- Transfersomes are chemically unstable due to their predisposition to oxidative degradable but expensive [31]
- Another obstacle to using Transfersome as a drug delivery system is the difficulty of achieving it natural purity phospholipids. Therefore, synthetic phospholipids can be used as alternatives [32].
- The cost of transfersomal formulations is associated with immature materials used on lipid excipients, as well as expensive tools needed to increase production. So, the most widely used lipid component is phosphatidylcholine, because it has a very low cost [6].

1.2 Mechanism of Action

Vesicles are known as colloidal particles, which are closed fluid chambers A concentric bilayer made of amphiphilic molecules. They are very useful as a vesicular drug Delivery systems, which deliver hydrophilic drugs implanted in a watery interior, And hydrophobic drugs are bound within the lipid bilayer [33]. About transfersomes, Highly degraded

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(ultra-flexible) and the vesicles that carry the drug they work on, there Skin transplantation is strongly associated with fluid transfer of transfersomes, hydrophilicity And the ability to maintain vesicle integrity (Figure 2).They penetrate well into the firm skin when used under unusual conditions; This special skin condition is especially needed to initiate transepidermal osmotic Gradient on whole skin [1,34]. According to a study by Cevc and Blume, hydrotaxis (xerophobia) It is the entry point of transfersomes, also referred to as transferosome's The tendency to seek moisture near the deeper layers of the skin rather than the dry outer surface due to The state of evaporation in the formation of transfersomal following its use in Skin (flawless condition) [37]. Differences in transdermal fluid performance, due to A natural transdermal gradient, creates a powerful effect on the skin Transfersomes vesicles, which force the expansion of the intercellular joint with very low resistance And thus producing flexible channels of 20–30 nm in diameter. These created channels allow you Ultra-deformable transfer, slimed transfersomes to the skin in relation to water absorption Gradient [38]. In addition, the osmotic gradient increases due to evaporation of the skin area Water due to body temperature, which makes its action as a driving force easier to transport flexible crossings Skin to bring therapeutic agents from the application area to the target area or system Treatment with effective therapeutic focus and minimal systemic toxicity [18]. Transfersomes Show higher penetration efficiency (with smaller skin channels) compared to normal Liposomes but have the same bilayered structure that helps to combine lipophilic as well Hydrophilic, as well as amphiphilic, drugs [39]. Transfersomes differ from liposomes, mainly due to In their soft, highly flexible and highly flawed synthetic membrane. Dependence on The shape of the area, as well as the shape of the lipid bilayer, make the vesicles self-contained as well Self-regulating. This structure enables vesicles of transfersomes to bypass many navigation barriers Successfully. Therefore, transfersome are supramolecular organizations composed of at least one type of Amphipathic agent and, by adding at least one type of bilayer lubricant agent (edge activator), Resulting in a significant increase in lipid bilayer flexibility and stiffness [8].

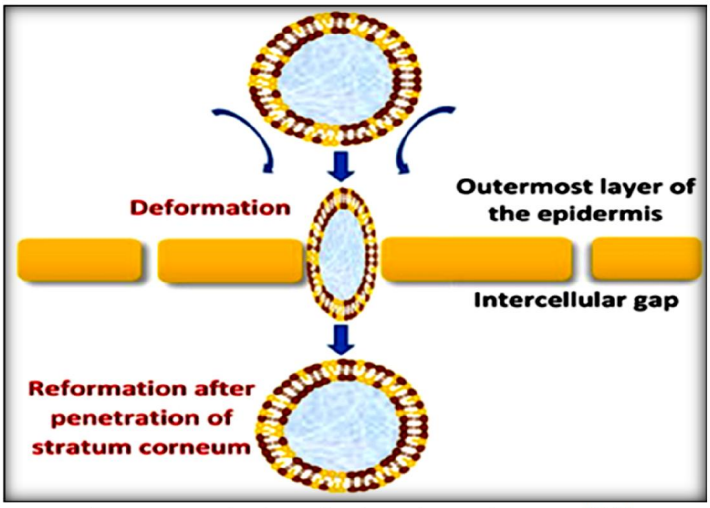

Figure 2: Mechanism of action of Transfersomes. [35,36]

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Fig. 3. Pictorial diagram of mechanism of action of transferosomes

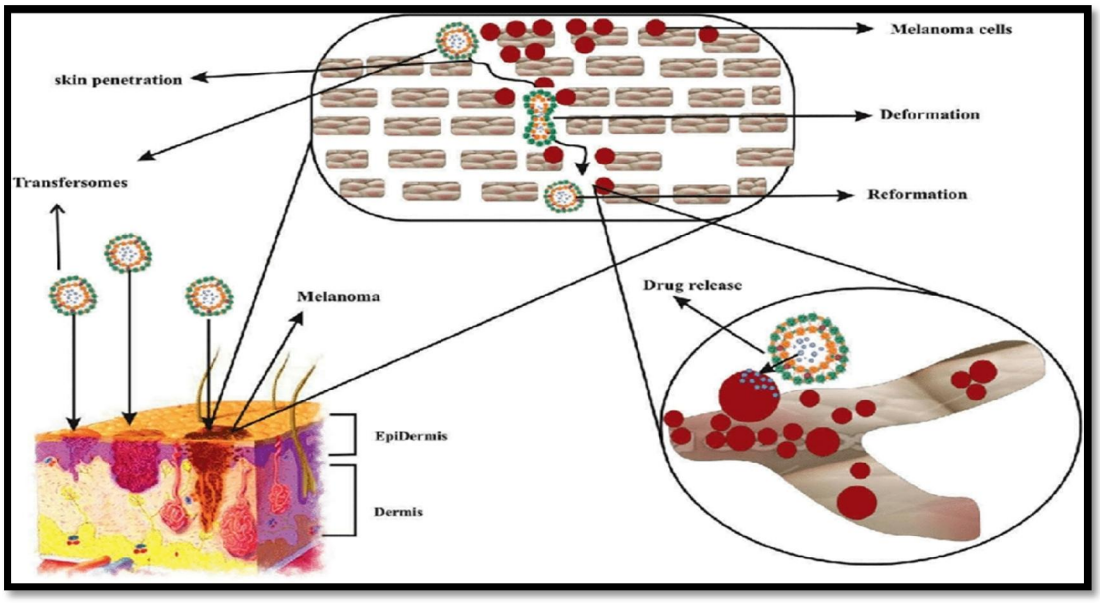

Figure 3: Mechanism of action of Transfersomes. [35,36]

Some transfersome have Other alcoholic beverages (ethanol or propylene glycol) in their as infusion supplements And, again, are used as cosolvents with good solving power. It is proposed that Ethanol be seduced Modification of the polar lipid bilayer head circuit. After ingestion, ethanol increases Fluid in the intercellular lipid matrix and later leads to a reduction in lipid congestion Picture [40]. Transfersomes can enter through the stratum corneum and reach the target sites, Which includes the dermis and blood circulation. Their ability to login depends on the disability of Transfersomal membrane, which can be caused by vesicle formation [41,42]. Therefore, The formation of the most suitable vesicles should be identified with each designed operation Testing procedures for each treatment agent to find the most qualified carriers Good disability, drug carrying capacity and stability.

1.3 Composition of Transfersomes:

Transfersomes are generally composed of

- Firstly, the main ingredient, an amphipathic ingredient (e.g., soy phosphatidylcholine, Egg phosphatidylcholine, etc.) that can be a mixture of lipids, which are the vesicle-forming Components that create the lipid bilayer [43].
- Secondly, 10–25% surfactants/edge activators; the most commonly used edge activators In transfersome preparations are surfactants as sodium cholates; sodium deoxycholate; Tweens and Spans (Tween 20, Tween 60, Tween 80, Span 60, Span 65 and Span 80) and dipotassium Glycyrrhizinate, which are biocompatible bilayer-softening compounds that increase the vesicles' Bilayer flexibility and improve the permeability [44].
- About 3–10% alcohol (ethanol or methanol), as the solvent and, finally, hydrating medium consist With either water or a saline phosphate buffer (pH 6.5–7)

II. METHOD OF PREPARATION

1) Film Hydration Technique/Rotary Evaporation-Sonication Method:

The phospholipids and edge activator (vesicle-forming ingredients) are dissolved during a Flask employing a volatile organic solvent mixture (example: chloroform and methanol during a Suitable (v/v) ratio). The lipophilic drug can be Incorporated in this step. In order to form a thin Film, the organic solvent is evapo- rated above the Lipid transition temperature under reduced pressure Using a rotary vacuum evaporator. Keep it under Vacuum to get rid of the ultimate traces of the Solvent. The deposited thin film is hydrated Employing a solution with the acceptable pH (example: pH 7.4) by rotation for a respective time At the corresponding tem- perature. The hydrophilic Drug incorporation can be done in this stage. The Resulting vesicles are swollen at room temperature And sonicated in a bath or probe sonicator to obtain

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Small vesicles. The vesicles are homogenized by Extrusion through a sandwich of 200 nm to 100 nm Polycarbonate membranes [45].

2) Vortexing-Sonication Method

The phospholipids, edge activator and the drug are mixed in a phosphate buffer. The mixture is Then vortexed until a milky transfersomal suspension is obtained. It is then sonicated, using a bath Sonicator, for a respective time at room temperature and then extruded through polycarbonate Membranes (example: 450 and 220 nm) [46].

3) Reverse phase evaporation method

This method is carried out as follows: lipids and Organic solvents were combined together in a Round bottomed flask under nitrogen purging Aqueous media containing edge activators. Depending on the drug's solubility, it's mixed with Either a lipophilic or a lipophobic media. After Sonication, the prepared material is left for 30 Minutes until it appears to be a homogeneous Combination. Organic phase is eliminated when Pressure is kept to a minimum. The substance Transforms into a viscous gel that creates Vesicles [47].

4) Suspension Homogenization Method

Transfersomes are prepared by mixing an ethanolic phospholipid solution with an appropriate Amount of edge activator. The prepared suspension is subsequently mixed with buffer to yield a total Lipid concentration. The resulting formulation is then sonicated, frozen and thawed respectively two To three times [48].

5) Centrifugation Process

The phospholipids, edge activator and the lipophilic drug are dissolved in the organic solvent. The solvent is then removed using a rotary evaporator under reduced pressure at the respective temperature. The remaining traces of solvent are removed under vacuum. The deposited lipid film is hydrated with the appropriate buffer solution by centrifuging at room temperature. The hydrophilic drug incorporation can be done in this stage. The resulting vesicles are swollen at room temperature. The obtained multilamellar lipid vesicles are further sonicated at room temperature [49].

Evaluation of Transfersomes: [50-52]

1. Vesicle size distribution and zeta potential:

Vesicle size, size distribution and zeta potential were determined by Dynamic Light Scattering system by Malvern Zeta sizer.

2. Vesicle Morphology

Vesicle diameter can be determined using photon correlation spectroscopy or dynamic light Scattering (DLS) method. Samples were prepared in distilled water, filtered through a 0.2 mm Membrane filter and diluted with filtered saline and then size measurement done by using Photon correlation spectroscopy or dynamic light scattering (DLS) measurements. Transfersomes vesicles can be visualized by TEM, phase contrast microscopy, etc. The Stability of vesicle can be determined by assessing the size and structure of vesicles over Time. Mean size is measured by DLS and structural changes are observed by TEM.

3. Drug content:

The drug content can be determined using one of the instrumental analytical methods such as Modified high performance liquid chromatography method (HPLC) method using a UV Detector, column oven, auto sample, pump and computerized analysis program depending Upon the analytical method of the pharmacopoeial drug.

4. Turbidity measurement:

Turbidity of drug in aqueous solution can be measured using nephelometer.

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5. Surface charge and charge density:
Surface Charge and charge density of transfersomes can be determined using zeta sizer.

6. Penetration ability
Penetration ability of Transfersomes can be evaluated using Fluorescence microscopy.

7. Confocal scanning laser microscopy study:
Light microscopy and electron Microscopy both face problem of fixation.

Applications of Transfersomes as the Transdermal Delivery System:
Over the past decades, the applications of the transfersomes in the field of transdermal drug Administration have been extensively studied. Some of these applications are described in the Section below.

1. Delivery of Antioxidants:
In 2017, Avadhani et al. developed nanotransfersomes containing epigallocatechin-3-gallate (EGCG) and hyaluronic acid by using a modified thin-film hydration method followed by the High-pressure homogenization technique in order to enhance their efficacies as UV radiation protectors, Antioxidants and antiaging substances [100]. In 2019, Wu et al. prepared transfersomes combined With resveratrol using the high-pressure homogenization technique. It was found that the obtained Transfersomes could improve the stability, bioavailability, solubility and safety of resveratrol [53].

2. Delivery of Anticancer Drugs:
A research conducted by Jiang et al. in 2018 was associated with the topical chemotherapy of Melanoma by transfersome-embedded oligopeptide hydrogels containing paclitaxel prepared by the Thin-film dispersion method. Transfersomes composed of phosphatidylcholine, tween80 and sodium Deoxycholate were shown to effectively penetrate into tumor tissues [54].

3. Delivery of Corticosteroids:
The biological activity and characteristics of halogenated corticosteroid triamcinolone-acetonide-loaded transfersomes prepared by the conventional thin-film hydration technique were studied by Cevc and Blume in 2003 and 2004. The results showed that transfersomes had increased the biological potency and prolonged effect, as well as the reduced therapeutic dosage [55].

4. Delivery of Anti-Inflammatory Drugs:
Diclofenac sodium, celecoxib, mefenamic acid and curcumin-loaded transfersomes were developed and studied for the purpose of topical administration by several research groups. Research findings suggested that transferomes could improve the stability and efficacy of the anti-inflammatory drugs [56].

5. Delivery of NSAIDs:
The typical problems Associated with NSAIDs like GI irritation can be Overcome by transdermal delivery using trans-Fersomes. Some drugs like diclofenac and Ketoprofen are already studied for their efficacy Using tranfersomes and ketoprofen formulation is Already approved by Swiss regulatory agency [57].

6. Delivery of Herbal Drugs:
Transfersomes of Capsaicin have been prepared by Xiao-Ying et al.Showing improved absorption through the topical Route when compared to pure capsaicin due to the Property of transfersome to supply nutrients locally By penetrating through the stratum corneum due to The presence of the surface-active agent in their Formulation [58].

7. Delivery of Anti-Inflammatory: Diclofenac sodium, celecoxib, mefenamic acid and curcumin-loaded transfersomes were developed And studied for the purpose of topical administration by several research groups. [59]

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Table 2. Examples of applications of transfersomes as a transdermal delivery system.

No.	Drug	Methods of Preparation and Formulation Details	Inference
1.	Insulin	Thin-film hydration technique (10 Pa), ethanolic SPC, SC (8.7 wt % SPC, 1.3 wt % SC, 8.5 vol % ethanol), triethanolamine–HCl buffer (pH 6.5) Subjected to intermediate-pressure homogenization or ultrasonication	Therapeutically significant hypoglycemia was induced in both mice and humans, with a good efficacy. as well as reproducibility
2.	Resveratrol	High-pressure homogenization technique (5 cycles, 1500 bar), PC, TW20, Plantacare® 1200 UP, TW80	Antioxidant activity was not affected by coating, improved instability, bioavailability, solubility and safety
3.	Epigallocatechin-3-gallate (EGCG) and hyaluronic acid	Modified thin-film hydration method followed by high-pressure homogenization technique, chloroform:methanol (4:1 *v/v*), SPC, SC, hydration by PBS (pH 6.8); after removing the film, the mixture was passed through a high-pressure homogenizer (1000–1200 bars, 10 cycles)	Promising free radical-scavenging effect with considerably high skin permeation and deposition of EGCG
4.	Triamcinolone-acetonide	Thin-film hydration technique (10 Pa; 12 h), methanol/chloroform (1:1 *v/v*), SPC as an ethanolic solution (1:1 *w/v*), TW80 (9:11 *w/w*) relative to SPC, buffer (pH = 6.5), homogenized by sonication	Prolonged anti-inflammatory activity and 10-fold dose reduction to achieve the therapeutic level compared to the conventional formulation
5.	Corticosteroids Glucocortico steroids Hydrocortisone and dexamethasone	Conventional film method (10 Pa, 12 h), methanol/chloroform (1:1 *v/v*), SPC, TW20 (1:1 molar ratio relatively to SPC), buffer (pH = 6.5), homogenized by gentle sonication	Improved biological potency, prolonged effect and reduced therapeutic dosage

III. CONCLUSION

Transfersomes are ultra-deformable carriers that facilitate the delivery of a diverse array of drug Molecules across the skin barrier with superior efficacy compared to the conventional vesicular systems. When tested in artificial systems. Transfersomes can pass through even tiny pores (100 mm) nearly as efficiently as water, which is 1500 times smaller. Drug laden transfersomes can carry unprecedented amount of drug per unit time across the skin (up to 100mg cm2h-1).Transdermal drug delivery system is frequently used due to its several advantages over other Routes drug delivery but the penetration of drug via the stratum corneum is a rate limiting Step, its major limitations like, it cannot be able to transport the larger size molecule. That is Why vesicular system like Transfersomes are developed to overcome these limitations.

REFERENCES

[1]. Chaurasiya, P.; Ganju, E.; Upmanyu, N.; Ray, S.K.; Jain, P. Transfersomes: A novel technique for transdermal drug delivery. J. Drug Deliv. Ther. 2019, 9, 279–285.

[2]. Modi, C.; Bharadia, P. Transfersomes: New dominants for transdermal drug delivery. Am. J. PharmTech. Res.2012, 2, 71–91.

[3]. Jain, A.K.; Kumar, F. Transfersomes: Ultradeformable vesicles for transdermal drug delivery. Asian J. Biomater. Res. 2017, 3, 1–13.

[4]. Elsayed, M.A.; Abdallah, O.Y.; Naggar, V.F.; Khalafallah, N.M. Lipid vesicles for skin delivery of drugs: Reviewing three decades of research. Int. J. Pharm. 2007, 332, 1–16.

[5]. Touitou, E.; Junginger, H.E.; Weiner, N.D.; Nagai, T.; Mezei, M. Liposomes as carriers for topical and transdermal delivery. J. Pharm. Sci. 1994, 83, 1189–1203.

[6]. Yadav, D.; Sandeep, K.; Pandey, D.; Dutta, R.K. Liposomes for drug delivery. J. Biotechnol. Biomater. 2017,7, 1–8.

[7]. Cevc, G. Transfersomes, liposomes and other lipid suspensions on the skin: Permeation enhancement, vesicle penetration, and transdermal drug delivery. Crit. Rev. Ther. Drug Carr. Syst. 1996, 13, 257–388.

[8]. Rajan, R.; Jose, S.; Mukund, V.P.B.; Vasudevan, D.T. Transferosomes—A vesicular transdermal delivery system for enhanced drug permeation. J. Adv. Pharm. Technol. Res. 2011, 2, 138–143.

IJARSCT
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International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, June 2022
Impact Factor: 6.252

[9]. Lymberopoulos, A.; Demopoulou, C.; Kyriazi, M.; Katsarou, M.; Demertzis, N.; Hatziandoniou, S.;Maswadeh, H.; Papaioanou, G.; Demetzos, C.; Maibach, H.; et al. Liposome percutaneous penetration in vivo. Toxicol. Res. Appl. 2017, 1, 1–6.

[10]. Li, J. Microneedle Patches as Drug and Vaccine Delivery Platform. Curr. Med. Chem. 2017, 24, 2413–2422.

[11]. Wang, M.; Marepally, S.; Vemula, P.; Xu, C. Inorganic Nanoparticles for Transdermal Drug Delivery and Topical Application. In Nanoscience in Dermatology; Elsevier: Amsterdam, The Netherlands, 2016; pp. 57–72.

[12]. Xu, B.; Jiang, G.; Yu, W.; Liu, D.; Zhang, Y.; Zhou, J.; Sun, S.; Liu, Y. H2O2-Responsive mesoporous silica nanoparticles integrated With microneedle patches for the glucose-monitored transdermal delivery of insulin. J. Mater. Chem. B 2017, 5, 8200–8208.

[13]. Pegoraro, C.; MacNeil, S.; Battaglia, G. Transdermal drug delivery: From micro to nano. Nanoscale 2012, 4, 1881–1894.

[14]. Fesq, H.; Lehmann, J.; Kontny, A.; Erdmann, I.; Theiling, K.; Rother, M.; Ring, J.; Cevc, G.; Abeck, D. Improved Risk-benefit ratio for topical triamcinolone acetonide in Transfersome in comparison with equipotent cream and ointment: A randomized controlled trial. Brit. J. Dermatol. 2003, 149, 611–619.

[15]. Cevc, G. Transfersomes: Innovative transdermal drug carriers. In Modified-Release Drug Delivery Technology,1st ed.; Rathbone, M.J., Hadgraft, J., Roberts, M.S., Eds.; Marcel Dekker, Inc.: New York, NY, USA, 2002; Volume 126, pp. 533–546. ISBN 0-8247-0869-5.

[16]. Rai, S.; Pandey, V.; Rai, G. Transfersomes as versatile and flexible nano-vesicular carriers in skin cancer therapy: The state of the art. Nano Rev. Exp. 2017, 8, 1325708.

[17]. Fernández-García R, Lalatsa A, Statts L, Bolás-Fernández F, Ballesteros MP, Serrano DR. Transferosomes as Nanocarriers for drugs across the skin: Quality by design from lab to industrial Scale. Int J Pharm. 2020;573:118817

[18]. Walve, J.R.; Bakliwal, S.R.; Rane, B.R.; Pawar, S.P. Transfersomes: A surrogated carrier for transdermal drug delivery system. Int. J. Appl. Biol. Pharm. Technol. 2011, 2, 204–213.

[19]. Sivannarayana, P.; Rani, A.P.; Saikishore, V.; VenuBabu, C.; SriRekha, V. Transfersomes: Ultra deformable vesicular carrier systems in transdermal drug delivery system. Res. J. Pharm. Dos. Forms Technol. 2012, 4,243–255.

[20]. Sachan, R.; Parashar, T.; Soniya, S.V.; Singh, G.; Tyagi, S.; Patel, C.; Gupta, A. Drug carrier transfersomes:A novel tool for transdermal drug delivery system. Int. J. Res. Dev. Pharm. Life Sci. 2013, 2, 309–316.

[21]. Li, J.; Wang, X.; Zhang, T.; Wang, C.; Huang, Z.; Luo, X.; Deng, Y. A review on phospholipids and their main Applications in drug delivery systems. Asian J. Pharm. Sci. 2015, 10, 81–98.

[22]. Bhasin, B.; Londhe, V.Y. An overview of transfersomal drug delivery. Int. J. Pharm. Sci. Res. 2018, 9,2175–2184.

[23]. Lei, W.; Yu, C.; Lin, H.; Zhou, X. Development of tacrolimus-loaded transfersomes for deeper skin penetration Enhancement and therapeutic effect improvement in vivo. Asian J. Pharm. Sci. 2013, 8, 336–345.

[24]. Pandey, A. Role of surfactants as penetration enhancer in transdermal drug delivery system. J. Mol. Pharm.Org. Process. Res. 2014, 2, 1–10.

[25]. Duangjit, S.; Opanasopit, P.; Rojanarata, T.; Ngawhirunpat, T. Characterization and in vitro skin permeation Of meloxicam-loaded Liposomes versus Transfersomes. J. Drug Deliv. 2010, 2011, 1–9.

[26]. Aggarwal, N.; Goindi, S. Preparation and evaluation of antifungal efficacy of griseofulvin loaded deformable Membrane vesicles in optimized guinea pig model of Microsporum canis—Dermatophytosis. Int. J. Pharm.2012, 437, 277–287.

[27]. Chen, J.; Lu, W.-L.; Gu, W.; Lu, S.-S.; Chen, Z.-P.; Cai, B.-C. Skin permeation behavior of elastic liposomes:Role of formulation ingredients. Expert Opin. Drug Deliv. 2013, 10, 845–856.

[28]. Dhopavkar S, Kadu P. Transfersomes-a Boon for transdermal delivery. Indo American Journal Of Pharmaceutical Sciences. 2017;4(9):2908-19.

[29]. Moawad, F.A.; Ali, A.A.; Salem, H.F. Nanotransfersomes-loaded thermosensitive in situ gel as a rectal Delivery system of tizanidine HCl: Preparation, in vitro and in vivo performance. Drug Deliv. 2017, 24, 252–

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, June 2022
Impact Factor: 6.252

260.

[30]. Bnyan, R.; Khan, I.; Ehtezazi, T.; Saleem, I.; Gordon, S.; Neill, F.O.; Roberts, M. Surfactant effects on lipid-based Vesicles properties. J. Pharm. Sci. 2018, 107, 1237–1246.

[31]. Suresh. D. Kumavat*. Transfersomes: A Promising Approach for Transdermal Drug Delivery System. Asian journal of Pharmaceutical sciences and research 2013;3.

[32]. Van Hoogevest, P.; Wendel, A. The use of natural and synthetic phospholipids as pharmaceutical excipients. Eur. J. Lipid Sci. Technol. 2014, 116, 1088–1107.

[33]. Mathur, M. Approaches for improving the pharmacological and pharmacokinetics properties of herbal drugs.Int. Res. J. Pharm. Appl. Sci. 2013, 3, 40–50.

[34]. Cevc, G. Transdermal drug delivery of insulin with ultradeformable carriers. Clin. Pharmacokinet. 2003, 42,461–474.

[35]. Jadupati, M.; Kumar, N.A. Transferosome: An opportunistic carrier for transdermal drug delivery system.Int. Res. J. Pharm. 2012, 3, 35–38.

[36]. Cevc, G.; Blume, G.; Schätzlein, A.; Gebauer, D.; Paul, A. The skin: A pathway for systemic treatment with Patches and lipid-based agent carriers. Adv. Drug Deliv. Rev. 1996, 18, 349–378.

[37]. Mandal, U.K.; Mahmood, S.; Taher, M. Experimental design and optimization of raloxifene hydrochloride Loaded nanotransfersomes for transdermal application. Int. J. Nanomed. 2014, 9, 4331–4346.

[38]. Cevc, G.; Schatzlein, A.G.; Richardsen, H. Ultradeformable lipid vesicles can penetrate the skin and other Semi-permeable barriers unfragmented. Evidence from double label CLSM experiments and direct size Measurements. Biochim. Et Biophys. Acta (BBA)-Biomembr. 2002, 1564, 21–30.

[39]. Chauhan, P.; Tyagi, B.K. Herbal novel drug delivery systems and transfersomes. J. Drug Deliv. Ther. 2018, 8,162–168.

[40]. Kumar, G.P.; Rajeshwarrao, P. Nonionic surfactant vesicular systems for effective drug delivery—An overview.Acta Pharm. Sin. B 2011, 1, 208–219.

[41]. Cipolla, D.; Wu, H.; Gonda, I.; Eastman, S.; Redelmeier, T.; Chan, H.-K. Modifying the release properties of liposomes toward personalized medicine. J. Pharm. Sci. 2014, 103, 1851–1862.

[42]. Dudhipala, N.; Mohammed, R.P.; Youssef, A.A.A.; Banala, N. Effect of lipid and edge activator concentration on development of Aceclofenac loaded transfersomes gel for transdermal application: In vitro and ex vivo skin permeation. Drug Dev. Ind. Pharm. 2020, 46, 1–28.

[43]. Iskandarsyah; Rahmi, A.D.; Pangesti, D.M. Comparison of the characteristics of transfersomes and Protransfersomes containing azelaic acid. J. Young-Pharm. 2018, 10, S11–S15.

[44]. Kotla, N.G.; Chandrasekar, B.; Rooney, P.; Sivaraman, G.; Larrañaga, A.; Krishna, K.V.; Pandit, A.; Rochev, Y. Biomimetic lipid-based nanosystems for enhanced dermal delivery of drugs and bioactive Agents. ACS Biomater. Sci. Eng. 2017, 3, 1262–1272.

[45]. Shakthi Apsara ThejaniOpatha, VarinTitapiwatanakun and RomchatChutoprapat *. Transfersomes: A Promising Nanoencapsulation Technique for Transdermal Drug Delivery.

[46]. El Zaafarany, G.M.; Awad, G.A.S.; Holayel, S.M.; Mortada, N. Role of edge activators and surface charge In developing ultradeformable vesicles with enhanced skin delivery. Int. J. Pharm. 2010, 397, 164–172.

[47]. Malakar J, Sen SO, Nayak AK, Sen KK. Formulation, optimization and evaluation of Transferosomal gel for transdermal insulin Delivery. Saudi Pharm J. 2012;20:355–63.

[48]. Ghai, I.; Chaudhary, H.; Ghai, S.; Kohli, K.; Kr, V. A review of transdermal drug delivery using nano-vesicular Carriers: Transfersomes. Recent Pat. Nanomed. 2012, 2, 164–171.

[49]. Chaurasiya P., Ganju E., Upmanyu N., Ray S.K., Jain P. Transfersomes: A novel technique for transdermal drug delivery. J. Drug Deliv. Ther. 2019;9:279–285. Doi: 10.22270/jddt.v9i1.2198.

[50]. Celtic Pharma Acquires Stake In Idea AG "21.7% Shareholding Purchased in Europe"s Leading targeted therapeutics Company IDEA prepares to Expand its late stage Clinical Development programmes," Hamiltion, Bermuda And Munich, Germany: September 28,2005.

[51]. Qvist M.H. Hoeck U. kreilgaard B. Madsen F. Hovgaard L. Froljaer S. Application of Confocal scan- ning microscopy in Characertisation of chemical enhancers in Drug in adhesive transdermal patches. AAPS Pharm

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
Volume 2, Issue 1, June 2022
Impact Factor: 6.252

Sci 2002;4:11-18.

[52]. Walve JR, Bakliwal SR, Rane BR, Pawar SP. Transfersomes: a surrogated carrier for Transdermal drug delivery system. Int J Applied Biology Pharma Technol 2011;2:204- 213.

[53]. Wu, P.-S.; Li, Y.-S.; Kuo, Y.-C.; Tsai, S.-J.J.; Lin, C.-C. Preparation and evaluation of novel transfersomes Combined with the natural antioxidant resveratrol. Molecules 2019, 24, 600.

[54]. Jiang, T.; Wang, T.; Li, T.; Ma, Y.; Shen, S.; He, B.; Mo, R. Enhanced transdermal drug delivery by Transfersome-embedded oligopeptide hydrogel for topical chemotherapy of melanoma. ACS Nano 2018, 12, 9693–9701.

[55]. Cevc, G.; Blume, G. Biological activity and characteristics of triamcinolone-acetonide formulated with the self-regulating drug carriers, Transfersomes®. Biochim. Et Biophys. Acta (BBA) Biomembr. 2003, 1614, 156–164.

[56]. Shabana, S.; Sailaja, A.K. Formulation and evaluation of diclofenac sodium transferosomes using different surfactants by thin film hydration method. Der Pharm. Lett. 2015, 7, 43–53.

[57]. Shaji J and Lal M: Preparation, optimization and Evaluation of transferosomal formulation for enhanced Transdermal delivery of a COX-2 inhibitor. Int J Pharm Pharm Sci 2014; 6: 467-77.

[58]. Benson HA: Transfersomes for transdermal drug delivery. Expert opinion on Drug Delivery 2006; 3(6): 727-37.

[59]. El Zaafarany, G.M.; Awad, G.A.S.; Holayel, S.M.; Mortada, N. Role of edge activators and surface charge In developing ultradeformable vesicles with enhanced skin delivery. Int. J. Pharm. 2010, 397, 164–172.