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Research Progress of Liposomes in the Anti-tumor Field

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Abstract. Liposomal nanocarriers built from phospholipid bilayers have garnered substantial research interest for anticancer work. Their desirable traits--good biocompatibility, low immunogenic potential, and flexible surface-tuning possibilities--make them appealing for tumor therapy. This review revisits liposome basics including structural features, common fabrication workflows and different classification schemes. Special attention goes to functional modification approaches reported in recent papers: long-circulating redesign, thermoresponsive formulations, pH-triggered vesicles and ligand-conjugated targeting constructs. I also compile published experimental outcomes for liposome-based interventions against breast cancer, lung cancer and glioma. Discussions cover active targeting workflows, drug release triggered by local tumor microenvironment cues, and strategies designed to cross the blood-brain barrier. Even with promising pre-clinical dataset accumulated over years, multiple practical barriers slow clinical translation. Variable EPR performance across animal species, unwanted side effects linked to PEG modification, and inconsistent formulation stability remain persistent bottlenecks. From my perspective, further work should prioritize stimulus-responsive liposome designs tailored toward actual tumor microenvironment features. Iterative improvement of manufacturing protocols will also prove critical if we hope to move more liposome candidates toward real-world clinical use.

Keywords: Liposomes, Anti-tumor, Drug delivery system, Targeted therapy

1. Introduction

Malignant neoplasms continue to drive high morbidity and mortality across global populations. Standard clinical regimens built on conventional chemotherapy and radiotherapy inflict notable damage on healthy non-tumor tissues. Rising drug-resistance rates further worsen patient quality-of-life and undermine overall therapeutic outcomes. Many research groups have turned toward custom-built nano-scale delivery systems to get around these clinical limitations [1]. Among diverse nanocarrier platforms available today, liposomes stand out for oncological applications. They carry low biosafety risk, deliver moderate selective cytotoxicity, and sustain drug release within blood circulation to lessen off-target injury to normal organs [1, 2].

Liposome delivery technology has advanced quickly in recent years. Researchers have rolled out many modification tactics: long-circulating surface engineering, active-targeting decoration, microenvironment-responsive membrane redesign, to name a few. These adjustments have greatly

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expanded what liposomes can achieve within oncology research. A small number of liposome-based products have already reached clinical practice. Even so, broader bench-to-bedside transition still faces real-world constraints. Suboptimal delivery efficiency, safety uncertainties and obstacles for large-scale industrial manufacturing hold back wider adoption [3].

This review collects recent research observations for liposome-centered anti-tumor investigations. I lay out core physicochemical properties of liposomes and describe the current landscape of modified liposome variants. Approved clinical liposome products are mentioned, alongside major complications observed during translational research. Some potential future research directions are touched upon, aiming to offer practical reference points for developing and deploying next-generation anti-cancer liposome therapeutics.

2. Basic introduction to liposomes

2.1. Structure and composition

Liposomes form spherical or ellipsoidal closed vesicles. They self-assemble once phospholipid molecules are placed within aqueous surroundings. Every phospholipid molecule holds one hydrophilic head group paired with two hydrophobic acyl tails. When submerged in water, phospholipid units spontaneously reorient: polar head groups face outward toward surrounding aqueous medium, and non-polar acyl chains fold inward. This arrangement creates sealed vesicle compartments. The inner aqueous cavity can trap water-soluble therapeutic substances, whereas lipid-rich bilayer regions accommodate hydrophobic payloads.

Lipid head groups may carry positive charge, negative charge, or adopt zwitterionic status. Electrostatic repulsion generated by charged lipid heads helps preserve colloidal stability of liposome suspensions. Changes in acyl-chain length, unsaturation levels and molecular symmetry directly alter membrane fluidity and permeability profiles [4].

Liposomes share many permeation traits with native biological membranes. Their solute-selective permeability largely mirrors that seen in living cell membranes. Temperature-dependent transmembrane transport patterns also show high similarity. Such observations reinforce the idea that phospholipid bilayers constitute the core structural foundation for biological membrane barrier functions [5]. Liposome preparations additionally serve as convenient experimental tools. Researchers use them to dissect molecular-scale interactions and barrier-related properties belonging to distinct membrane components.

2.2. Preparation methods

Several practical techniques exist for liposome production. Thin-film hydration, ultrasonication and reverse-phase evaporation represent the most widely-used laboratory options. For thin-film hydration, lipids and cholesterol get dissolved in chloroform. The mixture is stirred slightly above lipid phase-transition temperature, before rotary evaporation strips away organic solvent. A dry lipid film forms on the flask wall. Aqueous buffer is added to hydrate this film, followed by vortex mixing. Finished liposome suspensions are usually stored at 4 °C. Low-temperature storage slows hydrolytic degradation for lipids containing ester linkages [6].

Ultrasonication subjects multilamellar liposome suspensions to high-intensity acoustic energy. Sonication generates extreme local pressure, spot heating and fluid turbulence, triggering cavitation events. Resulting shear forces break down large multilayer assemblies. Lipid fragments reassemble

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into smaller unilamellar vesicles. Sonication power and treatment duration exert large influence over final particle dimensions and drug encapsulation yield [7].

Reverse-phase evaporation starts by forming water-in-oil emulsions. Lipid molecules organize into reverse micelles along interfaces separating water and organic solvent phases. Organic solvent removal drives bilayer assembly. Payload polarity strongly impacts encapsulation outcomes with this technique. Molecules of lower polarity tend to partition into organic fractions and integrate into growing lipid bilayers, achieving higher trapping efficiencies [8]. Each fabrication method brings its own set of pros and cons. Experimenters select protocols flexibly according to target particle size, physicochemical features of loaded agents and intended production scale.

3. Classification of liposomes

3.1. Conventional liposomes

Conventional liposomes are unmodified basic vesicle formulations. After intravenous injection, these liposomes become rapidly sequestered by the reticuloendothelial system (RES). Most accumulated material localizes in liver and spleen tissues. This property can be exploited for therapies targeting RES-rich organs. Still, non-specific RES uptake creates major delivery hurdles whenever therapeutic targets sit outside RES compartments [9].

3.2. Long-circulating liposomes

Long-circulating liposomes were developed to counter fast RES clearance of conventional liposomes. Targeted surface modification enables these vesicles to retain stability inside blood flow for extended periods. Improved tumor accumulation and sustained drug release can be realized. PEG and PEG-derivative conjugation remains the dominant modification strategy reported across publications. Polyethylene glycol acts as non-toxic, minimally immunogenic amphiphilic polymer. Once anchored onto liposome surfaces, hydrophilic PEG chains stretch outward and form hydration layers with surrounding water molecules. Added steric repulsion reduces RES recognition and phagocytic clearance, significantly extending liposome circulating half-life [10].

3.3. Specialized functional liposomes

Building on long-circulating performance, research teams have equipped liposomes with added functional capabilities. Microenvironment responsiveness and active-targeting capacity are two popular development directions, producing advanced functional vesicle platforms.

3.3.1. Thermosensitive liposomes

Thermosensitive liposomes incorporate organic-inorganic hybrid phospholipids alongside temperature-sensitive lipid fractions. Their overall structural integrity stays intact under normal conditions, yet drug cargo gets released upon heat stimulation. Further surface decoration with targeting peptides such as WSG can endow these vesicles with active-targeting behavior. Existing test data suggest satisfactory stability under storage conditions and simulated circulating environments. Drug release profiles show clear temperature-dependent trends [11].

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3.3.2. pH-sensitive liposomes

pH-sensitive liposomes achieve site-specific drug release by taking advantage of acidic tumor microenvironments. Normal tissues and circulating blood maintain pH values roughly between 7.4 and 7.5. Rapid metabolic activity within solid tumors pushes extracellular pH down to approximately 6.5-6.7 [12]. After tumor cells internalize liposomes via endocytosis, vesicles are trafficked toward endosomes and lysosomes where pH falls further to 4.0-6.5. Acidic surroundings trigger lipid-bilayer phase transitions. Encapsulated therapeutics leak out, supporting intracellular targeted delivery [13].

3.3.3. Ligand-modified liposomes

Antibodies, peptides, folic acid and other targeting moieties can be covalently attached onto liposome outer surfaces. Such surface-bound ligands selectively bind receptors overexpressed on tumor-cell membranes, establishing active-targeting functionality. This modification strategy increases local drug concentration within lesion sites. Off-target toxicity toward healthy tissues drops accordingly, and overall therapeutic index improves [14].

4. Applications of liposomes in the anti-tumor field

4.1. Breast cancer

Liposome-based breast-cancer therapy mostly depends on active-targeting delivery mechanisms. Surface-tethered ligands including antibodies, peptides and folate recognize overexpressed tumor-cell receptors such as HER2, folate receptor and CD44. Drug payloads are therefore directed toward tumor sites. Higher intratumoral drug concentrations, enhanced cellular internalization and reduced systemic adverse effects can be observed.

Post-intravenous administration, liposomes first passively deposit inside tumor tissue through the EPR effect. Ligand-receptor interactions then mediate active endocytic uptake by tumor cells. Certain liposome variants respond to local enzymatic activity or pH shifts to initiate cargo discharge. Liposomal carriers can also bypass efflux-pump-mediated resistance pathways like P-glycoprotein, helping treat otherwise drug-refractory tumor phenotypes. For breast-cancer cases complicated by brain metastasis, purpose-engineered liposomes may cross the blood-brain barrier to deliver agents into the central nervous system [15].

One recent study reported Chk1-targeted hesperidin liposomes. These constructs bind cell-cycle checkpoint kinase Chk1 overexpressed by breast-cancer cells. Measured cytotoxicity against MCF-7 cells yielded an IC_{50} value of 13.52 μg/mL. Using DMBA-induced rat breast-cancer models, the formulation shrank tumor masses and helped restore hematological and biochemical parameters toward normal ranges [16].

4.2. Lung cancer

Multiple multifunctional targeting liposome candidates have been constructed for lung-cancer intervention. Researchers synthesized DSPE-PEG_{2000}-OCT as targeting ligand and encapsulated chemotherapeutic drugs inside liposome compartments. The modified carriers guided drug accumulation within tumor foci. At cellular level, these liposomes boost drug uptake by malignant cells. Apoptosis-related protein expression gets modulated to trigger cancer-cell death. Meanwhile, angiogenesis, tumor migration and invasive capacity become suppressed. Intravenous injection into

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tumor-bearing mice drove effective liposome accumulation within tumor lesions. Tumor progression slowed, animal survival lengthened, and preliminary safety assessment showed encouraging results. These targeting liposome systems supply solid experimental groundwork for future lung-cancer therapeutic exploration [17].

Another research group built YSA-peptide-decorated oridonin-loaded long-circulating liposomes, with particle size sitting near 140 nm. YSA modification brought notable improvements in cellular uptake and cytotoxic performance against A549 lung-cancer cells. Pharmacokinetic measurements recorded elevated AUC values, extended half-life and prolonged in-vivo retention. Marked tumor-growth inhibition was demonstrated in nude-mouse xenograft models [18].

4.3. Glioma

One research group co-loaded lipophilic epirubicin and hydrophilic resveratrol within liposome bilayers. Dual-ligand surface modification with MAN plus WGA was implemented. This design lowered drug-related toxicity and improved biocompatibility. The resultant liposomes managed to traverse the blood-brain barrier and achieve glioma-directed delivery. C6 glioma cells efficiently internalized dual-modified vesicles. Cell proliferation and tumor-sphere formation were strongly inhibited, and apoptotic cell death got induced. In-vitro blood-brain-barrier models validated trans-barrier transport capacity. Following intravenous injection in tumor-bearing rats, liposomes reached intracranial tumor regions. Glioma growth was restrained and animal survival time prolonged. Histopathological examinations further confirmed in-vivo anti-glioma potency [19].

Targeting-ligand conjugation is not the only route toward blood-brain-barrier penetration. Adjustments to liposome membrane materials can also confer brain-targeting traits. One recent work described PMPC-modified liposomes built for siRNA delivery against glioblastoma. No extra targeting ligands were needed. Intrinsic brain-homing properties belonging to PMPC enabled blood-brain-barrier penetration. PLK1 siRNA was successfully delivered, producing prominent tumor-growth inhibition in orthotopic U87MG models as well as patient-derived CSC2 glioma-stem-cell models [20].

5. Summary and outlook

Liposomes display rich functional diversity as anti-cancer drug-delivery platforms. Passive targeting, active targeting and microenvironment-triggered drug-release mechanisms have all generated promising experimental outcomes for breast-cancer, lung-cancer and glioma research.

Translating pre-clinical findings toward real-world clinical settings still comes with considerable obstacles. Whether EPR effects operate reliably and consistently within human tumors remains debated among investigators. Doxil®, for instance, failed to produce meaningful improvement in intratumoral drug accumulation compared against free doxorubicin [21]. PEG-surface modification prolongs circulation time, yet it may aggravate cutaneous adverse events such as palmar-plantar erythrodysesthesia. Expectations built entirely around EPR-driven enrichment should therefore be kept realistic. Other unresolved challenges cover long-term shelf stability of liposome formulations and phototoxicity caused by certain photosensitizer payloads.

Going forward, stimulus-responsive liposome designs that combine tumor-microenvironment signatures together with externally applied physical stimuli could grant finer spatiotemporal control over drug-release events. Therapeutic efficacy might rise as a consequence. At the same time, manufacturing workflows still need further refinement. Boosting formulation safety and minimizing

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batch-to-batch variation stays high-priority work, if we hope to see broader clinical adoption for liposome-based anti-tumor medicines.

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