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Liposome:A Novel Drug Delivery System

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A B S T R A C T

Liposome was derived from two Greek words "Lipos meaning fat and Soma meaning body". Liposome were spherical shaped vesicles consist of phospholipids and cholesterol. Due to their size hydrophobic and lipophilic character they are very promising system for drug delivery. This novel drug delivery system aims to target the drug directly to the site of action. Liposomes are very biocompatible and stable and have unique property to entrap both hydrophilic drug and lipophilic drug to its compartment and lead to controlled release effect. They are of 0.05- 5.0 micrometer in diameter. Liposomes are used for the treatment of various diseases like tumors or cancer. Liposomal Drug Delivery System and various aspects related to liposome that can be studied Compared with traditional drug delivery systems, liposomes exhibit better properties, including site-targeting, sustained or controlled release, protection of drugs from degradation and clearance, superior therapeutic effects, and lower toxic side effects. This review describes liposomes structure, composition, preparation methods, and evaluation clinical applications

Keywords: liposome,phospholipid,MLV,OLV,Dispersion,Tumer

Introduction

The Greek words lipos, which means fat, and soma, which means body, were combined to create the spherical concentric vesicles known as liposomes.[1] They are concentric bilayered vesicles in which a membranous lipid bilayer mostly made of natural or synthetic phospholipid entirely encloses an aqueous volume. Liposomes range in size from 30 nm to micrometres, having a phospholipid bilayer that is 4-5 nm thick.[2] The innovative medicine delivery method known as liposomes promises to deliver the drug directly to the site of action. They have the capacity to accept both hydrophilic and lipophilic molecules, preserving the medicine from deterioration and allowing the controlled release of the active components.[3] To increase treatment efficacy and patient compliance, many delivery methods, including parenteral, pulmonary, oral, transdermal, ocular, and nasal routes, have been devised.[4]

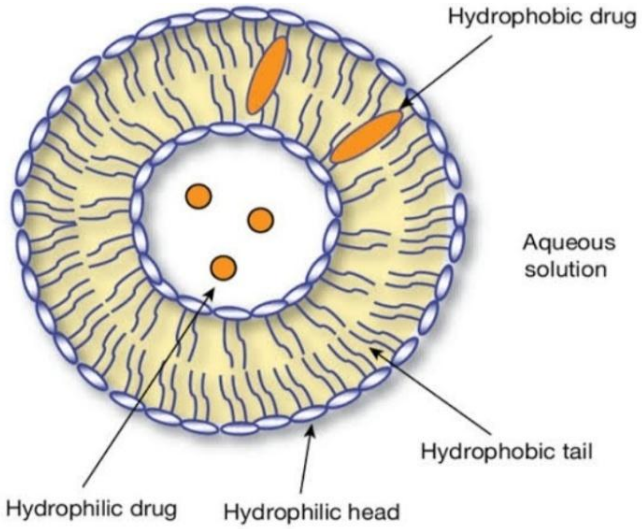


Figure 1: Structure of liposome

Structural components of liposome :

Phospholipids :

The majority of a liposome's structural elements are phospholipids. Phosphatidylcholine and phosphatidylethanolamine are the two most popular phospholipids utilised in liposomal preparation. Amphiphatic lipids are phospholipids. which consist of

- Hydrophilic polar head
- Hydrophobic tail

The composition of spontaneously occurring A glycerol moiety is joined to two acyl chains, which might be saturated or unsaturated, to form phosphatidylcholine. The arrangement of the lipid molecules' hydrocarbon chains determines the stability of the liposome membrane.[5]

Examples of phospholipids

1) Phosphatidylcholine
2) Phosphatidylethanolamine
3) Phosphatidylinositol
4) Phosphatidylserine

Cholestrol :

Another crucial part of the liposome's structure is cholesterol. It is a frequently employed sterol. The function of stability and rigidity is modulated by the presence of sterols. It cannot create a bilayer structure by itself.[6]]It is very heavily absorbed into phospholipids, reaching a molar ratio of 1:1 or 2:1 between phosphatidyl choline and cholesterol.[7] Cholesterol increases the fluidity and durability of cellular membranes and decreases the permeability of molecules that are soluble in water. Cholesterol blocked the interaction and instability of liposomes.[8]

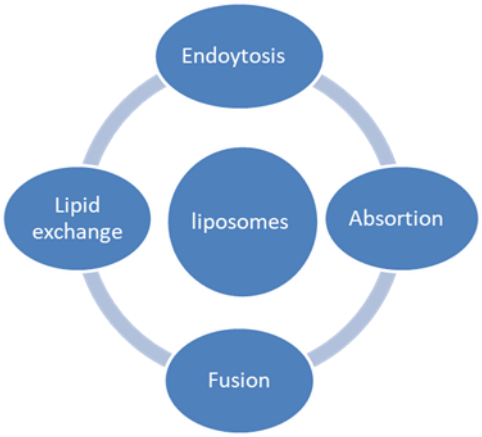
Advantages of Liposomes

- Amphiphatic in nature, entraps both types of medications, whether they are soluble in water or not.
- Liposomes increase the therapeutic index and effectiveness of drugs.[9]
- Liposomes are non ionic
- The drug's stability has improved.[10]
- Liposomes areBiocompatible in nature
- Liposomes help to stabilise proteins.[11]
- Site avoidance effect
- Liposomes lessen the encapsulated agent's toxicity
- Improved pharmacokinetic effects

Disadvantages of Liposomes

- The liposome have high production cost .
- Lipose having Low solubility.
- Liposome have Short half-life.
- Fewer stables.
- Leakage and fusion of encapsulated drug from liposome may occur.
- Sometime phospholipids may undergoes oxidation.[12]

Mechanism of Action of Liposomes.



Classification of liposomes .

1. Based on structure parameters liposome.[13]
    - Multi lamellar large vesicles (MLV) : Diameter size is More than 0.5 µm.
    - Oligolamellar vesicles (OLV) : Diameter size is 0.1-1.0 µm.
    - Multivesicular vesicle (MVV) : Diameter size is more then 1.0 µm.
    - Uni lamellar vesicles (ULV) :
        1) Medium sized uni lamellar vesicles (MUV) : Diameter size is More than 100nm.
        2) Small Uni lamellar vesicles (SUV) : Diameter size is 20-100 µm.
        3) Giant Uni lamellar vesicles (GUV) : Diameter size is More than 1.0 µm.
        4) Large Uni lamellar vesicles (LUV): Diameter size is More than 100nm.
2. Based on method of Liposome preparation. [14]
    - SUVs and OLVs made by reverse phase evaporation method (REV)
    - Multilamellar vesicle made by reverse phase evaporation method (MLV REV)
    - Stable plurilamillar vesicle (SPLV)
    - Frozen and thawed MLV (FATMLV)
    - Vesical prepared by extrusion technique (VET)
    - Dehydration rehydration method (DRV)
3. Based on composition and application of liposome .[15]
    - Conventional liposome
    - Fusogenic liposomes
    - Phsensitive liposomes
    - Cationic liposomes
    - Long circulatory liposomes
    - Immuno liposome

METHOD OF PREPARATION OF LIPOSOME

A) GENERAL METHOD OF PREPARATION

In an organic solvent, the lipid is dissolved. A thin lipid layer is left on the container wall after the solvent evaporates. The medication is mixed into an aqueous solution. The mixture is first stirred to create multi-lamellar vesicles, and then it is sonicated to create SUVs. The second technique involves sonicating the mixture and evaporating the solvent to produce LUVs. SUVs are created as a result of extrusion. If a drug is water soluble, it can be added to an aqueous solution or buffer; if it is hydrophobic, it can be added to an organic solvent. Gel chromatography can be used to separate liposomes and free drug.

B) SPECIFIC METHODS

1) Physical Dispersion Method

2) Solvent Dispersion Method

1) Physical dispersion method

a) Hand Shaken Method:

The lipid mixture and charged components are dissolved in a mixture of chloroform and methanol (2:1) before being added to a 250 ml round bottomed flask. The flask is fixed to a rotating evaporator that is coupled to a vacuum pump and rotates at a speed of 60 rpm. At roughly 30 degrees, the organic solvents evaportate. Following the appearance of a dry residue at the flask's walls, spinning is continued for an additional 15 minutes. After being separated from the vacuum pump, the evaporator is filled with nitrogen. After that, the flask is taken out of the evaporator and mounted on the lypholizer to remove any remaining solvent. The flask is then nitrogen flushed once more before 5 cc of phosphate buffer is added. Once more connected to the evaporator, the flask is rotated for 30 minutes at a speed of roughly 60 rpm to remove all of the lipid from its wall. Finally, a milky white suspension forms. To finish the swelling process before administering MLVs, the suspension is allowed to stand for two hours.

b) Non-hand shaking:

Similar to the shaking method, but with careful swell management. The conical flask's flat bottom is covered with the mixture of lipid solution in chloroform and methanol. By passing nitrogen through the flask, the solution evaporates at room temperature without being disturbed. Following drying, water-saturated nitrogen is fed through the flask until the dried film's opacity vanishes. Lipid is swollen by the addition of bulk liquid after hydration. The flask is tilted one way, 10 to 20 ml of 0.2M sucrose in distilled water are added, and then the flask is slowly brought back to its upright position. The lipid layer at the bottom of the flask is given a gentle wash with the solution. The flask is sealed and flushed with nitrogen before being left at 37 degrees for two hours to allow swelling. The vesicles are then combined to create a milky solution. For 10 minutes, the suspension is centrifuged at 1200 rpm. The MLV layer floating on the surface is eliminated. LUVs are created from the fluid that is still present.

c) Freeze-drying (lyophilization)

The liposomal goods are given this treatment to maintain them and increase their shelf stability. After combining the liposome suspension with a cryoprotective, primarily 5–10% sucrose or trehalose, freeze-drying entails deep freezing the mixture. The liquid samples were then transformed into fluffy solid particles by a sublimation stage that was performed at a very low temperature and under reduced vacuum. Liposomes containing thermosensitive biomolecules must now undergo lyophilization as a necessary step in the process.

2) Solvent Dispersion Method:

a) Ethanol injection method:

At 550°C to 65 °C, an aqueous solution of the substance to be encapsulated is gently injected with a solution of lipid dissolved in diethyl ether or an ether-methanol combination. The removal of ether under vacuum causes liposomes formation.

b)Ethanol Injection

A lipid solution of ethanol is rapidly injected to a hung excess of buffer. The MLVs are immediately fromed

c) Reverse Phase evaporation vesicles:

the two phase mixture that was bath sonicated. The droplets are directed to a semisolid gel under decreasing pressure in a rotating evaporator. The water compartment is now surrounded by a monolayer of phospholipids. A bilayer SUV with an outer layer for stable vesicles is created after certain water droplets and lipid monolayers are collapsed by mechanical shaking with a vortex shaker.

Characterization Of Liposomes :

1. Vesicle shape and lamellarity: An electron microscope was used to study the vesicle shape.
2. Particle size and distribution: The size determined by a laser diffraction analyzer with a minimum focus power of 5MW .[16]
3. Entrapment Efficiency - It establishes the quantity and rate of water-soluble substances' entrapment in the liposomes' aqueous compartment.

This can be calculated by a given formula

% Entrapment efficiency = Entrapped drug × 100/total drug.

4. Trapped volume : It is the volume of aqueous entrapped lipids per volume of lipids. There are ranges for this between 0.5 and 30 microliters/micromol.[17]
5. In vitro drug release can be accomplished using a Franz Diffusion cell, which has a 25 mm diameter. It has a 22 ml reservoir compartment that was filled with buffer that includes 20% v/v methanol to keep the sink state.
6. Percentage yield of liposomes :The prepared liposomes were made and collected, giving a percentage yield of liposomes. The amount of medication and components used to make the liposomes was divided by the measured weight.[18]

STABILITY OF LIPOSOMES

Therapeutic efficacy of drug molecule is governed by stability of liposomes. There are two types of stability

Physical Stability: The shelf life of liposomes is affected by a number of physical events, including fusion, aggregation, and changes in form and size. Leakage of medication ingredients is the main issue that arises. For determining stability, the shape and size distribution are crucial factors. The phospholipids' physical stability can be preserved by preventing excessive unsaturation. They must be kept in storage at 4°C without freezing or exposure to light.[19]

Chemical Stability: Unsaturated fatty acids called phospholipids are susceptible to hydrolysis, which might change a drug's stability. Antioxidants like butylated hydroxy anisole can be used to stop the oxidative breakdown of liposomes.[20]

Applications of Liposomes

- **Cosmetics with liposomes**

Because of how they function and how they release ingredients to the cells, they are employed in cosmetics.[10]

- **Liposome in Tumor Therapy**

Liposomes can be used as medication carriers and given intravenously. If liposomes with lipid are made even more hydrophilic, they can circulate in the bloodstream for a longer period of time. medications like mitoxantrone and doxorubicin. In this way, they can extravasate the vascular endothelium of the tumour.

- **Ophthlamic Problems**: Liposomes have been proven to be effective in treating a variety of eye disorders, including proliferative vitreous retinopathy, proliferative keratitis, corneal transplant rejection, uveitis, and ondopthelmitis. Recently, a liposomal formulation of the medication verteprofin, which has been shown to be beneficial against eye problems, was licenced.[20]
- **Pulmonary Application** – They are useful tools for pulmonary delivery of drugs due to their solubilization capacity.[21]
- **Site specific targeting**- The immune liposomes are able to recognize and binds to target cells with greater specificity.
- **Gene therapy**-

Liposomes are used widely in gene applications to cure diseases

- **Liposomes as protein drug delivery**-

They are used to enhanced drug solubilization.

- **Vaccine immunological adjuvants**

Delivering antigens enclosed in liposomes can improve the immune response. The liposome can include antigens within the bilayers or accommodate them in the aqueous cavity depending on how lipophilic the antigens are. Liposomes were initially utilised as immunological adjuvants to improve the immune response to diphtheria toxoid.[22]

CONCLUSION

Liposomes have been realized as extremely useful carrier systems for targeted drug delivery. Drugs encapsulated in liposomes can have a significantly altered pharmacokinetics. The efficacy of the liposomal formulation depends on its ability to deliver the drug molecule to the targeted site over a prolonged period of time, simultaneously reducing its (drug's) toxic effects. Only time will tell which of the above applications and speculations will prove to be successful. However, based on the pharmaceutical applications and available products, we can say that liposomes have definitely established their position in modern delivery systems.

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