REVIEW ARTICLE

Liposomal Drug Delivery System – A Review

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Abstract

A liposome is the drug delivery system used for the administration of various types of drugs, or active substance[1] is essential for the treatment of various types of disease. A liposome is a very effective drug delivery system to Target the active medicament to an effective part of the body without entrapping or affecting the other body part; that's why it is also called the targeted drug delivery system. Liposomes are available in various sizes to the range for treatment to various types of disease as the carrier for targeted the medicament or drug to active site at a predetermined rate and time range, without affecting the other body part for the treatment of a particular disease. they are colloidal spheres of cholesterol non-poisonous surfactants, sphingolipids, glycolipids, long-chain unsaturated fats, and even layer proteins and active atoms or it is also called vesicular system.[2] this review discusses the advantages and disadvantages, various methods of preparation, evaluation, etc.

Keywords:- Liposome, Evaluation, Drug delivery system, Vesicles.

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Introduction

The name liposome is derived from two Greek words: Lipo = "fat" and Soma = "body". A liposome is the drug delivery system which is structurally seeing like a colloidal, vesicular and made up one or more than one lipid bilayer (outer layer) in which the equal number of aqueous layer (inner layer) is inclosed into it shown in Figure 1 which contains a substance like peptides and protein, hormones, enzymes, antibiotics, antifungal and anticancer agent .in this delivery system drug achieve the long therapeutic effect for the treatment of particular disease without affected to another part of the body. [3]

Advantages of liposomes:-

Liposomes are biocompatible, completely biodegradable, non-toxic, flexible, and nonimmunogenic for systemic and nonsystemic administrations.

- Provide controlled and sustained release.
- It carries both water and lipid-soluble drugs.
- The drug can be stabilized from oxidation.
- Targeted drug delivery or site-specific drug delivery.
- Control hydration.

disadvantages of liposome:-

- Less stability.
- Low solubility.
- Short half-life.
- High production cost.
- Leakage and fusion of encapsulated drug/molecules.[4]

Types of Liposomes[5]

Liposomes are classified based on –

Based on Structural Parameters

Unilamellar vesicles

- Small unilamellar vesicles (SUV)
- Medium unilamellar vesicles (MUV)
- Large unilamellar vesicles (LUV)

Oligolamellar vesicles (OLV)

These are made up of 2-10 bilayers of lipids surrounding a large internal volume.

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Multilamellar vesicles (MLV)

MLV made up of several bilayers. And the preparation method differs from other vesicle preparation methods. They are arranged in a manner like an onion in which concentric spherical bilayers of LUV/MLV enclosing a large number of SUV etc.

Based on Method of Preparation

1. Reverse phase evaporation method (REV): single or oligolamellar vesicles.
2. MLV-REV: multilamellar vesicles made by a reverse-phase evaporation method.
3. SPLV: stable multilamellar vesicles
4. FATMLV: frozen and thawed MLV.
5. VET: vesicles prepared by the extrusion method.

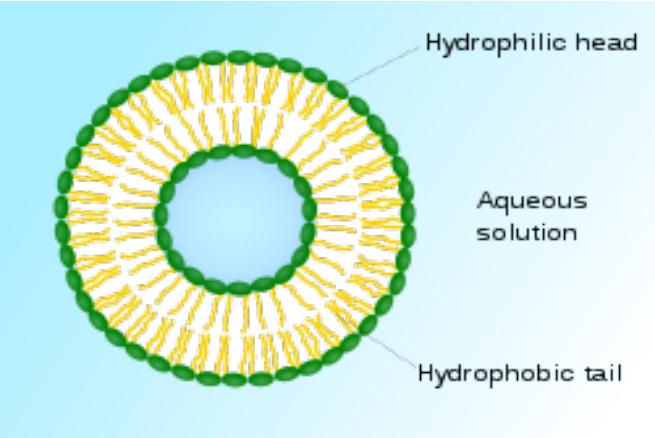

Figure 1: Structure of liposome

Table 1: Liposome classification

Liposomes type	*Size*	*No. of lamellae*
Small unilamellar vesicles(SUV)	20 nm-100 nm	single
Large unilamellar vesicles (LUV)	100 nm-400 nm	single
Glant unilamellar vesicles(GUV)	1-micro meter and large	single
Large multilamellar vesicles(MLV)	200 nm-~3micro meter	multiple
Multivesicular vesicles (MVV)	200 nm-~3micro meter	multiple

Based upon Composition and Application

1. Conventiuonal liposome.
2. Fusogenic liposomes (RSVE): reconstituted Sendai virus envelopes.
3. pH-sensitive liposomes.
4. Cationic liposomes
5. Long circulatory liposomes (LCL)
6. Immune-liposomes.

Material And Method

Composition of liposomes[6-7]

The major structural components are used in the preparation of liposomes are shown in Table 1.

1. Phospholipids

Phospholipids are the main component for the preparation of the liposome membrane. And they are further categorized into two category –

- Natural Phospholipids:-
  - ◊ egg phosphatidylcholine.
  - ◊ Soybean phosphatidylcholine.
- Synthetic Phospholipids:-
  - ◊ Dipalmitoyl phosphatidyl cloline (DPPC).
  - ◊ Dipalmitoyl phosphatidyl ethanolamine (DPPE)
  - ◊ Distearoyl phosphatidylserine (DSPC).
  - ◊ Dipalmitoyl phosphatidic acid (DPPA).
  - ◊ Dioleoyl phosphatidylglycerol (DOPG).

2. Sterols (Cholesterol)

Cholesterol and its derivatives are often used in the preparation of liposomes, and its help too-

- reducing the permeability of the membrane to a water-soluble molecule.
- Decreasing the fluidity or microviscosity of the bilayer
- Stabilizing the membrane in the presence of biological fluids such as plasma (this effect is used in the formulation of I .V. liposomes).

3. Sphingolipids

sphingosine is one of the most important parts of sphingolipids. Sphingolipids are obtained from plant and animal cells. Eg:- sphingomyelin and glycosphingolipids.

4. Cationic lipids

Eg:- DODAB/C (dioctadecyl dimethyl ammonium bromide or chloride, DOTAP

Dioleoyl propyl trimethyl ammonium chloride.

5. Other substances

- A variety of other lipids of surfactants are used to form liposomes.
- Many single-chain surfactants are used to form liposomes by mixing with cholesterol.
- Non-ionic lipids

6. Polymeric material.

Classification of liposomes[8]

Liposomes are classified into different types-

1. According to their size.
2. According to their number of lamellae (lipid bilayer).

Method of preparation of liposomes[9-12]

Two methods are used for the preparation of liposomes are:-

1. A general method of preparation
2. A specific method of preparation:- are two types-

a. Passive loading technique:-

1. Mechanical dispersion
   - Lipid hydration method
   - Micro emulsification
   - Sonication
   - French pressure cell method
   - Membrane extrusion
   - Dried reconstituted vesicles
   - Freeze-thaw method.
2. Solvent dispersion
   - Ethanol injection method
   - Ether infusion method
   - Double emulsification
   - Reverse-phase evaporation
3. Detergent removal

b. Active loading technique

1. Prollposome
2. Lyophilization.

A general method of preparation:- In all the methods which are used for the preparation of liposomes are involved basic four stages are:-

- Drying down lipids from an organic solvent.
- Dispersing the lipid in aqueous media.
- Purifying the final product.
- Analyzing the final product.

Passive loading technique

Mechanical dispersion

- Lipid hydration method:-

◊ on this method firstly prepare the homogeneous mixture of lipids. By dissolving and mixing a lipid component in an organic solvent (chloroform)

◊ Ones the lipid is thoroughly mixed in the organic solvent, the solvent is removed to yield a lipid film.

◊ The lipid film is thoroughly dried by placing the vial or flask on a vacuum pump overnight by removing the residual organic solvent.

◊ Lipid solution was frozen by placing the container on a block of dry ice or swirling the container in dry ice- acetone or alcohol.

- Micro emulsification:-

In this method, small vesicles are prepared by micro emulsifying lipid composition using high shearing stress generated from high-pressure homogenizer. (speed of rotation 20 to 200 for biological). These methods are used to prepare the small lipids vesicles on a commercial scale.

- Sonication:-

In this method lipids (MLVs) are sonicated with the help of a sonicator in this method two types of sonicators are used either bath type sonicator or probe sonicator for the preparation of liposome vesicles.

- French pressure cell method:-

This technique is basic, quick, reproducible; furthermore, it includes delicate treatment of temperamental materials. In this method, MLV expulsion through a small hole point at 20,000psi at temp 4°C. Furthermore, it likewise has a few focal points over the sonication technique. What's more, a few disservices resemble hard to accomplishing temperature and less working volume.

- Membrane extrusion:-

In this method the processed liposome has a narrow size distribution and selected average size less than about 0.4 microns.

- Dried reconstituted vesicles

In this method, liposomes are added to an aqueous solution containing a drug or mixed with a lyophilized protein, followed by dehydration or mixture.

- Freeze-thaw Method.

In this method the SUVs are quickly solidified, followed by moderate defrosting.

Solvent dispersion

- Ethanol injection method:-

In this method MLVs are formed by a lipid solution of ethanol are rapidly injected into an excess of a buffer. but some drawbacks of this method are the particles may be with heterogeneous size distribution (30-110).

- Ether infusion method

In this method, liposomes are prepared by dissolving a lipid solution in diethyl or ether methanol, and then the mixture is slowly injected into an aqueous solution of a drug, to be encapsulated at a temp of 55-65°C under the reduced pressure.

- Double emulsification

This method firstly prepared the emulsion by dissolving the drug in the aqueous phase(W1), which is then emulsified in an organic solvent of a polymer is called primary emulsion(W/O). After that this primary emulsion further mixed in an emulsifier-containing aqueous solution(W2) to make a W1/O/W2 double emulsion. And after than microspheres are obtained by removal of the solvent and filtration process.

- Reverse-phase evaporation

The lipid blend is taken in a round base flagon followed by the expulsion of dissolvable under diminished pressure by a rotational evaporator. The framework is cleaned with nitrogen and the lipid are re-broken down in the natural stages. The opposite stages vesicles will frame in these stages. The standard solvent utilized is diethyl ether and isopropyl ether. The fluid stage which contains medication to be epitomized is included after the lipids are re-scattered in these stages. The framework is held under persistent nitrogen; what's more, the two stages framework is sonicated until the blend turns out to be clear one-stage scattering. The blend is at that point set on the rotating evaporator, and the expulsion of natural dissolvable is done until a gel is shaped trailed by evacuation of non-embodied material. The subsequent liposomes are called switch stage dissipation vesicles.

Detergent removal

Detergents are used to solubilize the lipids at their critical micellar concentrations. LUVs are shaped by eliminating the detergent by dialysis and combining the micelles. In this method, the liposomes are formed in homogenous size. And the retention of detergent contaminants is the drawback of this method.

Active loading technique

1. *Prollposome:-* lipid and active substances (drug) are covered onto a solvent transporter to shape free-streaming granular material in supportive of liposomes which structure an isotonic liposomal suspension on hydration. The favorable to pro- liposome approach may give a chance for cost-effective large scale manufacturing liposomes containing particularly lipophilic drugs.
2. *Lyophilization:-* the expulsion of water from items in a solidified state at incredibly decreased weight is called lyophilization (freeze-drying). The cycle is commonly used to dry items that are thermolabile which might be annihilated by heat-drying. This method has an incredible potential to unravel long haul steadiness issues as for liposomal solidness. Spillage of entangled materials may occur during the cycle of freeze-drying and on reconstitution.

Result and Discussion

Evaluation of liposomes[13]

The purpose of the evaluation of liposome to ensure the in vivo and in vitro performance of liposomes. Evaluation parameter are categories into three broad categories are-

- Physical characterization:- Size, shape, surface feature, lamellarty, phase behavior and drug release profile.
- Chemical characterization
- Biological characterization:- To ensure the safety and suitability of formulation for therapeutic use.

Some parameters are

Vesicle shape and lamellarity

vesicle shape can be evaluated utilized electron microscopic techniques. Lamellarity of vesicles for example number of bilayers present in liposomes is decided to utilize freeze-fracture electron microscopy and p-31 nuclear magnetic resonance analysis.

Vesicle size and size distribution

Various techniques are used to describe the size and size distribution for eg. Light microscopy, fluorescent microscopy, electron microscopy, laser light scattering photon correlation spectroscopy, field flow fractionation, gel permeation, and exclusion. The most exact strategy for deciding the size of liposome is electron microscopy since it licenses one to see ever individual liposomes and to acquire accurate data about the profile of liposome. most of the evaluation methods are used for liposome are categorize into a various category:-

Microscopic, diffraction, scattering, and hydrodynamic techniques.

Encapsulation efficiency and trapped volume

This determines the amount and rate of entrapment of water-soluble agents in the aqueous compartment of the liposome.

Drug release

The component of medication discharge from liposome can be surveyed by utilizing very much aligned in vitro dispersion cells. The liposome-based definition can be helped by utilizing in vitro tests to foresee pharmacokinetics and bioavailability of medication previously utilizing expensive and tedious in vivo examinations. The weakening actuated medication discharge in cushion and plasma was utilized as an indicator for pharmacokinetic execution of liposomal details and another measure which decided intracellular medication discharge prompted by liposome debasement in the presence of mouse-liver lysosome lysate was utilized to evaluate The bioavailability of medication.

Application of liposome[14-16]

the application of liposomes are categorized into two categories are:-

- general application:- in this category, liposomes are used to treat respiratory disorders, eye disorders, vaccine adjuvant, brain targeting, and anti-infective agents.
- clinical application:-
  - ◊ cancer chemotherapy.
  - ◊ gene therapy.
  - ◊ liposomes for topical application.
  - ◊ liposomes as a carrier of the drug in oral treatment.
  - ◊ Liposomes for pulmonary delivery.
  - ◊ Against leishmaniasis.
  - ◊ Cell biological application.
  - ◊ Metal storage disease.
  - ◊ Ophthalmic delivery of drugs.

Conclusion

Liposome has been acknowledged as an incredibly valuable transporter framework for focused medication conveyance. The adaptability of their conduct can be used for the medication conveyance through any course of the organization and for any medication material regardless.

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