WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.453
Volume 14, Issue 4, 622-630. Review Article ISSN 2277–7105

"A REVIEW ON TRANSFERSOMES IN ADVANCED DRUG DELIVERY SYSTEMS"

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Article Received on
01 January 2025,

Revised on 21 Jan. 2024,
Accepted on 09 Feb. 2025

DOI: 10.20959/wjpr20254-35660

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ABSTRACT

A novel vesicular drug delivery method called transfersomes was created to improve medication penetration across biological membranes, especially the skin. Transdermal and targeted drug delivery have been transformed by these lipid-based, ultra-flexible, deformable carriers because they increase therapeutic efficacy, decrease systemic side effects, and improve bioavailability. The structure, composition, preparation techniques, mechanism of action, benefits, drawbacks, and most recent developments of transfersome-based drug delivery systems are all covered in detail in this review. Transdermal medication delivery devices are now much more effective thanks to recent developments in transfersome technology. Phospholipids and surfactants combine to form the specialized, elastic vesicles known as transfersomes, which help move medicinal substances over the epidermal barrier. This review focuses on the advancements in transfersome formulation, such as the incorporation of nanoparticles for better skin penetration, the use of penetration enhancers, and the adjustment of lipid composition. Important discoveries show that adding surfactants improves the permeability and flexibility of transfersomes, enabling the efficient administration of both hydrophilic and hydrophobic medications. Furthermore, new research suggests that iontophoresis and microneedles combined with transfersomes can increase drug delivery rates and bioavailability in general. Clinical uses of this technology have demonstrated promise in the treatment of long-term ailments such vaccine administration, hormone replacement therapy, and pain control. Transfersomes are a good choice for contemporary drug delivery systems because of their calability of manufacture and capacity to encapsulate a variety of pharmacological substances In conclusion, ongoing research into the mechanisms of skin

absorption and the development of novel formulation strategies are expected to propel transfersome technology to the forefront of transdermal delivery solutions, offering improved patient compliance and therapeutic outcomes.

KEYWORDS: Transfersomes, Advanced Drug Delivery Systems, Apllication.

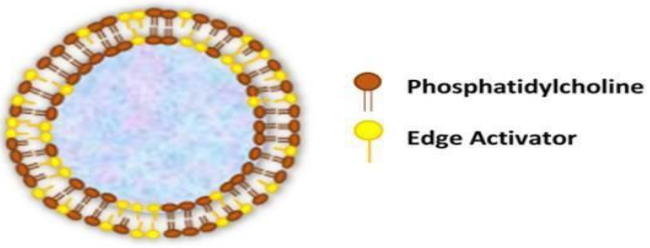
INTRODUCTION

Definition

Transfersomes are vesicular systems composed of phospholipids, surfactants, and edge activators that enhance the flexibility of lipid bilayers. Their unique deformability allows them to penetrate tight intercellular spaces and deliver drugs more efficiently.

Conventional drug delivery systems often face challenges such as poor solubility, low bioavailability, and systemic side effects. Transfersomes have emerged as a promising solution, particularly for transdermal and targeted delivery. These elastic vesicles can squeeze through narrow intercellular spaces, making them superior to traditional liposomes in delivering drugs across the skin and other biological barriers.

Transfersomes are lipid-based vesicular carriers engineered to improve the penetration and bioavailability of drugs. Unlike traditional liposomes, transfersomes possess extreme deformability, enabling them to traverse biological barriers such as the skin or mucosa. This makes them highly effective for transdermal, ocular, and systemic delivery of hydrophilic, lipophilic, or amphiphilic drugs.



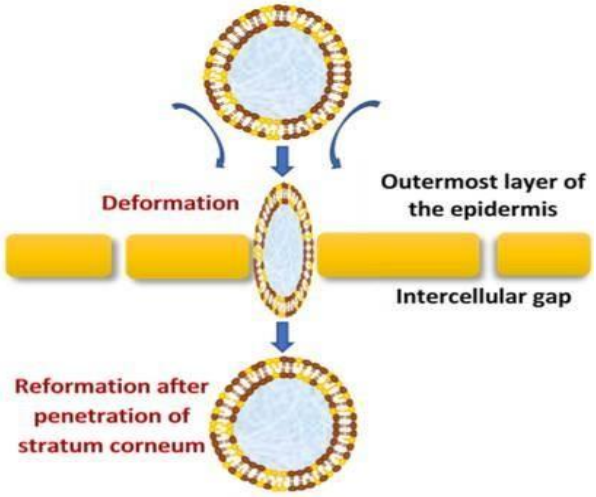
TRANSFERSOMES

Mechanism of Action

Transferosomes overcome the obstacle of skin penetration by squeezing themselves along the stratum corneum's internal sealing lipids. The method by which transferosomes improve the distribution of active compounds in and across the skin is still unknown. There are two processes by which transferosomes can penetrate the skin:

1. Transferosomes are drug vectors that stay intact after passing through the skin.
2. Transferosomes operate as penetration enhancers, breaking the stratum corneum's highly structured intercellular lipids and allowing drug molecules to penetrate into and through the stratum corneum.

Cevc and colleagues postulated the first mechanism, claiming that deformable liposomes penetrate the stratum corneum due to the skin's natural transdermal moisture gradient and subsequently enter the systemic circulation after passing the epidermis.



Composition of Transferosomes: Transferosomes are generally made up of 12

- First, main ingredient an amphipathic component (e.g. Soya phosphatidylcholine, egg phosphatidylcholine, etc.) that can be a combination of lipids that form the lipid bilayer.
- Second, biocompatible bilayer-softening chemicals used that increase the vesicles' bilayer flexibility and improve permeability, are the most commonly used edge activators in transferosome preparations.
- The solvent is approximately 3–10 % alcohol (ethanol or methanol), and the hydrating medium is either water or a saline phosphate buffer (pH 6.5–7).

Methods of Preparation

A. Thin film hydration process:

This approach consists of three phases and is used to prepare transferosomes.

1. By dissolving phospholipids and surfactant in a volatile organic solvent, a thin film is made from the vesicles-forming components (chloroform and methanol). A rotary evaporator is used to evaporate the organic solvent. The final one traces of solvent were eliminated overnight.

2. Rotation at 60rpm for 1hour at the appropriate temperature hydrates a prepared thin film with buffer (pH 6.5). The resultant vesicles were enlarged at room temperature for 2 hours.
3. The resulting vesicles were sonicated at room temperature or at 50°C for 30 minutes using a bath sonicator or a probe sonicated at 4°C for 30 minutes to prepare small vesicles. Manual extrusion of the sonicated vesicles 10 times through a sandwich of 200 and 100nm polycarbonate membranes homogenised the vesicles.14-15

B. Modified hand shaking:

To create transfersomes, the lipid film hydration technique is also utilised, and it comprises of the following steps:

1. In a 1:1 mixture of ethanol and chloroform, the drug, lecithin (PC), and edge activator were dissolved. Evaporation of organic solvent while hand shaking above the lipid transition temperature (43°C) was used to remove it. With rotation, a thin lipid coating formed inside the flask wall. The thin coating was left overnight to allow the solvent to evaporate completely.
2. The film was then hydrated for 15 minutes at the appropriate temperature with phosphate buffer (pH 7.4) and gentle shaking. At 2-8°C, the transferosome suspension was further hydrated for 1 hour16

APPLICATIONS

1. Transdermal Drug Delivery

Transfersomes have been widely explored for transdermal delivery due to their ability to penetrate deep into the skin.

Example: Diclofenac-loaded transfersomes for pain management.

2. Cancer Therapy

Transfersomes enhance the targeted delivery of chemotherapeutic agents, reducing systemic toxicity.

Example: Doxorubicin-loaded transfersomes have shown improved tumor targeting and reduced side effects.

3. Vaccine Delivery

Transfersomes serve as effective carriers for antigens, enabling transdermal vaccination and stimulating robust immune responses.

Example: Influenza and hepatitis vaccines have been studied with promising results.

4. Ocular Drug Delivery

Transfersomes improve drug delivery to the cornea and intraocular tissues, overcoming the challenges of conventional eye drops. Used for delivering drugs to the eye with improved bioavailability.

Example: Timolol-loaded transfersomes have been used to manage glaucoma effectively.

5. Cosmeceuticals

Transfersomes are increasingly used in the cosmetic industry to deliver anti-aging agents and nutrients deep into the skin.

Example: Vitamin C-loaded transfersomes have shown enhanced skin penetration and antioxidative effects.

6. Oral Drug Delivery

Transfersomes have revolutionized transdermal drug delivery by enabling the transport of large molecules like insulin and hormones. Used for drugs with poor bioavailability.

Example: Insulin-loaded transfersomes for oral diabetes therapy.

Challenges

1. Stability Issues:
   Transfersomes are prone to leakage and degradation under certain conditions.
2. Manufacturing Complexity:
   The preparation process requires precise optimization for reproducibility.
3. Skin Irritation:
   Edge activators may cause irritation or allergic reactions in sensitive individuals.
4. High Production Costs:
   Scaling up the production process is expensive and resource-intensive.

Recent Advances

These recent advances in transfersomes highlight their evolving role in drug delivery and personalized medicine. Let's delve into each innovation in detail:

1. Nano-Transfersomes

What it is: Smaller-sized transfersomes (nano-range, <100 nm) designed for enhanced tissue penetration.

Benefits: Improved drug absorption, deeper tissue targeting, and reduced systemic side effects.

Example: Nano-transfersomes loaded with anti-inflammatory drugs like ibuprofen have shown superior skin penetration and prolonged drug action.

2. Theranostic Transfersomes

What it is: Transfersomes combining therapeutic agents (drugs) and diagnostic agents (imaging molecules).

Benefits: Enables real-time monitoring of drug distribution and effectiveness, particularly in cancer treatment.

Example: Theranostic transfersomes containing doxorubicin (chemotherapy) and MRI contrast agents help visualize tumor response in real-time.

3. AI-Optimized Formulations

What it is: Application of artificial intelligence and machine learning to optimize transfersome compositions and predict stability.

Benefits: Faster and more precise formulation development, reduced experimental costs, and enhanced performance prediction.

Example: AI models are being used to predict the best lipid-to-edge activator ratios for maximum drug penetration and shelf stability.

4. Smart Transfersomes

What it is: Transfersomes engineered to respond to environmental stimuli like pH, temperature, or enzymes.

Benefits: Controlled and site-specific drug release, reducing unwanted drug leakage.

Example: pH-sensitive transfersomes loaded with insulin release the drug only in response to blood glucose levels, reducing the need for frequent injections.

5. Functionalized Transfersomes

What it is: Surface-modified transfersomes with ligands (e.g., antibodies, peptides) for

targeted drug delivery.

Benefits: Enhanced specificity for diseased cells, reduced off-target effects, and improved therapeutic outcomes.

Example: Functionalized transfersomes targeting HER2-positive breast cancer cells improve drug delivery efficiency and reduce to.

6. Combination Therapy

What it is: Transfersomes designed to co-deliver multiple drugs for synergistic effects. Benefits: Enhanced therapeutic efficacy, reduced drug resistance, and fewer side effects. Example: Transfersomes co-loaded with curcumin (anti-inflammatory) and methotrexate (chemotherapy) show improved anti-cancer activity compared to individual treatments.

Future Outlook

The integration of nanotechnology, AI, and bioengineering into transfersome technology is paving the way for more precise, effective, and patient-friendly drug delivery systems. Regulatory approvals and large-scale production will be the next steps toward clinical translation.

LIMITATIONS OF TRANSFERSOMES

- Stability issues – Prone to oxidation and hydrolysis.
- High cost of production – Complex formulation process.
- Storage concerns – Require specific temperature and conditions.
- Limited drug loading capacity – May not be suitable for high-dose drugs.

CONCLUSION

Transfersomes have emerged as a ground breaking advancement in drug delivery, offering superior drug penetration, sustained release, and targeted therapy. Despite some limitations, ongoing research and technological innovations continue to improve their stability, efficiency, and therapeutic potential. Transfersomes hold great promise for revolutionizing transdermal, ocular, cancer, and vaccine drug delivery in the coming years.

FUTURE PERSPECTIVES

- Development of more stable formulations.
- Large-scale production and commercialization.

- Clinical trials for more diverse applications.
- Exploring hybrid systems with nanoparticles for enhanced drug delivery

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