Review Article

International Journal of Indigenous Herbs and Drugs
Content Available at www.saap.org.in ISSN: 2456-7345

A review on: liposomes

K. Subba Reddy[1], M. Durga Srinivasa Rao[2], P. Venkatesh[3]
[1] B.Pharmacy final year student, Jagan's Institute of Pharmaceutical Sciences, Nellore
[2] Associate Professor, Dept. of Pharmaceutics, Jagan's Institute of Pharmaceutical Science, Nellore
[3] Principal Jagan's Institute of Pharmaceutical Science, Nellore

Article Info :

Article History
Received on: 28-11-2021
Revised on : 07-12-2021
Accepted on : 17-01-2022

Abstract

Liposomes, spherical shaped vesicles consisting of one or more phospholipid bilayers, were first described in the mid60s. Today, they are a very useful reproduction, reagent, and tool in various scientific disciplines, including mathematics and theoretical physics, biophysics, chemistry, colloid science, biochemistry, and biology. Among several talented new drug delivery systems, liposomes characterize an advanced technology to deliver active molecules to the site of action. Research on liposome technology has progressed from conventional vesicles to 'second-generation liposomes', in which long-circulating liposomes are obtained by modulating the lipid composition, size, and charge of the vesicle. Liposomes with modified surfaces have also been developed using several molecules, such as glycolipids. They are of 0.05- 5.0 micrometer in diameter. Liposomes are used for the treatment of various diseases like tumors or cancer. In this review article provides a Liposomal Drug Delivery System and various aspects related to liposome that can be studied.

Keywords: Liposomes, phospholipids, and drug delivery system.

***Corresponding Author**
K. Subba Reddy

DOI: https://doi.org/10.46956/ijihd.v7i1.271

Production and Hosted By
Saap.org.in

Introduction

Liposomes were spherical shaped concentric vesicles derived from two Greek words lipos means fat and soma means body [1]. Liposome were first made by Bangham et al in 1961, it was an accidental discovery in which he scattered the phosphatidyl choline molecule in water, during this he found that the molecule was forming a closed bilayer structure having an aqueous phase which were entrapped by a lipid bilayer [2]. Liposome very useful because act as a carrier for a variety of drugs, having a potential therapeutic action or other properties. Liposome is colloidal carriers, having a size range of 0.01–5.0μm in diameter. Drug encapsulated by liposome achieve therapeutic level for long duration as drug must first be release from liposome before metabolism and excretion [3]. They are small artificial vesicles of spherical shape that can be created from cholesterol and natural non-toxic phospholipids. Due to their size and hydrophobic and hydrophilic character (besides biocompatibility), liposome's are promising systems for drug delivery. There is a unique ability of liposomes to entrap drugs of both aqueous and the lipid phase and it makes them attractive drug delivery systems for hydrophilic and hydrophobic drugs [4].

Liposome properties differ considerably with lipid composition, surface charge, size, and the method of preparation. It has been displayed that phospholipids impulsively form closed structures when they are hydrated in aqueous solutions. Such vesicles which have one or more phospholipid bilayer membranes can transport aqueous or lipid drugs, depending on the nature of those drugs. Generally, liposomes are definite as spherical vesicles with particle sizes ranging from 30 nm to several micrometres. They consist of one or more lipid bilayers surrounding aqueous units, where the polar head groups are oriented in the pathway of the interior and exterior aqueous phases.

SOUTH ASIAN ACADEMIC PUBLICATIONS

Liposomes are the novel drug delivery system that aims to deliver the drug directly to the place of action. They have potential to accommodate both hydrophilic and lipophilic compounds to protect the drug from degradation and release the active ingredients in a controlled manner [5, 6].

Liposomal encapsulation technology (LET) is the newest delivery technique used by medical investigators to transmit drugs that act as curative promoters to the assured body organs. This form of delivery system proposal targeted the delivery of vital combinations to the body. LET is a method of generating sub-microscopic foams called liposomes, which encapsulate numerous materials. These 'liposomes' form a barrier around their contents, which is resistant to enzymes in the mouth and stomach, alkaline solutions, digestive juices, bile salts, and intestinal flora that are generated in the human body, as well as free radicals. The contents of the liposomes are, therefore, protected from oxidation and degradation. This protective phospholipid shield or barrier remains undamaged until the contents of the liposome are delivered to the exact target gland, organ, or system where the contents will be utilized [7].

The present review will briefly explain the comprehensively deliberate liposomes in terms of liposomes, explore the related problems and solutions proposed, with a focus on liposome preparation, characterizations, affecting factors, advantages, and disadvantages.

Types of Liposomes

Liposomes are highly versatile compounds and they can be fabricated with various combinations, their diversity and properties vary in structure, size, shape, and surface properties. One of the classification types of liposomes is founded on their size and amount of layers, for example, unilamellar and multilamellar liposomes. They can be subdivided into four main categories based on structural parameters:

- multilamellar liposomes/vesicles (MLV)(More than 0.5 μm)
- oligolamellar vesicles (OLV)(0.1-1.0 μm)
- multilamellar liposomes/vesicles (MVV)(More than 1.0 μm)
- unilamellar vesicles (ULV)(All size ranges).

Furthermore, the ULV can be divided into

- giant unilamellar liposomes/vesicles (GUV) groups(More than 1.0 μm),
- large unilamellar liposomes/vesicles (LUV)(More than 100nm),
- medium unilamellar vesicles (MUL)(More than 100nm)
- Small unilamellar liposomes/vesicles (SUV) (20-100 nm) and based on size.

In this regard, liposomes synthesis methods can be categorized as dehydration and rehydration (DRV), reverse phase evaporation (REV), particularly for SUL, OLV, and MLV liposomes, vesicles prepared by extrusion technique (VET), and frozen and thawed (FAT) for MLV preparation.

Based upon Conventional Liposomes classified as:

- Natural lecithin mixtures
- Liposome with glycolipids
- Synthetic identical chain phospholipids

Based upon Specialty liposomes

- Lipoprotein coated
- Carbohydrate coated
- Bipolar fatty acid
- Antibody directed

The structural components are

1) Phospholipids Phospholipids are the major structural components of liposome. The most common phospholipids used in liposomal preparation are Phosphatidylcholine (PC8). Phosphatidyl-choline is an amphiphatic molecule consist of-

- A hydrophilic polar head group, phosphocholine
- A glycerol bridge
- A pair of hydrophobic acyl hydrocarbon chains

The chemical structure of naturally occurring Phosphatidylcholine has a glycerol moiety attached to two acyl chains which may be saturated or unsaturated. The stability of liposome membrane depends on the packing of hydrocarbon chains of the lipid molecules. The nature of the fatty acid in lipid molecule, such as number of double bonds in the chain, is responsible for bilayer properties such as elasticity and phase behaviour [9]. Phospholipids are very abundant in nature and which contains choline is used for the preparation of liposomes.

Examples of phospholipids are-

- Phosphatidyl choline (Lecithin) PC
- Phosphatidyl ethanolamine(Cephalin)-PE
- Phosphatidyl serine (PS)
- Phosphatidyl Glycerol (PG)

Cholestrol Cholesterol is another important structural component of liposome. It is a commonly used sterol. The addition of sterols modulates the function of stability and rigidity. It does not by itself form a bilayer structure [10]. It gets incorporated into phospholipids in a very high concentration up to 1:1 or 2:1 molar ratio of cholesterol to phosphatidyl choline. The presence of cholesterol in the lipid bilayer enhances the stability and form highly ordered and rigid membrane structure(Li X et al., 2011). Cholesterol reduces the permeability of water soluble molecules and improves the fluidity and stability of biological membrane. The interaction and destabilization of liposomes was prevented by cholesterol [11].

Methods of Liposome Preparation

General methods of preparation

All the methods of preparing the liposomes involve four basic stages:

1. Drying down lipids from organic solvent.
2. Dispersing the lipid in aqueous media.
3. Purifying the resultant liposome.
4. Analyzing the final product.

SOUTH ASIAN ACADEMIC PUBLICATIONS

Method of liposome preparation and drug loading the following methods are used for the preparation of liposome:

1. Passive loading techniques
2. Active loading technique.

Passive loading techniques include three different methods

1. Mechanical dispersion method.
2. Solvent dispersion method.
3. Detergent removal method (removal of nonencapsulated material) [14].

Mechanical dispersion method

The following are types of mechanical dispersion methods:

- **Sonication** - Sonication is perhaps the most extensively used method for the preparation of SUV. Here, MLVs are sonicated either with a bath type sonicator or a probe sonicator under a passive atmosphere.
- **French pressure cell** - French pressure cell involves the extrusion of MLV through a small orifice
- **Freeze-thawed liposomes**- SUVs are rapidly frozen and thawed slowly. The short-lived sonication disperses aggregated materials to LUV. The creation of unilamellar vesicles is as a result of the fusion of SUV throughout the processes of freezing and thawing
- **Lipid film hydration by hand shaking, non-hand. Shaking or freeze drying**.
- **Micro-emulsification**. This method is used for preparing SLV. It can be achieved by microemulsifying lipid compositions using high shearing stress generated from high pressure homogenizer. Dried reconstituted vesicles: In this method liposomes are added to an aqueous solution containing drug or mixed with lyophilized protein, followed by dehydration of mixture.
- **Membrane extrusion**

Solvent Dispersion method

- **Ethanol injection:** A lipid solution of ethanol was added to an aqueous buffer which immediately forms MLV.
- **Ether infusion**: A solution of lipids dissolved in diethylether and is slowly injected to a solution of the material to be encapsulated at temperature 55-60 ◦ C29.

Detergent removal method:

Lipids were solubilized by detergents at their critical miscelles concentration. As detergent is removed, miscelles become richer in phospholipids and finally combine to form LUVs.

Active Loading Techniques

- **Proliposomes:** In this method lipid and drug were coated onto a soluble carrier to form free flowing granular material in pro-liposome which forms an isotonic liposomal suspension on hydration30.
- **Lyophillization:** The removal of water from products in a frozen state at a reduced pressure is called Lyophillization. This method is generally used to dry the products that are thermolabile.

Mechanism of transportation through liposome

The limitations and benefits of liposome drug carriers lie critically on the interaction of liposomes with cells and their destiny in vivo after administration. In vivo and in vitro studies of the contacts with cells have shown that the main interaction of liposomes with cells is either simple adsorption (by specific interactions with cell-surface components, electrostatic forces, or by nonspecific weak hydrophobic) or following endocytosis (by phagocytic cells of the reticuloendothelial system, for example macrophages and neutrophils).

Evaluations of Liposomes

1. Vesicle shape and lamellarity: The shape of the vesicles were studied by using electron microscope.
2. Particle size and distribution: The size analysed by an analyzer based on laser diffraction theory focused with minimum power of 5MW.
3. Entrapment Efficiency – It determines amount and rate of entrapment of water soluble agents in aqueous compartment of liposomes.
4. Trapped Volume – It is an important parameter related to liposomes .It is aqueous entrapped volume per quantity of lipids. This can vary from 0.5 to 30 microlitre/micromol.
5. In vitro drug release **–** This can be carried by using Franz Diffusion cell which has a diameter of 25 mm.

Applications of Liposomes

Respiratory Disorders- The liposomes have been found to possess beneficial effects in the treatment of several respiratory disorders, reason being their better sustained release, improved stability and reduced toxicity than ordinary aerosols. Liquid or dry form can be taken for inhalation of liposome and release of drug has been reported to occur during nebulization.

Ophthlamic Disorders- Dry eyes, keratitis, corneal transplant rejection, uveitis, ondopthelmitis and proliferative vitro retinopathy are the examples of eye disorders against which liposomes have been found to possess beneficial effects. The drug verteprofin that is found to be effective against eye disorders has been recently approved as liposomal formulation.

Tumor therapy- Carrier of small cytotoxic molecule and vehicles used for macromolecule such as cytokines.

Immunological adjuvants in vaccines - Liposomes used in immunoadjuvant, immunodiagnosis. ¬ Liposomes as protein drug delivery- They are used to enhanced drug solubilization

Pulmonary Application – They are useful tools for pulmonary delivery of drugs due to their solubilization capacity [12].

Liposomes in Cosmetics- They are used in cosmetics because their physiology is similar to the cell membrane and they release materials to the cells [16].

Site specific targeting- The immunoliposomes are able to recognize and binds to target cells with greater specificity.

Gene therapy- Liposomes are used widely in gene applications to cure diseases.

Conclusion

Liposomes have been used in a broad range of pharmaceutical applications and it have been realized as extremely useful carrier system for targeted drug delivery, and also Liposomes with enhanced drug delivery to disease locations, by ability of long circulation residence times, are now achieving clinical acceptance. Finally, liposomal drugs show reduced toxicities and retain improved efficacy compared with free complements. However, based on the pharmaceutical applications and available products, we can say that liposomes have definitely established their position in modern delivery systems.

References

1. Sahoo SK, Labhasetwar V: Nanotech approaches to drug delivery and imaging. DDT 2003, 8:24. 2. Gabizon A, Goren D, Cohen R, Barenholz Y: Development of liposomal anthracyclines: from basics to clinical applications. J Control Release 1998, 53:275–279.
2. Allen TM: Liposomes. Opportunities in drug delivery. Drugs 1997, 54:8–14.
3. Chrai SS, Murari R, Imran A: Liposomes: a review. Bio Pharm 2001, 14(11):10–14.
4. Andreas W, Karola VU: Liposome technology for industrial purposes. J Drug Deliv 2011, 2011:9.
5. Mayer, L.D., Hope, M.J., Cullis, P.R., Janoff, A.S. Solute distributions and trapping efficiencies observed in freezethawed multilmellar vesicles. Biochim. Biophys. Acta 1985; 817:193-196.
6. Vyas, S.P., Khar, R.K. 2006. Targeted And Controlled Drug Delivery: Novel Carrier Systems. Edition 1, CBS Publishers and Distributor, New Delhi.pp.421-427.
7. Maurya SD, Prajapati S, Gupta A, Saxena G, Dhakar RC, Formulation development and evaluation of ethosome of stavudine, Int J Pharm Edu Res. 2010; 13(16).
8. Hemanthkumar M, Spandana V: Liposomal encapsulation technology a novel drug delivery system designed for ayurvedic drug preparation. IRJP 2011, 2(10):4–7.
9. Samadikhah HR, Majidi A, Nikkhah M, Hosseinkhani S. Preparation, characterization, and efficient transfection of cationic liposomes and nanomagnetic cationic liposomes. Int J Nanomedicine, 2011; 6: 2275-2283.
10. Paecharoenchai O, Niyomtham N, Apirakaramwong A, Ngawhirunpat T, Rojanarata T, Yingyongnarongkul BE, et al. Structure Relationship of Cationic Lipids on Gene Transfection Mediated by Cationic Liposomes. AAPS Pharm Sci Tech, 2012; in press.
11. Li X, Chen D, Le C, Zhu C, Gan Y, Hovgaard L. Novel mucuspenetrating liposomes as a potential oral drug delivery system: preparation, in vitro characterization, and enhanced cellular uptake. Int J Nanomedicine, 2011; 6: 3151-3162.
12. Ejiogu Deborah Chioma. Formulation and evaluation of etodolac niosomes by modified ether injection technique. Universal Journal of Pharmaceutical Research. 2016; 1(1): 1- 6.
13. Elsaied Hamada Elsaied, Hamdy Mohamed Dawaba, Elsherbini Ahmed Ibrahim, Mohsen Ibrahim Afouna. Investigation of proniosomes gel as a promising carrier for transdermal delivery of Glimepiride. Universal Journal of Pharmaceutical Research. 2016; 1(2): 1-18
14. Riaz M: Liposome preparation method. Pak J Pharm Sci 1996, 9(1):65–77. 19. Himanshu A, Sitasharan P, Singhai AK: Liposomes as drug carriers. IJPLS 2011, 2(7):945–951.
15. 0. Schieren H, Rudolph S, Findelstein M, Coleman P, Weissmann G: Comparison of large unilamellar vesicles prepared by a petroleum ether vaporization method with multilamellar vesicles: ESR, diffusion and entrapment analyses. Biochim Biophys Acta 1978, 542(1):137–153.
16. Batzri S, Korn ED: Single bilayer liposomes prepared without sonication. Biochim Biophy Acta 1973, 298(4):1015–1019.
17. Szoka F Jr, Papahadjopoulos D: Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation. Proc Natl Acad Sci USA 1978, 75(9):4194–4198.
18. Handa T, Naito S, Hiramatsu M, Tsuboi M: Thermal SiO and H13CO+ line observations of the dense molecular cloud G0.11-0.11 in the Galactic Center Region. Astrophys J 2006, 636:261–266.
19. Daemen T, Hofstede G, Ten Kate MT, Bakker-Woudenberg IAJM, Scherphof GL: Liposomal doxorubicin induced toxicity: depletion and impairment of phagocytic activity of liver macrophages. Int Cancer 1995, 61:761–721.
20. Kirby CJ, Gregoriadis G: A simple procedure for preparing liposomes capable of high encapsulation efficiency under mild conditions. In Liposome Technology. 1st edition. Edited by Gregoriadis G. Boca Raton: CRC; 1984:19–27.

SOUTH ASIAN ACADEMIC PUBLICATIONS