

Nanotechnology-Based Drug Delivery Systems for Lung Cancer: A Focused Review on Nanocarrier Platforms

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Abstract – Lung cancer remains the leading cause of cancer mortality worldwide, largely due to late diagnosis, aggressive progression, and the limited effectiveness of conventional chemotherapies. Systemic agents such as paclitaxel, cisplatin, and docetaxel suffer from poor solubility, rapid clearance, nonspecific distribution, and dose-limiting toxicity, underscoring the need for more efficient delivery strategies. Recent advances in nanotechnology have introduced versatile drug delivery systems capable of enhancing drug stability, improving tumor accumulation, and enabling controlled and sustained release. This review provides a focused overview of major nanocarrier platforms, polymeric nanoparticles, lipid-based systems, inorganic nanomaterials, and hybrid nano systems, used to improve chemotherapeutic delivery in lung cancer. Their key material properties, drug-loading capabilities, and therapeutic advantages are summarized to highlight how nanotechnology can address the limitations of traditional treatments.

Keywords – Nanocarriers, lung cancer, polymeric nanoparticles, lipid-based drug delivery, inorganic nanomaterials

1. Introduction

Lung cancer continues to be a major global health burden and remains the foremost cause of cancer mortality worldwide [1-3]. Despite extensive advancements in oncology, the clinical success of conventional chemotherapeutics remains limited by nonspecific biodistribution, systemic toxicity, rapid drug metabolism, and the development of multidrug resistance [4-6]. Commonly used agents such as paclitaxel, cisplatin, and docetaxel suffer from poor aqueous solubility and inadequate tumor accumulation, resulting in suboptimal therapeutic responses [5, 7, 8]. These limitations emphasize the critical need for novel therapeutic strategies capable of improving drug selectivity, enhancing tumor uptake, and minimizing adverse effects.

In recent years, emerging therapeutic modalities have sought to address these shortcomings through more precise and efficient delivery mechanisms. Among these, nanotechnology has gained particular attention for its ability to overcome physicochemical and biological barriers associated with lung cancer treatment [9, 10]. Nanocarriers can protect drugs from degradation, improve their solubility, prolong systemic circulation, and allow sustained or stimuli-responsive release [11-13]. These advancements have positioned nanotechnology-based drug delivery systems as promising candidates to enhance therapeutic index and circumvent the drawbacks of traditional treatments [14].

Given the rapid evolution of nanomedicine, a comprehensive understanding of the available nanocarrier platforms is essential for guiding future research and clinical translation [15, 16]. Different classes of nanocarriers, polymeric nanoparticles, lipid-based systems, inorganic nanomaterials, and hybrid nanosystems, offer unique

advantages in terms of stability, biocompatibility, drug-loading capability, and controlled release mechanisms [17-20]. Examining these systems collectively provides valuable insight into how structural and material innovations can improve outcomes in lung cancer therapy.

Therefore, the aim of this review is to summarize and critically analyze current nanotechnology-based drug delivery systems focusing exclusively on carrier platforms used for lung cancer chemotherapy. By consolidating recent advancements and discussing the key features of major nanocarrier classes, this review provides a clear and focused perspective on their potential to serve as next-generation therapeutic tools. This work aims to support ongoing efforts to develop safer, more efficient, and clinically translatable nanomedicine strategies for lung cancer management.

2. Conventional Therapies and Their Limitations

Conventional lung cancer treatments primarily include chemotherapy, radiotherapy, surgical resection, and targeted small-molecule inhibitors [21-23]. While these modalities form the foundation of current clinical management, their efficacy remains restricted by several biological and pharmacological barriers [13, 24]. Chemotherapeutics such as cisplatin, paclitaxel, and docetaxel exhibit poor aqueous solubility, rapid systemic clearance, and limited tumor selectivity, often requiring high doses to achieve therapeutic levels [25-27]. Radiotherapy and surgery are effective only in early-stage diseases, yet most patients present at advanced stages where localized interventions offer minimal benefit [28, 29]. Furthermore, targeted therapies, though initially promising, lose effectiveness due to tumor heterogeneity and the rapid emergence of resistance mutations [30, 31].

These limitations result in suboptimal therapeutic responses, high recurrence rates, and severe systemic toxicity. Nonspecific biodistribution exposes healthy tissues to cytotoxic agents, leading to adverse effects such as nephrotoxicity, neurotoxicity, and myelosuppression[32, 33]. Additionally, poor penetration of drugs into dense tumor tissue and the development of multidrug resistance further compromise treatment outcomes[34-36]. The combined effect of these challenges underscores the urgent need for improved drug delivery strategies capable of enhancing therapeutic index, minimizing off-target effects, and overcoming resistance mechanisms in lung cancer therapy.

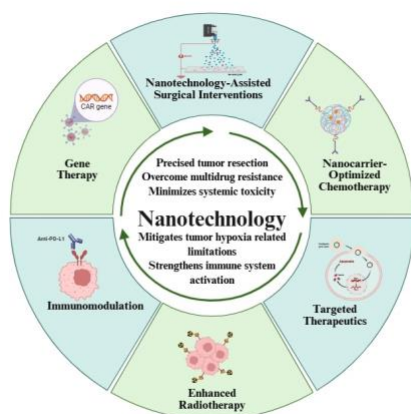


Figure 1. Nanotechnology-enhanced approaches improving precision in surgery, therapy, and drug delivery for cancer treatment.

3. Nanotechnology-Based Nanocarriers

3.1 Polymeric Nanoparticles

Polymeric nanoparticles (PNPs) represent one of the most established and versatile platforms in nanotechnology-based drug delivery for lung cancer[37, 38]. Their popularity arises from the tunable physicochemical properties of synthetic and natural polymers, which allow precise control over particle size, drug loading, degradation rate, and surface functionalization. These nanoparticles can encapsulate a broad range of chemotherapeutic agents, including highly hydrophobic molecules, protecting them from premature degradation and enhancing their bioavailability[39-41]. Materials such as PLGA, PEG-PLGA, chitosan, polycaprolactone (PCL), and poloxamers are widely utilized because they offer predictable degradation profiles and excellent biocompatibility[42-44].

One key advantage of polymeric nanocarriers lies in their ability to provide sustained and controlled drug release, which minimizes fluctuations in drug plasma levels and reduces the dosing frequency[45, 46]. Hydrophobic polymers like PLGA and PCL enable the encapsulation of poorly soluble drugs such as paclitaxel or docetaxel, dramatically improving their solubility and circulation stability [47, 48]. Natural polymers like chitosan provide additional benefits such as mucoadhesion, which enhances retention in the lung

mucosal environment and promotes localized drug accumulation[49, 50]. These tunable properties make polymeric nanoparticles suitable for both systemic and inhalation-based delivery routes, allowing targeted deposition within the respiratory tract.

Polymeric nanoparticles have been extensively explored in lung cancer models, demonstrating significant improvements in drug efficacy and safety. PLGA nanoparticles loaded with paclitaxel have shown enhanced solubility and reduced systemic toxicity compared to free drug formulations[51-53]. Likewise, PCL nanoparticles carrying docetaxel enable prolonged drug release due to their slow degradation rate, maintaining therapeutic concentrations at the tumor site for extended periods[54, 55]. Chitosan-based nanoparticles, due to their positive surface charge, adhere strongly to negatively charged airway epithelial surfaces, improving residence time and potentially increasing drug uptake in lung tumors[56].

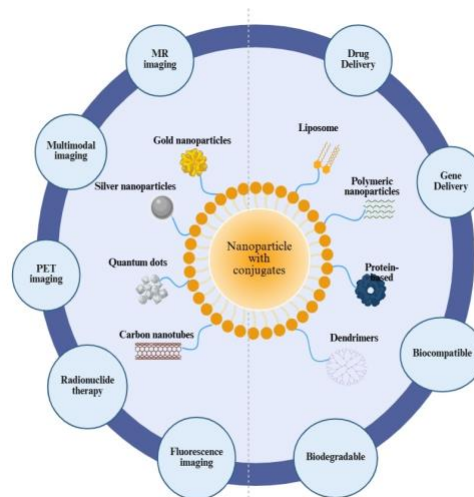


Figure 2. Multifunctional nanoparticles with diverse conjugates enabling applications in imaging, targeted delivery, and therapeutic interventions. This schematic highlight various nanoparticle types and their biomedical roles.

3.2 Lipid-Based Nanocarriers

Lipid-based nanocarriers are among the most clinically advanced drug delivery platforms due to their inherent biocompatibility, biodegradability, and structural similarity to biological membranes[57-59]. These carriers can encapsulate both hydrophilic and hydrophobic drugs and are particularly suitable for improving the solubility and stability of chemotherapeutics that are poorly soluble in water[60, 61]. Common lipid-based systems include liposomes, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers (NLCs), each offering unique advantages depending on the therapeutic goal and formulation strategy[62].

One of the key benefits of lipid nanocarriers is their ability to provide controlled and sustained drug release, which reduces burst release and prolongs drug circulation time[45, 63]. Liposomes, for instance, can be engineered with PEGylation or other surface modifications to evade immune clearance,

resulting in prolonged systemic retention. SLNs and NLCs incorporate solid and semi-solid lipid matrices that stabilize hydrophobic drugs and protect them from premature degradation, enhancing both intracellular uptake and therapeutic efficacy[64, 65].

In the context of lung cancer, lipid-based systems have demonstrated significant improvements over conventional formulations[66, 67]. Liposomes loaded with doxorubicin have shown reduced cardiotoxicity and enhanced tumor

penetration[68, 69]. SLNs encapsulating docetaxel improve solubility and stability, leading to more effective cytotoxicity against cancer cells[70, 71]. NLCs delivering paclitaxel demonstrate higher cellular uptake and stronger anti-tumor activity in vitro and in vivo, emphasizing their potential for enhanced chemotherapeutic performance as summarized in table-1.

Table 1: Different Nanocarriers for Lung Cancer Drug Delivery

Nanocarrier Type	Materials	Key Advantages	Examples / Functional Notes	Ref
Polymeric Nanoparticles (PNPs)	PLGA, PEG-PLGA, Chitosan	Biodegradable, tunable degradation	PLGA-paclitaxel: improved solubility, reduced toxicity	[72]
	PCL, Poloxamers, PLA, Eudragit	Sustained/controlled release, high drug loading	PCL-docetaxel: prolonged release, steady drug levels	[73]
	Chitosan derivatives	Protects labile drugs, mucoadhesive	Chitosan-various drugs: enhanced lung retention; PEG-PLGA-doxorubicin: extended circulation	[50, 74]
Lipid-Based Nanocarriers	Liposomes, SLNs	Biocompatible, can load hydrophilic & hydrophobic drugs	Liposomes-doxorubicin: reduced cardiotoxicity, improved tumor penetration	[75, 76]
	NLCs, Phospholipids	Reduces burst release, improves circulation	SLNs-docetaxel: enhanced stability, improved solubility	[77]
	Cholesterol, Stearic acid	Stabilizes labile drugs, flexible formulation	NLCs-paclitaxel: higher intracellular uptake, enhanced cytotoxicity	[72, 77]
Inorganic Nanocarriers	MSNs, AuNPs	High surface area, tunable pore size	MSNs-cisplatin: sustained release, reduced nephrotoxicity	[78]
	Iron oxide NPs, Cerium oxide NPs	Mechanical & chemical stability, multifunctional	AuNP-paclitaxel: enhanced cellular uptake; Iron oxide-docetaxel: magnetic guidance	[79]
	Quantum Dots, TiO ₂ NPs	Stimuli-responsive, imaging potential	Cerium oxide-doxorubicin: ROS modulation, synergistic therapy	[80]
Hybrid Nanocarriers	Lipid-Polymer Hybrids, Polymer-coated MSNs	Combines organic & inorganic benefits, improved stability	Lipid-polymer hybrids-paclitaxel: core-shell stability, enhanced tumor accumulation	
	MOFs, Core-Shell NPs	Reduced burst release, multifunctional	Polymer-coated MSNs: pH-triggered release, minimized leakage	[81, 82]
	Silica-Polymer Hybrids	High versatility, multi-drug loading	MOFs-gemcitabine: ultra-high loading; Hybrid silica-lipid NPs: improved bioavailability	[83]

3.3 Inorganic Nanocarriers

Inorganic nanocarriers offer unique physicochemical properties that are not achievable with organic or polymeric systems, making them attractive platforms for lung cancer drug delivery[84]. Materials such as mesoporous silica nanoparticles (MSNs), gold nanoparticles (AuNPs), iron oxide nanoparticles, and cerium oxide nanoparticles provide high structural stability, tunable porosity, and multifunctionality[33, 85]. Their robust architecture allows high drug-loading capacity, precise control over release kinetics, and the potential for integrating imaging or diagnostic functionalities alongside therapy[86].

A major advantage of inorganic nanocarriers is their large surface area and tunable pore structure, especially in MSNs, which enables encapsulation of high concentrations of chemotherapeutic agents while protecting them from premature degradation[87-89]. In addition, their mechanical and chemical stability allows for external modulation, such as pH-responsive, redox-sensitive, or magnetically guided drug release, which can improve tumor specificity and minimize systemic exposure[90].

In lung cancer applications, inorganic nanocarriers have shown significant therapeutic benefits. MSNs carrying cisplatin facilitate sustained release and reduce nephrotoxicity compared to free drug[91, 92]. Gold nanoparticles loaded with paclitaxel enhance cellular uptake and cytotoxicity in lung cancer cells[93, 94]. Iron oxide nanoparticles provide dual functionality as drug carriers and magnetically responsive agents for guided delivery[95]. Moreover, cerium oxide nanoparticles can act as ROS modulators while delivering anticancer drugs, further improving therapeutic efficacy[96, 97].

3.4 Hybrid Nanocarriers

Hybrid nanocarriers integrate the advantages of both organic and inorganic systems to create multifunctional platforms with enhanced stability, versatility, and therapeutic potential[98]. By combining polymers, lipids, or other organic materials with inorganic frameworks such as mesoporous silica or metal-organic frameworks (MOFs), hybrid nanocarriers achieve controlled drug release, improved structural integrity, and higher drug-loading capacity than single-component systems[99].

One key benefit of hybrid systems is their enhanced structural stability and reduced premature drug leakage[100, 101]. For example, lipid-polymer hybrid nanoparticles feature a polymeric core that provides mechanical support and sustains drug release, while the lipid shell enhances biocompatibility and improves circulation time[17, 102]. Similarly, polymer-coated MSNs prevent early release of encapsulated drugs and allow stimuli-responsive release under specific physiological conditions, such as pH changes in tumor tissues[103].

In lung cancer therapy, hybrid nanocarriers have demonstrated superior performance compared to conventional carriers. Lipid-polymer hybrids loaded with paclitaxel show improved tumor penetration and cytotoxicity due to the combined advantages of the polymer core and lipid shell[17, 104]. Polymer-coated MSNs provide controlled and targeted release, reducing systemic toxicity. MOFs, with their exceptionally high surface area and porosity, enable ultra-high loading of small-molecule drugs such as gemcitabine,

offering potential for combination therapy and enhanced therapeutic index[105, 106]. Overall, hybrid nanocarriers represent the next generation of drug delivery systems by offering multifunctionality, high loading efficiency, and precise control over drug release[107, 108]. Their flexible design and tunable properties make them particularly promising for overcoming the limitations of conventional therapies and advancing lung cancer treatment.

4 Conclusion and Future Perspectives

Nanotechnology-based drug delivery systems have markedly advanced lung cancer therapy by overcoming many limitations of conventional chemotherapeutics, such as poor solubility, rapid clearance, nonspecific distribution, and systemic toxicity. Polymeric nanoparticles, lipid-based nanocarriers, inorganic nanomaterials, and hybrid nanosystems each provide unique advantages, including sustained drug release, enhanced stability, high drug-loading capacity, and biocompatibility[109, 110]. These features collectively improve therapeutic efficacy and reduce adverse effects, positioning nanocarriers as versatile and promising tools in lung cancer management.

Looking forward, several areas warrant further exploration to fully realize the clinical potential of nanocarriers. Optimization of particle size, surface properties, and release kinetics will be critical to maximize tumor accumulation and minimize off-target effects[111, 112]. The development of multifunctional or stimuli-responsive systems capable of releasing drugs in response to pH, enzymes, or redox conditions could further enhance precision and therapeutic outcomes[90]. Moreover, rigorous evaluation of long-term safety, pharmacokinetics, and large-scale manufacturing feasibility is essential to ensure clinical translation.

Future research may also focus on integrating hybrid systems and combining multiple therapeutic agents to achieve synergistic effects while reducing systemic toxicity. With continued innovation in material design, fabrication techniques, and translational studies, nanocarrier-based drug delivery holds significant promise for the next generation of effective, safe, and targeted lung cancer therapies.

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