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Research Article

An Article on Curcumin Loaded Transferosomes as A Novel Drug Delivery System

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Abstract

Curcumin is a natural compound found in turmeric and has shown potential in treating a variety of diseases due to its anti-inflammatory and antioxidant properties. However, curcumin has low bioavailability and poor solubility in water, which limits its therapeutic efficacy. Transferosomes are specialized lipid vesicles that can encapsulate drugs and other bioactive molecules, allowing them to be delivered to specific target tissues. Curcumin, a natural compound found in turmeric, has been the subject of intense study due to its potential health benefits, including anti-inflammatory and antioxidant properties. Transferosomes are lipid-based nanoparticles that can encapsulate hydrophobic compounds like curcumin and improve their delivery to target tissues. They can also enhance the absorption of drugs through the skin or mucous membranes. Several studies have investigated the potential of curcumin loaded transferosomes in various applications, such as wound healing, cancer treatment, and anti-inflammatory therapy. These studies have shown promising results, indicating that transferosomes could be an effective drug delivery system for curcumin. However, more research is needed to optimize the formulation and improve the stability and shelf-life curcumin-loaded transferosomes. Additionally, the safety and toxicity of these nanoparticles need to be thoroughly evaluated before they can be used in clinical application. In our study we have observed drug content 4.47mg/ml and EE% was found to be 94.8%, the percentage of drug release of curcumin transferosomes was observed as 30.8%at time period of 4hr. [1]

Kew Words: rollator; walking aid; risks of an walking aid; support and balance control

Introduction

Curcumin is a natural polyphenol compound found in turmeric, which has been reported to have various pharmacological properties, including anti-inflammatory, antioxidant, and anticancer activities. However, its poor water solubility and low bioavailability limit its therapeutic potential. To overcome these limitations, curcumin can be loaded into transferosomes, which are lipid-based nanoparticles composed of phospholipids and surfactants that can encapsulate hydrophobic drugs and improve their solubility and bioavailability.[2] Transferosomes can also enhance drug delivery by penetrating through the skin and other biological barriers. Curcumin-loaded transferosomes have shown promising results in preclinical studies as a potential treatment for various diseases, including cancer, inflammatory disorders, and skin diseases. They have been shown to have improved

bioavailability and sustained release of curcumin, leading to enhanced therapeutic effects and reduced toxicity.[3]

Overall, curcumin-loaded transferosomes are a promising drug delivery system that can improve the therapeutic potential of curcumin and other hydrophobic drugs. However, more research is needed to optimize their formulation and evaluate their safety and efficacy in clinical trials.[4]

Composition of Transferosomes

Transferosomes are lipid vesicles or liposomes that are specially designed to improve the delivery of drugs and other substances through the skin or other biological membranes. The composition of transferosomes can vary depending on the specific application, but generally, they are made up of the following components:

1.Phospholipids: These are the main components of the transferosomes and form the lipid bilayer that encapsulates the drug or other substances. The most commonly used phospholipids are soya lecithin, phosphatidylcholine, phosphatidylethanolamine, and phosphatidylglycerol.

2.Surfactants: These are amphiphilic molecules that are added to the lipid bilayer to improve its flexibility and deformability. Examples of surfactants

used in transferosomes include SPAN 60,80, Tween 80, sodium cholate, and sodium deoxycholate.

3.Cholesterol: This is added to the transferosomes to increase their stability and rigidity.

4.Drug or other substances: Transferosomes can encapsulate a variety of drugs or other substances, such as peptides, proteins, and vaccines.

5.Other additives: Depending on the specific application, other additives may be added to the transferosomes to improve their performance. For example, propylene glycol can be added to improve the solubility of hydrophilic drugs.

The composition of transferosomes can be optimized for specific applications by adjusting the ratios of the different components and by using different types of phospholipids, surfactants, and other additives.[5]

Ingredients	Examples	Function
Phospholipid	Soya Lecithin, phosphatidylcholine, Egg phosphatidylcholine, Dipalmityl phosphatidylcholine Distearyl phosphatidylcholine	Vesicle forming component
Surfactant	Sodium cholate Sodium deoxy cholate Tween 80 Span 80	For providing flexibility
Alcohol	Ethanol Methanol	As a solvent
Dye	Rhodamine-123	For confocal Scanning laser Microscopy (CSLM) study
Buffering agent	Saline phosphate buffer (pH 6.5) 7% v/v ethanol Tris buffer (pH 6.5)	As a hydrating medium

Table 1: composition of transferosomes

The high deformability of transferosomes allows them to easily adapt to the skin's contours and penetrate through the pores and hair follicles. This makes them an effective carrier for delivering drugs across the skin barrier and into the deeper layers of the skin

Advantages of curcumin-loaded transferosomes

- Improved solubility and stability: Curcumin is highly hydrophobic and has poor solubility in aqueous solutions. Loading curcumin into transferosomes can improve its solubility and stability, thereby increasing its bioavailability and efficacy.
- Enhanced skin penetration: Transferosomes can penetrate the skin more efficiently than other drug delivery systems, such as liposomes, noisome, and ectosomes. This can help to deliver curcumin to the target site more effectively.
- Controlled release: Transferosomes can release their cargo in a controlled manner, allowing for sustained drug delivery and reducing the frequency of administration.
- Targeted delivery: Transferosomes can be modified with ligands or antibodies to target specific cells or tissues, improving the selectivity and efficacy of the treatment.
- Reduced side effects: By improving the bioavailability and efficacy of curcumin, transferosomes can potentially reduce the required dose and minimize the risk of side effects.[6]

Disadvantages of curcumin loaded transferosomes:

- Instability: Curcumin is known for its poor stability and low bioavailability. Loading it into transferosomes can improve its stability, but the vesicles themselves may be unstable and prone to degradation over time, which can limit their effectiveness.
  Low loading capacity: Transferosomes have limited capacity to encapsulate curcumin, which can result in low drug loading efficiency and require larger doses to achieve therapeutic effects.
- Cost: The production of transferosomes can be costly due to the complex process and the need for specialized equipment and materials.
- Complex formulation: The formulation of curcumin-loaded transferosomes can be complex, requiring optimization of lipid composition, surfactants, and other excipients to ensure the stability and effectiveness of the final product.
- Limited research: While there is growing interest in curcumin-loaded transferosomes, research on their safety and efficacy is still limited, and more studies are needed to fully understand their potential benefits and drawbacks.[7]

Material and methods:

The transferosomes were prepared by modified hand shaking, lipid film hydration technique. Preparing curcumin transferosomes by thin film hydration method involves the following steps:

Selection of lipid and surfactant: The first step is to select an appropriate lipid and surfactant combination that can form stable transferosomes. Phosphatidylcholine and cholesterol are commonly used lipids, and surfactants like Tween 80 or Span 80 can be used to stabilize the transferosomes.

2.Preparation of lipid film: The selected lipid and surfactant are dissolved in a suitable organic solvent like chloroform or methanol. The solvent is then evaporated using a rotary evaporator or a vacuum oven to form a thin lipid film on the walls of the glass vial.

3.Hydration of lipid film: The lipid film is hydrated with an aqueous solution containing curcumin. The hydration can be done by adding the aqueous solution dropwise to the lipid film and shaking the vial gently.

4.Sonication: The vial is then subjected to sonication using a probe so nicator or a bath so nicator to form transferosomes. Sonication helps in breaking down the lipid film into small vesicles and also disperses curcumin in the aqueous phase.

5.Purification and characterization: The transferosomes are purified by centrifugation and characterized for size, shape, and stability. The size of the transferosomes can be determined by dynamic light scattering, and their morphology can be observed using transmission electron microscopy.

Overall, the thin film hydration method is a simple and effective method for preparing curcumin transferosomes that can improve the bioavailability and therapeutic efficacy of curcumin.[8]

Characterization of curcumin loaded transferosomes:

- Particle size and size distribution: The size and size distribution of the transferosomes can be measured using techniques such as dynamic light scattering (DLS), laser diffraction, or transmission electron microscopy (TEM).
- Zeta potential: The surface charge of the transferosomes can be determined using zeta potential measurements, which can provide information about their stability and potential interactions with biological systems.
- Encapsulation efficiency: The amount of curcumin encapsulated within the transferosomes can be determined using spectrophotometric methods, such as UV-Vi's spectroscopy.
- Morphology: The morphology and structure of the transferosomes can be visualized using TEM or scanning electron microscopy (SEM).
- Drug release profile: The release of curcumin from the transferosomes can be evaluated using techniques such as dialysis or Franz diffusion cells.
- Stability: The stability of the transferosomes can be evaluated by measuring changes in size, morphology, or drug release over time under various storage conditions.
- In vitro and in vivo efficacy: The efficacy of the curcumin-loaded transferosomes can be evaluated using in vitro cell culture assays and in vivo animal models, to assess their potential therapeutic effects and safety.[9]

Evaluation:

1) **Drug content: -** 1 ml of suspension dissolved in 9 ml of methanol, shake it for 15-20 mins. then check under UV spectrophotometer.

$$\text{D.C} = \frac{\text{Practical DC}}{\text{Theoritical DC}} \times 100$$

2) **Entrapment efficiency:** -Take 1 ml of suspension and dissolved in 9ml of 7.4 buffer, sample was poured into the centrifuge tube and kept for ultra centrifugation for 45min at desired temperature for about 17000 rpm, then supernatant liquid was taken and check in UV.

$$\text{E.E} = \frac{\text{Amount of drug taken} - \text{Amount of drug Supernatent}}{\text{Amount of drug taken}} \times 100$$

3) **Diffusion study:** 50ml 0f frace diffusion having dialysis membrane the suspension is placed in donor compartment and receptor compartment buffer was taken. and stirring was carried out in receptor compartment, at every 30 mins interval, take out 1 ml and check for UV. [10]

Optimization of transferosomes preparation:

Transferosomes are lipid-based vesicles that have the ability to carry drugs across biological barriers. They are widely used in pharmaceuticals for the delivery of drugs that have poor water solubility, poor bioavailability or high toxicity. The optimization of transferosomes formulation is important to ensure that the vesicles are stable, biocompatible, and effective in drug delivery. Here are some strategies for optimizing transferosomes formulation.

1.Selection of lipid components: The lipid components used in transferosomes formulation play a crucial role in determining the stability, fluidity and permeability of the vesicles. It is important to select the appropriate lipids that can form a stable bilayer structure and allow for drug encapsulation. Different lipid combinations can be tested to optimize the formulation.

2.Optimization of drug loading: The loading of drugs into transferosomes can affect the stability, size, and encapsulation efficiency of the vesicles. Various methods can be used to optimize drug loading, such as adjusting the drug concentration, pH, temperature and sonication parameters.

3.Addition of stabilizing agents: Stabilizing agents such as surfactants, polymers, and antioxidants can be added to transferosomes formulation to increase the stability and shelf life of the vesicles. The type and concentration of stabilizing agents can be optimized to improve the formulation.

4.Optimization of size and shape: The size and shape of transferosomes can influence their ability to penetrate biological barriers and deliver drugs. Different sonication parameters, including time, power and frequency, can be optimized to control the size and shape of the vesicles.

5.Evaluation of in vitro and in vivo efficacy: The efficacy of transferosomes formulation can be evaluated in vitro and in vivo using different assays. In vitro assays such as drug release studies, stability studies, and cytotoxicity studies can be performed to evaluate the formulation. In vivo studies can be conducted to evaluate the pharmacokinetics, biodistribution, and efficacy of the formulation. In summary, the optimization of transferosomes formulation is a crucial step in developing an effective drug delivery system. Lipid selection, drug loading, stabilizing agents, size and shape optimization, and in vitro and in vivo evaluation are important strategies for optimizing the formulation.[11]

Stability of transferosomes: -

Transferosomes are highly flexible, self-optimizing, and elastic lipid vesicles that are able to encapsulate and transport a wide range of drugs across biological membranes. The stability of transferosomes depends on various factors such as the composition of the lipid bilayer, charge and size of the vesicles, and storage conditions. In general, transferosomes can be stored at refrigerated temperature (2-8°C) for a relatively long period of time, typically several months. However, the stability of transferosomes can be affected by several factors such as temperature, pH, ionic strength, and the presence of enzymes. For instance, high temperatures may cause the lipid bilayer to become unstable, leading to leakage of the encapsulated drug and eventual loss of activity. Similarly, changes in pH or ionic strength can cause the vesicles to undergo destabilization, leading to aggregation or fusion, which can alter their drug release characteristics. In addition, the presence of enzymes such as phospholipases or proteases can cause the lipid bilayer to be degraded, leading to destabilization and loss of the vesicles. To enhance the stability of transferosomes, different techniques have been used such as lyophilization, addition of stabilizing agents such as surfactants or polymers, and optimization of the lipid composition. Overall, the stability of transferosomes is an important consideration in their development and use as drug delivery systems, and their stability can be improved by optimizing their composition, storage conditions, and formulation technique.[12]

Safety measures of transferosomes

They are composed of phospholipids and surfactants, and are capable of encapsulating both hydrophilic and lipophilic drugs. Transferosomes have several advantages over other drug delivery systems, including their ability to improve drug absorption and bioavailability, and their ability to target specific tissues.[13]

However, like any other drug delivery system, transferosomes have safety considerations that need to be taken into account. Here are some important safety considerations related to transferosomes:

1.Toxicity: Some of the ingredients used in transferosomes, such as surfactants, can be toxic in high concentrations. Careful selection of the ingredients used in transferosomes is necessary to minimize toxicity.

2.Stability: Transferosomes are susceptible to degradation, particularly in the presence of enzymes and other biological substances. This can lead to the release of drugs at unintended sites and potentially cause adverse effects.[14]

3.Immunogenicity: The use of foreign substances, such as lipids and surfactants, in transferosomes can trigger an immune response in some individuals. This can lead to allergic reactions or other adverse effects.

4.Pharmacokinetics: The pharmacokinetics of transferosomes can differ from the pharmacokinetics of the drug alone. This can affect drug efficacy and safety, and careful characterization of transferosomes is necessary to ensure appropriate dosing.

5.Storage and handling: Transferosomes are sensitive to temperature and can be easily damaged during storage and handling. Proper storage and handling conditions should be established and followed to ensure the stability and efficacy of the drug. Overall, while transferosomes have many potential advantages as drug delivery systems, it is important to carefully consider their safety considerations and ensure that they are used appropriately to minimize the risk of adverse effects.[15]

Results and discussion:

Optical Microscopy: The transferosomes are observed under a projection microscope. The vesicles are obtained like Uni-lamellar and multi-lamellar structure as shown in figure 1

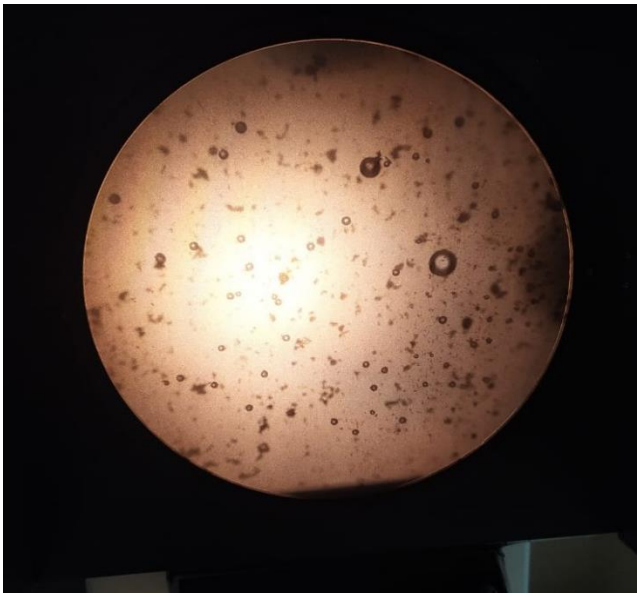

Figure1: Vesicles of Curcumin Transferosomes

Drug content was foundto be 4.47 mg/ml and the entrapment efficiency was found to be 94.87%. The diffusion studies were done by Franz diffusion cell by taking 7.4 phosphate buffer. The amount of drug release was done in a period of 5 hours and the percentage of drug release was 30.87% at 4th hour as shown in figure 2.

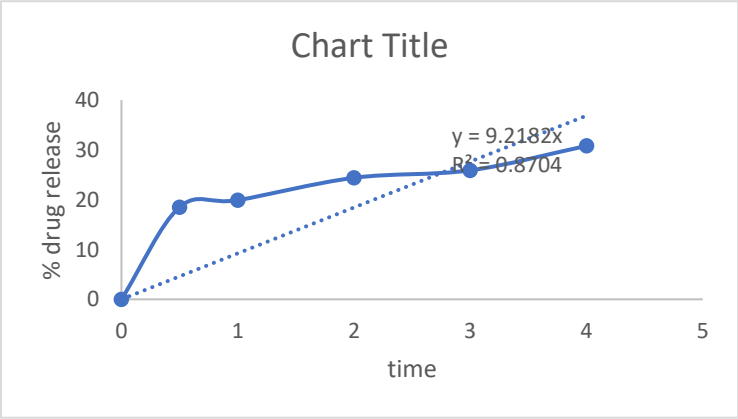

Figure 2: Invitro drug release of the formulation

Conclusion:

Curcumin has been shown to possess various biological activities, including anti-inflammatory, antioxidant, and anticancer properties. However, its poor solubility and bioavailability limit its therapeutic effectiveness. Transferosomes are lipid-based vesicles that can enhance the bioavailability and permeation of drugs across biological barriers. Several studies have investigated the use of transferosomes as a delivery system for curcumin. The results indicate that curcumin-loaded transferosomes have improved stability and bioavailability compared to free curcumin. Moreover, curcumin-loaded

transferosomes have demonstrated potential therapeutic effects in various preclinical models, including cancer, Alzheimer's disease, and inflammatory disorders. However, more research is needed to validate their safety and efficacy in humans. With our study we conclude that curcumin-loaded transferosomes have shown promising results as a potential drug delivery system for curcumin

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