Chapter

Liposomal Technology in Drug Formulations: Enhancing Therapeutic Efficacy and Safety

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Abstract

Liposomes are vesicular structures made of lipid bilayers that naturally develop when phospholipids scatter in water. These small vesicles included an aqueous core within a membrane made of lipid bilayers. Novel Drug Delivery Systems (NDDS) are intended to release medications at a controlled rate dependent on the body's needs during therapy while targeting specific locations of action. Liposomes, which are spherical structures made up of phospholipid bilayers, have gained popularity in therapeutic formulations due to their ability to encapsulate both hydrophilic and hydrophobic medicines. This dual encapsulation capability improves the therapeutic efficacy and safety of many medicines. Liposomes are ideal for targeted drug delivery due to their biocompatibility, biodegradability, and non-immunogenic qualities, which reduce systemic side effects and improve bioavailability. Recent advances in liposomal technology have resulted in formulations being employed in a variety of sectors, including cancer therapy, infectious disorders, and vaccine administration. This review examines the structural properties, preparation methodologies, and therapeutic applications of liposomes, emphasising their potential to change drug delivery systems. This chapter emphasises the crucial importance of liposomes in modern pharmaceutical sciences and their bright future in personalised medicine by examining current research and clinical applications.

Keywords: liposome, phospholipid structure, hydrophilic and hydrophobic drugs, formulation, drug delivery

1. Introduction

Liposomes represent spherical vesicles, comprising one or more phospholipid bilayers first described in the 1960s by the British haematologist Alec D. Bang ham with the ability to encapsulate both hydrophilic and lipophilic drugs. In 1965, researchers presented the first description of swelling phospholipid systems. Within a few years, a variety of enclosed phospholipid bilayer structures made up of single bilayers, dubbed 'bangosomes' and then 'liposomes', were described. Early pioneers such as Gregoriadis and Perrie demonstrated that liposomes can entrap

pharmaceuticals and be employed as drug delivery devices [1]. Due to this structure, liposomes have become a really effective drug delivery system through which they improve the therapeutic index of drugs by enhancing their bioavailability, prolonging circulation time, and reducing toxicity. Since these vesicles tend to imitate cell membranes, they are biocompatible and are, therefore, capable of delivering drugs to the site of their target either through passive or active targeting mechanisms. This drastically reduces side effects and increases the therapeutic value of the drugs being used [2].

Therefore, liposomes have been employed in many fields of medical science, ranging from oncology to infectious diseases and gene therapy. The ability of liposomes to encapsulate drugs either within their aqueous core or within their lipid bilayer enables them to protect labile drugs from degradation and allows for controlled release, hence making them an attractive vehicle for a number of therapeutic agents [3]. More recent advances in liposomal technology have improved circulation time in the bloodstream, through processes such as pegylation, offering new opportunities in both precision medicine and personalised therapies [4]. Liposomes are composed of amphiphilic phospholipids with a hydrophilic head and a hydrophobic tail, which allows them to seal themselves in aquatic environments. In recent years, major research has concentrated on the delivery of antibiotics [5, 6], genes [7, 8], antifungals [9, 10], anti-inflammatory [11, 12], and anticancer drugs [13, 14], which are also used in many pharmacological, biological, and medical applications.

2. Structure of liposome

The primary structural components of liposomes are phospholipids and cholesterol. The lipid bilayer is made up of phospholipids with a hydrophilic head and a hydrophobic tail group. The head attracts water, while the tail, which is formed of a long hydrocarbon chain, repels water. Phospholipids, the primary component of liposomes, can easily merge with skin lipids, enhancing medication penetration and localisation in the skin layers. The cholesterol absorbed into the lipid membrane increases the stability of liposomes while also reducing membrane permeability. As bilayer structures, liposomes in aqueous solution can encapsulate hydrophilic compounds in the aqueous compartment while hydrophobic substances can be accommodated in the lipid phase (**Figure 1**) [15].

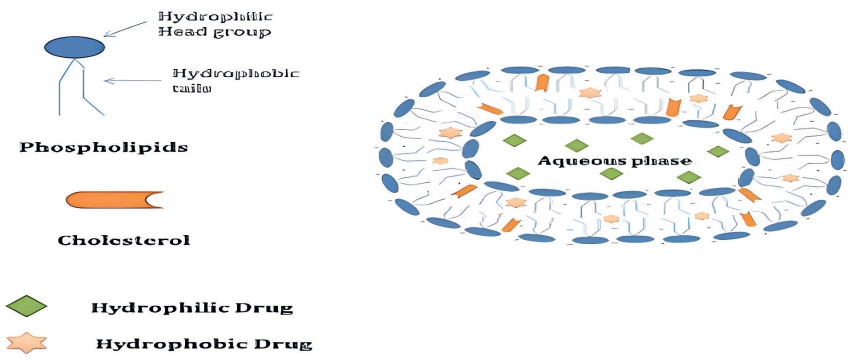

Figure 1.
Structure of conventional liposome encapsulating hydrophilic & hydrophobic drugs.

3. The way that liposomes work

A liposome is an aqueous solution surrounded by a hydrophobic membrane. Both hydrophilic and hydrophobic molecules can be found in liposomes because hydrophobic compounds are easily absorbed by lipid membranes. How far a medicine is positioned will depend on its lipid content and other physiochemical properties. When lipid bilayers combine with other cell bilayers (the cell membrane), liposomal contents are released, which subsequently deliver the required medication molecules to the site of action. The following factors contribute to the production of bilayers:

- Unfavourable interactions between the hydrophilic and hydrophobic phases can be mitigated by folding into closed, concentric vesicles.

- The massive free energy difference between the hydrophilic and hydrophobic environments is lessened by the formation of huge vesicles, due to the fact that spherical shapes have the least surface tension and are the most stable. The self-assembled structure that results in vesicles is therefore as stable as feasible.

Procedure for administering medication with liposomes:

1. *Adsorption*: The process of adsorption is how liposomes attach to cell membranes.

2. *Endocytosis*: The internalisation and engulfment of liposomes within the liposomes after their adsorption on the cell membrane.

3. *Fusion*: When liposomal lipid bilayers unite with the lipoidal cell membrane by lateral diffusion and lipid intermingling, liposome contents are directly delivered to the cytoplasm.

4. *Lipid exchange*: Because the phospholipids in the cell membrane and the liposomal lipid membrane are similar, lipid transfer proteins in the cell membrane can recognise liposomes and initiate lipid exchange.

For example, cancer cells need to consume enormous amounts of fat in order to meet their requirements for rapid development. They also recognise liposomes, which are filled with anticancer drugs, as a potential source of sustenance. When liposomes target them, they are absorbed. Anticancer medications destroy cancer cells as soon as they break free from the liposome and enter the location [16].

4. Classification of liposomes

Liposomes are categorised depending on the size and the number of bilayers. Unilamellar vesicles come in three different varieties: large (LUV), small (SUV), and multilamellar (MLV). Conventional liposomes (CL), pH-sensitive liposomes, cationic liposomes, long circulating liposomes (LCL), and immuno-liposomes are the different types of liposomes based on their composition. As illustrated in **Figure 2**, they are categorised as reverse phase evaporation vesicles (REV), French press vesicles (FPV), and ether injection vesicles (EIV) in accordance with the technique of preparation [17].

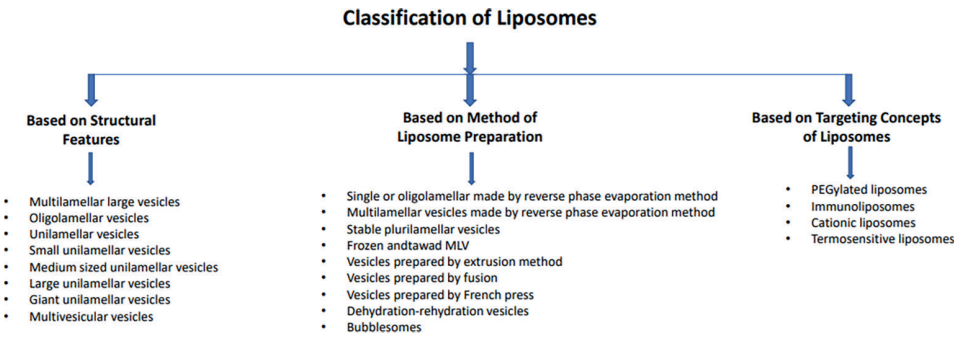

Figure 2.
Liposome classification.

5. Liposome stability

The stability of the liposomes throughout production, storage, and distribution determines the therapeutic efficacy of the drug molecule. The maintenance of the physical and chemical stability of the active molecule throughout the development and storage phases is ensured by a stable dosage form. In design-based stability tests, physical, chemical, and microbiological parameters are assessed, and product integrity is guaranteed throughout storage [18].

5.1 Physical stability

The size of the vesicles generated throughout the liposomal manufacturing stages varies. Vesicles assemble and enlarge to reach a thermodynamically favourable state during storage. Drug leakage from the vesicles during storage may cause fusion and breaking. The liposomal medicinal product's physical stability is lowered as a result. Therefore, vesicle size distribution and shape play a critical role in determining physical stability [19]. A variety of methods, including light scattering and electron microscopy, are employed to assess the morphology and size of the vesicles as well as their visual appearance. Although its content in the liposome structure cannot go above 50%, cholesterol reinforces the lipid membrane. Maintaining and stabilising the bioactive molecule at the liposome's centre is crucial. Maintaining pH levels and preventing excessive unsaturation of phospholipids during simple peroxidation are two ways to preserve physical stability. It is necessary to keep them chilled at 4°C to prevent freezing and exposure to light.

5.2 Chemical stability

Chemically unsaturated fatty acids known as phospholipids are prone to oxidation and hydrolysis, which could compromise the stability of the medicinal product. The stability of a liposomal formulation is greatly influenced by pH, ionic strength, solvent system, and buffering species. The production of hydroxy and cyclic peroxidases as a result of free radical generation during the oxidation process is known as oxidation degradation. To avert oxidative disintegration, liposomes can be shielded from sunlight, supplemented with antioxidants like butylated hydroxyl toluene (BHT) or α-tocopherol, manufactured in an inert atmosphere

like nitrogen or argon, or treated with EDTA to remove traces of heavy metals [20]. Lyso-phosphatidylcholine is produced when the ester bond at the C-4 position of the glycerol moiety of phospholipids is hydrolysed. The liposomal contents' permeability is increased as a result. Therefore, it is essential to regulate the lysoPC limit in lysosomal pharmaceutical products. Phosphatidylcholine and lysoPC-free liposomes can be combined to achieve it [21].

6. Properties of liposomes

Liposomes are spherical vesicles consisting of one or more phospholipid bilayers, used in drug delivery and other applications due to their unique properties. Below are the key properties of liposomes:

6.1 Biocompatibility and biodegradability

Liposomes are biocompatible and biodegradable because they are made of phospholipids, which are also found in biological membranes. Their suitability for medication administration is improved and the danger of toxicity is reduced because of this feature [3].

6.2 Amphiphilicity

Both hydrophilic and hydrophobic areas are present in liposomes. Medications soluble in water can be encapsulated by the hydrophilic core, while medications soluble in lipids can be included by the hydrophobic bilayer. A large variety of medications can be delivered because of this dual capability [2].

6.3 Size and charge variability

Depending on the makeup of the phospholipids, liposomes can have a size ranging from 50 nm to several micrometres with a surface charge that is neutral, positively charged (cationic), or negatively charged (anionic). Their size and charge affect how quickly they circulate through the bloodstream and are absorbed by cells [22].

6.4 Controlled release of encapsulated drugs

Drugs that have been encapsulated can be released gradually and under control using liposomes. The liposomal membrane's composition can be altered to control this release, as can the use of stimuli-responsive components that release the medication in response to changes in temperature or pH [23].

6.5 Low immunogenicity

When liposomes are properly formed, such as by adding polyethylene glycol (PEGylation), they can elude the immune system and avoid being quickly cleared by the mononuclear phagocyte system (MPS). As a result, the drug's bioavailability is improved and its bloodstream circulation time is prolonged [24].

6.6 Encapsulation efficiency

Liposomes are highly effective at encapsulating pharmaceuticals that are hydrophilic, hydrophobic, or amphiphilic. They can thereby deliver a variety of therapeutic agents with greater versatility, enhancing medication solubility and stability, and lowering toxicity [25].

6.7 Enhanced permeability and retention (EPR) effect

Liposomes' increased permeability and retention effect allows them to accumulate in tumour tissues. Because the vascularisation of tumours is often more permeable than that of healthy tissues, liposomes can effectively and passively target tumour locations and deliver anticancer medications [26].

7. Advantages of liposomes

- *Biocompatibility and biodegradability:* Because liposomes are formed from natural phospholipids, the carriers themselves are biocompatible and biodegradable, with essentially no risk of toxicity, and they are easily metabolised within the body without causing harm to the host (**Figure 3**) [27].

- *Improved drug delivery:* Liposomes have the capacity to encapsulate both hydrophilic and hydrophobic pharmaceuticals, increase the solubility profiles of poorly soluble medications, and protect drugs from degradation. This increases the bioavailability and therapeutic index of the medicines [2].

- *Targeted delivery:* Liposomes can be modified to have surface ligands that allow them to target specific cells or tissues, reducing off-target effects while increasing drug accumulation at the intended region. This is especially advantageous in cancer therapy since targeting tumour cells can reduce systemic toxicity [28].

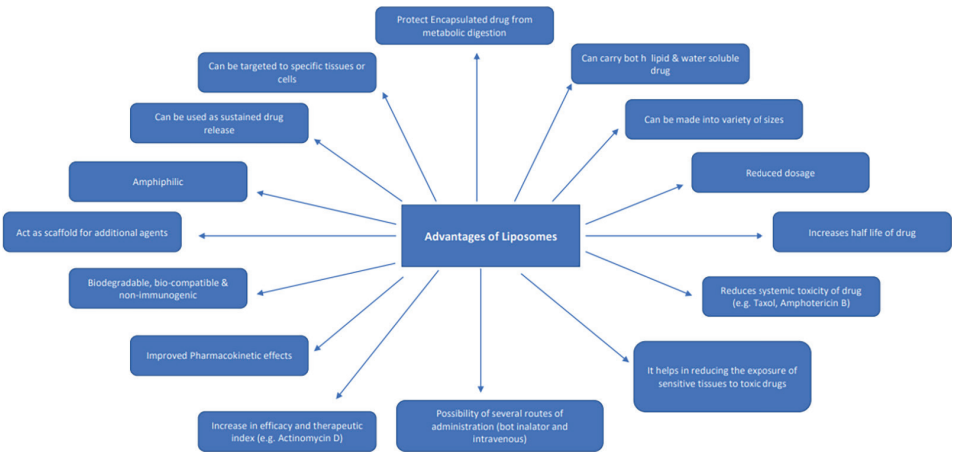

Figure 3.
Advantages of liposome [16].

- *Reduced toxicity:* This reduces the exposure of normal tissues to harmful medicines, lowering side effects and boosting patient tolerance [2].

- *Controlled release:* Liposomes can be engineered to release their components at a regulated and predetermined time, allowing medications to be delivered in a sustained form for a longer period of time, resulting in reduced frequency dosing and higher patient compliance [3].

8. Disadvantages of liposomes

- *Stability issues:* Liposomes are therefore susceptible to instability in terms of encapsulated drug leakage, fusion, and phospholipid oxidation, all of which significantly impair their effectiveness and shelf life [2].

- *High production costs:* Liposome synthesis and purification can be complex and expensive, which may limit their widespread application, particularly in resource-limited situations [29].

- *Rapid clearance by the reticuloendothelial system (RES):* Liposomes are quickly recognised and eliminated by the mononuclear phagocyte system (MPS) in the liver and spleen, potentially limiting their circulation time and efficacy [28].

- *Limited drug loading capacity:* The amount of pharmaceuticals that can be incorporated into liposomes may be limited depending on the type of liposome and the drug's qualities. This may have an impact on the dosages that can be administered [29].

- *Immunogenicity potential:* Liposomes, particularly non-PEGylated or unmodified ones, have the potential to stimulate the immune system, resulting in hypersensitivity reactions or accelerated clearance from the circulation [2].

9. Methods for preparation

The Bangham technique (thin film hydrolysis), ether/ethanol injection, reverse phase evaporation, detergent depletion, heating, microfluidic channel, membrane extrusion, homogenisation, and sonication are examples of conventional liposome synthesis techniques. Researchers have been using dual asymmetric freezing and freeze drying for almost 10 years. Supercritical fluid (SCF) and centrifugation (DAC) for the delivery of liposomal drugs. Drug delivery techniques that are cutting edge include lysolipid and depo-foam liposomes.

9.1 The Bangham method of thin film hydration

The Bangham technique was the first widely utilised technique to create liposomes [30, 31]. With this technique, lipids are dissolved in an organic solvent (dichloromethane, ethanol, chloroform, or a mixture of methanol and chloroform). The solvent that is organic is melted in a vacuum at 45–60°C to form a thin coating of

lipid. After 2 hours of steady agitation in aqueous solutions at 60–70°C, the thin lipid layer swells and forms round, closed liposomes [32].

9.2 Methods of injecting ethanol/ether

In 1973, Batzri and Korn presented the ethanol injection technique [33]. Lipids are dissolved in an organic solvent (such as ethanol, diethyl ether, or an ether-methanol mixture) and then injected into an aqueous phase to create liposomes. At 55–65°C or with less pressure, encapsulate the material. Moreover, heating is necessary to extract the organic solvent from the liposomes since ether is incompatible with aqueous media [34]. The inkjet method was created by Hauschild et al. as a contemporary ethanol injection technique. Using this method, a drug solution, whether hydrophilic, lipophilic, or both, was dissolved in ethanol and converted into an inkjet device that allowed for the large-scale production of liposomes with remarkable control over particle size [35].

9.3 Method of reverse phase evaporation

The reverse phase evaporation method [36], developed by Szoka and Papahadjopoulos, involves dissolving medications in aqueous media and lipids in an organic solvent. After that, the mixture is sonicated to create inverted or emulsion-free micelles. A rotary evaporator is used to progressively evaporate the organic solvent, turning the micelles into a viscous or gel-like substance. The gel collapses at a crucial stage, releasing some inverted micelles. Liposomes are produced when more phospholipids surround the remaining micelles in a bilayer. A modified reverse-phase evaporation approach was proposed by Handa et al. [37], with the primary benefit being the liposome's excellent encapsulation.

9.4 Freeze-drying method

Liu et al. discovered the lyophilisation monophasic solution method for liposome manufacturing. This method involves dissolving the lipid and medicine in tert-butyl alcohol at 450°C, while the lyoprotectant dissolves in water. The two resulting solutions are combined to form a third identical monophasic solution, which is then filtered and freeze dried to produce proliposomes. The freeze-drying process consists of two steps. The substance is frozen at −40°C and dried at ambient temperature, yielding liposomes with a mean diameter of 100–300 nm [38].

9.5 Dual asymmetric centrifugation method (DAC)

In contrast to the standard centrifugation procedure, which calls for the vials to be rotated on their own centre axis, the DAC method involves rotating sealed vials on the main rotational axis at a defined speed and distance in addition to rotating on their own axis. The primary rotation forces the sample outward, and the adhesion between the sample and the rotating vial causes the revolution around its own centre to force the sample material in the opposite direction. Hence, mechanical turbulence and capitations introduce energy into the sample preparation process, resulting in the production of nano-liposomes with an optimum size distribution of approximately 60 nm [39].

9.6 Supercritical fluid methods (SCF)

Supercritical fluid extraction, supercritical-assisted liposome formation (super Lip) [40], depressurisation of an expanded liquid organic solution-suspension method (DELOS), supercritical anti-solvent method (SAS), supercritical reverse phase evaporation method (SCRPE), and particles from gases [41, 42] are examples of SCF methods that have been developed as green techniques to overcome the limitations of toxicity and degradability of conventional methods. Because it is inflammable, affordable, non-corrosive, non-toxic, acceptable to the environment, and appropriate for thermolabile chemicals, CO2 is the most often used supercritical gas [43].

9.7 Formation of liposomes

The following factors determine whether the liposome preparation technique is best:

- The physicochemical properties of the liposomal components and the substance to be entrapped;
- The imprisoned substance's effective concentration and possible toxicity;
- Extra procedures needed for the vesicles' application or delivery;
- The vesicles' ideal dimensions, polydispersity, and shelf life for the planned use; and,
- The ability to produce safe and effective liposomal products on a wide scale and the reproducibility of batch-to-batch production.

10. Characterisation of liposomes

10.1 Size and size distribution

When it comes to regulating the in vivo release of drug-loaded liposomes, vesicle size is crucial. Liposomes' average size is determined by their manner of production and phospholipid content.

Numerous methods are used to analyse size and size distribution, such as:

1. Microscopic methods include SEM, freeze-fracture TEM, negative stain TEM, and optical microscopy. Liposomes are imaged using SEM and TEM techniques, which are also utilised to measure the inter-bilayer distance and bilayer thickness [44]. Atomic force microscopy (AFM), a very high-resolution scanning probe microscopy that creates 3D micrographs with resolution of nanometres and A0 scale to analyse the liposome shape, stability, size, and dynamic process of lipid nano-capsules, is one of the recently developed microscopic techniques [45].

2. Hydrodynamic methods include gel exclusion chromatography, analytical centrifugation, field flow fractionation, ultracentrifugation, and others that are

used to analyse size distribution, elution properties, and liposome homogeneity in addition to estimating a compound's molecular mass [46].

3. Lipid vesicle size can be determined using diffraction light scattering techniques such quasi-elastic light scattering, laser light scattering, and photon correlation spectroscopy.

Liposomes smaller than 1 μm in size can have their mean diameter measured using these methods. Depending on whether a liposome formulation is intended for parenteral, topical, or inhalation application, it is important to keep an eye on its size. Liposomal size can be modified by a number of techniques, including homogenisation, extrusion, and sonication.

10.2 Calculating lamellarity

The quantity of lipid bilayers enclosing the lipid vesicles is known as lamellarity. Liposome size, homogeneity, and lamellarity can all be determined by means of cryo-electron microscopy, 31P-nuclear magnetic resonance (NMR), and small-angle X-ray scattering (SAXS) techniques [47].

10.3 Zeta potential

The main factor influencing cellular absorption and customised drug delivery is the zeta potential. By generating an electric field in response to incident laser scattering on moving particles, the laser Doppler electrophoresis and Zetasizer assess the zeta potential of liposomal dispersion. The zeta potential is affected by a number of variables, including pH, ionic strength, and particle concentration. The total surface charge and blood circulation time of liposomes are influenced by their lipid composition, specifically the positive- and negative-charged phospholipids [48].

10.4 Efficient encapsulation/entrapment

The percentage of water-soluble medicine and aqueous phase that are encapsulated during liposome production is known as encapsulation efficiency. The percentage of entrapment per milli gramme of lipid is how it should be shown. Drug bioavailability will increase with improved entrapment efficiency [49]. Solid phase extraction, size exclusion chromatography, hollow fibre centrifugal ultrafiltration and centrifugation ultrafiltration, mini-column centrifugation, and protamine aggregation are some of the techniques used to determine entrapment efficiency. Liposomes can be purified and separated using the mini-column centrifugation method; for negatively charged and neutral liposomes, the protamine aggregation method is employed. An indirect method of gauging encapsulation efficiency is to calculate the percentage of the drug's value that remains unencapsulated after being subtracted from the total amount to be used [50].

10.5 In vitro drug release studies

An in vitro diffusion cell or a dialysis bag is used for the 370°C in vitro drug release experiments. To replicate in vivo conditions, the cell or bag needs to be dampened with receptor media that contains pH 7.4 buffer and continuously agitated under sink

conditions. A fresh medium volume was added to the receptor media at regular intervals, and the required amount of the medium was taken. The concentration was then assessed using UV-visible spectrophotometry and HPLC. The release of water-soluble drugs is influenced by the cholesterol concentration in liposomal formulations; an increase in cholesterol concentration accelerates the release of the drug [51].

10.6 In vivo performance

The pharmacokinetic characteristics of individual vesicles can impact the in vivo performance of liposome-containing drugs. Intravenous liposome delivery is used to examine the in vivo effectiveness of liposomal drug delivery methods by showing rapid clearance from the liver and spleen. Greater than 0.5 μm liposomes were phagocytosed, but liver parenchymal cells absorbed liposomes smaller than 0.1 μm. Liposomes with cholesterol increase stability by stopping drug leakage. Hyaluronic acid was used to functionalise magnetic liposome nanocomposites loaded with the anticancer medication imatinib. Fluorescence photos were obtained at 2, 4, and 8 hours after injecting these magnetic liposomes into a mouse model to examine their in vivo behaviour. When the fluorescence signal is at its highest, magnetic liposomes are absorbed and retained [52].

11. Applications of liposomes

Drug delivery systems: Liposomes are extensively employed as drug delivery vehicles for a wide range of drugs including anticancer agents, antibiotics, antifungal, and antiviral drugs. Drugs formulated in the form of liposomes are administered with the aim of enhancing their stability, solubility, and bioavailability, and reducing toxicity and side effects.

- *Anticancer therapy*: The wide use of liposomes is their application in the delivery of chemotherapy drugs such as doxorubicin (e.g., Doxil) and daunorubicin (e.g., DaunoXome). In this application, the drug is intended to be delivered to the target tumour cells, thus minimising systemic exposure to the drug and therefore reducing the side effects [53].

- *Antibiotic delivery*: Liposomal formulations have been shown to improve antibiotic delivery for drugs such as amphotericin B (AmBisome) in fungal infections. The liposomal form reduces the nephrotoxicity and some other adverse reactions to the drug [54].

Gene delivery: Liposomes can be used for delivering genetic materials, such as DNA, RNA, and small interfering RNA (siRNA), into cells for their use in gene therapy. This helps shield the genetic materials from degradation; enhance cellular uptake of the said material; and hence facilitate handling genetic disorders, cancers, and viral infections.

- *Gene therapy*: Liposomal gene delivery, which is also known as lipoplex, is currently used for the delivery of genes that either serve to replace a defective gene or suppress the expression of a harmful gene. Liposomes are under clinical trials to treat cystic fibrosis, haemophilia, and several cancers (**Table 1**) [55].

Disease	Liposomal drug	Clinical applications	Outcome	References
Systemic Fungal Infections	*AmBisome* (Liposomal Amphotericin B)	Treatment of cryptococcosis and candidiasis	Decreased nephrotoxicity and improved antifungal efficacy	[56]
Kaposi's Sarcoma	*Doxil* (Liposomal Doxorubicin)	Treatment of AIDS-related Kaposi's sarcoma	Improved tumour targeting and reduced systemic toxicity	[53]
Rheumatoid Arthritis	Liposomal Prednisolone	Anti-inflammatory therapy	Reduced inflammation with fewer side effects	[2]
Alzheimer's Disease	Liposomal Curcumin	Cognitive enhancement in Alzheimer's patients	Better brain penetration and reduced amyloid plaques	[57]
Breast Cancer	*Mylotarg* (Liposomal Gemtuzumab Ozogamicin)	Treatment of HER2-positive breast cancer	Enhanced targeting of cancer cells, leading to better outcomes	[58]
Hepatitis A	Liposomal Hepatitis A Vaccine	Preventive vaccine for hepatitis A infection	Enhanced immune response and prolonged protection	[59]
Cardiovascular Disease	Liposomal Statins	Targeted delivery for atherosclerosis management	Reduced plaque size and inflammation with fewer side effects	[60]
Pancreatic Cancer	Liposomal Irinotecan (*Onivyde*)	Treatment of metastatic pancreatic cancer	Improved overall survival and progression-free survival compared to standard therapy	[61]
Triple-Negative Breast Cancer	Liposomal Doxorubicin and Cyclophosphamide	Treatment of early-stage triple-negative breast cancer	Higher pathological complete response and better tolerability than free drugs	[62]
Non-Small Cell Lung Cancer (NSCLC)	Liposomal Cisplatin	Treatment of advanced NSCLC	Reduced nephrotoxicity and enhanced efficacy compared to free cisplatin	[63]
Ovarian Cancer	*Doxil* (Liposomal Doxorubicin)	Treatment of advanced ovarian cancer	Reduced cardiotoxicity and prolonged drug circulation	[64]
	Liposomal Paclitaxel	First-line treatment for ovarian cancer	Increased tumour response rate and reduced peripheral neuropathy compared to free paclitaxel	[65]
Colorectal Cancer	Liposomal Irinotecan (*Onivyde*) plus Fluorouracil and Leucovorin	Second-line treatment for metastatic colorectal cancer	Significantly improved survival compared to other irinotecan formulations	[66]

Disease	Liposomal drug	Clinical applications	Outcome	References
Glioblastoma	Liposomal Temozolomide	Treatment of recurrent glioblastoma	Enhanced brain tumour penetration and improved survival rates in clinical trials	[67]
HIV/AIDS (Kaposi's Sarcoma)	*Doxil* (Liposomal Doxorubicin)	Treatment of Kaposi's sarcoma in HIV patients	Reduced systemic toxicity and prolonged drug exposure	[68]
Prostate Cancer	Liposomal Docetaxel	Treatment of castration-resistant prostate cancer	Increased median survival and improved quality of life	[69]
Hepatocellular Carcinoma	Liposomal Doxorubicin	Advanced hepatocellular carcinoma treatment	Higher drug concentration in tumours with fewer side effects	[70]

Table 1.
Recent clinical examples of liposomal drug delivery systems.

Vaccine delivery: The usage of liposomes as adjuvants in vaccine formulations increases the immune response to antigens and allows for better vaccination. Liposomal vaccines can deliver antigens more efficiently and give sustained release, leading to prolonged immune stimulation.

- *COVID-19 vaccines*: The mRNA vaccines have used lipid nanoparticles to protect them from any form of degradation; these have included Pfizer-BioNTech and Moderna vaccines. These nanoparticles protect the mRNA from any form of degradation and at the same time facilitate its delivery into cells so that it may be used for generating the antigen that then provokes an immune response [71].

Cosmetics and dermatological applications: Liposomes are also used in cosmetic formulations to improve the delivery of active substances into the skin. They have been found to increase the stability and penetrability of vitamins, antioxidants, and moisturisers, hence presenting more effective cosmetics.

- *Anti-ageing creams*: The liposomes in the creams can act as carriers for the deeper penetration of retinoids, peptides, and other active molecules, thereby increasing their activity to diminish wrinkles and fine lines [72].

Diagnostic imaging: Liposomes can be filled with contrast agents and applied to various diagnostic imaging methods including MRI and nuclear imaging. Such liposomal contrast agent increases the visibility of tumours, inflamed tissues, or other pathological sites.

- *MRI contrast agents*: Gadolinium- or iron oxide nanoparticle-based liposomes are applied as contrast agents in MRI for improved imaging of tumours and other abnormalities in soft tissues [73].

Pulmonary delivery: Inhalable liposomal carriers allow for the targeting of drug delivery to the lungs and exhibit potential in treating specific respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and lung infections.

- *Inhalation therapies*: Liposomes have been developed that encapsulate corticosteroids, antibiotics, and bronchodilators and deliver them precisely to the lungs. Such developed formulations might be beneficial in reducing the systemic side effects because of an increased local drug concentration [74].

12. Conclusion

Drug delivery systems are majorly advanced by liposomes, as they assure improved bioavailability of the therapeutic agents, their selective delivery, and reduced toxicity. In addition to encapsulating hydrophilic drugs, their ability to encapsulate hydrophobic drugs as well, coupled with excellent biocompatibility, makes them versatile carriers for a wide range of pharmaceutical applications. Although key challenges still remain on issues like stability, scalability, and cost-effectiveness, their potential continues to be enhanced with ongoing research and technological innovations in the field of liposomal therapies. As these continue to develop, liposomes have the potential to be a game-changing influence in the way that personalised medicine and treatment outcomes for many diverse medical specialties are approached.

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