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# A Review on Liposomes As A Novel Drug Delivery System

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**Abstract:** *Liposomes are an unique and innovative medication delivery system. Liposomes have several advantages over other drug delivery systems, including site targeting, delayed or controlled release, protection of drugs from degradation and clearance, improved therapeutic effects, and less negative side effects. Because liposomes are effective drug carriers in pre-clinical and clinical studies, they have many benefits and uses. Additionally discussed were issues with liposomal stability, efficient targeting techniques, and some of its drawbacks. Many drugs' biodistribution has been changed because of the creation of liposomes, which has enhanced the drugs' therapeutic properties.*

**Keywords**: Liposomes, Drug delivery, Novel Delivery, Application

## I. INTRODUCTION

The Greek words 'Lipos' which means fat and 'Soma' that means body, was combined to form spherical concentric vesicles called liposomes. 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) [1] . 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[2] . 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 sites. Liposomal drug delivery is gaining interest due to its contribution to various areas like drug delivery, cosmetics, and biological membrane structure [3]. A liposome is a tiny bubble (vesicle), with a membrane composed of a phospholipid bilayer. Membranes are usually made of phospholipids like phosphatidylet-hanolamine and phosphatidylcholine. Phospholipids are amphiphilic with its polar head as hydrophilic and hydrocarbon tail as hydrophobic [4].

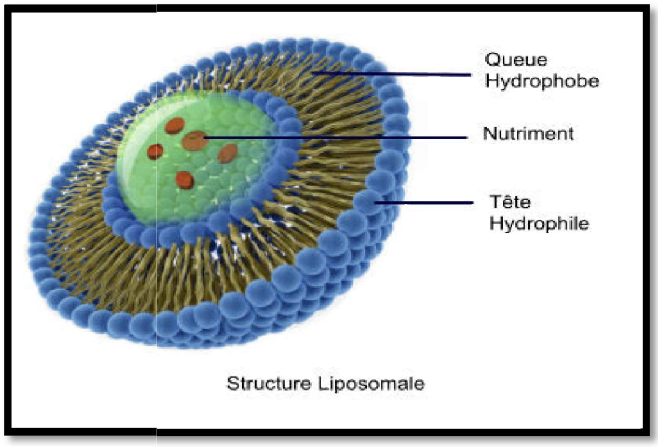


Fig.1[1]

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**Structure of liposomes:**

**Phospholipids:**

The main structural elements of liposomes are phospholipids. These come from the phosphatidic acid[5].Glycerol moieties form the backbone of the molecules[6]

• Naturally occurring phospholipids used in liposome:

Phosphatidylethanolamine

Phosphatidylcholine

Phosphatidylserine

• Synthetic phospholipids used in the liposomes are:

Dioleoyl phosphatidylcholine

Disteroyl phosphatidylcholine

Dioleoyl phosphatidylethanolamine.[7]

**Cholesterol:**

Another component in the formation of liposomes is cholesterol. During the preparation of liposomes, cholesterol molecules position themselves with their hydroxyl group oriented towards the aqueous core whereas the hydrophobic group is inserted in the hydrocarbon core region of the bilayer.[7] Low-cholesterol liposomes interact with transferring, macroglobulin, and albumin, which are plasma proteins. These proteins have a tendency to remove large amounts of phospholipids from liposomes, which weakens the vesicles' monolayer and causes physical damage.[8]

## II. HISTORY OF LIPOSOMES

Liposomes were first discovered in the mid-1960s by British haematologist Dr. Alec D. Bangham [2]. He was studying the structure of cell membranes and stumbled upon the liposome while using an electron microscope[5] . Liposomes are tiny spherical structures made up of lipid bilayers, similar to the structure of cell membranes. Dr Bangham's ground breaking work laid the foundation for understanding and developing liposomes for various applications[8]. In the following decades, liposomes gained recognition for their potential in drug delivery. Their ability to encapsulate drugs and transport them to specific sites in the body revolutionized the field of pharmacology [9].

**Classification of Liposomes:** [10,11,12,13]

1) Classification of liposome depending upon size and shape

- Multilamellar vesicles (MLV)
- Large unilamellar vesicles (LUV)
- Small unilamellar vesicles (SUV)

2) Classification of liposome according to composition

- Conventional liposome
- PH- sensitive liposome
- Cationic liposome
- Long circulating liposome
- Immuno- liposome

3) Classification of liposome depending upon production method

A) Passive loading technique

a) Mechanical dispersion method

- Lipid hydration by hand shaking or freeze drying
- Micro emulsification

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- Sonication
- French pressure cell

b) Solvent dispersion method

- Ethanol injection
- Ether injection
- Double emulsion vesicle
- Reverse phase evaporation

c) Detergent removal method

- Dialysis
- Detergent removal of mixed micellar
- Dilution

B) Active loading technique

**Advantages of Liposomes**:[1,7,14,15]

- Targeted Drug Delivery: Liposomes can encapsulate drugs and deliver them to specific target tissues or cells, allowing for targeted therapy. This minimizes the exposure of healthy tissues to the drug, reducing side effects.
- Improved Bioavailability: Liposomes can encapsulate poorly water-soluble drugs, improving their solubility and bioavailability, which can be a critical factor in drug effectiveness.
- Sustained Release: Liposomes can release drugs gradually over time, leading to sustained therapeutic effects and reducing the need for frequent dosing.
- Protection of Sensitive Compounds: Liposomes can protect sensitive drugs or bioactive compounds from degradation due to environmental factors, such as enzymes, pH changes, or oxidation.
- Versatility: They can be tailored in terms of size, composition, and surface modifications to optimize their performance for specific drugs or therapeutic applications.
- Reduced Toxicity: Liposomal drug delivery can reduce the toxicity of certain drugs by minimizing their exposure to healthy tissues while targeting diseased cells.
- Enhanced Cellular Uptake: Liposomes can improve the cellular uptake of drugs or therapeutic agents, making them more effective in treating diseases.
- Cosmetic Applications: Liposomes are used in cosmetics to enhance the penetration of active ingredients into the skin, improving their efficacy.

**Disadvantages of Liposomes**:[1,7,14,16]

- Uniformity: Achieving uniformity in liposome size and composition can be difficult, affecting their performance and reproducibility.
- Short Circulation Half-Life: Liposomes can be rapidly cleared from the bloodstream by the body's immune system, limiting their time window for drug delivery.
- Immunogenicity: Some liposome formulations may trigger an immune response, potentially causing adverse reactions in the body.
- Limited Drug Loading: Liposomes have a finite capacity for drug loading, which can be a limitation when trying to deliver high doses of certain drugs.
- Complexity: The development of liposomal formulations requires expertise and can be a complex process, which may limit their accessibility to researchers and manufacturers.

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- Expense: Producing liposomal formulations can be costly, which may lead to higher drug prices for liposome based therapies.
- Compatibility Issues: Some drugs may not be suitable for encapsulation in liposomes due to compatibility issues, limiting the range of drugs that can benefit from liposomal delivery.
- Clinical Translation: Despite promising results in preclinical studies, not all liposome-based therapies have successfully transitioned to clinical use, highlighting challenges in translating laboratory findings to real-world applications.
- Interaction with Biological Systems: Liposomes may interact with proteins or cells in ways that affect their stability, drug release, or performance composition, liposomes may not be readily biodegradable, which can raise environmental concerns.
- Storage Stability: Liposomes can be prone to instability during storage, leading to aggregation, leakage of encapsulated substances, or changes in size and structure.
- Scalability: Scaling up the production of liposomes can be challenging and costly, which may limit their widespread use in large-scale pharmaceutical manufacturing.

## III. METHODS OF PREPARATION

**Mechanism of formation of Liposomes:** [16,18]

Liposome performs their motion by four distinct Mechanism:

• Endocytosis – This take location via phagocytic cells of reticuloendothelial system together with neutrophils.

• Adsorption – It occurs to the cellular surface through non precise electrostatic forces or by using interplay with cell surface additives.

• Fusion- It takes place by means of the insertion of liposomal bilayer into plasma membrane with continuous release of liposomal content into the cytoplasm.

• Lipid exchange- on this transfer of liposomal lipids to the cellular membrane without association of liposomal contents.

**Methods Of Preparation**[17]

**Passive loading technique**

**A. Mechanical dispersion method**

- Sonication
- French pressure cell
- Membrane extrusion
- Microencapsulation
- Lipid hydration method
- Membrane extrusion

**B. Solvent dispersion method**

- Ethanol injection
- Ether injection
- Double emulsion
- Reverse phase evaporation

**C. Detergent removal method**

**Active loading technique**

- Proliposomes
- Lyophilisation

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**A. Mechanical dispersion method**

**Sonication:**

Sonication is the method most commonly used to prepare SUVs. Here, MLVs are subjected to passive sonication utilizing a probe-style or bath-style sonicator. The main disadvantages of this approach are its incredibly small interior capacity, ineffective encapsulation, phospholipid degradation and removal of large molecules, metal contamination from the probe tip, and the presence of MLV in addition to SUV.[19]

**French Pressure Cell**:

French pressure cells use the technique of ejecting MLV through a tiny opening. One notable feature of the French press vesicle method is that the proteins seem to be somewhat unassuming during the sonication process. It's important to note that French press vesicles, which are produced by sonication or detergent removal, appear to have a far longer memory for encapsulated solutes than SUVs. The method requires careful handling of unstable materials. In certain aspects, the procedure is better than the sonication technique. Consequently, the liposomes have a size similar to sonicated SUVs. The method's drawbacks are that the working volumes are quite small—the limit is 50 mL—and that it can be difficult to obtain the high temperature.[19]

**Micro emulsification method:**

This method is used in the commercial development of small lipid spheres. A homogenizer's shearing stress could be used to micro-emulsify fatty mixes in order to accomplish this. By raising the rotation rate from 20 to 200, microemulsion can be created for natural applications.[19]

**B. Solvent dispersion method**

**Ethanol injection:**

An ethanol lipid solution is instantly injected into a vast excess of buffer. At once, the MLVs are generated. The population's heterogeneity (30 to 110 nm), the liposomes' extreme dilution, the challenge of eliminating all of the ethanol due to its formation of an azeotrope with water, and the high probability of the various biologically active macromolecules becoming inactive in the presence of even trace amounts of ethanol are some of the method's shortcomings.[17]

**Ether Injection Method:**

A solution of lipids dissolved in diethyl ether or ether/methanol mixture is slowly injected to an aqueous solution of the material to be encapsulated at 55-65°C or under reduced pressure. The subsequent removal of ether under vacuum leads to the formation of liposomes. The main drawbacks of the method are population is heterogeneous (70-190 nm) and the exposure of compounds to be encapsulated to organic solvents or high temperature.[17]

**Reverse phase evaporation technique:**

The waterin-oil emulsion is first formed by quickly sonicating a two-phase structure containing phospholipids in naturally dissolvable materials like isopropyl ether, diethyl ether, or a mixture of isopropyl ether and chloroform with aqueous buffer. A polymer is formed when natural substances break under lighter weights. The main benefit of method is that the liposomes were densely packed (about 80%)[20]

## IV. APPLICATIONS

- Liposomes are commonly used as drug delivery vehicles to encapsulate and deliver both hydrophobic and hydrophilic drugs.
- They can improve drug solubility, stability, and bioavailability.
- Liposomal drug formulations can target specific tissues or cells, reducing systemic side effects.[21]
- Liposomal formulations of chemotherapy drugs, like Doxil (liposomal doxorubicin), are used to treat cancer.

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- They can improve drug circulation time and reduce damage to healthy tissues.[22]

## V. CONCLUSION

Modern ophthalmology and general medicine use liposomes. It is a useful medical tool because of its capacity to increase treatment rates, lower toxicity, supply targeted medications, and advance imaging technology. The primary technique for incorporating hydrophilic and hydrophilic nanoparticles into liposomes is presented in this work, along with the suitable strategy for effective experimental techniques. One of the greatest choices for delivering nanocarriers, delivering certain organs or regions, and targeting receptors is liposomes. To get better benefits, liposome formulations need to be well-designed to have less adverse effects and higher bioavailability.

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