The Bioscan AN INTERNATIONAL QUARTERLY JOURNAL OF LIFE SCIENCES 21(2): S.I (2), 1404-1427, 2026 www.thebioscan.com

LIPOSOME-BASED DRUG DELIVERY SYSTEMS: FORMULATION, CHARACTERIZATION AND BIOMEDICAL APPLICATIONS

Dr. Vidyavathi M[1], Kondamuri Pushpalatha* [1,2].

[1]Institute of Pharmaceutical Technology, Sri Padmavati Mahila Visvavidyalayam, Tirupati, Andhra Pradesh-517502, India.

[2]School of Pharmacy, Aditya University, Surampalem, Andhra Pradesh -533437, India.

***Corresponding Author address:**

Kondamuri Pushpalatha,

Research scholar,

Institute of Pharmaceutical Technology,

Sri Padmavati Mahila Visvavidyalayam,

Tirupati, Andhra Pradesh-517502, India

Email: kondamuripushpalatha@gmail.com

DOI: https://doi.org/10.63001/tbs.2026.v21.i02.S.I(2).pp1404-1427

KEYWORDS
Liposomes, Drug Delivery, Nanomedicine , Phospholipid bilayer, Targeted Therapy, Gene Therapy

Received on:
29-04-2026
Accepted on:
17-05-2026
Published on:
27-05-2026

Abstract

Liposomes are small, spherical shaped vesicles made up of phospholipid bilayer surrounding an aqueous core. Because they are capable of entrapping both hydrophilic and lipophilic substances. They are naturally compatible with biological system, so they became important part in modern drug delivery systems. Liposomes are discovered in the 1960s by Alen Behngam and have since significantly evolved. Scientist have sophisticated in many ways, turning them from simple laboratory tool to carriers for targeted delivery and nano medicine. This review discusses the classification, structure and composition of liposomes, methods of preparation, characterization techniques and various applications across various fields. It also gives an analysis about surface modification approaches like stimuli-responsive formulations, surface modification approaches to overcome existing limitations. By combining the fundamental principles with modern development. This review aims to present a broad point on liposomal technologies and serve as valuable area for scientists and healthcare professional who involved in development of modern or targeted drug delivery.

INTRODUCTION

Liposomes are vesicles that exist tiny sacs created through spontaneously organising fat-based double membranes. Initially, it was explained by Alec Bangham along with their associates in 1961 during their research about fat-derived dispersions[1].

The discovery marked a significant turning point in pharmaceutical drug delivery research. These innovative vesicular systems closely resemble the structural characteristics of biological membrane, which makes them especially suitable for carrying a wide spectrum of therapeutic and diagnostic agents. The amphiphilic nature of phospholipids having hydrophobic tails and hydrophilic head groups are fundamental to the assembly of these vesicles. This molecular arrangement enables liposomes to encapsulate hydrophilic drugs within their internal aqueous compartment while embedding lipophilic drugs within the surrounding bilayer. Apart from functioning as drug carriers, liposomes also play an important role in protecting therapeutic molecule from early enzymatic breakdown. They modify the drug's distribution pattern within the body, which in turn helps to reduce systemic adverse effects[2,3]. In many formulations, liposomes are specifically engineered to enable slow and regulated release of the encapsulated compound. These combined features greatly improve the overall safety profile and enhance the therapeutic performance of the loaded medication[4]

At first, the promise of liposomes in medicine appeared limited because they were unstable and were cleared quickly from circulation. With continued experimentation, researchers began modifying the lipid ingredients, refining the preparation process, and adding surface coatings such as poly ethylene glycol (PEG) to improve their stability. These refinements gradually turned liposomes from simple laboratory models into dependable nanocarriers for drug delivery. The steady progress in this field has shaped the direction of modern pharmaceutics, giving rise to several clinically approved liposomal formulations. By carrying drugs mainly to the tissues that need them, liposomes increase absorption where it matters most and reduce harmful effects elsewhere. For this reason, they have become an important part of today's movement forward precision and targeted therapy[5,6].

In nanomedicine, formulation factors such as size, charge, lipid composition, and surface modification play a crucial role in clinical performance of liposomes. These affect biological mechanisms such as immune evasion, stability, biodistribution and drug release. Thus, establishing the connection between formulation and biological constraints, such as clearance, stability and manufacturability is important to enhance clinical translation of liposomes

[7,8]. This review spans publications over the past two decades, but focuses on clinically and advanced stage liposome formulations. The literature was reviewed for its insights into formulation, biological implications and translational potential

Advantages:

- **Biocompatibility and biodegradability:** They are made up of biological lipids, so they are naturally accepted by the body and they are decomposable, hence prolonged accumulation and adverse effects are reduced [1,2].
- **Targeted and controlled drug release:** Liposomes can facilitate targeted delivery through modification of surface by using binding molecules, enables active targeting and structural configuration permits prolonged and regulated drug release, hence dosing frequency is reduced and enhances therapeutic efficiency [29,30].
- **Reduced Toxicity and improved pharmacokinetics:** Entrapment of drug in the lipid bilayers gives protection to the sensitive drugs from the breakdown, thereby reducing systemic exposure, resulting in enhanced pharmacokinetic properties and reduced toxic effects [3,4].
- **Encapsulation versatility:** Liposomes are able to enclose both hydrophilic and lipophilic drugs in the bilayer, which can be suitable for wide range therapeutic substances [5,6,30]

Limitations:

- **Stability Issues:** Liposomes are having structural instability such as, clumping and fusion and molecular degradation like peroxidation, hydrolysis, results in leakage of drug from the vesicles or decomposition in its shelf life [31,32].
- **High production cost:** Liposome production needs exact dimensions and aseptic environment so their production cost is more complex and expensive [33].
- **Batch to Batch Variability:** The standards of physical properties like size, shape and encapsulation efficiency in the largescale production is a major difficulty because of the rigorous quality control [34].
- **Immune clearance:** Regardless of improvements like PEG Modification, Reticulo-endothelial system, identifies and eliminates the liposomes, so the therapeutic efficacy and time of systemic circulation may be restricted [35].

These challenges with liposomes. Such as stability, rapid clearance and batch-to-batch variability, are related to the formulation. For example, liposomal size and surface modification affect reticuloendothelial system (RES) clearance, while lipid composition and cholesterol content affect membrane stability and drug leakage. As such, fine-tuning these factors is essential to enhance the translatability of the liposomes

STRUCTURE AND COMPOSITION

Liposomes can be made with biological or synthetic compounds and it can encapsulate both lipophilic and hydrophilic drugs. They are dual in nature because it having one hydrophilic polar segment (eg., phosphotidyl choline, phosphotidyl ethanol amine, phosphotidyl glycerol, phosphotidyl serine and a one lipophilic non-polar segment i.e., a pair of lipid-based hydrocarbon chains[5] , as shown in Fig.1. The selection of particular lipid types significantly affects the vesicle's structural characteristics, like as electrical potential of bilayer flexibility, and transition of phase, temperature. For example, lipid molecules containing saturated fatty hydrocarbon chains are likely to create increasingly rigid bilayers, whereas those with double-bonded chains lead to greater flexible membranes[19]. Cholesterol is frequently included within the fat-based membrane, generally in concentrations varying between 30-50%. Its inclusion strengthens bilayer durability, decreases leakage for hydrophilic compounds, as well as prevents fat solidification, thus boosting the general strength of the vesicle-based structure[6,9]

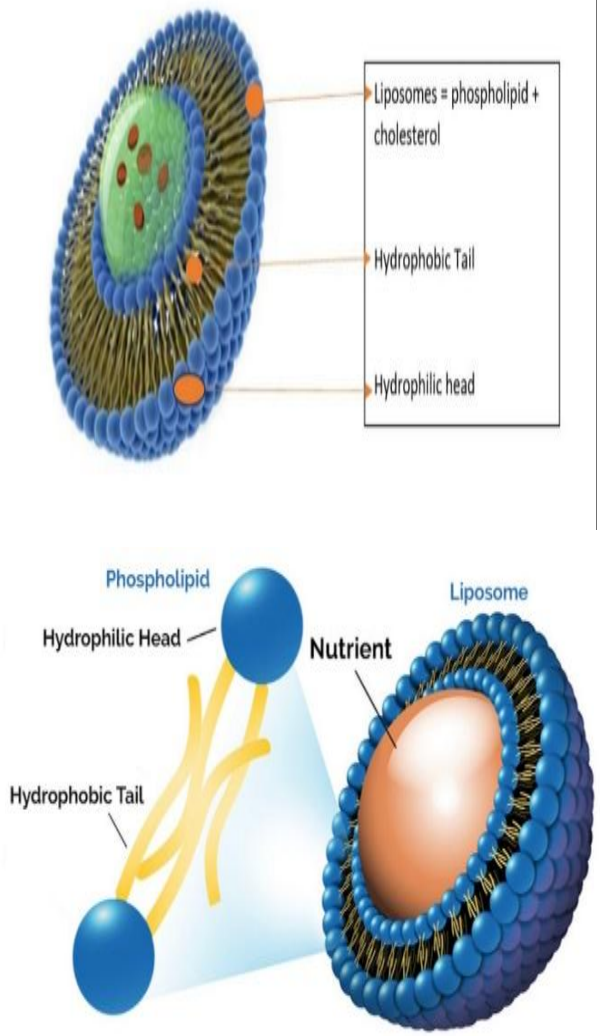

Fig. 1: Structural components of design[9]

CLASSIFICATION OF LIPOSOMES:[2]

Liposomes may be generally categorised depending upon their physical characteristics, such as layer arrangement and dimension, as well as functionality via their modification of composition or particular alterations for specific uses, and they are shown in Fig.2.

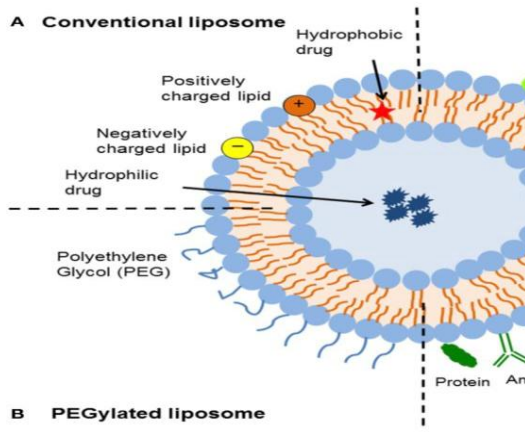

Fig. 2: Schematic representation of the different types of liposomes [10]

1. **Based on Lamellarity and size:**

- **Unilamellar vesicles:** These liposomes are defined by one solitary phospholipid bilayer surrounding a water-based interior. They are commonly employed to entrap both lipophilic and lipophobic therapeutic compounds
    - **Small Unilamellar Vesicles(SUV):** Usually have a width smaller than 100nm, frequently ranging from 20-50nm [11]. small size enables improved entry into specific tissues and may affect the duration of the blood flow and absorption mechanism
    - **Large Unilamellar Vesicles(LUV)**[13]: These vesicles typically exhibit sizes larger than 100nm. Large unilamellar vesicles have a greater aqueous core, rendering them appropriate for greater amounts of lipophilic drugs. They are often created by using the membrane-passage method or the removal of surfactant techniques.
- **Multilamellar Vesicles**[12]**:** They consist of several layered lipid membranes similar to a layered-sphere structure, with water-based partitions divided by lipid layers. Multilamellar Vesicles are generally greater compared to unilamellar vesicles, commonly more than 500nm up to a few microns, and provide large entrapment potential, especially for lipophilic drugs. Inside, their increased dimension may cause fast removal from the body.
- **Multivesicular Vesicles**[2,13]**:** They differ from multilamellar vesicles, such as liposomes include several

irregularly arranged water-based partitions inside a single large liposome divided by non-uniform phospholipid bilayers. Multivesicular vesicles are generally bigger and are intended for prolonged release of therapeutic compounds, frequently employed for site-specific release uses, because of their distinctive internal arrangement and extended delivery rate profiles

2. **Based on composition and surface modification:**

- **Conventional Liposomes:** It is made mainly from biological lipid molecules along with cholesterol without particular targeting binding agents or extended–circulating characteristics[17]

- **PEGylated Liposomes: Liposomes are altered using** PEG strands on their surface. PEG Coating forms a water-attracting barrier surrounding the vesicle, lowering protein tagging from plasma proteins and later absorption through the reticuloendothelial system (RES), thus extending its biological half-life [21]

- **Ligand–Targeted Liposomes:** Such vesicles contain particular binding molecules like immunoglobulins, peptides, nucleic acid binders, and sugars linked to their surface, which identify and adhere to targeted cell-surface proteins or target markers on intended biological cells such as tumour cells. This mechanism allows targeted delivery of drug[23]

- **Cationic Liposomes:** It contains cationic lipid molecules like DOTAP, DOPE, which can bind to electronegative genetic biomolecules like DNA, RNA through electrostatic force for the application of genetic transfer, along with this it may also binds with anionic cellular membrane walls due to its cationic potential[22]

- **Stimuli-Responsive Liposomes:** These liposomes are mostly used to discharge the entrapped content. This discharge may occur by the effect of internal factors like pH, Enzymatic action, Oxidation-reduction balance or the external factors like temperature, radiation, high frequency sound waves. Such a mechanism enables the possibility of regulated as well as drug release of site-specific therapeutic agents at the location of the pathological area[32].

This accurate lipidic structure carrier dimension, surface potential as well as the selected formulation technique represent essential factors which together control the entrapment effectiveness, Durability, as well as drug release in the body association with liposome-based preparations[12,29].

METHOD OF PREPARATION

The production of lipid-based carriers includes different approaches; every method provides specific benefits with respect to expandability, entrapment, effectiveness, as well as regulation with respect to physical and chemical characteristics. The selection of procedure commonly relies upon the category of lipid, encapsulated Drug, size of lipid vesicle, layer structure, and targeted purpose.

1. **Thin film hydration method:** This is also called as Bengham method. This method continued to be one of the most commonly used and basic techniques in the preparation of liposome [1,13] Method is shown in fig.3.

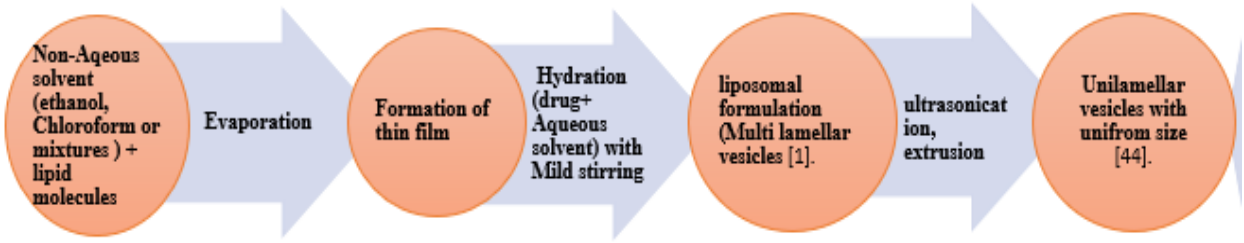

Fig. 3: Preparation of Liposome by thin film hydration technique

2. **Reverse-Phase Evaporation Technique**[2,6,13]: This method is especially efficient in attaining significant entrapment of water-soluble drugs. Method is shown in fig.4.

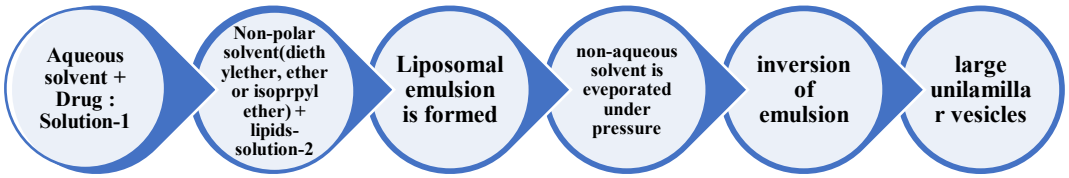

Fig. 4: Preparation of Liposomes by Reverse-Phase Evaporation Technique

This approach is noted because of its capacity to encapsulate a significant proportion of hydrophilic substances, rendering it extremely effective for hydrophilic substances; however, remaining non-aqueous solvent could be a problem.

3. **Ethanol Injection and Detergent Removal:**

Ethanol Injection Method[14]**:** It is an easy method, commonly employed in limited-scale preparations and for producing small unilamellar vesicles and the method is shown in fig.5

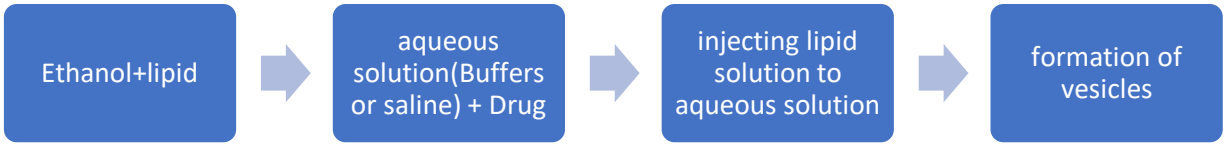

Fig. 5: Preparation of Liposome by Ethanol Injection method.

This method can result in relatively low encapsulation efficiencies for hydrophilic drugs and may produce a broad size distribution, requiring subsequent sizing steps.

- **Detergent Removal (Dialysis or Gel filtration):** This approach depends on the slow elimination of surfactants extracted from blended aggregates made of phospholipids, in addition to surfactants. Phospholipids and surfactants are initially combined to produce aggregates that dissolve the drug. Through dialysis, gel filtration, Chromatography, or hydrophobic resin adsorption, detergent slowly reaches to critical micellar

concentration and then spontaneously forms as liposomes. The present method enables effective regulation of liposome dimensions, layer structure, and it proves specifically beneficial to integrating lipid bilayer polypeptides into lipid vesicles [38].

4. **Mechanical Dispersion Methods:** These techniques consist of applying physical force to phospholipid mixtures to produce lipid vesicles. Usually employed with the purpose of decreasing size and uniformity. This can be achieved by
   - **Sonication**[15]**:** This technique uses ultrasound waves to disintegrate multilamellar vesicles into small unilamellar vesicles. This method uses high-frequency sound waves (ultrasound) to disrupt MLVs and form SUVs. To achieve the disintegration, probe and bath sonication techniques are used. This technique is effective in generating small lamellar vesicles. Sonication may cause degradation of phospholipids, called oxidation, and irregular distribution of temperature, possibly altering the stability of therapeutic agents.
   - **Extrusion:** It includes transferring pre-prepared multilamellar vesicles derived from the thin-film hydration technique, continuously using rigid polymer layers having specific opening diameters like 50- 400 nanometres. That machine-assisted technique decreases the size of liposomes and yields consistent batches composed of unilamellar vesicles. This is a frequently employed technique intended for producing liposomes for the purpose of healthcare-related applications because of their expandability, consistency, and capability to generate aseptic preparations[13,48-51].
   - **French Press**: It includes propelling a phospholipid mixture across a narrow orifice subjected to elevated pressure. The frictional stress produced led to the development of minute, consistent lipid vesicles. It is an effective method for producing SUVs and LUVs with high encapsulation efficiency, but it can be a batch process and may generate heat[52].
   - **High-Pressure Homogenization:** Similar to the French press, this method uses high pressure to force lipid dispersions through a narrow

gap, creating intense shear forces that break down larger vesicles into smaller, more uniform liposomes. It is suitable for large-scale production and can produce stable formulations [49,51].

5. **Microfluidics and supercritical fluid methods:** These methods are the most advanced
   - **Microfluidics:** It is employed with exactly designed micro pathways to regulate the fast and consistent blending of lipid-based mixtures with hydrophilic phases. This extremely regulated combining setting enables for exact regulation of the kinetics of vesicle creation, resulting in the generation of extremely consistent vesicles with narrow dimensions, frequently in the nanometre scale. Microfluidic methods are progressively favoured for clinical–grade preparations because of their accuracy, expandability, and capacity to create sterile preparations with limited lot—to-lot inconsistency[52]
   - **Supercritical Fluid method:** Developing methods such as supercritical anti-solvent or fast expansion of supercritical mixtures provides a solvent-free or minimal amount of solvent substitutes for vesicle formulation. These techniques exploit the distinct characteristics of supercritical substances (such as carbon dioxide) as dissolving agents or precipitating agents to precipitate lipids and create liposomes within well-ordered circumstances, providing benefits in aspects of cleanness, lowered non-aqueous solution residues, and ecological sustainability, although encouraging, they are yet mostly in the experimental stage for industrial drug manufacturing[16,35-39].

CHARACTERIZATION

Characterization of liposomes is important to know the structure, size, shape, consistency, and stability of the formed vesicles, and also to compare the relationship between in vitro and in vivo behaviour. Based on the characterizations of the liposomes, we may be able to analyze the effect of the safety and therapeutic efficacy of the liposomes.

1. Size and Zeta Potential [41,50]**:** These are essential characterizations for nano particle systems, affecting absorption, dispersion and stability.

- **Dynamic Light Scattering:** This is commonly used to determine

the vesicle diameter by examining the differences in diffused illumination generated by particle Brownian motion of nano sized particles in suspension. Dynamic Light Scattering offers data regarding mean particle dimension (Z-mean) and polydispersity Index.

- **Particle Tracking Analysis:** It provides an analysis of individual particles and provides the particle distribution and size and number of particles. It can also identify small groups and gives an optical observation of particle movement[53].
- **Electron Microscopy:** Methods For the determination of shape, size and structure and their interactions can be studies by using electron microscopy like Transmission Electron microscopy, Scanning Electron Microscopy or Cryogenic imaging. Cryogenic imaging gives vesicle dimensions along with image and also provide detailed information about structure of phospholipid bilayer[53].
- **Zeta Potential:** Zeta potential determined by using Electrophoretic light Scattering. It reflects the surface voltage on the surface of liposome. It is an essential indicator of colloidal stability. The zetapotential (total charge of surface) usually exceeding ± 30 millivolts indicates a strong electric repelling force among liposome, that avoids clumping and enhances long term stability of liposomes[11]
- **Entrapment Efficiency:** This is used to measure the quantity of substance entrapped in the lipid vesicle. This includes isolation of un entrapped drug from the liposomes, the isolation can be done by using various methods such as ultracentrifugation, gel filtration chromatography (Sephadex cartridge), membrane diffusion or microfiltration. The quantity of drug within the lipid vesicle (by disruption of vesicle) or the unbounded drug content can be measured by instrumental methods like ultraviolet-visible spectrophotometer, High

efficiency liquid chromatography or fluorescence assays[60].

% Entrapment Efficiency = Total amount of drug- Free drug in the supernatant/ Total amount of drug * 100

- **Drug loading**: It is denoted the weight proportion of the drug inside the lipid vesicle. This measures the concentration of drug per individual mass[20]

Drug Loading = Weight of the drug in Liposomes/ Weight of total drug * 100

2. Bilayer integrity and stability[46]: These are Conducted to evaluate structural integrity and stability This can be evaluated by following methods

- **Differential Scanning Calorimetry[49-51]:** Differential Scanning Calorimetry (DSC) is employed to measure the thermal responses associated with phase transitions occurring within the phospholipid bilayer. The main transition temperature and the degree of cooperativity observed during this shift provide valuable information into the fluidity and structural organization of the phospholipid bilayer. These characteristics influenced by factors such as the type of fatty acid in the layer, proportion of cholesterol, and the nature of drug-phospholipid interactions. Any alterations in the transition temperature or the appearance of secondary thermal signals may indicate disturbances in bilayer integrity or phase separation induced by the entrapped drug.
- **Fluorescence Assay[45]:** This method is primarily based on the entrapment of self-quenching fluorescent markers, such as carboxy fluorescein or calcein at high concentrations within liposomes. When the encapsulated dye diffuses into surrounding medium, dilution alleviates the self-quenching effect, resulting in a distinct and quantifiable increase in fluorescence intensity(dequenching). The observed fluorescence enhancement that serves as sensitive parameter for evaluating membrane integrity and overall stability.
- **Physical Stability Test:** The physical stability of liposomes

in its shelf life can be determined by evaluating the vesicle diameter, polydispersity index, and zetapotential. Techniques employed for the determination of vesicle aggregation and sedimentation are Dynamic light scattering and optical density analysis[56].

- **Chemical Stability Tests[55,58]:** Chemical stability is determined to know extent of lipid and drug degradation in the formulation. Lipids are mostly prone to deterioration because of hydrolytic cleavages of ester linkages. To evaluate degradation analytics are used, they are HPLC (High Performance Liquid Chromatography), TLC (Thin Layer Chromatography) and GC (Gas Chromatography). These methods are also used to identify lipid oxidation and measuring the integrity of entrapped drug during and after formulation.
- **In-vitro Release profiles[42-44]:** This is conducted to know drug release from the lipid vesicle Typical techniques comprise membrane diffusion bags, Diffusion cells (example: Franz diffusion cell), or Flow-through Systems. The liposomes are placed onto the semipermeable membrane, under sink conditions, drug release will be calculated. It is determined by using UV-Visible Spectroscopy and High-Performance Liquid Chromatography.
- The liberation rate profiles may be affected by lipid composition, Cholesterol level, interactions of drug and lipid, as well as environmental stimuli such as temperature, pH, for trigger-sensitive lipid vesicles. Quantitative models like zero-order, first-order, higuchi-type, and korsmeyer-peppas equations are frequently used to interpret drug release information and comprehend the fundamental processes (eg, Such as diffusion through lipid membrane, degradation of the delivery system).

Other Advanced Characterization Techniques:

- **Fourier-Transform Infrared Spectroscopy[45]:** it is utilized for detecting chemical moieties as well as examining intermolecular

associations inside the lipid vesicle, verifying lipid composition, drug entrapment, along with possible interaction of drug and lipid through the examination of changes in distinctive spectral peaks .

- **Small–Angle X-ray Scattering and Small–Angle Neutron Scattering[55]:** These methods offer in-depth data regarding the inner layer structure, distance between layers, as well as the general morphology of lipid vesicles in suspension. These are especially valuable in examining the organization of phospholipid bilayers as well as entrapped compounds.
- **Atomic Force Microscopy**: Atomic Force microscopy provides high-resolution surface visuals of liposomes, allowing the observation of each particle, their dimensions, shape and the outer structure. It may employ to examine their association with different cells[47].
- **Nuclear Magnetic Resonance Spectroscopy[56]:** It may be employed to investigate the atomic–level motion of fatty molecules inside the double layer, evaluate the entrapment of the drug, and monitor the release of the drug. Nuclear magnetic resonance is particularly useful in examining the lipid phase properties as well as interactions between lipid and drug within the bilayer.
- **Cryo-Electron Tomography:** a sophisticated variant of cryo-electron microscopy, which enables three-dimensional modelling of lipid vesicles offering exceptional resolution regarding their inner layer structure, as well as the spatial arrangement of entrapped substance inside the particles[57].
- **Inductively coupled plasma mass spectroscopy:** it is used for the measurement of ultra-trace metals, which may be significant when metal-based compounds or imaging enhancers are entrapped inside lipid vesicles or for identifying contaminants originating in the process of manufacturing[58].
- **Circular Dichroism Spectroscopy:** When protein molecules are unified in the liposomes, the secondary

configuration of the proteins is analysed by using Circular Dichroism Spectroscopy (eg, site-specific transport or immunogenic components). Circular dichroism spectroscopy may evaluate their structural stability and entrapment [59].

- **Differential Configuration:** A traditional technique for isolating lipid vesicles according to their diameter and density, frequently employed alongside alternative dimension-measuring methods or too refining lipid vesicle formulation[59].
- **Field-Flow Fractionation:** It is a non-disruptive isolation method, which is capable of isolating lipid vesicles according to dimension, shape, as well as density, offering high-resolution dimensional profiles and enabling segmentation of heterogeneous mixtures without disrupting the liposomes [59].

BIOMEDICAL APPLICATIONS:

1. **Drug delivery:** Liposomes have phospholipid bilayers in their composition. Hence, it can increase the efficacy and stability of the drugs by enhancing the solubility and permitting the delivery of drugs to the targeted site like cells and organs[18-20]. A notable milestone within this field is Doxil(polyethylene glycol-coated lipid vesicle, doxorubicin), the first FDA-authorized lipid vesicle-based medication. Its polyethylene glycol layer offers immune–evasive features extending the time of circulation and lowering the cardiotoxicity frequently linked to unencapsulated doxorubicin in oncology patients[4,16]. Additional remarkable cases include Myocet(non-PEG-Coated lipid vesicle doxorubicin) and Daunoxome (lipid vesicle daunorubicin). Other notable examples include Myocet® (non-PEGylated liposomal doxorubicin) and DaunoXome® (liposomal daunorubicin) [20].
2. **Vaccine delivery:** Lipid vesicles function as powerful immune enhancers or carriers within immunization preparations, significantly improving substantially improving antigen absorption by immune-presenting cells and triggering strong antibody-mediated immunological reactions[21]. Their role became especially important during the rapid development of mRNA COVID-19 Vaccines (e.g., Pfizer-BioNTech and Moderna), where lipid-based nanoparticles (which are distinct from classical liposomes but share

similar lipid-based delivery principles) revolutionized vaccine delivery by protecting the fragile mRNA and helping it enter into cells effectively[27].

3. **Gene Therapy:** Liposomes with a cationic nature have developed into potential non-viral-based carriers for genetic transfer. The polar head of the bilayer have strong affinity for non-polar genetic materials such as DNA and RNA, leading to the formation of stable lipid-nucleic acids complexes. These assemblies facilitate cellular uptake and enable the subsequent escape of genetic material from endosomal compartments. It also provides various advantages like decreased immune activation and easy to manufacturing relevant to achieve efficient gene transfer[18,19,33].
4. **Antimicrobial therapy:** Liposomal formulation assists in overcoming defence mechanisms through modifying ADME properties and biological dispersions, thereby it enhances the bioavailability and decreases the toxicity of anti-microbial substances[41,47]. Ambisome (Vesicular polyene antifungal B) is widely accepted and significant therapy for mycotic diseases, with decreased kidney toxicity when compared with traditional antifungal B preparations[26,36,37].
5. **Diagnostic imaging:** Radio labelled or Fluorescent labelled liposomes are used in imaging the malignancy and heart-related ailments. It may bind specifically to particular biomarkers allows direct tracking of biological dispersion illness, imaging and evaluation of therapeutic activity[36].

A number of liposomal formulations have effectively moved from research to clinical practice, highlighting the significance of liposomal nanocarriers. For instance, Doxil® (PEGylated liposomal doxorubilicin) is the first FDA-approved nanomedicine and used to treat ovarian cancer and Kaposi's sarcoma due to its longer circulation time and lower cardiotoxicity [4,23]. Likewise, AmBisome® (liposomal amphotericin B) is a well-accepted antifungal agent that exhibit much lower renal toxicity than free amphotericin B [26].

Other notable liposomal products include DaunoXome® (liposomal daunorubicin) for kaposi's sarcoma and Myocet® (non-PEGylated liposomal doxorubicin) for cancer treatment with reduced cardiotoxicity [22]. These formulations demonstrate the benefits of liposomal entrapment in terms of the

therapeutic index through altered pharmacokinetics and biodistribution. However, the clinical application of liposomes is limited by their biological performance, production scale-up and storage stability. However, although PEGylation increases the circulation time, it may decreases cellular uptake (the PEG dilemma). As such, achieving a balance between formulation and clinical needs is essential in liposomal drug development.

Table 1: Clinically approved liposomal formulations and their therapeutic applications

Product	Drug	Type	Indication	Key Advantage	Limitation	Reference
Doxil®	Doxorubicin	PEGylated liposome	Cancer	Reduced Cardiotoxicity	Hand-foot syndrome	65,66
AmBisome®	Amphotericin B	liposome	Fungal infections	Reduced nephro toxicity	High cost	19
DaunoXome®	Daunorubicin	liposome	Kaposi's Sarcoma	Improved PK	Limited Use	20
Myocet®	Doxorubicin	Non-PEGylated liposome	Cancer	Reduced toxicity	Shorter circulation	26

FUTURE PROSPECTIVES

- **Artificial Intelligence and Computational Design:** Developing enhanced vesicles using Predictive algorithms[62]
- **Personalized Medicine:** Lipid vesicles are developed by aligning with genomic and biochemical characteristics[64]
- **Multifunctional Liposomes:** Liposomal systems can be integrated with additional nano-

carriers like Branched polymers, colloidal gold particles[63].

- **3D Printed Liposomes and Bio printing**: Those prospects can be useful in exploring various opportunities in tissue repair and personalized treatments[64]
- **Global Access and Affordability:** This Liposomal approach reduces production cost and enhances distribution in economically challenged areas[63].

Conclusion: Liposomes have become central modern medicine, especially in the delivery of drug and vaccine technology. They have essential biocompatibility and flexibility allowing them to carry both hydrophilic and lipophilic drugs and release them in a controlled manner across various diseases. Liposomes have advance in preparation methods, surface engineering and emerging nanotechnology have further widened their performance and application. The liposomes are also playing an important role in development of personalised and next generation therapeutic strategies. The existed limitation can be overcome by continued optimization, standardised manufacturing and collaborative research**.**

Author Contribution: K. Pushpalatha performed to literature survey, Drafting the manuscript, data compliation and preparation of the review article. Dr. M.Vidyavathi contributed to conceptualization, critical revision, supervision

Acknowledgment: Nil

Conflict of interest: The Authors declared there is no conflict of interest

REFERENCES:

1. Wadhwa S, Garg V, Gulati M, Kapoor B, Singh SK, Mittal N. Nanovesicles for nanomedicine: theory and practices. Pharmaceutical Nanotechnology: Basic Protocols. 2019 May 31:1-7.
2. Akbarzadeh A, Rezaei-Sadabady R, Davaran S, Joo SW, Zarghami N, Hanifehpour Y, Samiei M, Kouhi M, Nejati-Koshki K. Liposome: classification, preparation, and applications. Nanoscale research letters. 2013 Feb 22;8(1):102.
3. Shetye L, Sherlekar A, Mendhulkar V. Liposome-Based Drug Delivery—A New Therapeutic Paradigm. InAdvanced Drug Delivery: Methods and Applications 2023 Oct 25 (pp. 21-48). Singapore: Springer Nature Singapore.
4. Barenholz YC. Doxil®—The first FDA-approved nano-drug: Lessons

learned. Journal of controlled release. 2012 Jun 10;160(2):117-34.

5. Lasic DD. Liposomes: From Physics to Applications. 1993 Jan.
6. Szoka Jr F, Papahadjopoulos D. Procedure for preparation of liposomes with large internal aqueous space and high capture by reverse-phase evaporation. Proceedings of the national academy of sciences. 1978 Sep;75(9):4194-8.
7. Sercombe L, Veerati T, Moheimani F, Wu SY, Sood AK, Hua S. Advances and challenges of liposome assisted drug delivery. Frontiers in pharmacology. 2015 Dec 1;6:286.
8. Basak S, Das TK. Liposome-based drug delivery systems: from laboratory research to industrial production—instruments and challenges. ChemEngineering. 2025 May 27;9(3):56.
9. JAFARI M, MALAEKEH NB, Nasirli H, Hosseinzadeh H. Formulation of topical liposomes encapsulated with triamcinolone and comparison of their anti-inflammatory effects with available conventional topical ointment in mice. Iranian Journal of Basic Medical science, 2005: 195-201.
10. Liu W, Ye A, Han F, Han J. Advances and challenges in liposome digestion: Surface interaction, biological fate, and GIT modeling. Advances in Colloid and Interface Science. 2019 Jan 1;263:52-67.
11. Hope MJ, Bally MB, Webb G, Cullis PR. Production of large unilamellar vesicles by a rapid extrusion procedure. Characterization of size distribution, trapped volume and ability to maintain a membrane potential. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1985 Jan 10;812(1):55-65.
12. Kim S, Turker MS, Chi EY, Sela S, Martin GM. Preparation of multivesicular liposomes. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1983 Mar 9;728(3):339-48.
13. Aksoy AS. Liposomes: Composition, preparation techniques, and diverse applications in food science. Istanbul Aydin Üniversitesi Dergisi Anadolu Bil Meslek Yüksekokulu. 2024 Jul 1;19(70).
14. Deamer D, Bangham AD. Large volume liposomes by an ether vaporization method. Biochimica et Biophysica Acta (BBA)-Nucleic Acids and Protein Synthesis. 1976 Sep 7;443(3):629-34.
15. Batzri S, Korn ED. Single bilayer liposomes prepared without sonication. Biochimica et Biophysica Acta (BBA)-

Biomembranes. 1973 Apr 16;298(4):1015-9.

16. Mitragotri S, Burke PA, Langer R. Overcoming the challenges in administering biopharmaceuticals: formulation and delivery strategies. Nature reviews Drug discovery. 2014 Sep;13(9):655-72.
17. Alavi M, Rai M, Varma RS, Hamidi M, Mozafari MR. Conventional and novel methods for the preparation of micro and nanoliposomes. Micro Nano Bio Aspects. 2022 May 1;1(1):18-29.
18. Hoseini B, Jaafari MR, Golabpour A, Momtazi-Borojeni AA, Karimi M, Eslami S. Application of ensemble machine learning approach to assess the factors affecting size and polydispersity index of liposomal nanoparticles. Scientific reports. 2023 Oct 21;13(1):18012.
19. Blume A. Apparent molar heat capacities of phospholipids in aqueous dispersion. Effects of chain length and head group structure. Biochemistry. 1983 Nov 1;22(23):5436-42.
20. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. Advanced drug delivery reviews. 2013 Jan 1;65(1):36-48.
21. Gabizon AA. Pegylated liposomal doxorubicin: metamorphosis of an old drug into a new form of chemotherapy. Cancer investigation. 2001 Jan 1;19(4):424-36.
22. Khademi F, Taheri RA, Momtazi-Borojeni AA, Farnoosh G, Johnston TP, Sahebkar A. Potential of cationic liposomes as adjuvants/delivery systems for tuberculosis subunit vaccines. Reviews of Physiology, Biochemistry and Pharmacology, Vol. 175. 2018 Apr 27:47-69.
23. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines—a new era in vaccinology. Nature reviews Drug discovery. 2018 Apr;17(4):261-79.
24. Li SD, Huang L. Gene therapy progress and prospects: non-viral gene therapy by systemic delivery. Gene therapy. 2006 Sep;13(18):1313-9.
25. Drulis-Kawa Z, Dorotkiewicz-Jach A. Liposomes as delivery systems for antibiotics. International journal of pharmaceutics. 2010 Mar 15;387(1-2):187-98.
26. Stone NR, Bicanic T, Salim R, Hope W. Liposomal amphotericin B (AmBisome®): a review of the pharmacokinetics, pharmacodynamics, clinical experience and future directions. Drugs. 2016 Mar;76(4):485-500.

27. Silindir M, Erdoğan S, Özer AY, Maia S. Liposomes and their applications in molecular imaging. Journal of drug targeting. 2012 Jun 1;20(5):401-15.
28. Maeda H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review. Journal of controlled release. 2000 Mar 1;65(1-2):271-84.
29. Pasarin D, Ghizdareanu AI, Enascuta CE, Matei CB, Bilbie C, Paraschiv-Palada L, Veres PA. Coating materials to increase the stability of liposomes. Polymers. 2023 Feb 3;15(3):782.
30. Kesharwani R, Jaiswal P, Patel DK, Yadav PK. Lipid-based drug delivery system (LBDDS): An emerging paradigm to enhance oral bioavailability of poorly soluble drugs. Biomedical Materials & Devices. 2023 Sep;1(2):648-63.
31. Urbinati G, Marsaud V, Renoir JM. Anticancer drugs in liposomal nanodevices: a target delivery for a targeted therapy. Current topics in medicinal chemistry. 2012 Aug 1;12(15):1693-712.
32. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nature reviews Drug discovery. 2014 Nov;13(11):813-27.
33. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, Okoroafor CC, Eze SC, Kalu OL, Odoh EC, Nwadike UG. Advances in drug delivery systems, challenges and future directions. Heliyon. 2023 Jun 1;9(6).
34. Shoaib A, Javed S, Tabish M, Khan ME, Zaki M, Alqahtani SS, Sultan MH, Ahsan W, Afzal M. Applications of nanomedicine-integrated phototherapeutic agents in cancer theranostics: A comprehensive review of the current state of research. Nanotechnology Reviews. 2024 May 24;13(1):20240023.
35. Laura Immordino M, Dosio F, Cattel L. Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential. International journal of nanomedicine. 2006 Sep 15;1(3):297-315.
36. Al Bostami RD, Abuwatfa WH, Husseini GA. Recent advances in nanoparticle-based co-delivery systems for cancer therapy. Nanomaterials. 2022 Aug 4;12(15):2672.
37. Kuriakose AE, Nguyen TP, Noukeu LC, Sabhani M, Le D, Nguyen KT. Stem cells as drug delivery vehicles. Encyclopedia of tissue engineering and regenerative medicine. London, UK: Elsiever. 2019 Jan 1:197-210.

38. Helenius AR, Simons KA. Solubilization of membranes by detergents. Biochimica et Biophysica Acta (BBA)-Reviews on Biomembranes. 1975 Mar 25;415(1):29-79.
39. Chakravarty P, Famili A, Nagapudi K, Al-Sayah MA. Using supercritical fluid technology as a green alternative during the preparation of drug delivery systems. Pharmaceutics. 2019 Nov 25;11(12):629.
40. Wang SX, Wen X, Wu J. The development and application of a liposomal delivery system in biomedical sciences. historical, clinical and molecular perspectives. 2017:53.
41. Chaves MA, Ferreira LS, Baldino L, Pinho SC, Reverchon E. Current applications of liposomes for the delivery of vitamins: A systematic review. Nanomaterials. 2023 May 5;13(9):1557.
42. Jantzen GM, Robinson JR. Sustained-and controlled-release drug delivery systems. Drugs and The Pharmaceutical Sciences. 2002;121:501-28.
43. Drummond DC, Meyer O, Hong K, Kirpotin DB, Papahadjopoulos D. Optimizing liposomes for delivery of chemotherapeutic agents to solid tumors. Pharmacological reviews. 1999 Dec 1;51(4):691-743.
44. Costa P, Lobo JM. Modeling and comparison of dissolution profiles. European journal of pharmaceutical sciences. 2001 May 1;13(2):123-33.
45. Lewis RN, McElhaney RN. Fourier transform infrared spectroscopy in the study of lipid phase transitions in model and biological membranes: practical considerations. Methods in membrane lipids. 2007 Jan 1:207-26.
46. Seth A, Kaushik D, Ghosh SK. X-ray scatterings to probe the structure and assembly of biomimetic membranes. The European Physical Journal Special Topics. 2024 Dec;233(21):2941-63.
47. Dufrêne YF. Atomic force microscopy in microbiology: new structural and functional insights into the microbial cell surface. MBio. 2014 Aug 29;5(4):10-128.
48. Olson F, Hunt CA, Szoka FC, Vail WJ, Papahadjopoulos D. Preparation of liposomes of defined size distribution by extrusion through polycarbonate membranes. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1979 Oct 19;557(1):9-23.
49. Rigaud JL, Lévy D. Reconstitution of membrane proteins into liposomes. InMethods in enzymology 2003 Jan 1 (Vol. 372, pp. 65-86). Academic Press.
50. Hope MJ, Bally MB, Webb G, Cullis PR. Production of large unilamellar

vesicles by a rapid extrusion procedure. Characterization of size distribution, trapped volume and ability to maintain a membrane potential. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1985 Jan 10;812(1):55-65.

51. Laouini A, Jaafar-Maalej C, Limayem-Blouza I, Sfar S, Charcosset C, Fessi H. Preparation, characterization and applications of liposomes: state of the art. Journal of colloid Science and Biotechnology. 2012 Dec 1;1(2):147-68.
52. Cheng Y, Hay CD, Mahuttanatan SM, Hindley JW, Ces O, Elani Y. Microfluidic technologies for lipid vesicle generation. Lab on a Chip. 2024;24(20):4679-716.
53. Filipe V, Hawe A, Jiskoot W. Critical evaluation of Nanoparticle Tracking Analysis (NTA) by NanoSight for the measurement of nanoparticles and protein aggregates. Pharmaceutical research. 2010 May;27(5):796-810.
54. Sopyan I, Gozali D. A Review: A Novel of Efforts to Enhance Liposome Stability as Drug Delivery Approach. Systematic Reviews in Pharmacy. 2020 Jun 1;11(6).
55. Semeraro EF, Marx L, Frewein MP, Pabst G. Increasing complexity in small-angle X-ray and neutron scattering experiments: from biological membrane mimics to live cells. Soft Matter. 2021;17(2):222-32.
56. Bhaumik A. Aspects of structural biology studied by liquid and solid-state NMR, Newdelhi:Springer;2007.
57. Nogales De La Morena E, Mahamid J. Bridging structural and cell biology with cryo-electron microscopy. Nature: New biology. 2024 Apr 1;628(8006).
58. Su CK, Sun YC. Considerations of inductively coupled plasma mass spectrometry techniques for characterizing the dissolution of metal-based nanomaterials in biological tissues. Journal of Analytical Atomic Spectrometry. 2015;30(8):1689-705.
59. Kelly SM, Price NC. The use of circular dichroism in the investigation of protein structure and function. Current protein and peptide science. 2000 Dec 1;1(4):349-84.
60. Qian S, Li C, Zuo Z. Pharmacokinetics and disposition of various drug loaded liposomes. Current drug metabolism. 2012 May 1;13(4):372-95.
61. Park YH, Kim WS, Lee DW. Size analysis of industrial carbon blacks by sedimentation and flow field-flow fractionation. Analytical and bioanalytical chemistry. 2003 Feb;375(4):489-95.

62. Parmar P, Porwal S, Dwivedi S, Koka SS, Darwhekar GN. The Role of Liposomes in Artificial Intelligence: A Promising Synergy. International Journal of Pharmacy & Life Sciences. 2024 Sep 1;15(9).
63. Szoka, F. C. (2019). Liposomal drug delivery: current status and future prospects. Membrane fusion, 845-890.
64. Peng, H., Han, B., Tong, T., Jin, X., Peng, Y., Guo, M., ... & Wang, Q. (2024). 3D printing processes in precise drug delivery for personalized medicine. Biofabrication, 16(3), 032001.
65. Papahadjopoulos D, Allen TM, Gabizon A, Mayhew E, Matthay K, Huang SK, Lee KD, Woodle MC, Lasic DD, Redemann CJ. Sterically stabilized liposomes: improvements in pharmacokinetics and antitumor therapeutic efficacy. Proceedings of the National Academy of Sciences. 1991 Dec 15;88(24):11460-4.
66. Allen TM, Hansen C, Martin F, Redemann C, Yau-Young A. Liposomes containing synthetic lipid derivatives of poly (ethylene glycol) show prolonged circulation half-lives in vivo. Biochimica et Biophysica Acta (BBA)-Biomembranes. 1991 Jul 1;1066(1):29-36.