

Recent Update on Transferosomes as Transdermal Drug Delivery System

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Abstract

A primary goal of these delivery systems was to provide patients with greater convenience. This drug delivery technology is a specially constructed artificial vesicle that resembles cell vesicles and is appropriate for controlled and potentially targeted medication administration. Because they are formed of natural phospholipids, like liposomes, they are biodegradable and biocompatible. They are made up of phospholipids such as phosphatidyl choline, edge activators such as sodium cholate, and a little amount of ethanol. Transferosome drug delivery works via two processes. For starters, as drug vectors, they remain intact after penetrating the skin. Second, they operate as penetration enhancers, breaking the stratum corneum's highly structured intercellular lipids. Based on data that it is effective without causing skin irritation, this medication delivery technique is preferred for the treatment of skin cancer. This review gives an important overview of transferosomes as drug delivery vesicles' properties, composition, manufacturing processes, formulation examples, characterization, succinct assessments of published publications and applications, and so on.

Keywords: transferosomes; vesicular drug delivery systems; transdermal

Introduction

Novel drug delivery system aims to deliver the drug at a rate directed by need of body during the period of treatment, and channel the active entity to the site of action. Biological origin of these vesicles was first reported in 1965 by 'Bingham' and has been given name as 'Bingham bodies'. Vesicular drug delivery systems have been used to improve the therapeutic index, solubility, stability, and rapid degradation of drug molecule. The targeted vesicles are classified into the following types based on their composition. Lipoidal biocarriers for site specific targeting: Liposomes Emulsomes Enzymosomes Ethosomes Sphingosomes Transferosomes Pharmasomes Virosomes. Non-lipoidal biocarriers for site specific targeting [1].

In past few years we are in search of a therapeutic and efficient drug delivery system which provides many benefits over conventional drug delivery system like avoidance of first pass metabolism, predictable and extended duration of action, utility of short half-life drugs, improving physiological and pharmacological response, avoiding the fluctuation in drug levels, inter- and intra-patient variations, minimizing undesirable side effects and most importantly, which provides patients convenience [2].

We found many benefits of conventional dose forms, but also significant downsides. Oral medications face a hostile environment in the GI tract, solubility difficulties, first pass metabolism, and a bitter taste. The main disadvantages of parenteral preparations are allergic reactions, needle pain, infection risk, emboli, and cost. Topical medicines produce local irritation, itching, erythema, and reduced stratum corneum permeability [3]. Transdermal delivery is an attractive approach because it allows for easy drug delivery. The stratum corneum permeability is a key problem of dermal and transdermal medication delivery systems. The stratum corneum is the epidermis' topmost layer, made composed of keratinized, flattened epidermal cells. Water-tight cells with a strong flexible membrane impede chemical transfer, rendering this route of administration insufficient for therapeutic application. Electrophoresis, sonophoresis, and iontophoresis are some of the technologies investigated and developed to overcome these issues. Non-ionic surfactant vesicles such as niosomes and proniosomes are colloidal carriers [4]. Other vesicular systems used are liposomes, dendrosomes, niosomes, exosomes, microemulsions. Using rational membrane design as a particular

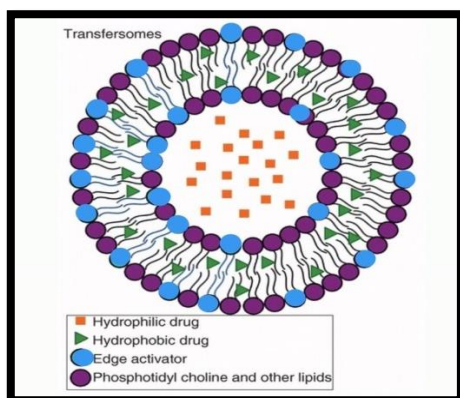


form of composite body known as “transferosomes”, an unique vesicular drug carrier system is developed. Transferosomes are the most promising way to build an unique dosage form that delivers the medicine slowly and safely with minimal side effects. Gregor Cevc proposed the concept of transferosomes in 1991. Transferosomes The is a trademark of IDEA AG and refers to patented drug delivery. The name is a mix of *transfero* and *soma*. *Transfero* means to carry across in Latin, and *soma* means body in Greek, therefore it is a “carrying body”. Transferosomes are artificial vesicles meant to mimic a cell vesicle or a cell in exocytosis, making them ideal for controlled and potentially targeted medication delivery [5].

Salient Features of Transferosomes: These are made up of natural phospholipids like liposome therefore these are biodegradable and biocompatible [6].

1. They act as a carrier for low to High molecular weight drugs such as analgesic, corticosteroids, anesthetics, sex hormones, albumins, insulin, anticancer etc.
2. These molecules possess wide range of solubilities as they are made up of hydrophilic and hydrophobic moieties.
3. Transferosomes have high entrapment efficiency, for example for lipophilic drugs the entrapment efficiency is nearly equal to 90%.
4. The transferosome molecules encapsulate the drug and protect it from metabolic degradation. example: proteins and peptides
5. Transferosomes acts as a depot as they release the drug slowly and gradually.
6. Transferosomes are used as topical and as well as for systemic delivery of the drugs.
7. Transferosome preparation involves simple and easy procedures and avoid use of unacceptable pharmaceutical Excipients.
8. The formulation is short, simple, and easy to scale up.
9. Transferosomes possesses high deformability which helps in better penetration of vesicles.
10. They can deform and pass-through narrow constructions (5 to 10 times less diameter of their own size) without any significant loss of the drugs.

Structure and Composition of Transferosomes: Transferosomes are the mixed lipid aggregates composed of *phospholipids* like phosphatidyl choline- an amphipathic ingredient and a lipid bilayer softening compound usually known as *edge activator* which forms the vesicle.



Phospholipids:

- Vesicles composed of phospholipids as the main ingredient like soya phosphatidylcholine, egg phosphatidylcholine, dipalmitoyl phosphatidylcholine, etc., 10-25% surfactant for providing flexibility, various solvents as ethanol, methanol and hydrating medium consisting of saline phosphate buffer (pH 6.5-7). Dyes like Rhodamine 123, Nile red etc.
- Phosphatidylcholine is a fatty composition which can be from both human and vegetable origin, is mainly an unsaturated fatty acid. These unsaturated fatty acids are mainly linoleic acid up to 70% of the total fatty acids.
- Foremost reason behind the ability of phospholipids to fluidize the lipid bilayer is soy phosphatidylcholine which has a very low phase-transition temperature of below 0°C in water-containing systems, which can be determined by measuring the increase of the trans epidermal water loss (TEWL) after application for a short period of time [7].

Edge activators:

- The edge activator is added to increase lipid bilayer flexibility and permeability it is also known as “bilayer softening component”, it may be a biocompatible surfactant or an amphiphilic drug.
- An edge activator chiefly consists of single chain surfactant of nonionic nature which causes destabilization of the lipid bilayer Thus by increasing its fluidity and elasticity [8]. Flexibility of the transferosome membrane can be modified by mixing suitable surface-active agents in proper ratios.
- most used edge activators which are biocompatible and increase the vesicle’s bilayer flexibility as well as improve the permeability in transferosome 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.

Advantages:

1. Transferosomes increases the duration of drug in systemic circulation due to its encapsulated form which increases half-lives of the drugs [8].
2. Both Hydrophilic and hydrophobic moieties can be encapsulated.
3. The vesicles of transferosomes are capable of entrapping hydrophilic, lipophilic, amphiphilic particles.
4. These are nontoxic in nature.
5. These have ability to target the specific organ for drug delivery.
6. Transferosomes avoids first pass metabolism which increase their bioavailability.
7. They have potential to increase transdermal flux and improve site specificity of biologically active agents.
8. These are made up of pharmaceutically acceptable ingredients which are nontoxic and are prepared by using standard methods, optimized on case-by-case basis.
9. They protect the drugs from metabolic degradation by encapsulation and prevent undesirable side effects.
10. Transferosomes are highly recommend for predictable and extended duration of activity, for sustained release of drugs.
11. Transferosomes are used for delivery of numerous active



compounds such as insulin, proteins, peptides, corticosteroids, anticancer drugs, analgesics, anesthetics, herbal medicines, and NSAID's.

12. These are made up of natural phospholipids like liposome hence these are promisingly biocompatible biodegradable.
13. Transferosomes accommodate a variety of agents Independent of their molecular weight, size, structure, polarity.
14. Transferosomes are the versatile and efficient molecules in effective drug delivery.
15. These are ultra-deformable and elastic in nature they squeeze themselves in narrow constructions of skin that are very minute, such as 5 to 10 times less diameter than the vesicle diameter.
16. Transferosomes are the unique drug carrier systems that deliver therapeutic agents with wide range of solubilities as these are composed of hydrophilic and hydrophobic moieties.
17. These can be easily administered in unconscious and comatose patients.
18. These can be used with drugs which have narrow therapeutic index.
19. Equivalent therapeutic effect is achieved in transdermal drug delivery with lower daily dose of a drug than the required dose.
20. Self-administration is possible in this system of drug delivery which is noninvasive, painless, and simple application which increases patient compliance.

DISADVANTAGES:

1. Due to their predisposition to oxidative degradation these are chemically unstable.
2. Purity of natural phospholipids is the main criteria in adoption of transferosomes as drug delivery vehicles.
3. Drug molecules which are used for transferosome delivery must be potent because patch size limits amount that can be delivered.
4. Drugs which require high blood levels cannot be administered.
5. Transferosome molecules permeate the skin slowly as these are hydrophilic in nature.
6. It may cause hypersensitivity reaction in some cases.
7. Transferosomes are chemically unstable because of their susceptibility to oxidative degradation.
8. Transferosomes are not suitable for higher doses of drugs.
9. Along with these limitations the high expense of the product is also a major drawback for the wide acceptance of transferosome [9].

Method of Preparation

These are divided into two procedures which are involved in the preparation of transferosomes. They are as follows: 1) Thin film hydration technique 2) Modified hand shaking method [10].

1) Thin film hydration technique:

Preparation consists of three stages.

1. A) The first step is to dissolve phospholipids and surfactants in alcohol to form a thin film of vesicles. B) The aforementioned dissolved solution is heated to a temperature above the lipid's

temperature. Keep them under the rotatory evaporator so the organic solvent can escape. C) If any invisible solvents are present, it is kept in a vacuum at night to eliminate the

2. Hydrate the film with a sufficient buffer at 60 rpm for roughly an hour. The vesicles are left to swell for 2 hours at room temperature.
3. Sonicate the prepared vesicles for 30 minutes at 50°C using a bath sonicator.

Revised Hand Shake Method

1. Prepare a 1:2 mixture of chloroform and ethanol, then dissolve lecithin, a surfactant and drug, in the mixture.
2. The organic solvent is evaporated from the mixture using the lipid transition temperature.
3. The generated thin lipid layer is left over to eliminate any remaining organic solvent.

Sonication method:

Phospholipids, medication, and activator in phosphate buffer A milky transferosomal suspension is obtained by continuous stirring. It is then passed through polycarbonate membranes after a period of ultra-sonication in a bath sonicator at ambient temperature [11].

Suspension homogenization:

Transferosomes are made by dissolving ethanolic phospholipid solution with an edge activator in it. The prepared mixture is led to a lipid concentration. The next formulation is sonicated, cooled, then defrosted twice or three times.

Centrifugation:

It's mixed with the lipophilic drug, catalyst, and phospholipids. The solvent is subsequently removed using a rotatory evaporator at lower pressure and temperature. Solvents are eliminated by staying in the dark. The settled lipid film is humidified with an appropriate buffer solution by centrifugation. This is the phase for hydrophilic drug penetration. At room temperature, these vesicles swell. The obtained multilamellar lipid vesicles are sonicated [11].

Evaporation method:

The phospholipids, a catalyst are combined in a round bottomed flask, and then lipophilic medicines can be added. Using rotatory evaporation, the solvent was then removed to form lipid films. These films are dissolved in an organic solution containing isopropyl ether/diethyl ether. The aqueous and organic phases are then combined to form a bi-phase system. A hydrophilic medication can be imposed now. This system is sonicated in a bath sonicator until an emulsion is obtained. The organic solvent is evaporated from the thick gel to produce a vesicular suspension [12].

Hi-pressure homogenization:

The phospholipids edge activator and medicine are mixed constantly in distilled water. The mixture is then shaken using



ultrasonics. The resultant mixture is then homogenised under high pressure. Finally, the transferosomes are stored properly.

Injection of ethanol:

To obtain a transparent and organic phase, dissolving the phospholipid, edge activator, and lipophilic drug in ethanol using a magnetic continuous stirrer until a clear solution is obtained. To make an aqueous phase, add water miscible compounds to phosphate buffer. This is the time to interpret the hydrophilic medication. The organic and aqueous phase solutions are heated to 45-50 c. The ethanolic phospholipid solution is gradually introduced into the aqueous solution while stirring. To remove the ethanol, the dispersion is placed in a vacuum evaporator and subsequently sonicated to reduce particle size [13].

Characterisation of transferosomes:

Entrapment efficacy:

It is known by splitting the opaque drug. After centrifugation, vesicles can be broken down. The systemic approach is used to study medication amount [14]. Dynamic light scattering and photon-association spectroscopy are used to determine vesicle diameter.

Cslm study:

This method involves separating transferosomes from liposomes, niosomes, and studying transferosome absorption. The concept is a lipophilic fluorescent marker that can emit light. And the light released can be utilised elsewhere.

Measurement of deformability/permeability:

The transferosome mixture is transferred in numerous filters with pore diameters ranging from 50 to 400 nm. Dynamic light scattering is recognised to determine particle size distribution in vesicles contracted to every filter. The following formula can be used to determine deformability [15].

$D=J(rv/rp)$ So, 5 min suspension extruded = J, rv= vesicle size, rp= barrier pore size

In -vitro drug release:

Using a cellophane membrane, transferosome dissolution is heated to 32°C. and the results. This procedure should be mentioned at intervals. Detection is done by UV, HPLC, and HPVLC. The amount of free medicines should be broken up and measured.

Vesicles type:

TEM, phase contrast microscopy should be used to see transferosome vesicles. The size and structure of vesicles determine their capacity. DLS calculates mean size and TEM detects structural differences.

Vesicles per cubic mm:

Transferosomes without ultrasonic energy are hydrated five times with 0.9 percent NaCl solution. The process is then studied using a hemocytometer and an optical microscope. The algorithm below counts and measures transferosomes in small squares [16].

Total number of transferosomes counted x dilution factor = 4000. Penetration ability:

Fluorescence microscopy can estimate it.

Turbidity measurement:

The turbidity of medication in water is measured using a nephelometer.

Surface charge density:

Zetasizer can estimate it. Drug content: HPLC method uses UV detector, column frequently, pump, and auto sample to estimate drug content.

Occlusive effect:

Skin occlusive aids medication penetration in topical formulations. Likewise. It damages elastic vesicles. Hydro taxis is a critical step in vesicle penetration from non-aqueous to aqueous surfaces. Occlusion affects hydration forces hinder skin evaporation [16].

Concise evidence of published Transferosomal gel formulations and its influence on pharmacology:

Khaled M.Hosny et al (2021) studied amphotericin nanotransferosome nasal gel as an antifungal therapy for fungal sinusitis. It is based on rhinosinusitis, which is classified as allergic, mycetoma, chronic, or acute invasive. The purpose of this study is to determine the efficacy of amphotericin gel loaded with nanotransferosomes in situ against aspergillus flavus, a mould that causes allergic rhinosinusitis. A Box-Behnken design was used to optimise the formulation of nanotransferosomes in order to examine interactions and match the pre-requisites of selected locations. The improved formulation contained 300 mg soyabean lecithin, 200 mg amphotericin B (AMP), and 150 mg clove oil, resulting in a particle size of 155.09nm, an entrapment efficacy (EE) of 84.30 percent, an inhibitory zone of 16.0mm, and a serum creatinine concentration of 0.1197mmol. The optimised formulation was then evaluated for several characteristics, and it released 79.25 percent AMP and demonstrated penetration through the nasal membrane, whereas other experiments did not reach complete absorption. The in vivo tests performed on animal models revealed no significant difference in various kidney function parameters, implying that the nasal in situ gel loaded with AMP-clove oil nanotransferosomes may be a promising novel carrier that enhances antifungal activity while minimising AMP nephrotoxicity [17].

Antonio José Guillot et al (2021) studied Mithramycin Nano-Encapsulation in Transferosomes and Polymeric Micelles for Sarcoma Treatment. Mithramycin, a natural antibiotic, has anti-sarcoma activity but also systemic toxicity. The nano delivery method of mithramycin displays good therapeutic window. Transferosomes and PLGA polymeric Micelles are coupled to



enhance polydispersity index and encapsulation efficiency. This preparation is produced through thin film hydration and ethanol injection technique. This work presents a novel formulation for improved encapsulation of mithramycin for potential therapeutic usage [18].

Oral Gel Loaded with Fluconazole-Sesame Oil, Development, Optimization, and Assessment of Antifungal Activity by **Hela M. Alkhalidi et al.** Oral candida is a fungus that infects the skin or mucous membranes. It is caused by overgrowth of 150 candida species, but mostly candida albicans. This fungus infection can be acute or chronic. This work used thin-layer evaporation to create fluconazole-loaded sesame oil Nano transfersomes (FS-NTF) to treat oral candidiasis. The box-Behnken design was used to determine how vesicle size, EE, zone of inhibition, and ulcer index interact. The final FS-NTF formulation included hyaluronic acid hydrogel (HA-FS-NTF). Pseudoplastic flow was detected. Ex vivo permeability was observed to be greater in HA-FS-NTF (400g/cm²) than HA-FS-NTF (294g/cm²). In immunosuppressed animals with candida infection, the improved formulation had an inhibitory zone of 14.330.76 and an ulcer index of 0.6370.29. Fluconazole has proven to be an effective and safer oral treatment for candidiasis [19].

Durgesh Thakre et al. (2021) studied itraconazole-loaded transfersomes for treating fungi. Itraconazole is an antifungal drug used to treat a variety of fungi. Several carrier systems including antifungal medicines have shown promise in treating skin infections. This study looked into the possibility of transfersosomal gel formulations for transdermal delivery of Itraconazole and evaluated the effects of lipid, ethanol, drug, and stirrer time. Measurement of gel viscosity, vesicle size, surface charge, entrapment efficacy, PH, drug content extrudability, spreadability, stability, and in vitro drug dispersion. The manufactured gel had a viscosity of 3240cps, a percent assay of 98.560.23, an extrudability of 145g, and a spreadability of 9.85 (g.cm/sec). The Franz diffusion cell method reported 92.230.21% drug release from transfersomes in 12 hours. The first 30 minutes had a 12.250.32% drug release, which is high. The gel was optimised for fungal effect. Due to its high deformable capacity, Transfersomal gel allows for greater skin penetration and targeted medication release [20].

Khomendra Kumar Sarwa et al. The topical antiarthritic potential of capsaicin (an active principle of capsicum) was investigated in arthritic rats. Capsaicin was applied topically to rats via the transfersosomal vesicular system. These nano-sized transfersomes with a negative surface charge (-14.5 mV) and appropriate structural flexibility resulted in 60.34 percent entrapment efficacy, 220 nm biomembrane penetration, and 76.76 percent drug release from vesicular system in 24 hours. The antiarthritic efficacy of our produced capsaicin-loaded transfersosomal formulation was compared to that of a conventional gel formulation (Thermagel, standard). Our formulation has superior inhibitory action than the commercial Thermagel formulation at the same dosage level, possibly due to Thermagel's lower permeability across dermal barriers than our specially engineered transfersosomal delivery method. The innovative vesicular system's tolerance indicates greater topical administration of such an irritant [21].

Silvia during, Puteri **D. Nastitiand et al (2020)** studied Andrographolide transdermal gel. It is vital in evaluating transfersome use. It has two steps. The first step involves adjusting the ratio of span 80 to phospholipids to test the effect on transfersome deformability (P1-P4). Using four formulations, we tested the effect of altering Andrographolide ratios in transfersomes on entrapment efficiency (F1-F4). The particle size was 524.02 nm and the entrapment efficiency was 97.02+0.01. In the first phase, the transfersome and non-transfersome Andrographolide gels had penetration fluxes of 23.26 2.34 and 1.28 0.82g/cm.h. This medication is a promising transdermal delivery method for Andrographolide [22].

Taxifolin-loaded lipid nanovesicles for beverage fortification were studied by **Forough Hasibi et al (2020)**. To increase bioavailability, transfersomes, niosomes, and liposomes made by ethanol injection technique (EIM) and supplemented with soybean lecithin, tween 80, span 60, and cholesterol were utilised. It's an antioxidant. Sizes should be between 98 and 215 nm. The zeta potential should be -20.40 to -32.20 nv. 72-75 percent encapsulation efficiency Maximum lecithin and tween 80 formulations with and without cholesterol. Size is 200 nm. It is an antioxidant flavanone that is utilised to protect the circulatory system. Low bioavailability in food and medicine. Nanocarriers are physically stable and encapsulate well. They added tween 80 and soya lecithin as stabilisers to ensure Taxifolin distribution to foods like beverages [23].

An increased and longer-lasting ocular delivery study was conducted by **Karthik Yadav Janga et al. (2019)** on the efficiency of the electron driven sole-to-gel transfersomes. The in situ gelling system was constructed using NT transfersome formulations (FNs) with a 1:1 molar ratio of phospholipid-to-Span and low quantities of tocopheryl polyethylene glycol succinate (TPGS). The molar ratios of phospholipid, sorbitan monostearate (Span), and TPGS were tuned. FN-loaded formulations (FNGs) with gellan gum (0.3 percent w/v) formed an in-situ gel in simulated tear fluid. Studies on corneal epithelial cell cytotoxicity and histopathology confirmed the improved formulations' ocular safety and cytocompatibility. Transcorneal permeability experiments showed better NT from transfersome formulations compared to control solution. The electrolyte-sensitive FNGs delivered more NT to the ocular tissues than the FNs and FNGs. As a drug delivery platform for better topical ocular pharmacotherapy, Gellan gum-based in situ hydrogels of transfersomes are successful [24].

Astried Leonyza and Silvia surini (2019) have been investigating the optimization for percutaneous peptide and protein delivery of sodium transfersomas based on deoxycholate. This study's major goal is to develop and characterise transfersomes for percutaneous peptide and protein delivery. This study was a pilot study for the topical delivery of rHEGF in transfersomes. This approach used phosphatidylcholine and sodium deoxycholate as vesicle formers to create transfersomes. The TF1, TF2, TF3, and TF4 formulations were optimised with phospholipid and surfactant ratios of 90:10, 85:15, 80:20, and 75:25, respectively. They were then characterised by particle size distribution, polydispersity index, zeta potential, vesicle shape, and deformability index. There was no significant difference in the polydispersity index between the two formulations. TEM



revealed transfersome spherical and unilamellar vesicles. A peptide and protein formulation using sodium deoxycholate-based transfersomes may be possible for percutaneous delivery [25].

Pey-Shiuan Wu et al. (2019) studied the Preparation and Evaluation of Novel Transfersomes Combined with the Natural Antioxidant Resveratrol. And revealed that Resveratrol (trans-3, 5, 40 -trihydroxystibene, RSV) is a kind of polyphenol which has anti-inflammatory, antioxidant, anti-allergy, and anti-cancer properties, as well as being a scavenger of free radicals and prevents cardiovascular diseases. It is quite unstable in light, heat, and other conditions, and decays easily due to environmental factors. For these reasons, the author used a new type of carrier, transfersome, to encapsulate RSV. Transfersome consists of phosphatidyl choline (PC) from a liposomal system and non-ionic edge activators (EA) which enhance the flexibility of the lipid bimolecular membrane of transfersome. They summarize all the tested parameters, the best production condition was 5% PC/EA (3:1) and 5% ethanol in distilled water, with an ultrasonic bath and stirring at 500 rpm, which is followed by high pressure homogenization. The optimal particle size was 40.13 ± 0.51 nm and the entrapment efficiency (EE) found was $59.93 \pm 0.99\%$. The results indicated that the RSV transfersomes D1–20(W) and D3–80(W) are the best groups. For the in vitro transdermal delivery, D1-20(W) had the highest cumulative amounts. For cell viability, the D3–80(W) group had the lowest cytotoxicity. Therefore, the author has successfully prepared RSV transfersomes and also improved the stability, solubility, and safety of RSV [26].

Pey-Shiuan Wu et al. (2019) investigated Novel Transfersomes Combined with Resveratrol. Resveratrol is a form of polyphenol, and has the propensities anti-inflammation, antioxygen, antisocial and anti-cancer, as well as the scavenger of free radicals and cardiovascular disease preventing. and it has also been found to be a scavenger of free radicals. Light, heat and other variables are highly unstable, and due to environmental causes it swiftly decays. The author employed the transfersome, a new carrier type, to encapsulate the RSV for these reasons. Transfersome is made of PLSP and non-ionic edge activators (EA) which improve lipid-biomolecular membrane flexibility of the transfersome. It is also composed of phosphatidyl choline (PC). They sum up all the factors evaluated, the optimal conditions for production were 5 percent PC/EA (3:1) and 5 percent ethanol, which is distilled, with an ultrasonic bath and 500 rpm rising. The ideal size for the particle was 40.13 ± 0.51 nm, with capture effectiveness (EE) of $59.93 \pm 0.99\%$. RSV transfers D1–20(W) and D3–80(W) were the best groups, according to the results. D1-20(W) had the largest cumulative quantities for in vitro transdermal administration. The lowest cytotoxicity for cell viability was in the D3–80(W) group. The author has therefore prepared RSV transfers successfully and increased RSV stability, solubility and safety [26].

To provide topical antioxidants, **Sopan Nangare et al. (2019)** developed a freeze-dried mulberry leaves extract-based transfersomal gel containing quercetin via thin layer hydration. The medicine was encapsulated in a selection of transfer formulations. This was explored. Particulate size and zeta, EE trap effectiveness (percentage), polydispersity index, in vitro drug release, drug content were used for batch optimization. An

optimised MF5 batch gives 86.23% and 95.79% of the quercetin release in the vesicles trap efficiency (percent). It has an average diameter of 118.7nm and a capacity for -45.11mV zeta vesicles. The formula MG1 provides superior antioxidant function, spreadability and trap efficiency, ex vivo release of medicines, homogeneity, drug content and stability compared to the formulation. Hence, an MG1 mulberry blade extract batch transfersomes gel offers a huge antioxidant potential, creating new possibilities in the topical application of acne vulgaris therapy [27].

Sameh Hosam Abd El-Alim et al. (2019) compared liposomes, ethosomes, and transfersomes as carriers for improving diflunisal transdermal administration. They tested it in vitro and in vivo. The ethosomes and transfersomes were studied and compared to regular liposomes. We made ethanol-containing ethosomes (10, 30, and 50%) and transfersomes with various edge activators (sodium deoxycholate, cholate, and taurocholate). Our results showed very high capture efficiency (46.73–65.99%), nanometric vesicle sizes (453.10–796.80 nm) and negative Zeta potentials (45.40–86.90 mv). Diflunisal release from nanovesicular hydrogels was longer than from dispersions. Diflunisal penetration and flux across skin layers was superior in both carriers than liposomal hydrogel [28].

Mengbing Chen colleagues (2018) studied carvedilol loaded Nano-transfersomes for topical skin cancer chemoprevention. The beta blocker carvedilol is known to prevent skin cancer in vivo and in vitro. Because beta blockers may induce difficulties in the cardiovascular system, carvedilol loaded transfersomes are used as target sites. Carvedilol, Tween 80 and soyphosphatidylcholine are chosen in the ratio 1:0.5:3. It stops DNA damage and apoptosis. Topical medication administration is used for chemoprevention of skin tumours, specifically carvedilol. Topical administration of carvedilol loaded transfersomes results in slower drug release and reduced systemic side effects. Among 30 formulations, F18 loaded carvedilol formulation with suspending agents and surfactants were chosen for topical distribution. This is recommended because the medicine is absorbed deeper into the skin, resulting in better pharmacological effects and fewer side effects. More research is being done to develop this medication into a gel or sunscreen [29].

Conclusion:

Transfersomes are ultra-deformable vesicles that handle transport related challenges such as Due to the skin's barrier qualities, high molecular weight medicinal compounds cannot be delivered transdermally. The deformable particles in transfersomes can transport medications over biological permeability barriers like skin. These elastic vesicles deform to enter the skin via pores. They are great for delivering peptides and proteins. To improve transdermal flux of medicinal medicines, these Transfersomes can adapt to environmental stress by squeezing themselves through skin pores that are many times narrower than normal. Transfersomes have a structure that combines hydrophilic and hydrophobic molecules, allowing for a wide range of solubility. Transfersomes have a number of advantages over other vesicular systems, including skin penetration, stability, systemic drug release, and deformability. Other vesicular systems are less efficient and less safe than



transfersomes. In the aforementioned review, we examined new publications, preparation methods, characterisation, and other aspects of this transdermal drug delivery system.

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