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COMPHREHENSIVE REVIEW ON LIPOSOME DRUG DELIVERY SYSTEM

Sravani V.[1], Moulika P.*[2], Nithisha Ch, Sahithya R., Nagini T. and Bhargavi V.

[1]UG Scholar, Department of Pharmaceutics Joginpally B. R. Pharmacy College, Moinabad Telengana.

[2]Assistant Professor, Department Pharmaceutics, Joginpally B. R. Pharmacy College Moinabad Telengana.

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***Corresponding Author**
Moulika P.
Assistant Professor,
Department Pharmaceutics,
Joginpally B. R. Pharmacy
College Moinabad
Telengana.

ABSTRACT

Liposomes are spherical vesicles composed of one or more concentric phospholipid bilayers that surround an aqueous core. An amazing method of delivering medication are benign and biodegradable liposomes. While reducing systemic toxicity, they have enhanced therapeutic treatment efficacy by stabilizing molecules, breaking down cellular and tissue absorption barriers, and boosting drug biodistribution to target sites in vivo. Emphasizing their fundamental principles, this review gives a general picture of liposomes. First addressed were the essential design elements of a suitable liposomal formulation; then, liposome manufacture and drug loading techniques came second. Before use, liposomes must be completely examined to guarantee in vitro and in vivo performance. Several properties—including size, polydispersity index, zeta potential, shape, lamellarity, phase behavior, encapsulation efficiency, and in vitro drug release—used to define liposomes were investigated. Along with liposome stability and constraints, the topic covered liposome functionalization and successful targeting strategies. At last, the goal of this work is to investigate the present market for liposomes as a method of drug delivery in several therapeutic uses.

KEYWORDS: Liposomes, Spherical vesicles, Phospholipid bilayers, Biodegradable.

INTRODUCTION

Discovered by Dr. Alec D. Bangham in 1961, liposomes have become among the most researched medication delivery strategies because of their adaptability.[1] Phospholipids make up these bilayer vesicles, which arrange around an aqueous core. Liposomes are valuable for many therapeutic uses since they may encapsulate a broad spectrum of drugs, including both hydrophilic and lipophilic compounds.[1] Liposome surface characteristics like size, charge, and functionalization can be changed to target particular cells or tissues—especially cancer cells.[2] Greek words "Lipos" meaning fat and "Soma" meaning body form the basis for the name liposome. Liposomal drug delivery techniques are being used increasingly. Applied in cosmetic and pharmaceutical sectors to move different substances. In culinary and manufacturing sectors, liposomal encapsulation is applied to maintain the functionality of unstable compounds. Liposomes are particularly promising in cancer treatment because they may be tailored to take advantage of the tumor microenvironment, which includes acidic pH, hypoxia, and high temperatures.[3] Furthermore, surface alterations such as the attachment of ligands (e.g., transferrin, folate, or antibodies) allow for targeted targeting of tumor cells or CSCs.[1, 4] This tailored strategy not only raises medication concentration at the tumor site, but it also improves therapeutic efficacy and reduces systemic toxicity.[1,2] Recent improvements in liposome formulations, particularly the introduction of stimuli-responsive liposomes, have further boosted their potential for cancer treatment, allowing regulated drug release occurs in response to specific stimuli, such as changes in pH or temperature at the tumor site.[3]

Basic Structure and Properties of Liposomes

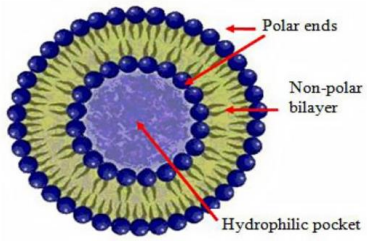


Figure 1: shows the basic structure of a liposome.[5]

COMPOSITION

Liposomes are microscopic vesicles containing one or more lipid bilayers. The key Components include: Phospholipids, the primary components of liposomes, contain

hydrophilic (water-loving) heads and hydrophobic (water-repelling) tails, allowing them to form bilayers in aqueous conditions.[6,1] Phosphatidylcholine, phosphatidylserine, and phosphatidylethanolamine are among the most often employed phospholipids in liposome formulations.

Cholesterol: Cholesterol is commonly included in liposome formulations to promote membrane stability and reduce permeability. It improves liposome stability by keeping the lipid bilayer rigid and intact.[4]

Liposomes can encapsulate hydrophilic and hydrophobic medicines using their water core and lipid bilayer, respectively. Liposomes can transport a variety of medicinal compounds due to their dual encapsulation ability.[7]

Dimensions, Surface, and Form

Liposomes' behavior in the body is heavily influenced by their size, surface charge, and shape. Liposome sizes range from 20 nm to several micrometres. greater liposomes, such as Large Unilamellar Vesicles (LUVs) and Multilamellar Vesicles (MLVs), can transport greater payloads, although they may be removed more quickly by the reticuloendothelial system.[8,9] Smaller liposomes, such as Small Unilamellar Vesicles (SUVs), offer superior tissue penetration and longer circulation durations. Liposomes' surface charges can be positive, negative, or neutral. Positively charged cationic liposomes may improve cellular absorption, whereas negatively charged anionic liposomes prevent aggregation and interact with certain biological components. Neutral liposomes are less reactive with biological systems.[10] Liposomes are normally spherical, however their form varies depending on production procedures and lipid makeup. These shape differences can alter liposome stability and drug release properties.[11]

LIPOSOME TYPES

Liposomes are classified depending on their structure and function.

Conventional Liposomes

Benefits: These simple liposomes, which have an aqueous core and phospholipid bilayer, can transport both hydrophilic and hydrophobic medicines. Still, the reticuloendothelial system[12] rapidly removes them and their circulation length is just fleeting.

Drawbacks: Polymers like polyethylene glycol (PEG) cover stealth liposomes, therefore lowering reticuloendothelial clearance and extending circulation time.[13]

Cationic Liposomes

Benefits: Effective in nucleic acid absorption and gene transfer.

Drawbacks: Cationic liposomes can interact with negatively charged cell membranes due their positive charge.[14]

Targeting Liposomes

Benefits: These liposomes are functionalized with particular ligands, such peptides or antibodies.

Drawbacks: which enable them to bind to receptors on target cells hence enhancing drug delivery specificity.[15]

Multilamellar vesicles (MLVs)

Benefits: Made of numerous concentric lipid bilayers that offer more pharmaceutical stability and protection.

Drawbacks: Multilamellar vesicles (MLVs) Their drug releasing properties, meanwhile, are slower.[16]

Advantages and disadvantages

Conventional Liposomes

Benefits: Simple preparation and the capacity to condense a large spectrum of drugs are among the advantages. Drawbacks: Short circulation time and fast reticuloendothelial system clearance are drawbacks.[17]

Stealth Liposomes

Benefits: Longer circulation time, better targeting, and lower immune system clearance are among the benefits. Drawbacks: The polymer covering could set up immunological responses; processing is more difficult.[13]

Cationic Liposomes: Benefits: Among the advantages are better cellular absorption and effective gene transfer. Drawbacks: Reduced stability in biological environments and perhaps toxicity resulting from the positive charge.[14]

Liposomes with particular goal in mind

Benefits: Low off-target effects and strong selectivity for target cells are benefits. Drawbacks: Complicated preparation and immunological sensitivity to certain ligands.[15]

Multipurpose vesicles: Benefits: Among the benefits include better controlled release and more pharmaceutical stability.

Drawbacks: Tissue penetration may be hampered by the delayed drug release.[16]

Method of liposome-based medication delivery

Encapsulating Drugs: Liposomes' unusual structure—an aqueous core surrounded by a lipid bilayer—allows them to encapsulate hydrophilic and hydrophobic drugs. The stability and solubility of the medicine are enhanced by this two-fold encapsulating ability.

Hydrophilic Drugs: Their stability and solubility are enhanced by their safe environment and watery core of the liposome.[18,19,20]

Hydrophobic drugs: These are absorbed into the lipid bilayer of the liposome, therefore guaranteeing stability and stopping breakdown.[19,20,21]

Drug release mechanism: Liposomes allow drugs to be released steadily and under control. One can reach this by several means.

PH-Sensitive Release: Liposomes can be made to release their contents in reaction to pH changes, such those of the acidic environment of endosomes or tumor tissues.[20, 22, 23,24]

Liposomes can also be produced to react to particular stimuli including light, temperature, or enzymes, therefore offering exact control over drug release.[21,22]

Enhanced permeability and retention define the EPR effect.

A main mechanism driving liposome generation in tumor tissues is the EPR effect.

This influence occurs because of the different properties of the lymphatic system and tumor vasculature.

High Permeability: Because tumor blood vessels expand rapidly and haphazardly, liposomes can more easily extravasate from the bloodstream into tumor tissue than normal tissues.[23,24,22]

Inadequate Lymphatic Drainage: Because tumours typically lack a well-developed lymphatic system, liposomes become trapped in tumor tissue for extended periods of time, promoting drug accumulation at the tumour site.[23,24,22]

Targeting Strategies for Liposomal Drug Delivery

1. Passive Targeting using the EPR Effect

Macromolecules like liposomes can be selectively concentrated in tumor tissues thanks to the Enhanced Permeability and Retention (EPR) effect, which takes advantage of tumor vasculature's unique properties. This technique depends on the disorganized and leaky tumor blood arteries have extensive inter-endothelial gaps and poor lymphatic drainage.[25]

Mechanism of EPR Effect

Leaky Tumor Vasculature: Tumors with rapid and unregulated angiogenesis typically have an abnormal vascular system. Larger breaches in blood arteries (200 nm to 1 µm) let nanoparticles such as liposomes to escape and gather in tumour tissues.[4]

Liposome properties for EPR exploitation

Size: For best use exploiting the EPR effect, liposomes spanning 50 to 200 nm are most appropriate. These liposomes can pass through the tumour vasculature without quick immune system destruction.[1]

Surface Modifications: Liposomes can circulate for longer times without being identified by the mononucleated phagocyte system (MPS) by linking polyethylene glycol chains to their surface[1], hence boosting their concentration in tumors.

Uses in cancer treatment: One of the finest examples of applying the EPR effect is Doxil® (liposomal doxorubicin). Lower systemic toxicity and enhanced treatment efficacy follow from liposomal doxorubicin accumulating selectively in tumor tissues.[26]

Difficulties and Restraints: Tumor heterogeneity: different EPR effects result from even the same tumor as well as from various tumor kinds.

Tumor size, blood flow parameters, and lymphatic drainage can all have a significant impact on the level of EPR-mediated drug transport.[25]

Limited Penetration: Although liposomes accumulate in tumor tissues, strong extracellular matrices and high interstitial fluid pressure can prevent them from entering deeper tumor sites.[1]

2. Active Targeting via Surface Modification

Active targeting techniques modify the surface of liposomes by attaching specific molecules (ligands, antibodies, or peptides) to overexpressed receptors on cancer cells or tumor vasculature to increase drug delivery selectivity and effectiveness.

Surface modifications are classified as follows

1. Ligand-based targeting

Folate Receptor Targeting: Folate receptors are overexpressed in several malignancies, including glioblastoma, breast, and ovarian cancers. Liposomes functionalized with folate can preferentially bind to these receptors, resulting in increased cancer cell internalization.

Integrin Targeting: RGD peptides in liposomes can target integrins like αvβ3, which are expressed by tumor cells and endothelial cells in the tumor vasculature. This enhances medicine delivery to tumor vasculature and cancer cells.[28]

2. Based Targeting

Monoclonal Antibodies (mAbs): Liposomes coated with monoclonal antibodies that target tumor-specific antigens enable selective adhesion to tumor cells. Herceptin® (trastuzumab) is one treatment option for HER2-positive breast cancer.[27]

3. Peptide-based targeting

Tumor-Specific Peptides: Liposomes can transport specific substances to tumor cells by attaching to receptors such neuropilin-1 and αvβ3 integrins.[28]

4. Antibody Aptamers-Based Targeting

Aptamers are short nucleic acid sequences that bind to certain cell surface targets and can be used as liposome targeting agents. Unlike antibodies, they have a high level of specificity and low immunogenicity.

FORMULATION AND MANUFACTURING OF LIPOSOMAL DRUG DELIVERY SYSTEMS

Liposomal drug delivery systems (LDDS) can deliver a wide range of medical medications, making them a versatile and promising approach. Because they can encapsulate hydrophilic and lipophilic medicines, increase drug stability, and raise bioavailability.

Techniques for manufacturing liposomes

1. Thin-Film Hydration Approach: Bangham et al. (1965) first reported the thin-film hydration procedure, which is now one of the most popular methods for liposome manufacturing. This method includes the stages shown below.

Solvent Evaporation: Using an organic solvent such as methanol or chloroform, phospholipids and other lipid components are dissolved. The solution is then evaporated using a rotary evaporator, leaving behind a thin layer of lipids on the container's surface. Hydration: To form liposomes, the thin film is hydrated with water solution.

Hydration: To form liposomes, the thin film is hydrated with an aqueous phase, commonly water or buffer. The hydration process causes lipid molecules to self-assemble into bilayer structures. The thin-film hydration process is popular because it is inexpensive, simple to apply, and reproducible. However, in terms of size and encapsulation efficacy, it frequently generates varied liposome populations.

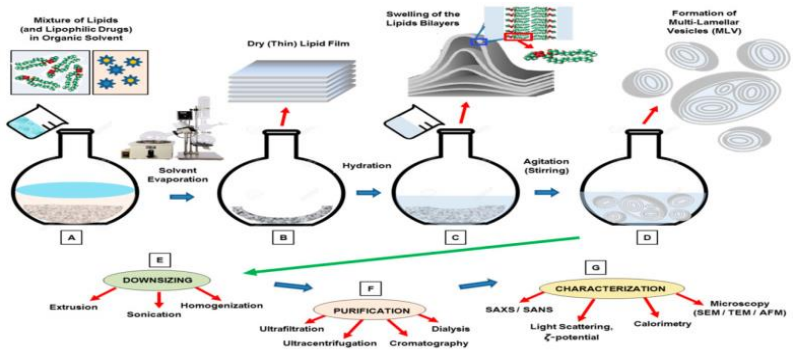


Figure 2: The thin-film hydration technique (also known as the Bangham method) is the oldest, most common, and simplest procedure for making MLV.[42,43,44]

Schematically, the main phases of liposome synthesis employing the thin-film hydration approach are shown. Dissolved in an organic solvent (A), the lipid components come first then lipophilic drugs/macromolecules. The solvent evaporates, leaving B—thin, dry lipid coating. The lipid film is next rehydrated in a saline buffer (which finally contains hydrophilic dugs that have to be gathered), generating swelling of the lipid bilayer stacks (C). The repeated stirring or agitation of the sample promotes the generation of (polydispersed) multilamellar vesicles (D). Reducing the liposomes (E), purifying (F), and characterizing (G) are the last phases of the production process.

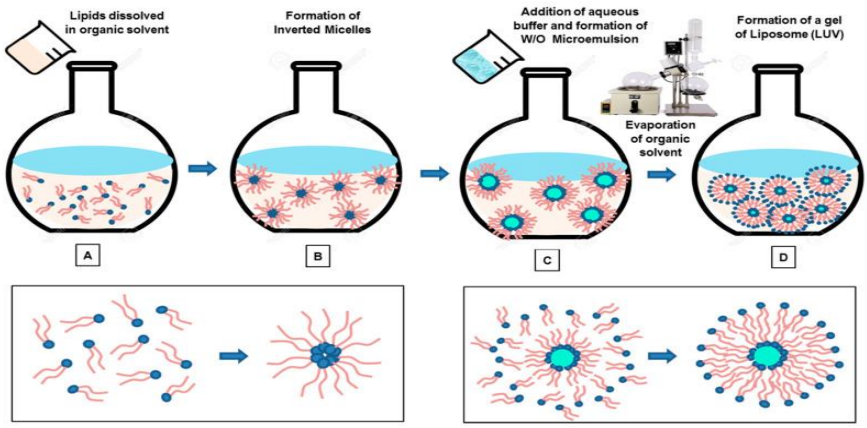
2. The Reverse-Phase Evaporation Method

Szoke and Papahadjopoulos (1978) first described the reverse-phase evaporation method (REV), which is particularly useful for producing large unilamellar vesicles (LUVs). Steps are as follows.

Water-in-oil Emulsion Formation: To make a water-in-oil emulsion, lipids are dissolved in an organic solvent and mixed with an aqueous phase.

Evaporation: When the organic solvent is removed at a lower pressure, a gel-like substance called a reverse-phase vesicle forms.

Resuspension: The liposomes are finally resuspended in an aqueous solution after the leftover organic solvent has been removed. Although this approach can encapsulate both hydrophobic and hydrophilic drugs, it may be difficult to replicate and remove the solvent.



Reverse-phase evaporation's fundamental phases are shown graphically below. In organic solvent (A), lipids dissolve; inverted micelles develop in B. The homogenous dispersion of a W/O microemulsion is facilitated by adding an aqueous medium (buffer) then emulsification of the solution. A viscous gel forms and finally collapses to generate liposomes (D) when the organic solvent is finally removed from the solution via revolving evaporation under vacuum. Figure 3.[45,46,47]

3. Extrusion Method

Extrusion is a method for reducing liposome size and boosting homogeneity. It generates uniform liposome sizes by passing a liposomal suspension through a polycarbonate membrane with predefined pore widths. The acts consist of.

Making Liposome Suspension: Liposomes are created using thin-film hydration or another process.

Extrusion: To reduce the size of the liposomes and produce a more uniform population, the liposomal suspension is repeatedly passed over a membrane with a predefined pore size.

This approach is commonly used to manufacture tiny unilamellar vesicles (SUVs) and is highly effective at adjusting liposome size. However, because of shear pressures, it may take longer and result in lower encapsulation efficiency.

Challenges of Liposome Manufacturing

1. Scale-Up tasks: Transposing liposome production from the lab to the industrial level is among the most challenging chores. Many factors complicate the change, including: Reproducibility: Liposome size, charge, and encapsulation efficiency could change with increasing production volume.

Process Parameter Management: Maintaining exact control over important variables including temperature, hydration time, and fat content gets more challenging as the operation size increases.

Cost-effectiveness: Higher manufacturing costs result from need for more raw materials and improved machinery in bigger batches, therefore promoting cost-effectiveness. To solve these problems and provide better control over the size and content of liposomes on a more extensive level, the sector is looking at substitutes including microfluidic devices.

2. Reproducibility and Accuracy: Maintaining homogeneity over several production batches is one of the toughest challenges in liposomal drug delivery systems. The characteristics of the final product depend much on lipid concentration, solvent quality, and hydration conditions. attaining great repeatability calls for.

Standardized procedures: Approaches of preparation should abide by accepted guidelines. Advanced monitoring methods: It track properties including liposome size distribution and encapsulation efficiency over manufacturing.

Stability Issues Using Liposomes: Liposomal compositions have to be stable if they are therapeutally valuable. Liposomes could start to be physically and chemically unstable.

1. Physical Stability: Aggregation: Van der Waals pressures allow liposomes to mix and produce a diverse size distribution.

Leakage: Unstable formulations of encapsulated pharmaceuticals might cause membrane instability that results in leakage.

Osmolarity Stability: Liposomes can experience osmotic lysis under either high or low osmolarity settings.

Approaches for enhancing physical stability: Including stabilizing molecules, like cholesterol, stiffens thse liposomal bilayer.

Usually referred to as PEGylation, polyethylene glycol coating lowers aggregation by steric hindrance.

2. Chemical Integrity: Oxidation: Lipid oxidation can compromise drug release characteristics and lead to liposomal compositions breaking down.

Hydrolysis: Phospholipids can hydroly over time to produce lysophospholipids.

3. Storage environment and shelf-life: Variables including pH, temperature, and light exposure help to determine the shelf life of liposomal compositions. Common storage techniques meant to extend shelf life consist in the following.
Freeze and dry liposomal substances can increase their shelf life by preventing oxidation and hydrolysis. Usually kept in dark settings and at low temperatures (like 4°C), liposomes help to prevent deterioration from lipid oxidation. Use more stable lipids like sphingomyelin or distearoylphosphatidylcholine to increase chemical stability.

Advances and Novelties in Liposomal Drug Delivery Systems: In recent years, liposomal drug delivery systems have developed dramatically. These developments seek to increase target specificity, medication bioavailability, and reduce off-target consequences. Perfect for exact and controlled medication administration, liposomes are nanoscale vesicles with an aqueous core and a lipid bilayer that can include hydrophobic or hydrophilic medicines.

1. Smartly designed targeted liposomes with unique characteristics: Liposomal systems evolved "smart" characteristics that boost their sensitivity to particular environmental stimuli

such pH, temperature, and enzyme presence. More focused and controlled pharmaceutical release made possible by these sensitive liposomes helps to lower side effects.

Liposomes responding to pH: Tumor microenvironments could be the perfect target for drug release since they are typically more acidic than normal tissues. The pH-sensitive linkers utilized in pH-sensitive liposome creation lead them to dissolve or change structure in acidic conditions, allowing for controlled release at the tumor site or within certain intracellular compartments such as lysosomes. Liposomes functionalized with pH-sensitive polymers, such as poly(ethylene glycol)-b-poly(lysine) (PEG-b-PLL), have been shown to release their contents in acidic conditions found in tumors.[29]

Temperature-Responsive Liposomes: Localized hyperthermia or external heating can activate these liposomes, causing a phase shift at a specific temperature (for example, during cancer treatment). Because poly(N-isopropylacrylamide) (PNIPAM) suddenly transforms from a hydrophilic to a hydrophobic state at temperatures close to 37°C, it is commonly used in these systems. When used in conjunction with hyperthermia treatment, these devices might generate localized heating, resulting in medication release.[30]

Enzyme-Responsive Liposomes: These are designed to release their cargo in response to specific enzymes. Many cancer cells express high levels of matrix metalloproteinases (MMPs), which can break down specific liposomal membrane components and release the drug. This feature reduces toxicity to healthy organs while increasing selectivity for malignant cells.[1]

2. Gene Therapy and Immunotherapy

Liposomal systems have made important advances in cancer immunotherapy by transferring genetic resources like as DNA, mRNA, and siRNA, as well as immunomodulatory medicines. These methods improve the efficacy of gene-based treatments by increasing cellular absorption and shielding the fragile genetic material from degradation.

Gene Therapy: Liposomes are used in gene therapy to carry mRNA and siRNA. Therapeutic proteins can be expressed by mRNA vaccines or therapies, whereas siRNA-based therapies target specific genes involved in disease processes. Liposomal systems, namely lipid nanoparticles (LNPs), have proven critical to the efficacy of mRNA vaccines, particularly the COVID-19 vaccine. In addition to promoting cellular absorption and ensuring optimal

mRNA release within the cell, these lipid nanoparticles protect mRNA from degradation. Liposome-based gene transfer appears to be a potential treatment method for cancer, genetic disorders, and other ailments.[31,32]

Cancer Immunotherapy: Liposomes are increasingly used to deliver cytokines (such as interleukins) or immune checkpoint inhibitors (such as anti-PD-1 and anti-CTLA-4 antibodies) directly to tumours. The immune system can target and remove cancer cells because these immunomodulatory medications activate the immune system. Liposomes have the advantage of customized dispersion, which reduces systemic side effects and improves therapeutic efficacy. Liposomal formulations have been used to co-deliver immunotherapies and chemotherapeutic medicines, thereby improving anti-tumor immune responses.[33,34]

3. Overcoming Biological Barriers in Nanomedicine with Liposomes

Liposomes' ability to precisely transfer and encapsulate a range of therapeutic compounds to disease locations makes them an essential component of nanomedicine, particularly in cancer therapy. One key area of research is their ability to cross biological barriers such as the blood-brain barrier (BBB).

Blood-Brain barrier (BBB) penetration: Treating brain tumors (like glioblastoma) and central nervous system (CNS) diseases presents a major challenge for blood-brain barrier (BBB) penetration. Small size and surface changes of liposomes could enable them to pass the blood-brain barrier more effectively than conventional medications. Targeting drug distribution across the blood-brain barrier requires functionalizing liposomes with particular ligands, such transferrin or polypeptides. Moreover, doxorubicin and other chemotherapeutic drugs have showed promise in liposomal formulations for overcoming this barrier and raising treatment efficacy in brain tumors.[1]

The effect on tumor targeting of improved permeability and retention (EPR): Liposomes and other nanoparticles can preferentially cluster in tumor tissue by leveraging the EPR phenomenon—that which results from tumor blood capillaries being more permeable than healthy blood arteries. Targeting tumor-specific ligands (like folic acid or HER2 antibodies) on the surface of liposomes helps to maximize drug delivery's selectivity to tumor cells.[29] Particularly with the creation of smart liposomes that react to enzyme, pH, or temperature stimuli, liposomal drug delivery techniques have made significant strides in recent years. By enabling targeted, controlled drug distribution, these developments reduce side effects and

increase treatment efficacy. Immunomodulators are delivered in part by liposomes. Gene therapy and immunotherapy make use of drugs and genetic materials including siRNA and mRNA, therefore providing fresh hope for the treatment of cancer and genetic disorders. Moreover, liposomes help to break down biological barriers, especially the blood-brain barrier, thereby enhancing the possibilities for cancer treatment with nanomedicine.

Applications

Clinical Use of Liposomal Drug Delivery for Cancer Treatment

Because of capacity to improve drug targeting, increase pharmacokinetics, and lower toxicity as compared to conventional formulations, liposomal drug delivery systems (DDS) have become important instruments in cancer treatment.

Liposomes are spherical vesicles made up of lipid bilayers that encapsulate therapeutic chemicals, allowing for regulated and sustained release as well as more specific targeting of cancer cells.

Table 1: FDA-approved cancer drugs based on liposomes.

Drug Name	Doxil (Doxorubicin Liposome Injection)	Marqibo (Vincristine Liposome Injection)	Depocyt (Cytarabine Liposome Injection)
Approval History	Approved by the FDA in 1995 for Kaposi's sarcoma; later expanded to include breast cancer, ovarian cancer, and multiple myeloma.[35]	FDA-approved in 2012 for acute lymphoblastic leukemia (ALL) in adults.[37]	Approved by the FDA in 1999 for treating lymphomatous meningitis.[39]
Clinical Use	Used for advanced ovarian cancer, breast cancer, and multiple myeloma. Liposomal formulation reduces cardiotoxicity compared to conventional doxorubicin.[4]	Allows higher doses of vincristine while reducing neurotoxicity typically associated with conventional vincristine treatments[37]	Delivers cytarabine to the central nervous system (CNS), overcoming the blood-brain barrier for treating cancers of the brain and spinal cord[39]
Clinical Findings	Improves survival rates in ovarian cancer patients and reduces cardiotoxicity; common side effects include hand-foot syndrome and infusion-related reactions.[36,4]	Demonstrated enhanced efficacy in relapsed/refractory ALL with improved overall survival and remission rates; challenges include long-term side effects and optimal dosing[38,37]	Significantly improves survival and time to progression in patients with CNS lymphoma and other brain-related cancers[39]

Clinical Trials and Key Results

Table 2: Several clinical trials have examined liposomal medication compositions, concentrating on their pharmacokinetics, effectiveness, and safety. These trials revealed both triumphs and challenges.

Drug Name	Doxil in Ovarian Cancer	Marqibo in Acute Lymphoblastic Leukemia (ALL)	Depocyt in Lymphomatous Meningitis
Trial	Phase III trial compared Doxil with conventional doxorubicin for advanced ovarian cancer[36]	Phase II study evaluating Marqibo's efficacy in relapsed/refractory ALL[38]	Phase III study assessing Depocyt's efficacy in treating lymphomatous meningitis in non-Hodgkin lymphoma patients[39]
Findings	Doxil improved progression-free survival (PFS) and reduced cardiotoxicity compared to conventional doxorubicin; side effects included hand-foot syndrome and infusion reactions.[4]	Marqibo showed enhanced efficacy with improved overall survival (OS) and remission rates; long-term side effects and optimal dosing regimen need further investigation[37]	Depocyt significantly improved survival and time to progression in CNS lymphoma patients, demonstrating potential as a critical therapy for central nervous system cancers[39]

Challenges of Clinical Trials

Several obstacles still exist in optimizing liposomal medication delivery in cancer treatment:

Encapsulation Efficiency: Maximising medication efficacy requires excellent encapsulation efficiency in liposomal compositions. Suboptimal encapsulation could result in insufficient therapeutic effects.[1]

Lack of Predictive Biomarkers: There is a scarcity of accurate biomarkers to predict patient responses to liposomal medicines, impeding the development of tailored treatment regimens.[40]

Combination Therapy: Improving Outcomes

To maximize overall therapeutic efficacy, liposomal formulations have also been investigated for use in combination treatments combining other modalities including chemotherapy, immunotherapy, and radiotherapy.

1. Liposomal chemotherapy and drugs

It has been shown that combinations of liposomal formulations like Doxil with other chemotherapy medications have synergistic effects. While reducing systemic toxicity, liposomes can raise the concentration of both medications at the tumor site (1).

2. Liposomal therapies and immunotherapy

Combining liposomes with immune checkpoint inhibitors—such as anti-PD-1/PD-L1 inhibitors—showcases promise. By delivering immuno-modulating medicines straight to the tumor microenvironment, these combinations might increase immune responses and reduce systemic toxicity.[41] Combining Doxil with immune checkpoint inhibitors seems to enhance therapy outcomes according preclinical studies.[41]

3. Radiotherapy and liposomal medicines

One can use liposomal compositions to make tumors more radiation sensitive. By encapsulating radiation-sensitizing compounds, liposomes reduce harm to healthy tissues and improve radiation targeting to cancer cells.[1]

By improving medication delivery, pharmacokinetics, and reduction of systemic toxicity, liposomal drug delivery systems have made major contributions to cancer therapy. Approved by the FDA, Doxil, Marqibo, and Depocyt are liposomal medications with positive clinical results.

Still, issues including side effects, manufacturing complexity, and the need for predictive biomarkers are enduring. Liposomal drugs taken in combination with chemotherapy, immunotherapy, and radiation could greatly enhance therapy outcomes and overcome drug resistance.

CONCLUSION

In essence, liposome-based drug delivery systems are a flexible and interesting approach for enhancing the therapeutic efficacy of several medications. Excellent for targeted and regulated medication release, their special structural characteristics—biocompatibility, biodegradability, and ability to encapsulate both hydrophilic and lipophilic compounds—make Liposomes have been demonstrated to increase medicinal ingredient bioavailability, lower systemic toxicity, and improve pharmacokinetics. Moreover, developments in surface

modification and targeting technologies have expanded their possible uses especially in gene therapy, cancer treatment.

Liposome compositions for medical usage still present difficulties even with their several advantages. One has to take into account manufacturing costs, production scalability, and stability as well as issues. Moreover, long-term safety and efficacy traits in humans have to be investigated extensively to guarantee that liposome-based treatments are effectively applied.

Promising technology that is always developing thanks to continuous study aiming at overcoming present constraints and optimizing its therapeutic potential is liposome drug delivery systems. Depending on further developments, liposomes could be crucial in the direction of personalized treatment and exact drug delivery.

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