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Liposomes as Therapeutic Vehicles: Advancing Targeted Drug Delivery in Healthcare

Varsha R. Gaikwad[1], Shaikh Sabiya[2], Khan Sahil[3], Choudhary Tariq[3], Kesarwani Aayush[3], Ansari Nehad[3], Ansari Anzal[3], Ambika Nand Jha[4,*]

Abstract

Liposomes represent an innovative approach to targeted drug delivery. These tiny, lipid-based vesicles can encapsulate medications, allowing them to travel directly to diseased cells while minimizing impact on healthy tissues. By using liposomes, medications can improve their effectiveness while reducing side effects, leading to better overall treatment results. Their structure enables a controlled release of the drug, which can be particularly beneficial for therapies requiring sustained action. This technology holds promise for various medical applications, including cancer treatment and vaccine delivery, making it a significant advancement in improving how we administer and target therapeutic agents within the body. The unique structure of liposomes allows for controlled drug release, which is particularly advantageous for therapies necessitating sustained action over time. In the context of oncology and genetic disorders, liposomes are revolutionizing treatment paradigms. Their capacity to encapsulate various therapeutic agents, such as small molecules, proteins, and nucleic acids, allows for targeted delivery to specific tissues in need. Their unique ability to encapsulate therapeutic agents allows for targeted delivery directly to affected cells, minimizing side effects and enhancing treatment efficacy. By modifying the liposome's surface, researchers can create formulations that selectively bind to specific cell types, making them invaluable for personalized medicine. This focused strategy enhances patient outcomes and paves the way for the development of novel therapies. As research advances, liposomes hold great promise for transforming how we approach disease treatment and management, paving the way for more effective and individualized healthcare. In this article, we will delve into the intriguing history of liposomes, tracing their discovery and examining their various applications in the medical field. We'll delve into how they function, enabling targeted delivery of drugs and enhancing treatment efficacy. Their ability to encapsulate various therapeutic agents has led to breakthroughs in treating conditions like cancer and genetic disorders. With ongoing research, liposomes continue to reveal new possibilities in personalized medicine, transforming patient care.

Keywords: Cancer treatment, controlled release, liposomes, targeted drug delivery, therapeutic agents

***Author for Correspondence**
Ambika Nand Jha
E-mail: nandjha99@gmail.com

[1]Assistant Professor, Department of Pharmacognosy, Shri Pandit Baburao Chaughule College of Pharmacy, Bhiwandi, Maharashtra, India
[2]Assistant Professor, Department of Pharmaceutical Chemistry, Shri Pandit Baburao Chaughule College of Pharmacy, Bhiwandi, Maharashtra, India
[3]Student, B. Pharm., Shri Pandit Baburao Chaughule College of Pharmacy, Bhiwandi, Maharashtra, India
[4]Assistant Professor, Department of Pharmacy Practice, School of Pharmacy, Sharda University, Greater Noida, Uttar Pradesh, India

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INTRODUCTION

Little fat bubbles called liposomes have been around for over 50 years. They were first discovered by Alec Bangham in the 1960s, and since then, scientists have been trying to figure out how to use them to help people [1, 2]. One of the cool things about liposomes is that they can carry all sorts of things inside them, like medicine,

proteins, and even DNA. The good thing about liposomes is that they are good at protecting the things inside them from getting damaged [3]. They are also biocompatible, which means they will not hurt the body. But there are some downsides to liposomes too. They can be hard to make and store, and sometimes they do not work very well. So, what makes a good liposome? It should be stable, spacious, and made from safe, durable materials that won't harm the body [4–6]. In this article, we will talk about the history of liposomes, what they are good for, and what makes them work. We will also explore the several kinds of liposomes and how they are ready. By the end of it, you should have a pretty good understanding of what liposomes are and how they can be used to help people.

Table1. Liposome classification

Classification Based on	Subcategory	Discription/Size Range/Composition
Size	1. Small unilamellar vesicles (SUVs). 2. large unilamellar vesicles (LUVs). 3. Multilamellar vesicles (MLVs).	1. 20 to 50 nm. 2. 50 to 150 nm. 3. 150 to 500 nm.
Composition	1. Conventional liposomes. 2. PEGylated liposomes. 3. Cationic liposomes.	1. Phospholipids, cholesterol. 2. PEG, phospholipids. 3. Cationic lipids, cholestrol.
Charge	1. Neutral liposomes. 2. Cationic liposomes. 3. Anionic liposomes.	1. No net charge. 2. Positive net charge. 3. Negative net charge.

Liposomes can be categorized into different types based on their size, composition, and charge, as outlined in Table 1. Recognizing these distinctions is essential for choosing the right liposome type for applications [7–9].

Liposomes vary in size, encompassing small unilamellar vesicles (SUVs) and large multilamellar vesicles (MLVs). SUVs are generally preferred for drug delivery applications, whereas MLVs are commonly utilized in the development of vaccines.

- *Composition:* Conventional liposomes are composed of phospholipids and cholesterol. PEGylated liposomes have an added layer of polyethylene glycol (PEG), which enhances their stability and circulation time. Cationic liposomes contain positively charged lipids, making them suitable for gene delivery.
- *Charge:* Neutral liposomes have no net charge, while cationic and anionic liposomes have positive and negative charges, respectively. The charge of liposomes influences how they interact with cells, as well as their effectiveness in delivering drugs or genetic material.
- *Applications:* Liposomes are like superheroes in the medical world! They can be used to deliver drugs and treatments to specific parts of the body, making them super effective.
- *Cancer therapy:* Liposomes are like special delivery trucks that bring cancer-fighting drugs right to the tumor. They can be designed to target specific types of cancer, like breast or lung cancer, and can even be used with other treatments like radiation therapy.
- *Infectious diseases:* Liposomes can help fight off bad guys like bacteria and viruses. They can carry antibiotics and antivirals directly to the source of the infection, making them effective.
- *Gene delivery:* Liposomes can even help fix faulty genes! They have the capability to transport functional copies of genes into cells, which can aid in the treatment of genetic conditions, such as cystic fibrosis.
- *Vaccine development:* Liposomes can be used to make vaccines more effective. They can boost the immune system's ability to combat illnesses, such as the flu and HPV.
- *Ocular delivery:* Liposomes can deliver drugs directly to the eyes, which can help treat conditions like macular degeneration and glaucoma.
- *Dermal delivery:* Liposomes can be used in creams and ointments to deliver drugs through the skin, which can help treat conditions like acne and psoriasis.

- *Mucosal delivery:* Liposomes can deliver drugs through mucous membranes, which can help treat conditions like respiratory infections and STDs.
- *Parenteral delivery:* Liposomes can be injected into the body to deliver drugs systemically or locally, depending on what is needed.
- *Nanotechnology:* Liposomes can even be combined with nanotechnology to create nanoliposomes, which are like tiny little drug delivery robots! In summary, liposomes are amazing and have lots of potential applications. They can be used to deliver drugs and treatments in a targeted way, making them effective [10, 11].

Drug Selection Criteria for Liposomal Formulations

When developing liposomal formulations, selecting the right drug is critical for ensuring therapeutic efficacy and safety. The following criteria must be carefully evaluated:

1. *Solubility:* A drug's solubility is a primary consideration in liposomal formulation. The drug must either be water-soluble or have a strong affinity for lipids, as this property influences its ability to be effectively encapsulated within the liposome. Drugs that are poorly soluble may not be able to achieve adequate concentrations within the liposomal carrier, potentially limiting their therapeutic effects. Moreover, enhancing the solubility of hydrophobic drugs can be achieved through various formulation techniques, such as using surfactants or co-solvents, ensuring that they can be effectively delivered in a liposomal form [12, 13].
2. *Stability:* Stability is another essential criterion for drug selection. The encapsulated drug should resist degradation, hydrolysis, or oxidation during storage and after administration. An unstable drug may result in inadequate treatment results or a heightened risk of toxicity. Formulation scientists often employ techniques, such as freeze-drying or the addition of stabilizing agents to enhance the stability of liposomal formulations. Additionally, understanding the degradation pathways of the drug helps in designing liposomes that protect the active ingredient [13, 14].
3. *Potency:* The potency of a drug reflects its capacity to achieve a desired therapeutic effect even at low concentrations. Highly potent drugs can achieve effective treatment outcomes with minimal dosages, which is particularly advantageous in reducing the potential for side effects. Evaluating the potency is crucial, especially in oncology and chronic diseases, where treatment regimens often involve multiple drugs [12–14].
4. *Toxicity:* A drug's toxicity profile must be carefully assessed to avoid adverse effects that could outweigh its therapeutic benefits. Low toxicity is especially vital when designing liposomal formulations, as the delivery system itself can influence the distribution and metabolism of the drug. Ideally, the drug should have a wide therapeutic window, meaning there is a substantial difference between effective and toxic doses [15].
5. *Molecular weight:* The molecular weight of the drug can significantly impact its pharmacokinetics and encapsulation efficiency. In general, drugs with lower molecular weights are more easily encapsulated and can be efficiently released from liposomes. However, very small molecules may escape during the formulation process. Therefore, finding an optimal molecular weight that balances these factors is key.
6. *pH sensitivity:* The pH stability of the drug is crucial, as it must remain effective across various physiological environments. Some drugs can degrade at specific pH levels, while others may require certain conditions for optimal activity. Formulation strategies can include pH-adjusting agents to maintain drug stability within the liposomal carrier and ensure appropriate release profiles.
7. *Interactions:* Potential interactions between the drug and liposomal components must be evaluated to ensure that the drug does not adversely affect liposome stability or functionality. For example, certain drugs may cause aggregation or destabilization of liposomes, which could compromise drug delivery. Comprehensive compatibility testing can help identify and mitigate such issues.

8. *Therapeutic index:* A favorable therapeutic index is critical for drug selection, indicating that the drug can be effective without causing significant toxicity. Drugs with a narrow therapeutic index require careful dosing and monitoring, making them less desirable for liposomal formulation unless specific strategies are employed to enhance safety and efficacy.
9. *Route of administration:* The selected drug must align with the planned route of administration, whether it be intravenous, oral, or topical. Each route has distinct challenges regarding the drug's absorption, distribution, metabolism, and excretion (ADME). For example, drugs designed for oral use often require specific formulation adjustments to endure the conditions of the gastrointestinal tract and to optimize absorption. These considerations are crucial for ensuring that the drug remains effective and safe, as the route of administration can significantly influence how the body processes and utilizes the medication. Proper compatibility is essential for achieving the desired therapeutic outcomes [16–19].
10. *Regulatory considerations:* Compliance with regulatory guidelines is essential when selecting drugs for liposomal formulations regulatory agencies like the FDA demand thorough information regarding the safety, efficacy, and manufacturing procedures of drugs. Understanding the regulatory landscape can guide the formulation process, helping to streamline the path to market [20, 21].
11. *Composition and excipients in liposomal formulations:* Liposomes are sophisticated drug delivery systems that rely on a carefully selected composition of excipients to enhance their functionality and overall performance. These excipients can be categorized into three main groups: lipids, aqueous core components, and additional ingredients [22–25].

LIPIDS

1. *Phospholipids:* Phospholipids, the essential components of liposomes, are amphipathic molecules that feature a hydrophilic (water-attracting) head and hydrophobic (water-repelling) tails. When exposed to aqueous environments, phospholipids spontaneously form bilayers, creating the structure that encapsulates therapeutic agents. Commonly used phospholipids include phosphatidylcholine and phosphatidylserine. Their selection impacts the liposome's stability, encapsulation efficiency, and release characteristics.
2. *Cholesterol:* Cholesterol is often incorporated into liposomal formulations to enhance membrane properties. It increases the fluidity and stability of the phospholipid bilayer, making the liposomes less permeable and more resilient to environmental stressors. Cholesterol helps modulate the release rates of encapsulated drugs, allowing for controlled release profiles that can improve therapeutic outcomes.
3. *Neutral lipids:* Additional lipids, such as sphingomyelin and ceramides, can be included to modify membrane characteristics. These neutral lipids can enhance liposome stability and provide specific functionalities, such as increasing the liposome's circulation time in the bloodstream or improving the targeting of the liposome to specific tissues.

AQUEOUS CORE COMPONENTS

1. *Buffering agents:* Salts like phosphate or citrate maintain the pH and osmotic balance within the liposome.
2. *Stabilizers:* Sugars or polyols like sucrose or trehalose help preserve liposome structure during freeze-drying or storage.
3. *pH adjusters:* Acids or bases like HCl or NaOH adjust the pH to optimize drug stability or liposome functionality.

Additional Ingredients

1. *Targeting ligands:* Molecules like antibodies, peptides, or carbohydrates attached to the liposome surface facilitate targeted delivery.
2. *Pegylation agents:* Polyethylene glycol (PEG) molecules enhance the circulation time of liposomes and decrease their immunogenicity.

3. *Preservatives:* Antimicrobial agents like parabens or benzyl alcohol prevent contamination and spoilage.
4. *Lyoprotectants:* Agents like mannitol or dextran protect liposomes during freeze-drying and reconstitution.

Importance of Excipients

Excipients significantly impact liposome performance, influencing:

1. *Stability:* Lipid composition, cholesterol content, and pH control affect liposome integrity.
2. *Targeting:* Targeting ligands and surface modifications enhance delivery specificity.
3. *Release kinetics:* Lipid composition, aqueous core components, and lyoprotectants regulate drug release.
4. *Immunogenicity:* Pegylation and surface modifications reduce immune responses.

MANUFACTURING

The manufacturing process for liposomes involves a complex, multi-step procedure that demands careful attention to various factors to guarantee the production of high-quality liposomes. In this section, we will explore the methods employed in creating our liposome formulation.

1. *Lipid selection and preparation:* The first step in manufacturing liposomes is to select and prepare the lipids. We use a combination of phospholipids, cholesterol, and other lipids to create a stable and flexible membrane. The lipids are sourced from reputable suppliers and are tested for purity and quality.
2. *Film hydration method:* We use the film hydration method to manufacture our liposomes. This involves dissolving the lipids in a solvent, such as chloroform or methanol, and then evaporating the solvent to form a thin film. The film is subsequently hydrated with a solution that includes the drug or therapeutic agent.
3. *Extrusion method:* After hydration, the liposomes are extruded through a series of filters to ensure uniform size and distribution. This step is critical in determining the final size and quality of the liposomes.
4. *Sonication method:* Alternatively, we use sonication to manufacture our liposomes. This involves using high-frequency sound waves to disrupt the lipid film and create liposomes.
5. *Lyophilization:* Once the liposomes are manufactured, they are lyophilized to remove excess water and preserve the formulation. This step is critical in ensuring the stability and shelf-life of the liposomes.
6. *Quality control:* Throughout the manufacturing process, we conduct rigorous quality control tests to ensure the liposomes meet our specifications. These tests include size distribution, encapsulation efficiency, and stability studies.
7. *Scale-up and commercial production:* After successful small-scale production, we scale up the manufacturing process to commercial levels. This involves transferring the process to larger equipment and ensuring that the liposomes meet the same quality standards as the small-scale batches. By using a combination of film hydration, extrusion, sonication, and lyophilization, we can produce liposomes that meet our specifications and are suitable for targeted therapy.

EVALUATION

To ensure the quality and efficacy of our liposome formulation, we conduct a comprehensive evaluation comprising various tests. These tests assess the physical, chemical, and biological properties of liposomes, guaranteeing they meet the required standards [26, 27].

Physical Characterization

1. *Size distribution:* We use dynamic light scattering (DLS) to determine the liposome size and distribution.
2. *Zeta potential:* This test measures the liposome surface charge, ensuring stability and preventing aggregation.

3. *Morphology:* Transmission electron microscopy (TEM) or scanning electron microscopy (SEM) visualizes the liposome shape and structure.

Chemical Characterization

1. *Encapsulation efficiency:* We measure the amount of drug encapsulated within the liposomes using techniques like HPLC or spectroscopy.
2. *Drug release kinetics:* In vitro release studies evaluate both the rate and extent of drug release from the liposomes.
3. *Stability studies:* We evaluate the liposome stability under various conditions (temperature, pH, and storage) to ensure shelf-life.

Biological Evaluation

1. *Cell culture studies:* In vitro cytotoxicity and cellular uptake studies assess the liposome biocompatibility and targeting efficiency.
2. *In Vivo studies:* Animal models evaluate the liposome biodistribution, pharmacokinetics, and therapeutic effectiveness.
3. *Immunogenicity tests:* We assess the immune response to the liposomes to ensure safety.

Functional Evaluation of Liposomal Formulations

Functional evaluation is a critical aspect of developing liposomal formulations, ensuring that they meet the desired therapeutic goals. Two key parameters in this evaluation are targeting efficiency and therapeutic efficacy [28].

1. *Targeting efficiency:* One of the primary advantages of liposomal drug delivery systems is their ability to specifically target certain cells or tissues, which enhances therapeutic outcomes while minimizing side effects. To assess targeting efficiency, various methods are employed, including the use of fluorescent markers or radio labeling to track the distribution of liposomes in biological systems. In vitro studies often involve cultured cells that express specific receptors or markers associated with the target tissue. By quantifying the uptake of liposomes in these cells compared to non-target cells, researchers can evaluate how effectively the liposomes are binding and delivering their cargo. In vivo studies may involve animal models where liposome distribution is monitored through imaging techniques or tissue sampling, providing insights into how well the formulation targets the intended site, such as tumors or inflamed tissues. This information is crucial for optimizing liposome design, including modifications to the lipid composition or surface characteristics, to enhance targeting capabilities.
2. *Therapeutic efficacy:* Assessing therapeutic efficacy involves both in vitro and in vivo studies that measure the liposome's effectiveness in treating specific diseases. In vitro studies typically include experiments that expose target cells to liposomal formulations to determine their cytotoxic effects, drug release profiles, and ability to induce desired biological responses. These tests provide preliminary data on the liposome's potential effectiveness before moving to more complex in vivo models. In vivo studies involve administering the liposomal formulation to animal models that replicate the disease conditions. Researchers assess factors, such as tumor size reduction, survival rates, and overall health outcomes. By comparing these results to control groups receiving standard treatments or placebo, the therapeutic efficacy of the liposomal formulation can be established (Table 2).

Table 2. Marketed examples of liposomal formulations.

S.N.	Brand Name	Company	Strength	Cost (INR)
1.	Doxil	Johnson and Johnson	2mg/ml	120,000/vial
2.	Ambisome	Gilead Sciences	50mg/vial	90,000/vial
3.	Abelcet	Sigma Tau Pharmaceuticals	100mg/vial	70,000/vial
4.	Myocet	Sopherion Therapeutics	50mg/25ml	50,000/vial

CONCLUSIONS

Liposomes have emerged as a highly effective and innovative drug delivery system, significantly enhancing therapeutic efficacy while minimizing toxicity. Their unique structure, consisting of phospholipid bilayers that encapsulate drugs, allows for precise targeting of therapies to specific sites in the body. This ability is especially beneficial for treating complex diseases, where conventional methods might be insufficient. The versatility of liposomal formulations facilitates a range of therapeutic applications, including controlled release mechanisms that prolong drug action and improve bioavailability. This allows drugs to stay active in the bloodstream for extended periods, potentially lowering the frequency of dosing and enhancing patient adherence to treatment plans. Marketed liposomal products, such as liposomal doxorubicin and amphotericin B, showcase their effectiveness in managing conditions like cancer and severe infections, respectively. As ongoing research delves deeper into the development of liposomal technologies, we anticipate the introduction of new formulations that can address unmet medical needs. For instance, advancements in formulation techniques and materials may lead to more stable liposomes with enhanced loading capacities. This is crucial for optimizing the delivery of potent drugs, especially those with poor solubility. Moreover, liposomes hold significant promise in the realm of personalized medicine. Their ability to be engineered for specific patient profiles allows for tailored therapeutic strategies that can maximize efficacy and minimize adverse effects. This strategy is especially advantageous in oncology, where tumor heterogeneity frequently complicates treatment outcomes. By leveraging the targeting capabilities of liposomes, clinicians may be able to deliver chemotherapy more effectively to cancer cells while sparing healthy tissues. The potential applications of liposomes extend beyond conventional drug delivery. In gene therapy, liposomes can serve as carriers for genetic material, facilitating the delivery of plasmids or RNA molecules to target cells. This could lead to breakthroughs in treating genetic disorders and various cancers. Furthermore, the advancement of liposomal vaccines has gained significant attention, especially regarding infectious diseases. Liposomal formulations can enhance the immunogenicity of vaccines by delivering antigens in a way that stimulates a robust immune response. Looking ahead, the continued evolution of liposomal technology promises not only to expand the range of treatable conditions but also to enhance existing therapies. As researchers uncover new methods for improving liposome stability, targeting, and release profiles, the clinical landscape will likely see a proliferation of liposomal-based treatments. This progress is supported by regulatory bodies recognizing the potential of liposomes, paving the way for quicker approvals and market availability. In summary, liposomes have fundamentally transformed the field of drug delivery, providing a sophisticated and targeted approach to disease management. Their ability to encapsulate various therapeutic agents, along with their adaptability for different applications, positions them as a cornerstone of modern medicine. With ongoing research and innovation, liposomes are set to play an increasingly vital role in improving patient outcomes across a spectrum of diseases, ultimately redefining how therapies are developed and administered. The future of liposomal formulations is bright, heralding new avenues for treatment that promise to enhance the quality of care and patient experiences in the years to come.

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