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Transferosomes: Novel Therapeutic Approach using Drug Delivery

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Abstract

Recent years have seen a significant increase in interest in innovative drug delivery systems because of their advantages over traditional medication administration methods. This work presents a novel method of drug delivery by discussing the idea of a herbal medication in transferosomes. Transferosomes are extremely pliable vesicles that have recently been presented as novel medication carriers. They have the ability to transport large molecules through intact mammalian skin. The use of lipid vesicles as a drug delivery method for skin therapy is still controversial, despite garnering more attention this year; most relevant papers emphasise the localization effect of liposomes, with the transport mechanisms mentioned in a few cases, depending on the formulation. A novel and cutting edge medication delivery technique called transferosomes has been created to get around the clarity issue and break through the skin barrier along the transcutaneous gradient. These are certain kinds of liposomes that have phosphatidylcholine water as an edge activator, or that contain it. Biocompatible and biodegradable properties are two advantages of transferosomes. It prevents the medicinal product from being broken down by metabolism.When coupled to generate transferosomes, both hydrophilic and hydrophobic compounds have a wider range of solubility. These carriers are extremely adaptable and excellent at holding a wide range of medications, regardless of their size, molecular weight, polarity, or form. Transferosomes have the ability to transport both high and low molecular weight drugs, including insulin, sex hormone, albumin, corticosteroids, and anti-cancer medicines. Many medications, including those used to treat cancer, atopic dermatitis, hypertension, anti-edema, analgesics, anti-inflammatory agents, and cutaneous leishmaniasis, exhibit activity in transferosomes.

Keyword: Novel drug System; Types; Classification; Methods of Preparation.

INTRODUCTION

Innovative medication delivery methods have been created to address a number of problems with traditional drug delivery. Transferosome is a trademark registered by the German company IDEA AG, which refers to its proprietary drug delivery technology. The name mean 'carrying body' and is derived from the Latin word 'transferre', meaning 'to carry across' and the Greek word 'soma', meaning 'a body'. Transfersomes are unique forms of liposomes made of phosphatidylcholine plus an edge activator. They are a relatively new and innovative medication delivery technology. The recently introduced unique drug carriers are transfersomes, highly malleable vesicles that can transport big molecules through intact mammalian skin.In its broadest definition, a transfersome is a device that naturally penetrates skin to transfer medications from the application to the intended location.[1-3] Although it has received more attention this year, the use of lipid vesicles as a drug delivery method for skin therapy is still

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debatable; most pertinent papers highlight the liposomes' localization effect, with the transport mechanisms being mentioned in a few instances, depending on the formulation.[4,5] Transferosomes have been employed in the treatment of numerous illnesses, including those involving the skin, eyes, brains, etc. For instance, according to accounts in the literature, chemotherapy administered traditionally to treat infections within the cells is not as successful in treating cancer since it cannot penetrate the cells. As a result, new carriers with the capacity to enter cells deeply, such transferosomes, were developed.[41,42] Microporous barriers can be effectively crossed by transferosome vesicles, even when the porous are considerably smaller than the vesicle. Phospholipids and edge activators (EAs) such as sodium cholate (NaCo), sodium deoxycholate, Span 60, Span 65, Span 80, Tween 20, Tween 60, Tween 80, and dipotassium glycyrrhizinate are the main components of transfersomes, which are elastic nanovesicles.[6] Transfersomes sin some situations, help the medication stay in the skin's upper layers.[7] Transfersomes have been investigated as drug delivery vehicles for many medications via transdermal or dermal delivery. [8-12] Transferosomes are a new and innovative drug delivery system that have been developed to overcome the problem of clarification and penetrate the skin barrier along the transcutaneous gradient. They are specific types of liposomes that contain or have phosphatidylcholine water as an edge activator. The primary application of transferosomes in skin care is due to their very flexible and self-optimized membranes.[13]

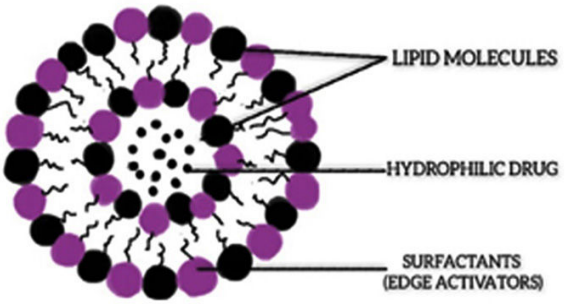


Fig. 1: structural feature of transferosomes

METHOD OF PREPARATION

Phosphatidylcholine tends to be mixed with sodium cholate or another biocompatible surfactant in ethanol. A appropriate buffer is then added to achieve a 10% w/w total lipid content.After that, the suspension is frozen, thawed, and sonicated two or three times to promote vesicle growth. Pressure homogenization, ultrasonication, or any other mechanical technique is then used to get the desired vesicle size. Dynamic light scattering analysis indicates that the final vesicle size for a typical transfersome preparation including 8.7% by weight SPC, 1.3% by weight sodium cholate, and up to 8.5% by volume ethanol is about 120 nm.For each drug, a unique carrier composition must be determined through experimentation in order to produce transfersomes with the maximum deformability and stability.[45]

Table 1: A different additives used in the formulation of transferosomes

Examples	Class	Uses
Egg phosphatidyl, cholineSoya phosphatidyl choline, dipalamitoyl phosphatidyl choline	Phospholipids	Vesicles forming component
Ethanol, methanol, isopropyl alcohol, chloroform	Solvents	As a solvent
Sod. Cholate, sod. Deoxycholate, tween-80, tween-20, span-80	Surfactants	Vesicles forming components [edge activators]
Saline phosphate buffer [pH 6.4], phosphate buffer [pH 7.4]	Buffering agent a hydrating	As medium
Rhodamine -123, rhodamine-DHPE, fluorescein DHPE nile red	Dye	For CSLM study

Advantages of transferosomes:[30-36]

1. One can attain high trapping efficiency.
2. Transferosomes are Biocompatible and biodegradable.
3. It guards against the medication product's breakdown via metabolism.
4. Transferosomes serve as a store for slow, progressive release.
5. Both hydrophilic and hydrophobic chemicals have a wider range of solubility when they are combined to form transferosomes.
6. This tailored drug delivery technology also allows for self-administration.
7. Drugs having a limited therapeutic window can also be treated with transferosomes.

8. Enhancing the bioavability is crucial.
9. Transferosomes have a near-90% entrapment efficiency when used with lipophillic drugs.
10. Additionally, transferosomes shield the medicine within from breakdown by proteins and peptides, for example.
11. Because of the compact and straightforward production procedure, scaling up is easy.
12. Regardless of their size, molecular weight, polarity, or shape, these carriers are incredibly versatile and effective in holding a wide variety of drugs. Both high and low molecular weight medications, such as albumin, corticosteroids, sex hormone, insulin, and anti-cancer agents, can be carried by transferosomes.
13. They prevent the body's metabolism from dissolving the drug inside.
14. Scalability is easy because the technique is uncomplicated and doesn't require the use of ingredients that are undesirable for pharmaceutical usage.

Disadvantages of transferosomes

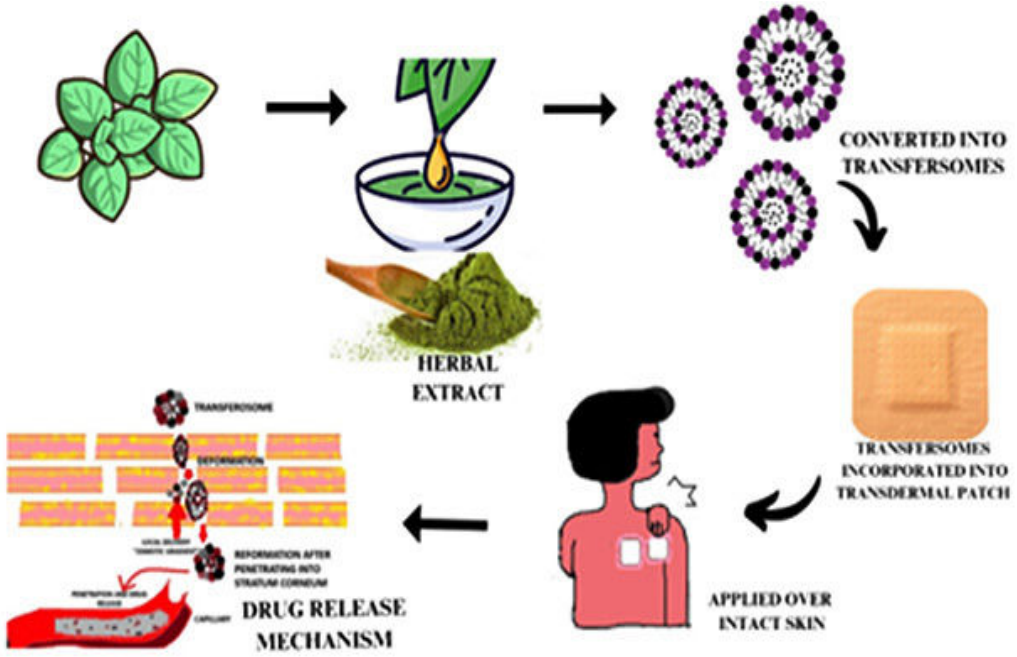
1. Transferosomes are prone to oxidative destruction, they are chemically unstable.
2. Another factor that opposes the use of transferosomes as drug delivery vehicles is their natural phospholipid purity.
3. Transferosomes are costly.

Limitations for transferosomes

1. Transferosomes are prone to oxidative destruction, which makes them chemically unstable. Purity of natural phospholipids is an additional factor that works against the use of transferosomes as drug delivery systems. Formulations for transferosomes are expensive.[15,16]
2. When inert gases like nitrogen and argon are introduced into the aqueous medium, transfersome oxidation can be considerably reduced.[26] Lowering the temperature and shielding it from light during storage might help lessen the likelihood of oxidation.[27] Post-preparation techniques like freeze- and spray-drying can increase transfersomes' storage stability.[28]
3. The challenge of achieving natural phospholipid purity poses another barrier to the drug delivery method of transfersomes. Consequently, artificial phospholipids could be utilised as a substitute.[25]

Mechanism of transferosomes

Transfersomes are drug delivery mechanisms that can pass through healthy skin. The great elasticity (deformability) of the vesicle bilayers and their ability to form an osmotic gradient across the skin are thought to be the two primary factors that determine of the unhindered passage of such carriers. Due to their extreme deformability, transfersomes create a transepidermal osmotic

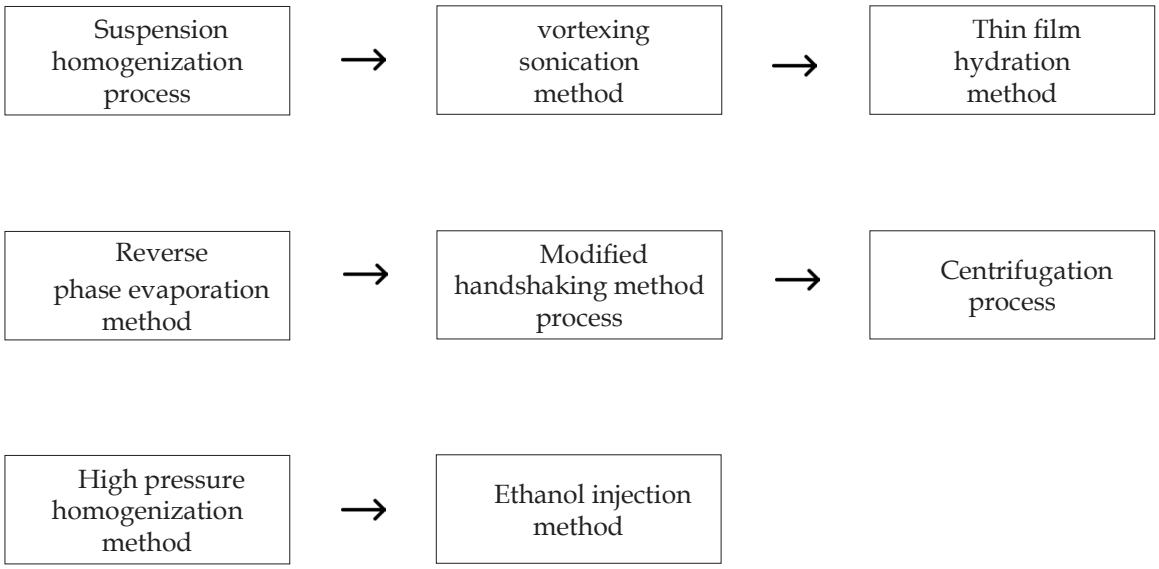


gradient in conjunction with EAs. They also press between the cells of the stratum corneum to transport drugs throughout the entire skin. Transfersomes are able to flex and squeeze through narrow openings that are 5 to 10 times smaller than their own diameter without suffering appreciable damage. This system's high deformability facilitates improved penetration of intact vesicles.[44]

Table 2: Herbal formulation based on transferosomal drug delivery system:[39,40]

Plant / constituent	Biological activity	Application of transferosomal technology
Curcumin	Antioxidant and anti-cancer	improvement of penetration
Colchicine	Anti-gout	reduction in related GIT adverse effects connected with transferosomal technology

Method of preparation of transferosomes[21-24]



Applications of transferosomes

Drugs are effectively loaded onto transfersomes to give targeted and regulated medication delivery to different body regions.

1. Due to the integration of phospholipids, transfersomes have the potential to increase the stability of labile medicines and provide regulated release of the supplied substance.[17,18]
2. **Transdermal immunization:** Hepatitis-B vaccinations used topically have had positive outcomes. Zidovudine's AUC was found to be 12 times greater than that of the standard control dosage. Selectivity in deposition in RES, which is where HIV typically resides was raised as well.
3. There are several GI adverse effects linked to NSAIDS. These can be avoided by employing highly deformable vesicles for transdermal administration.
4. **Delivery of anti-cancer drugs;** Anti-cancer medications are delivered using transfersomes, which are particularly useful in the treatment of skin cancers.[37] Skin cancer treatment with methotraxate-loaded transfersomes was attempted. The most effective way for tamoxifen (TAM), an anti-breast cancer drug, to pass through skin is via transfersomes and even at modest doses of 0.1–0.2 mg/kg/day, it acts as an anti-estrogen to speed up the formation of the mouse uterus.[19] 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.[29]

Delivery of various therapeutic agents[20]

Table 3: Various Drugs used with Transfersomal drug delivery system

Drug	Category	Therapeutic activity
Dexamethasone	Corticosteroid Drug	Anti-edema activity
Diclofenac	NSAID agent	Formulation optimization
Tacrolimus	Immunosuppressive	Atopic dermatitis
Pentoxifyllin	Xanthenes Derivative	Chronic occlusive arterial disease.
Eprosartan Mesylate	Angiotensin receptor blockers (ARBs)	Management of Hypertension
Ciprofloxacin	Quinolone Antibiotic	Treatment of otitis media
Timolol maleate	Nonselective β-adrenergic blocker	Management of Hypertension
Ketoconazole	Azoles antifungal	Antimicrobial activity
Diclofenac diethylamine, Curcumin	NSAID and natural Phenol curcuminoid	Analgesic and Anti-inflammatory
Itraconazole	Antifungal triazoles	Formulation Optimization
Paromomycin sulfate	Antibiotic	cutaneous leishmaniasis
Risperidone	Antipsychotics	Formulation Optimization
Minoxidil and caffeine	Antihypertensive vasodilator	Treatment of alopecia
Raloxifene Hydrochloride	Selective oestrogen receptor modulator (SERM)	Treatment of osteoporosis
sinomenine hydrochloride	Alkaloid	Formulation optimization Treatment of Rheumatism
Embelin	Benzoquinone derivative	Treatment of Cancer
Indinavir sulfate	protease inhibitor included in highly potent antiretroviral treatment to treat HIV/AIDS	Treatment against AIDS with other protease inhibitors, nucleoside analogues or reverse transcriptase inhibitors
Stavudine	Reverse transcriptase inhibitors	Prevention and treatment of HIV/AIDS

Delivery of herbal drugs

Since herbal medications may permeate the stratum corneum and deliver nutrients locally to maintain its functionality, they can also be integrated into transferosomes. It is made up of the flattened, keratinized remnants of developing epidermal cells. Various techniques were explored to overcome this barrier, such as electrophoresis, chemical permeation enhancers, immunotophoresis, microemulsions, and novel lentiviral carriers that facilitate the delivery of drugs through the skin, such as liposomes, noisomes, Twosomes, and transferosomes.[43] Topical delivery of curcumin and capsaicin via transferosomal formulations was demonstrated.[30]

Transfersomes facilitate the easy transportation of large molecules and weight compounds across the skin. Mammalian skin can be used to distribute substances like insulin and leukocytic generated interferon (INF).[46]

Leukocytic generated interferon-α (INF-α) is one of the interferons that have also been transported via transferosomes.Transferosomes assist in achieving a bioavailability that is somewhat comparable to subcutaneous injection. It has been discovered that human serum albumin or gap junction protein, when applied transdermally and enclosed in transferosomes, effectively elicits an immunological response.[37,38]

CONCLUSION

The goal of herbal medicine's innovative medication delivery system is to create a controlled release, high effectiveness drug formulation that also improves bioavailability. Transferosomes are a revolutionary concept that naturally permeate human skin to function as a carrier for drug delivery. Transferosomes are specialized vesicles or particles designed to quickly change their shape in reaction to stress from the outside world. In addition to acting as drug carriers for non-invasive, targeted drug delivery and prolonged release of therapeutic compounds, transferosomes can navigate a range of transport barriers. Its primary drawbacks are the stratum corneum's barriers and skin irritation; however, transfersomes showed the ability to get around these restrictions and effectively carry therapeutic substances into internal circulation.

In this type of delivery, Drug release can also be controlled according to the requirement. Thus, this approach can overcome theproblems which occur in conventional techniques.

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