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FORMULATION TECHNIQUES AND CHARACTERIZATION OF LIPOSOMES: AN OVERVIEW

Madhavi Sirsat*[1], Vaishnavi Hiwale[2], Pallavi Sambarkar[3] and Amol Wadhave[4]

[1,2]Students SDMVM's Diploma in Pharmacy Chh. Sambhajinagar.
[3]Lecturer SDMVM's Diploma in Pharmacy Chh. Sambhajinagar.
[4]Principal SDMVM's Diploma in Pharmacy Chh. Sambhajinagar.

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***Corresponding Author**
Madhavi Sirsat
Students SDMVM's Diploma in Pharmacy Chh. Sambhajinagar.

ABSTRACT

Liposome was derived from two Greek words "Lipos" meaning fat and "Soma" meaning body. Liposomes where spherical shaped vesicles and have diameter of 50-300 nm. consist of phospholipids and cholesterol vesicles which are under extensive investigation as drug carriers for improving the bioavailability and delivery of therapeutic agents. Liposomes have immense capability to prevent the degradation of drugs, reduce side effects and thus increasingly used for targeted drug delivery. The drugs can either incorporated inside aqueous space (hydrophilic drugs) or inside phospholipids bilayer (hydrophobic drugs). Liposomes can be manufactured in different lipid compositions it shows variation in particle size, Size distribution, surface, number of lamella and encapsulation efficacy. The present review paper explains about introductory, classification of liposomes, structural components of liposomes, methods of preparation and application of liposomes are explained detailed. They are recently used for various nanoscale drugs formulation. The possible use of liposomes in the therapy of cancer has also been investigated. Because liposomes are non-toxic, biodegradable, immunogenic and biocompatible. These liposomes are generally administrated by intra-venous route. The formulated liposome is evaluated by Zeta Sizer, entrapment efficiency. Research on liposome technology has progressed from conventional vesicles to 'second- generation liposomes. Liposomes with modified surfaces have also been developed using several molecules such as glycolipids or sialic acid, antineoplastic agents, doxorubicin and daunorubicin and cytarabine are advanced stages of clinical testing in humans. The review covers various aspects of liposome-based drug delivery, including their structure, formulation methods, advantages, limitations, and recent breakthroughs in the field. Furthermore, we discuss the diverse range of drugs and therapeutic agents that can be encapsulated within liposomes, as well as their clinical applications in targeting specific diseases.

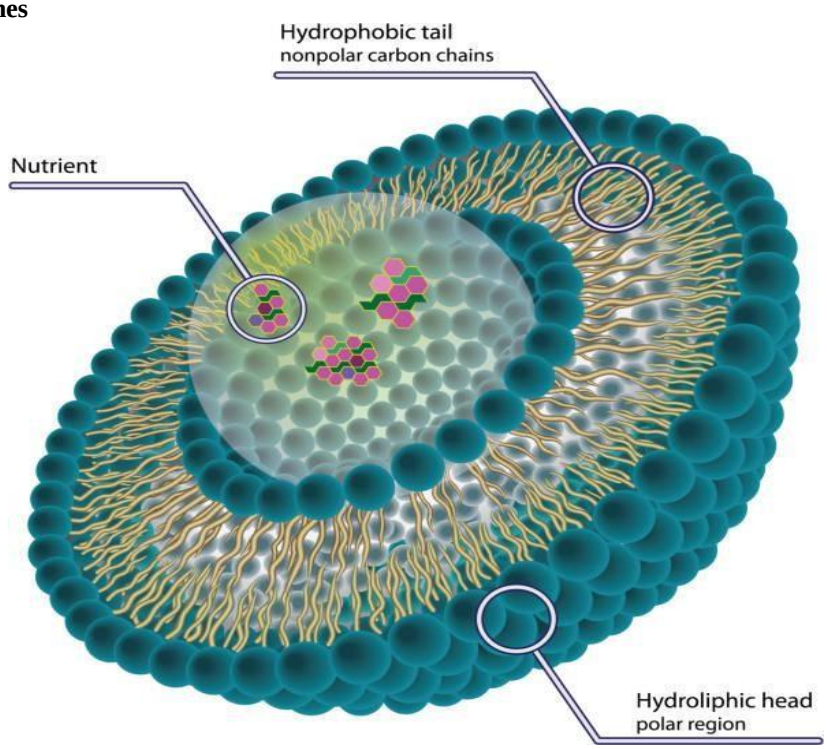
KEYWORDS: Liposome; Controlled Release; Targeted Drug Delivery; Novel Delivery.

INTRODUCTION

Liposomes are round sac phospholipid molecules. It encloses a water droplet especially as form artificially to carry drug into tissue membrane. Liposome is a nanoparticle (size-100nm). Liposome were first described by Bangham in 1961, it turned into an accidental discovery in which he scattered the phosphatidyl choline molecule in water, for the duration of this he located that the molecule was forming a closed bilayer shape having an aqueous segment which were entrapped by means of a lipid bilayer. Liposomes are useful because they act as carriers for a variety of drugs and have potential therapeutic or other properties. Various carriers such as nanoparticles, microparticles, polysaccharides, lectins, and liposomes can be used to target drug to a specific site. Liposomal drug delivery is gaining interest due to its contribution to various areas like drug delivery, cosmetics, and biological membrane structure.[1] free drug injected into the bloodstream usually reaches a therapeutic level for a brief period of time because of excretion and metabolism.[1] Liposomes are concentric, bilayer vesicles with a diameter of 0.01 to 5.0 µm. They can be composed of membrane proteins, long chains of fatty acids, glycolipids, cholesterol, sphingolipids and non-toxic surfactants.[2] Whenphospholipids are dispersed in water, vesicular structures known as liposomes.[2] When phospholipids are dispersed in water, vesicular structures known as liposomes. These structures have an inner aqueous phase is surrounded by phospholipid bilayer membranes. Encased in a sphere-shaped container, the liquid interior held materials such as proteins, enzymes, hormones, antimycotic and anticancer medicines and even plasmids. The majority of liposomes are made of biocompatible

and biodegradable substances that can hold hydrophilic and hydrophobic molecules together on a single substrate. Current studies concentrate more on the development of multifunctional liposomes with sophisticated in vitro characteristics and long-circulating stealth liposomes.

Structure of liposomes



Classification of liposomes

The liposome size can vary from very small (0.025 µm) to large (2.5 µm) vesicles. Moreover, liposomes may have one or bilayer membranes. The vesicle size is an acute parameter in determining the circulation half-life of liposomes, and both size and number of bilayers affect the amount of drug encapsulation in the liposomes On the basis of their size and number of bilayers, liposomes can also be classified into one of two categories:

1. Multilamellar vesicles (MLV).
2. Unilamellar vesicles.

Unilamellar vesicles can also be classified into two categories

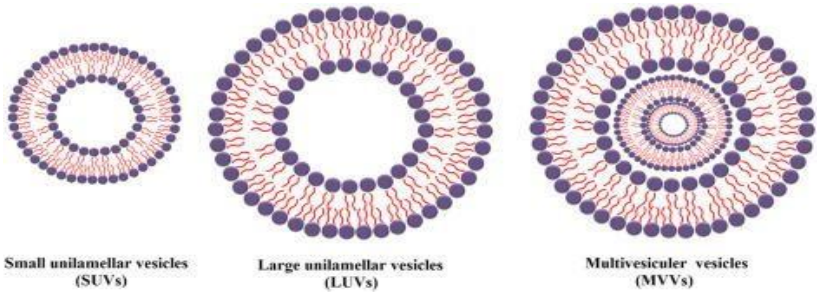
1. Large unilamellar vesicles (LUV).
2. Small unilamellar vesicles (SUV).

In unilamellar liposome's, the vesicle has a single phospholipids bilayer sphere enclosing the aqueous solution. In multilamellar liposome's, vesicles have an onion structure10. Classically, several unilamellar vesicles will form on the inside of the other with smaller size, making a multilamellar structure of concentric phospholipids spheres separated by layers of water. Multi lamellar vesicles are made up of two or more bilayers and are larger than 0.1µm. Their formulation process, which involves hydrating lipids in excess of an organic solvent or using thin film hydration approach is straight forward and incredibly portable. When stored for a long time, they remain mechanically stable. Because of their size, the reticuloendothelial system (RES) cells can remove them quickly, which makes them useful for a variety of purposes that target the RES organs.

Large unilamellar vesicle

The size of these liposomes is higher than 0.1µm and they are especially big unilamellar vesicles with a single bilayer. Since they can contain a huge volume of fluid in their cavity, they have a better encapsulation efficiency. They can be helpful for encasing hydrophilic medications due to their high.

Small unilamellar vesicles have a single bilayer and they are smaller than MLV and LUV, measuring less than 0.1µm and they are distinguished by having a long circulation half-life and a low entrapped aqueous volume to lipid ratio.



Composition of liposomes

The chemical components of liposomes include the phospholipid molecules and/or lipids with different head groups. Different lipid components can adjust the process parameters and biopharmaceutical parameters of colloidal vesicles, thus affecting the application of liposomes. In order to prepare liposomes with expected physicochemical properties, it is necessary to select various chemical and physical parameters of phospholipids to ensure the expected optimal formulation.

Phospholipids

Structurally, liposomes are spherical or multilayered spherical vesicles made by the self-assembly of diacyl-chain phospholipids (lipid bilayer) in aqueous solutions. The bilayer phospholipid membrane has a hydrophobic tail and a hydrophilic head that leads to the formation of an amphiphilic structure. Liposomes can be made from both natural and synthetic phospholipids. The charge of the hydrophilic group provides stability bthrough electrostatic repels. The hydrophobic group of lipids varies in the acyl chain length, symmetry, and saturation.[4]

Cholesterol

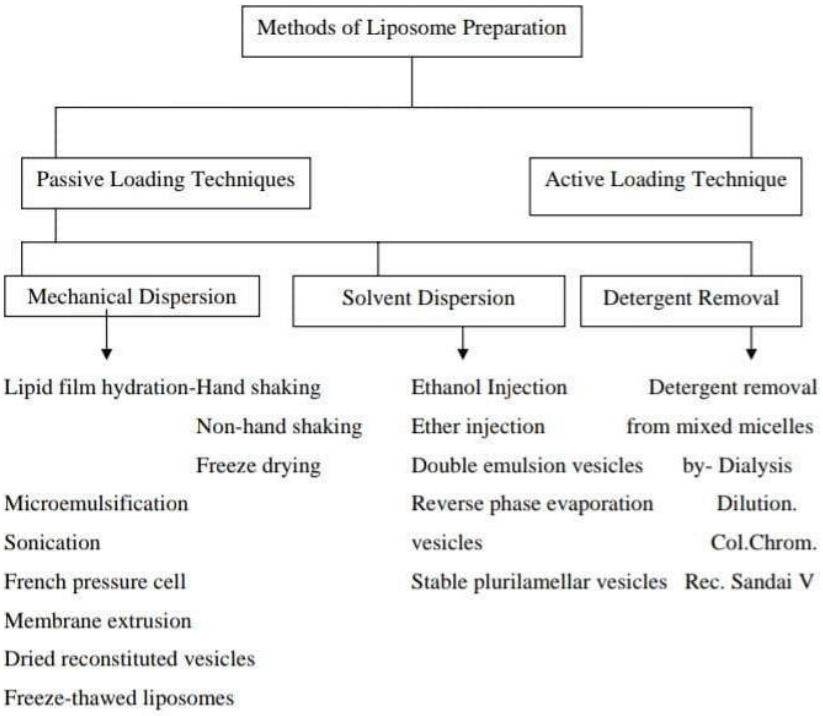
Cholesterol Without producing a bilayer structure on its own, cholesterol may be present in membranes in extremely higher quantities; for in-stance, a 1:1 or even 2:1 molar ratio of cholesterol to phosphati-dylcholine. In the membrane, cholesterol is located in the centrethe bilayer, parallel to the acyl chains, wherein the hydroxyl group faces the aqueous region.

Although interactions between hydrophobic and specified head groups have been associated also with high solubility of cholesterol in phospholipid liposomes, it is unknown how cholesterol is organised in the bilayer.[5]

Method of preparation

The preparation of all types of vesicular systems requires the input of energy.[6] Generally all the methods of liposome preparation involve three basic stages

1. Drying down of mixture of lipids from an organic solvent.
2. Dispersion of lipids in aqueous media.
3. Separation and purification of resultant liposomes. The various methods of preparation of liposomes are as under.[6]



Advantages of liposomes

- Some of the advantages of liposome are as follows:
- Provides selective passive targeting to tumour tissues (Liposomal doxorubicin). ☐ Increased efficacy and therapeutic index.
- Increased stability via encapsulation.
- Reduction in toxicity of the encapsulated agents. ☐ Site avoidance effect.
- Improved pharmacokinetic effects (reduced elimination, increased circulation life times). Flexibility to couple with site specific ligands to achieve active targeting[7]

Evaluation of liposomes

Liposomal processing and formulation for specified purpose are characterized to ensure their predictable in vivo and in vitro performance. The characterization parameters for purpose of evaluation could be classified into three categories.

1. Physical characterization.
2. Chemical characterization.
3. Biological characterization.

1. Drug entrapment studies

To aliquots of liposome sample (0.5 ml), 5 ml of 10% sodium lauryl sulfate (SLS) was added and the volume was made up to 50 ml. The sample was warmed on a water bath at 70°C for 30 min. Similarly, a blank liposome (without drug) suspension (0.5 ml), 5 ml of 10% SLS were taken in a 50 ml volumetric flask and the volume was made up with distilled water. The blank was warmed on a water bath at 70°C for 30 min. The absorbance of the test solution was taken in a UV spectrophotometer at 263 nm against the blank solution.

2. Percentage of entrapment efficiency

It was determined by using the ratio of the entrapped drug (mg) to the total drug (mg), which may be expressed by the following formula.[9]

Pharmacokinetics of liposomaes

Liposomal drugs can be applied through various routes, but mainly i.v. and topical administration is preferred. After reaching in the systemic circulation or in the local area, a liposome can interact with the cell by any of the following methods.

Endocytosis by phagocytotic cells of the R.E.S such as macrophages and Neutrophils.

Adsorption to the cell surface either by non specific weak hydrophobic or electrostatic forces or by specific interaction with cell surface components Fusion with the plasma cell membrane by insertion of lipid bilayer of liposome into plasma membrane with simultaneous release of liposomal contents into the cytoplasm.

Transfer of liposomal lipids to cellular or sub cellular membrane or vice versa without any association of the liposome contents.

It is often difficult to determine what mechanism is operative and more than one may operate at the same time.[10]

Drug loding of liposomaes

Drug loading can be attained either passively (i.e., the drug is encapsulated during liposome formation) or actively (i.e., after liposome formation). Hydrophobic drugs, for example amphotericin B taxol or annamycin, can be directly combined into liposomes during vesicle formation, and the amount of uptake and retention is governed by drug-lipid interactions.

Trapping effectiveness of 100% is often achievable, but this is dependent on the solubility of the drug in the liposome membrane.[11]

CONCLUSION

Liposomes have been used in a broad range of pharmaceutical applications. Liposomes are showing particular promise as intracellular delivery systems for anti-sense molecules, ribosomes, protein/peptides and DNA. Liposomes enhanced drug delivery to disease locations and longer residence times and achieve clinical acceptance. Liposomal drugs exhibit reduced toxicities and enhanced efficacy. Nowadays liposomes are used as carriers for a wide variety of drugs. Liposomes serve as versatile carriers. Liposomes have emerged as a promising class of drug delivery systems that offer significant advantages for enhancing the therapeutic efficacy and safety of various drugs. While challenges remain, the continued innovation and refinement of liposomal technologies hold great promise for the future of drug delivery in the pharmaceutical industry. Liposomes represent an exciting and versatile approach to drug delivery, with the potential to revolutionize the pharmaceutical industry by improving drug efficacy, reducing side effects, and enabling precise targeting of therapies. Further advancements in liposomal technology are likely to expand their use in a wide range of medical applications.

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