

Impacts of Liposomes and Their Application in Cancer Therapy

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Abstract: Cancer is one of the leading causes of mortality worldwide. Systemic toxicities and multi-drug resistance associated with chemotherapies have prompted the discovery and researches towards the development of alternative approaches. Nanotechnology has evolved as a promising approach in cancer studies to make diagnostic more precise, improve therapeutic outcomes by offering a target drug delivery system. Healthy cells damages can be minimized; therapeutic agents can reach specific cells or tissues by bypassing biological barriers through engineered Nanoparticles. Liposomes are self-assembled, uni-lamellar or multi-lamellar spherical vesicles primarily composed of phospholipids from either animal plant or origin. The amphipathic nature of Liposomes makes it possible to encapsulate hydrophilic drugs within the aqueous core and hydrophobic drugs in the lipid bilayer, which protects the drugs from environmental degradation during systemic circulation. Due to the biocompatibility, structural versatility, and ability to improve the therapeutic of anticancer agents, liposomes are the most widely investigated nanocarriers in oncology. The impact of liposomes and their applications in cancer therapy were explored in this review.

Keywords: Cancer, Drug Resistance, Liposomes, Nanotechnology, Nanoparticles, Oncology.

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I. INTRODUCTION

Conventional cancer treatments are often associated with challenges such as drug resistance, systemic toxicity and lack of specificity. This resistance is as a result of multiple factors, including drug deactivation, changes in drug targets, drug efflux, evasion of apoptosis, DNA damage repair, cell heterogeneity, and immune system escape within the tumor microenvironment (TME) (Li *et al.*, 2021). The International Agency for Research for Cancer (IARC) estimated cancer to be the leading cause of death globally in 2022, with approximately 20 million new cases and 9.7 million deaths (Bray *et al.*, 2024). Among the risk factors cancer, elevated levels of reactive oxygen species (ROS) are a major concern, while non-destructive concentrations of free radicals are normally regulated by antioxidants under physiological conditions (Sorriento, 2024). However, over production or uncontrolled accumulation of these reactive species can

directly or indirectly contribute significantly to oxidative damage of essential biomolecules, activating molecular and cellular pathways linked to inflammation and carcinogenesis (An *et al.*, 2024). As a result, there is need to explore an alternative therapeutic approach for the treatment and management of this life threatening disease.

Nanotechnology offers reliable approaches for enhancing the targeted delivery of anti-cancer drugs by the use of drug-loaded nanomaterials (NMs) (Salem *et al.*, 2023). These nanomaterials are designed based on tumor's etiology to effectively overcome drug resistance, reduce systemic toxicity and increase specificity (Yao *et al.*, 2020). Despite their minute size, nanomaterials (NMs) provide a large surface area for attaching biomolecules, thereby, enhancing drug's efficacy (Cao *et al.*, 2021). Liposomes, polymeric micelles, dendrimers, and inorganic nanoparticles are examples of developed nanomaterials (NMs) used in cancer

diagnosis and treatment. Their unique properties, such as biocompatibility, permeability, stability, retention, and targeted delivery, make them effective for these applications (Sabir *et al.*, 2025). The choice of nanomaterials (NMs) depends on the treatment type, by considering factors like size, shape, and physicochemical properties. For instance, micelles are useful for delivering hydrophobic and bipolar drugs, whereas gold nanoparticles and liposomes are suited for liver and blood cell uptake (Kim and Khang, 2020).

Liposomes boost drug effectiveness by reducing side effects and targeting delivery. They're a versatile platform for hydrophilic and lipophilic molecules, improving solubility, bioavailability, stability and targeted delivery. Their biocompatibility and customizable pharmacokinetics make them a valuable tool in clinical and industrial settings (Sercombe *et al.*, 2015).

II. LIPOSOMES

Liposomes are tiny spherical vesicles (50-500 nm diameter) made up of one or more lipid bilayers, as a result of emulsifying lipids (natural or synthetic) in an aqueous medium (Mekuye and Abera 2023). Liposomes typically composed of sterols, surfactants, and phospholipids (natural or synthetic) which are synthesized from egg yolk, soybean, and hydrogenated phosphatidylcholine (Ahmed *et al.*, 2019). These components are biodegradable, non-toxic, and perfect for industrial production. The amphipathic nature of liposomes makes it possible to encapsulate both hydrophilic and hydrophobic drugs. The Addition of cholesterol into liposomes helps to modulate membrane permeability, improve stability, and fluidity of bilayer membrane in biological fluids like blood and plasma (Nsairat *et al.*, 2022). Liposomes make cancer treatments more effective by reducing undesired toxicity to healthy cells and tissue; prolong half-life, improve drug solubility, pharmacokinetics, and bioavailability.

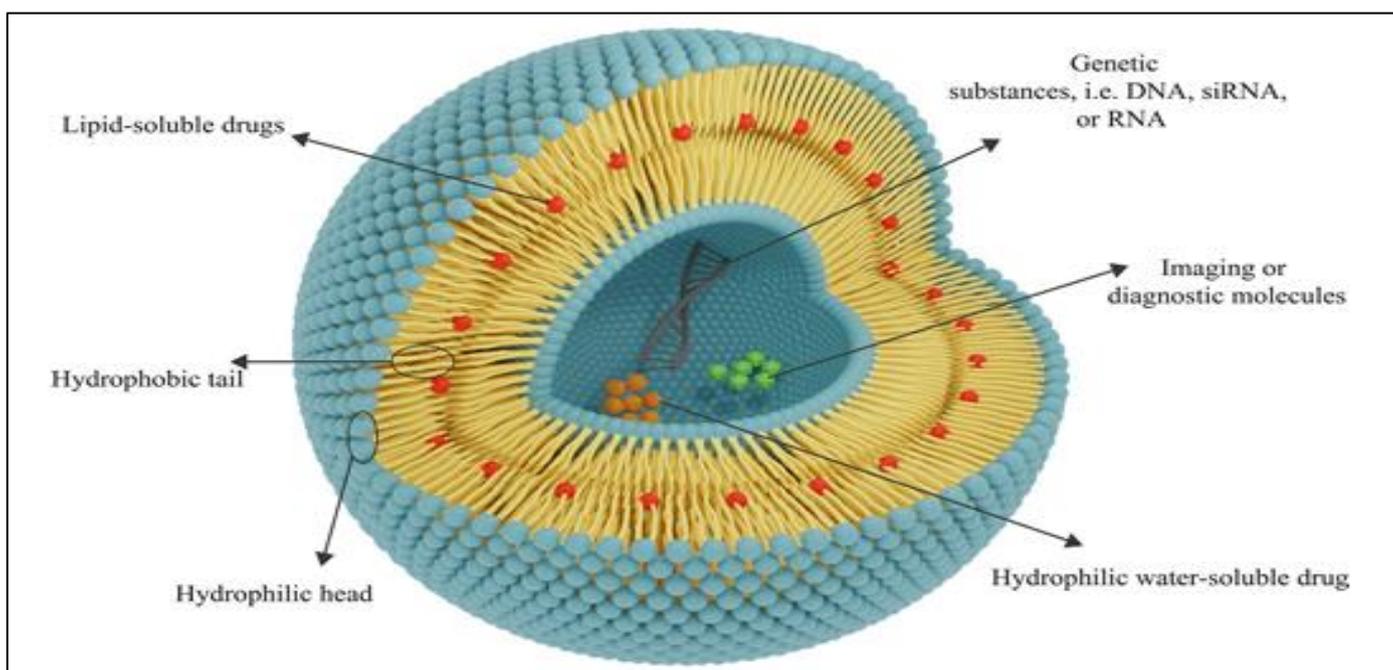


Fig 1 Structure of the Liposome Consisting Phospholipid Layers. Hydrophilic Drugs are Entrapped in the Central Hydrophilic Nucleus, and Hydrophobic Drugs are Placed in the Lipophilic Area.

In cancer treatment, liposomes have been utilized as ideal drug-delivery systems (DDSs) to deliver anti-cancer agents/drugs. There are two factors to consider when designing liposomal DDSs for cancer treatment; encapsulated drugs/therapeutic substances and surface modification (Cheng *et al.*, 2025). These nano-DDSs are phagocytized by mononuclear phagocyte system (MPS) in liver and spleen, to further prolonged drug half-life, improve drug solubility and stability, reduce drug immunogenicity and antigenicity, polyethylene glycol (PEG) is used to modify liposome surface. PEGylated liposomes are harder to be recognized by MPS therefore are delivered to target site more efficiently (Rommasi and Esfandiari 2021). Liposomes can be tweaked with surface modifications to evade the immune system, circulate longer, and release drugs in response to tumor

triggers (Large *et al.*, 2021). Some liposomal treatments are already approved, like Doxil, the first FDA-approved liposomal nano-DDS. Doxil delivers doxorubicin, is PEGylated, and treats various cancers (Sheoran *et al.*, 2022; Cheng *et al.*, 2025).

➤ Structural and Physicochemical Properties of Liposomes Relevant to Cancer Therapy

The efficacy of liposomes in cancer therapy is significantly impacted by factors like composition, size, surface charge, and lamellarity. Phospholipid-cholesterol bilayers mimic biological membranes, ensuring biocompatibility and minimal immunogenicity (Wang *et al.*, 2023). Particle size is crucial for tumor targeting. Nanoscale liposomes (50-200 nm) accumulate in tumors via the EPR

effect, due to leaky blood vessels and poor lymphatic drainage. Surface charge impacts circulation and uptake of near-neutral or slightly negative liposomes reduce protein binding (Collin *et al.*, 2020). Lamellarity affects drug loading and release of unilamellar vesicles are preferred for cancer treatment due to uniform size and predictable release. These factors contribute to liposomes' effectiveness in cancer therapy.

➤ *Liposomes in Targeted Delivery*

Liposomes top the list of nanocarriers for targeted drug delivery. Two key techniques boost their effectiveness: passive targeting and active targeting, both aiming to increase specificity and reduce side effects (Palange, 2023).

• *Passive Targeting (Non-Conjugated)*

Passive targeting relies on the enhanced permeability and retention (EPR) effect of cancerous cells. In comparison to normal tissue, cancer tissue forms plentiful aberrant vascular and excessive vascular permeability factors, and lack of lymphatic drainage. These features help liposomal DDSs target cancer cells and achieve enrichment at target site. This boosts specificity and reduces toxicity to healthy tissues, resulting in fewer side effects (Schirmacher, 2019).

• *Active Targeting (Ligand-Conjugated)*

Active targeting uses ligands that bind to specific receptors, guiding liposomes to target sites and reducing off-target effects. These ligands attach covalently or non-covalently, helping liposomes accumulate where needed. Liposomes can be engineered with ligands, antibodies, or peptides to target specific cells or tissues, leveraging receptor-mediated endocytosis. This is super useful in cancer therapy, where tumor cells often overexpress certain receptors, reducing harm to healthy cells and boosting treatment effectiveness (Desai *et al.*, 2025). Transferrin receptor (TfR), folate receptor (FR), estrogen receptor (ER) and hyaluronic acid receptor are vastly investigated ligand-binding targets. TfRs are glycoproteins that bind to iron in blood plasma. TfR plays important roles in cellular iron uptake. In normal cells, TfR is highly expressed on placental tissue, immature erythroid cells and other rapidly dividing cells (Cheng *et al.*, 2025). Tumor cells are rapidly proliferating cells and TfR is highly expressed in many cancer cells. Researches show that TfR is heavily distributed in blood-brain barrier and glioblastoma multiforme (GBM) cells (Johnsen *et al.*, 2019). TfR is also found to be highly expressed in other solid tumors such as breast cancer and hepatocellular carcinoma.

➤ *Liposomes Improved Bioavailability and Drug Solubility*

Liposomes significant advantage is their ability to enhance poorly water-soluble drug's solubility. Hydrophobic drugs can be encapsulated within the lipid bilayer, while hydrophilic drugs can be trapped in the aqueous core, thus increasing the bioavailability and therapeutic potential of many compounds (Ray *et al.*, 2021).

➤ *Reduced Toxicity and Side Effects*

Liposomes minimize the toxic impact of drugs like doxorubicin (Doxil®) and amphotericin B (AmBisome®),

reducing side effects such as heart and kidney damage. By controlling release and targeting specific tissues, liposomes protect healthy cells, making treatments safer (Barenholz, 2012; Desai *et al.*, 2025).

➤ *Controlled and Sustained Drug Release*

Liposomes can be designed to provide controlled and sustained drug release. The release rate can be manipulated by altering the lipid composition, surface charge, or addition of stimuli-responsive materials like pH-sensitive liposomes. This is applicable for treatments where prolonged therapeutic action is required, like in cancer therapy and other chronic conditions (Wahab *et al.*, 2021).

➤ *Biocompatibility and Biodegradability*

The natural composition of liposomes makes them biocompatible and biodegradable, minimizing immune responses and inflammatory reactions (Li *et al.*, 2018). These features make them suitable for a wide range of pharmaceutical and cosmetic applications (Desai *et al.*, 2025).

III. LIPOSOMAL SYSTEMS IN CANCER THERAPY

➤ *Conventional Liposomes*

The first generation of liposomes to be developed and investigated for cancer therapy were the conventional liposomes. While they demonstrated reduced toxicity compared to free drugs, their rapid clearance by the reticuloendothelial system limited clinical effectiveness. These first-generation liposomes serve as the foundation for subsequent liposomal formulations (Rommasi and Esfandiari 2021).

➤ *Stealth (PEGylated) Liposomes*

PEGylation represents a major advancement in liposome technology. By coating the liposomal surface with polyethylene glycol chains, these formulations exhibit prolonged systemic circulation and reduced protein adsorption. PEGylated liposomal doxorubicin is a key example, demonstrating reduced cardiotoxicity and improved patient tolerance when compared to conventional doxorubicin (Palange, 2023).

➤ *Targeted Liposomes*

Targeted liposomes are tagged with ligands like peptides, antibodies, or small molecules that recognize tumor-specific receptors. These approaches enhance selective uptake by cancer cells and minimizes off-target effects. Targeted liposomes have shown promise in delivering cytotoxic agents, genes, and RNA directly to malignant cells (Sanna, 2014).

➤ *Stimuli-Responsive Liposomes*

Stimuli-responsive liposomes are designed to release their payload in response to tumor-specific conditions such as acidic pH, enzymatic activity or elevated temperature. These smart systems offer controlled and site-specific drug release, enhancing therapeutic outcomes while reducing systemic toxicity (Wang *et al.*, 2023).

➤ *Clinically Approved Liposomal Anticancer Formulations*

Liposomal formulations, like doxorubicin, are approved and used to treat various cancers, including breast cancer, ovarian cancer, Kaposi's sarcoma and multiple myeloma. Liposomal daunorubicin and cytarabine have also shown improved safety and efficacy profiles in hematological malignancies (Cheng *et al.*, 2025). These approved liposomal formulations prove their worth, paving the way for next generation liposomal nanomedicines.

➤ *Advantages of Liposomes in Cancer Therapy*

Liposomal drug delivery has various advantages in oncology including improved pharmacokinetics, enhanced tumor accumulation, reduced dose-limiting toxicity and the ability to co-deliver multiple therapeutic agents. Liposomes encourage combination therapies by encapsulating synergistic drug pairs, thereby addressing resistance mechanisms and tumor heterogeneity (Aminolroayaei *et al.*, 2023).

➤ *Challenges Associated with Liposome Delivery Systems*

Liposomes have shown promising potentials in drug delivery system, but still have some limitations, which include limited drug loading for certain compounds, batch-to-batch variability, stability issues upon storage, and high production costs. In addition, the EPR effect varies significantly among patients and tumor types, resulting to inconsistent therapeutic outcomes. Immunogenic reactions to PEG and difficulties in large-scale manufacturing further complicate clinical translation. Addressing these challenges is essential for the broader adoption of liposome-based cancer therapies

IV. CONCLUSION

Liposomes have reduced the limitations associated with chemotherapy, by enhancing the bioavailability, target delivery, stability, controlled drug release, and reduced side effects of the drug agent. Biocompatibility and biodegradability of liposomes are due to their chemical properties making it a good drug delivery system. Liposomes offer numerous advantages over chemotherapeutic drug. Liposomal drugs have high encapsulation capability, showing a significant anticancer activity with decreased toxicity.

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