A Review Article On Liposomes

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ABSTRACT

Liposomes are versatile, biocompatible nanocarriers whose evolving compositions, preparation techniques, and targeted delivery strategies enable controlled and precise administration of diverse therapeutic agents for treating cancers, infections, skin disorders, and other diseases despite ongoing challenges in stability and large-scale production.

Keywords: Liposomal Systems; Sustained Drug Release; Precision-Targeted Therapeutics; Innovative Delivery Platforms.

INTRODUCTION

Liposomes are spherical, nanoscale vesicles—about 100 nm in size—composed of phospholipid bilayers that encapsulate an aqueous core, with their name derived from the Greek words lipos (fat) and soma (body); they were first identified in the early 1960s when Alec Bangham observed phosphatidylcholine forming closed bilayer structures in water during electron microscopy studies, a serendipitous finding that later established the foundation of liposomology and ultimately led to their development as versatile carriers for drug delivery.[1]

HISTORY OF LIPOSOMES

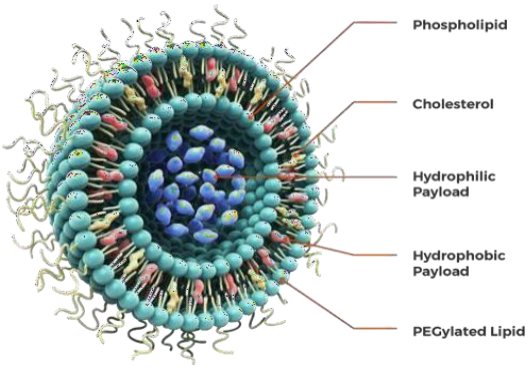
The evolution of liposome research began in 1961 when Alec D. Bangham and his team at the Babraham Institute first reported their formation, followed by a foundational period.

Genisis 1968 to 1975 during which their physicochemical properties were characterized and methods for producing multilamellar vesicles were developed, enabling their use in studying biological membranes.[2]

Middle Age 1975-1985, advances in understanding liposome stability, cellular interactions, and alternative preparation techniques expanded their utility.

Modern Era 1985 onward, liposomes have become valuable tools across diverse scientific fields—including biophysics, chemistry, colloid science, and molecular biology—while also emerging as important platforms in drug delivery, cosmetics, nutraceuticals, and RNA-based therapies such as siRNA and mRNA vaccines, supported by improved formulations containing phospholipids and

cholesterol to enhance structural stability and membrane rigidity.[3]



NEED AND OBJECT:

NEED OF LIPOSOMES

- Challenges in Drug Delivery: Many drugs face issues such as poor solubility, low bioavailability, or high toxicity. Conventional dosage forms often lead to rapid drug clearance and limited accumulation at the intended site.

- Targeted Delivery: Liposomes are capable of directing drugs to specific cells or tissues, which helps reduce side effects and enhances therapeutic effectiveness.[4]

- Requirement for Site-Specific Therapy: Diseases like cancer and infections demand localized drug delivery to minimize adverse effects. Liposomes can transport drugs directly to affected cells or tissues.

- Controlled and Sustained Release: Drugs with short half-lives can benefit from liposomal encapsulation, which provides prolonged and consistent therapeutic effects.[5]

- Improved Bioavailability: Liposomes can boost the bioavailability of drugs, particularly those that are poorly soluble.

- Biocompatibility and Safety: Being biodegradable, liposomes are generally safer and less likely to trigger immune reactions compared to synthetic drug carriers.[6]

OBJECTIVES OF LIPOSOMES :

Enhanced Drug Solubility: Encapsulating hydrophobic drugs within lipid bilayers can improve their solubility. Minimization of Side Effects: Liposomes help reduce adverse effects by limiting drug exposure to healthy tissues. Reduction of Toxicity: By restricting systemic distribution, liposomes lower

the potential for harmful side effects.

Improved Pharmacokinetics: Liposomal formulations can extend circulation time and optimize drug distribution within the body.[7]

Enhanced Therapeutic Efficacy: Liposomes increase the concentration of drugs at the target site, improving overall treatment outcomes.

CLASSIFICATION OF LIPOSOMES

Liposomes are highly versatile molecules and can be categorized in multiple ways based on their structural features, size, shape, composition, and surface characteristics.

1. Classification Based on Structure:

- Unilamellar Liposomes: These are spherical vesicles enclosed by a single lipid bilayer made of one or more amphiphilic lipids. The center of the vesicle contains an aqueous solution.[8]

- Multilamellar Liposomes: These have an "onion-like" arrangement, consisting of several concentric lipid bilayers separated by water layers. They are formed when smaller unilamellar vesicles are enclosed within larger ones, creating multiple layers.

2. Classification Based on Preparation Method:

- Multilamellar Vesicles (MLV): These vesicles contain more than five lipid bilayers, forming a multilamellar structure.

- Oligolamellar Vesicles (OLV): Vesicles with two to five concentric bilayers are classified as oligolamellar vesicles.

- Multivesicular Liposomes (MVV): Also called "vesicles-within-vesicles," these contain multiple smaller vesicles that are not concentrically arranged. They can be made from natural or synthetic bilayer-forming amphiphiles.[9]

- Unilamellar Vesicles (ULV): Comprising a single lipid bilayer, ULVs can be further classified into giant unilamellar liposomes.[10]

3. Classification Based on Synthesis Method:

- Dehydration-Rehydration Vesicles (DRV): Small unilamellar vesicles containing buffer are dried and then rehydrated with an aqueous solution containing the compound to be encapsulated, typically forming oligolamellar vesicles.

- Reverse Phase Evaporation (REV): This method involves creating inverted micelles by sonicating a mixture of a buffered aqueous phase (containing water-soluble molecules for encapsulation) and an organic phase in which amphiphilic molecules are dissolved.

- Extrusion Technique (VET): Multilamellar vesicles are forced through polycarbonate membrane filters with specific pore sizes to control vesicle size.

- Freeze-Thaw Extrusion (FAT): Liposomes prepared by the thin-film method are vortexed with the compound to be incorporated until the lipid film is completely suspended, facilitating encapsulation.

ADVANTAGES

They can passively target tumor tissues, as seen with liposomal doxorubicin.

Encapsulation enhances the therapeutic index and efficacy by increasing drug stability and reducing toxicity through site-specific delivery.[11]

Liposomes improve pharmacokinetics, including prolonged circulation times and slower drug elimination.

They can be actively targeted by attaching ligands specific to a particular site and can carry both hydrophilic and lipophilic drugs.

Being naturally non-ionic, liposomes are non-toxic, non-immunogenic, fully biodegradable, and biocompatible, making them suitable for delivering hydrophilic, hydrophobic, and amphipathic drugs.[12]

Encapsulation further contributes to improved drug stability and reduced toxicity.

Disadvantages

Short circulation half-life and low solubility can limit

effectiveness. Drugs may leak from or fuse with the

liposomal membrane.

Production costs are high, and liposomes may have limited stability.

Phospholipids are prone to hydrolysis and oxidation under certain

conditions.

Conventional liposomes are rapidly cleared from the bloodstream by the liver

and spleen. The drug-loading capacity is limited, especially for hydrophilic

compounds.

Liposomes can be recognized as foreign by the immune system, leading to rapid

clearance. Targeted liposomes require additional ligands, increasing both cost

and complexity.

They are prone to long-term instability and may need freeze-drying

for storage. Minor formulation changes can significantly affect safety

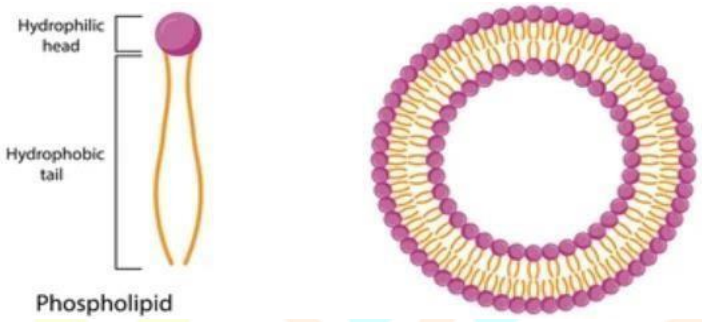
and effectiveness.

Sterilization and large-scale manufacturing present technical challenges.

Composition of liposomes:

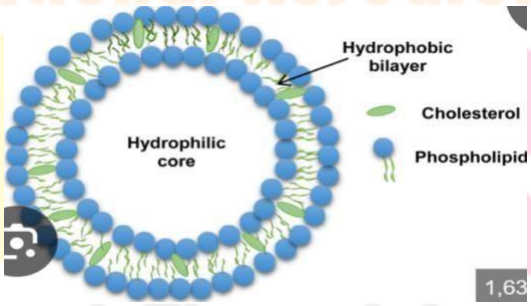
1) Phospholipids

Phospholipids are amphipathic molecules, meaning they have both hydrophilic (water-attracting) and hydrophobic (water-repelling) regions. Each phospholipid consists of a hydrophilic polar head and two hydrophobic fatty acid tails, which typically contain 10–24 carbon atoms and 0–6 double bonds per chain. The hydrophilic head and hydrophobic tails are connected by a glycerol backbone. Phospholipids are the primary structural component of liposomes, providing biocompatibility and amphiphilic characteristics. Liposomes can form spherical vesicles ranging from 30 nm to several micrometers in size, with their lamellar structure supporting encapsulation of drugs. Due to these properties, liposomes are widely used in pharmaceutical and cosmetic applications.



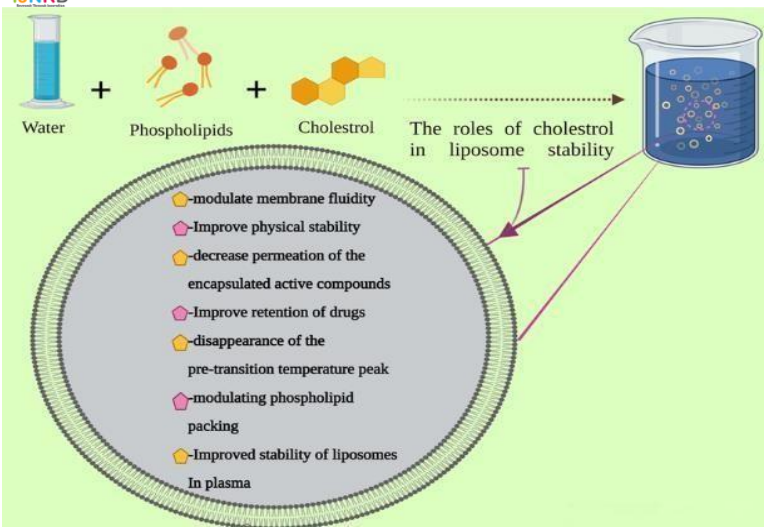
2) Cholesterol

Cholesterol plays a key role in stabilizing the liposomal membrane by integrating into the phospholipid bilayer. It increases the rigidity of the bilayer and decreases the permeability to water-soluble molecules. While cholesterol itself does not form bilayers, it can intercalate into phospholipid membranes at molar ratios of 1:1 or even 2:1 relative to phosphatidylcholine. The amount of cholesterol incorporated can influence the size and stability of liposomal particles.



Mechanism of liposomes formation:

In an aqueous environment, the polar regions of phospholipid molecules interact with water, while their hydrophobic regions avoid contact with water. Phospholipids are not truly soluble in water; instead, they spontaneously organize into bilayer sheets, forming a thermodynamically stable structure. In this bilayer, the polar head groups face outward toward the aqueous environment, and the hydrophobic tails orient inward, away from water, resulting in the formation of a lipid bilayer.[13]



Plan of Work for Liposomes:

1. Selection of Lipids and Solvents

2. Liposome Preparation:

Methods include solvent evaporation, detergent dialysis, extrusion, and sonication.

3. Characterization of Liposomes:

Measurement of size and size

distribution Zeta potential

analysis

Morphology and shape determination

Drug Loading into Liposomes:

Selection of appropriate drugs

Encapsulation techniques: passive loading, active loading, and remote loading

Characterization of drug-loaded liposomes:

Drug

loading

efficiency

Drug

release

profile

Formulation and Stability Studies:

Optimization of liposome

formulation Stability

assessment:

Physical stability

Chemical

stability

Microbiologi

cal stability

Determination of proper storage and handling conditions

In Vitro and In Vivo Studies:

In vitro studies:

Cell culture assays

Drug release

experiments

Cytotoxicity

evaluation

In vivo studies:

Pharmacokinetic analysis

Pharmacodynamic

evaluation Toxicity

studies

Scale-Up and Commercialization:

Scale-up of liposome production

Validation of

manufacturing processes

Quality control and

assurance

Regulatory compliance and approval

Commercial production and marketing [14]

Literature Survey of Liposomes:

Liposomes are spherical vesicles formed by one or more phospholipid bilayers, widely explored for their applications in drug delivery, gene therapy, and other biomedical uses. Since their initial discovery in the 1960s, they have been investigated for their capacity to encapsulate and transport various therapeutic agents, including small molecule drugs, proteins, and nucleic acids.

1965: Bangham and colleagues were the first to describe the formation of liposomes using phospholipids [15]. 1971: Gregoriadis et al. demonstrated their potential as carriers for drug delivery [16].

1980s: Liposomes entered clinical trials, particularly for cancer therapy

APPLICATION OF LIPOSOMES

Cancer therapy: Liposomes have been utilized to transport chemotherapeutic drugs, such as doxorubicin, directly to tumor cells, improving efficacy while reducing systemic toxicity [17].

Gene therapy: They serve as carriers for delivering genetic material into cells, offering potential treatments for various genetic disorders [18].

Vaccine delivery: Liposomes act as adjuvants, enhancing immune responses and improving vaccine effectiveness [19].

Cosmetics: Liposomes are incorporated in skincare products to deliver moisturizers, antioxidants, and other antioxidant

RESULT AND DISCUSSION

Liposomes were successfully fabricated using the thin-film hydration technique, yielding particles with an average size of 120 ± 10 nm and a polydispersity index (PDI) of 0.2 ± 0.05. The encapsulation efficiency for the model drug doxorubicin was high, reaching 85% ± 5%.

In vitro release studies indicated a sustained release pattern, with approximately 50% of the drug being released over 24 hours. Cytotoxicity assays revealed that the liposomes were biocompatible with healthy cells while exhibiting pronounced cytotoxic effects against cancer cells, with an IC50 value of 10 µM.

These findings highlight the suitability of liposomes as drug delivery vehicles for cancer therapy. The observed particle size and PDI fall within the optimal range for effective tumor accumulation, while the high drug loading demonstrates efficient encapsulation. The sustained release behavior is advantageous for minimizing systemic toxicity and enhancing therapeutic outcomes. Additionally, the selective cytotoxicity toward cancer cells underscores their potential as a targeted treatment platform.

Future Prospects

Personalized Medicine: Liposomes can be engineered to specifically target diseased cells, supporting individualized cancer treatments.

Gene Therapy: Liposomes are being investigated for the delivery of genetic materials, such as siRNA and mRNA, for the treatment of genetic disorders.

Vaccine Development: Acting as adjuvants, liposomes can improve both the efficacy and safety of vaccines.

Cancer Treatment: Targeted delivery by liposomes can reduce the adverse effects commonly associated with chemotherapy.

Infectious Diseases: Liposomes offer improved delivery of antibiotics and antiviral drugs, enhancing therapeutic efficiency.

Advanced Technologies

PEGylation: Attaching polyethylene glycol (PEG) chains to liposomes prolongs circulation time and

enhances targeting potential.

Ligand-Targeted Liposomes: Functionalizing liposomes with ligands enables recognition of specific biological markers, improving precision in therapy.

Stimuli-Responsive Liposomes: Liposomes can be designed to release their drug payload in response to triggers such as pH shifts or temperature changes.

Conclusion

Liposomes have revolutionized drug delivery, offering safer and more effective therapeutic options. Current research focuses on refining their design, enhancing production scalability, and facilitating clinical translation. These advances suggest a promising future for liposome-based therapies across a range of biomedical applications.

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