Available online on 15.09.2026 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

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Review Article

# Advanced Nanocarriers for Cancer Therapies: Recent Developments and Clinical Challenges

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## Article Info:

Article History:

Received 27 June 2026
Reviewed 09 Aug 2026
Accepted 01 Sep 2026
Published 15 Sep 2026

Cite this article as:

Rehmani A, Rahangdale PG, Meshram PD, Advanced Nanocarriers for Cancer Therapies: Recent Developments and Clinical Challenges, Journal of Drug Delivery and Therapeutics. 2026; 16(9):285-298
*DOI:*
*https://doi.org/10.22270/jddt.v16i9.7989*

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## Abstract

Cancer remains a major global health challenge, accounting for substantial morbidity and mortality despite advances in surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapies. However, the clinical effectiveness of these treatments is frequently limited by poor drug specificity, systemic toxicity, multidrug resistance, rapid drug clearance, and inadequate accumulation within tumor tissues. Advanced nanocarrier systems have emerged as a promising strategy to overcome these limitations by improving drug solubility, pharmacokinetics, tumor-targeted delivery, and therapeutic efficacy. This review critically summarizes recent developments in advanced nanocarriers for cancer therapy, emphasizing their design principles, therapeutic applications, clinical translation, and the key challenges influencing their future clinical adoption. The selected studies were critically analyzed to compare different nanocarrier platforms, targeting strategies, therapeutic performance, clinical progress, biosafety, manufacturing considerations, and regulatory perspectives. Recent advances demonstrate that lipid-based, polymeric, inorganic, biomimetic, and hybrid nanocarriers significantly enhance targeted drug delivery, improve therapeutic efficacy, and reduce systemic toxicity. Multifunctional and stimuli-responsive nanoplatforms have further expanded opportunities for precision oncology, although challenges related to safety, scalability, and regulatory approval remain. Advanced nanocarriers represent a promising platform for next-generation cancer therapeutics. Continued optimization of nanocarrier design, comprehensive safety evaluation, standardized manufacturing, and well-designed clinical studies will be essential to facilitate their successful translation into routine oncology practice.

**Keywords:** *Advanced Nanocarriers; Cancer Therapy; Targeted Drug Delivery Nanomedicine; Precision Oncology.*

## 1. INTRODUCTION

Cancer remains one of the most significant public health challenges worldwide and is a leading cause of morbidity and mortality across all age groups. Despite remarkable progress in molecular biology, diagnostic technologies, and therapeutic interventions, the incidence of cancer continues to rise due to population aging, lifestyle changes, environmental exposures, and genetic predisposition. Conventional treatment modalities, including surgery, chemotherapy, radiotherapy, hormone therapy, and targeted therapies, have substantially improved patient survival; however, their clinical effectiveness is often compromised by poor tumor selectivity, systemic toxicity, multidrug resistance, tumor heterogeneity, and disease recurrence[1-2]. These limitations underscore the urgent need for innovative therapeutic strategies capable of delivering anticancer agents with greater precision, efficacy, and safety. Nanotechnology has emerged as a transformative discipline in oncology, offering advanced drug delivery platforms that can overcome many of the shortcomings associated with conventional therapies. Nanocarriers possess unique physicochemical characteristics, including nanoscale dimensions, high surface area-to-volume ratio, tunable surface chemistry, and the ability to encapsulate diverse therapeutic molecules. These properties enable enhanced drug solubility, prolonged circulation time, controlled and stimuli-responsive drug release, improved pharmacokinetic profiles, and preferential accumulation within tumor tissues through both passive and active targeting mechanisms. Furthermore, advances in multifunctional nanocarriers have facilitated the integration of therapeutic and diagnostic functions, giving rise to theranostic systems that support personalized cancer management[3].

Recent developments in nanomedicine have expanded the repertoire of nanocarrier platforms, including lipid-based nanoparticles, polymeric nanoparticles, dendrimers, inorganic nanoparticles, biomimetic nanocarriers, and hybrid nanostructures. These systems have demonstrated significant promise in improving the

delivery of chemotherapeutic drugs, nucleic acids, proteins, peptides, and immunotherapeutic agents while minimizing off-target toxicity. In addition, the incorporation of targeting ligands, imaging agents, and stimuli-responsive materials has enhanced treatment specificity and therapeutic outcomes in various preclinical and clinical studies[4-5]. Nevertheless, several biological, manufacturing, regulatory, and translational challenges continue to limit the widespread clinical adoption of nanocarrier-based cancer therapeutics.

### 1.1 Global Burden of Cancer

Cancer is one of the leading causes of death worldwide and represents a substantial socioeconomic burden on healthcare systems. According to the International Agency for Research on Cancer, approximately 20 million new cancer cases and nearly 10 million cancer-related deaths were reported globally in 2022, with these numbers expected to increase substantially over the coming decades due to demographic changes and increased exposure to modifiable risk factors. Lung, breast, colorectal, prostate, and stomach cancers remain among the most frequently diagnosed malignancies, while lung cancer continues to account for the highest number of cancer-related deaths[6]. The global cancer burden is driven by multiple factors, including tobacco consumption, alcohol use, unhealthy diets, obesity, physical inactivity, chronic infections, environmental pollutants, occupational hazards, and inherited genetic mutations. Moreover, disparities in healthcare infrastructure, access to early diagnosis, screening programs, and advanced treatment options contribute significantly to variations in cancer incidence and survival rates between developed and developing countries. The increasing prevalence of cancer highlights the need for innovative therapeutic approaches that improve treatment efficacy while reducing adverse effects and healthcare costs[7-8].

### 1.2 Limitations of Conventional Cancer Therapies

Conventional cancer treatments-including surgery, chemotherapy, radiotherapy, hormone therapy, and molecular targeted therapy—remain the cornerstone of cancer management. Although these approaches have significantly improved survival outcomes for many patients, they are associated with several important limitations. Chemotherapeutic agents often exhibit poor selectivity, leading to damage of healthy tissues and causing adverse effects such as myelosuppression, gastrointestinal toxicity, cardiotoxicity, nephrotoxicity, and neurotoxicity. In addition, repeated administration of anticancer drugs frequently results in multidrug resistance through mechanisms such as increased drug efflux, enhanced DNA repair, mutation of drug targets, and activation of survival signaling pathways[9].

Radiotherapy may damage surrounding healthy tissues despite advances in precision treatment, whereas surgical intervention is often ineffective for metastatic or inaccessible tumors. Furthermore, tumor heterogeneity, abnormal tumor vasculature, elevated interstitial fluid pressure, and the immunosuppressive tumor microenvironment significantly reduce therapeutic effectiveness. These challenges emphasize the necessity for advanced drug delivery systems capable of selectively targeting malignant tissues while minimizing systemic toxicity[9-10].

### 1.3 Emergence of Nanocarriers in Oncology

The application of nanotechnology in oncology has revolutionized the design and delivery of anticancer therapeutics. Nanocarriers typically range from 1 to 200 nm in size and are engineered to encapsulate, protect, and transport therapeutic agents directly to tumor tissues. Their nanoscale dimensions facilitate improved cellular uptake, prolonged circulation time, enhanced drug stability, and controlled drug release. Importantly, nanocarriers can exploit the enhanced permeability and retention (EPR) effect for passive targeting while also being functionalized with antibodies, peptides, aptamers, or small molecules for active targeting of cancer-specific biomarkers[11].

Modern nanocarrier systems encompass lipid-based nanoparticles, polymeric nanoparticles, dendrimers, micelles, inorganic nanoparticles, carbon-based nanomaterials, extracellular vesicles, and biomimetic nanocarriers. Recent advances have enabled the development of multifunctional nanoplatforms capable of simultaneous drug delivery, gene therapy, immunotherapy, imaging, and real-time therapeutic monitoring. Stimuli-responsive nanocarriers that respond to pH, temperature, enzymes, redox conditions, ultrasound, magnetic fields, or light have further enhanced treatment precision and therapeutic outcomes. These innovations position nanocarriers as a cornerstone of precision oncology and next-generation cancer therapeutics[11-12].

This review aims to provide a comprehensive and critical overview of recent advances in nanocarrier-based cancer therapies. It discusses the fundamental principles governing nanocarrier design, classification, physicochemical characteristics, and mechanisms of tumor targeting. The review further examines major nanocarrier platforms, including lipid-based, polymeric, inorganic, biomimetic, carbon-based, and hybrid systems, together with their applications in chemotherapy, gene therapy, immunotherapy, photothermal therapy, photodynamic therapy, radiotherapy, and combination therapies.

## 2. FUNDAMENTALS OF NANOCARRIERS FOR CANCER THERAPY

Nanocarriers have revolutionized cancer therapeutics by enabling the targeted and controlled delivery of therapeutic agents to malignant tissues while minimizing systemic toxicity. Conventional chemotherapy is often associated with poor pharmacokinetics, rapid drug degradation, nonspecific biodistribution, multidrug resistance (MDR), and severe adverse effects resulting from the exposure of healthy tissues to cytotoxic drugs. Nanotechnology addresses these challenges through the engineering of nanoscale delivery systems capable of encapsulating, protecting, and selectively transporting anticancer agents to tumors[13]. Owing to their tunable physicochemical

properties, nanocarriers improve drug solubility, prolong circulation time, facilitate tumor accumulation, and enable controlled or stimuli-responsive drug release. Modern nanocarriers are designed not only to deliver chemotherapeutic drugs but also to transport nucleic acids, proteins, peptides, immunotherapeutics, photosensitizers, imaging agents, and gene-editing tools. Furthermore, multifunctional nanoplatforms integrate therapeutic and diagnostic capabilities (theranostics), allowing simultaneous tumor imaging, drug delivery, and treatment monitoring. Their interactions with the tumor microenvironment (TME), cellular membranes, intracellular organelles, and immune system significantly influence therapeutic outcomes[14]. Understanding the fundamental principles governing nanocarrier design, tumor targeting, and intracellular trafficking is therefore essential for developing effective next-generation cancer nanomedicines.

### 2.1 Classification Of Nanocarriers

Nanocarriers are nanoscale drug delivery systems, typically ranging from **1 to 1000 nm**, with most clinically relevant formulations measuring **20–200 nm**. These engineered systems encapsulate or conjugate therapeutic agents, protecting them from premature degradation while improving drug solubility, bioavailability, circulation time, and tumor-specific accumulation (**Table 1**). By enhancing pharmacokinetic properties and reducing systemic toxicity, nanocarriers have become indispensable in modern cancer therapy. Based on their composition and structural characteristics, nanocarriers are broadly classified into lipid-based, polymeric, inorganic, biomimetic/biological, and hybrid systems. Each class possesses unique advantages in terms of drug loading, targeting capability, controlled release, and multifunctionality[15]. Lipid-based carriers such as liposomes and lipid nanoparticles offer excellent biocompatibility and have achieved significant clinical success. Polymeric nanocarriers provide controlled drug release and versatile surface modification, whereas inorganic nanoparticles possess unique optical, magnetic, and imaging properties suitable for theranostic applications. Biomimetic nanocarriers, including exosomes and cell membrane-coated nanoparticles, enhance immune evasion and biological compatibility. More recently, hybrid nanocarriers have integrated the strengths of multiple materials to achieve targeted, stimuli-responsive, and personalized drug delivery, representing the next generation of cancer nanomedicine[16-17].

**Table 1:** Classification of advanced nanocarriers used in cancer therapy, highlighting representative examples, key advantages, and their major therapeutic applications in targeted drug delivery and precision oncology.[18-20]

| Nanocarrier Class | Representative Examples | Major Advantages | Major Applications |
|---|---|---|---|
| Lipid-based nanocarriers | Liposomes, Solid lipid nanoparticles (SLNs), Nanostructured lipid carriers (NLCs), Lipid nanoparticles (LNPs), Nanoemulsions | High biocompatibility, excellent drug encapsulation, prolonged circulation, controlled drug release | Chemotherapy, gene delivery, immunotherapy |
| Polymeric nanocarriers | PLGA nanoparticles, Polymeric micelles, Dendrimers, Nanogels, Polymersomes | Controlled drug release, high stability, surface functionalization, targeted delivery | Drug delivery, gene therapy, combination therapy |
| Inorganic nanocarriers | Gold nanoparticles, Iron oxide nanoparticles, Mesoporous silica nanoparticles, Calcium phosphate nanoparticles, Quantum dots | Magnetic, optical, and photothermal properties; high drug loading; imaging capability | Theranostics, photothermal therapy, MRI, targeted drug delivery |
| Biomimetic/Biological nanocarriers | Exosomes, Cell membrane-coated nanoparticles, Virus-like particles, Albumin nanoparticles | Excellent biocompatibility, immune evasion, prolonged circulation, natural targeting | RNA delivery, immunotherapy, precision medicine |
| Hybrid nanocarriers | Lipid–polymer hybrid nanoparticles, Polymer–inorganic hybrids, Multifunctional nanoplatforms | Combines advantages of multiple materials, stimuli-responsive release, multifunctionality | Personalized cancer therapy, theranostics, co-delivery of drugs and genes |

Overall, nanocarriers have emerged as versatile and highly efficient drug delivery platforms that address many limitations of conventional cancer therapies. Their diverse structural designs, improved targeting capabilities, controlled drug release, and multifunctional properties enhance therapeutic efficacy while reducing systemic toxicity. Continued advancements in nanocarrier engineering are expected to further improve precision oncology and accelerate the clinical translation of next-generation cancer therapeutics.

### 2.2 Physicochemical Properties Influencing Therapeutic Performance

The therapeutic performance of nanocarriers is primarily governed by their physicochemical properties, including particle size, shape, surface charge, hydrophobicity, drug loading capacity, encapsulation efficiency, surface functionalization, and colloidal stability. These characteristics collectively influence the biodistribution, pharmacokinetics, circulation time, tumor penetration, cellular uptake, and overall therapeutic efficacy of nanomedicines. Among these, **particle size** is one of the most critical factors, as nanoparticles smaller than 10 nm are rapidly eliminated through renal filtration, whereas particles larger than 200 nm are more susceptible to uptake by the mononuclear phagocyte system (MPS)[21]. Nanocarriers within the optimal size range of **30–150 nm** generally exhibit prolonged circulation and enhanced tumor accumulation through the enhanced permeability and retention (EPR) effect. Additionally, nanoparticle **shape and morphology** influence blood circulation and cellular internalization, with rod-shaped nanoparticles often demonstrating prolonged circulation and higher cellular uptake compared to spherical particles. **Surface charge** also plays a vital role in determining biological interactions; positively charged nanoparticles exhibit enhanced cellular uptake due to electrostatic interactions with negatively charged cell membranes but may induce higher protein adsorption and cytotoxicity, whereas neutral or slightly negative PEGylated nanoparticles provide improved systemic stability and prolonged circulation. Furthermore, **surface functionalization** with polyethylene glycol (PEG), antibodies, peptides, aptamers, vitamins, or other targeting ligands enhances receptor-mediated targeting while reducing immune recognition and facilitating stimuli-responsive drug release under conditions such as acidic pH, elevated glutathione levels, reactive oxygen species, enzymatic activity, or external triggers including light and magnetic fields. High **drug loading and encapsulation efficiency** ensure sufficient therapeutic payloads while minimizing premature drug leakage during circulation, thereby improving treatment efficacy. Equally important is the **physical and chemical stability** of nanocarriers, as aggregation or degradation can compromise circulation time, targeting efficiency, and drug integrity. Therefore, careful optimization of these physicochemical parameters is essential for developing safe, stable, and highly effective nanocarriers capable of achieving precise and efficient cancer therapy[22-23].

### 2.3 Tumor Microenvironment And Nanocarrier Interactions

The tumor microenvironment (TME) is a complex and dynamic network composed of cancer cells, stromal cells, immune cells, blood vessels, extracellular matrix (ECM), and various signaling molecules that collectively regulate tumor progression and therapeutic response. Unlike normal tissues, tumors are characterized by abnormal vasculature, hypoxia, acidic pH, elevated interstitial fluid pressure, and poor lymphatic drainage, which present both challenges and opportunities for nanocarrier-based drug delivery. Nanocarriers interact with the TME through mechanisms such as the enhanced permeability and retention (EPR) effect, receptor-mediated targeting, and stimuli-responsive drug release[24]. Tumor-specific conditions, including acidic pH, elevated glutathione (GSH), reactive oxygen species (ROS), and overexpressed enzymes, facilitate localized drug release, thereby enhancing therapeutic efficacy while minimizing systemic toxicity. Furthermore, surface modifications such as PEGylation and biomimetic coatings improve circulation time, reduce immune clearance, and promote selective accumulation of nanocarriers within tumor tissues, ultimately enhancing targeted cancer therapy.

### 2.4 Passive and Active Targeting Mechanisms

Targeted drug delivery is a key advantage of nanocarrier-based cancer therapy, as it enhances drug accumulation at tumor sites while minimizing toxicity to healthy tissues. **Passive targeting** primarily exploits the enhanced permeability and retention (EPR) effect, where nanoparticles (typically **30–150 nm**) preferentially accumulate in tumors due to their leaky vasculature and impaired lymphatic drainage, resulting in prolonged retention and increased local drug concentration. However, the EPR effect varies among different tumor types and patients, limiting its effectiveness when used alone (**Fig. 1**). To improve specificity, **active targeting** involves surface functionalization of nanocarriers with ligands such as monoclonal antibodies, peptides, aptamers, folic acid, hyaluronic acid, and transferrin, which selectively bind to overexpressed receptors including EGFR, HER2, CD44, folate receptor, and VEGFR on cancer cells[25]. This ligand–receptor interaction promotes receptor-mediated endocytosis, enhances intracellular drug delivery, and reduces off-target effects. Furthermore, advanced nanocarriers integrate passive and active targeting with **stimuli-responsive** drug release mechanisms, enabling controlled payload release in response to tumor-specific conditions such as acidic pH, hypoxia, elevated glutathione (GSH), reactive oxygen species (ROS), enzymes, or external stimuli including ultrasound, magnetic fields, and near-infrared (NIR) light. These multifunctional strategies significantly improve targeting accuracy, therapeutic efficacy, and the development of precision cancer nanomedicine[26].

### 2.5 Cellular Uptake And Intracellular Drug Trafficking

Following their accumulation within tumor tissues, nanocarriers must efficiently enter cancer cells and release their therapeutic payload at specific intracellular sites to achieve maximum therapeutic efficacy. Cellular uptake occurs primarily through endocytic pathways, including clathrin-mediated endocytosis, caveolae-mediated endocytosis, macropinocytosis, phagocytosis, and receptor-mediated endocytosis, with the uptake mechanism largely influenced by nanoparticle size, shape, surface charge, and ligand functionalization. Surface modification with antibodies, peptides, aptamers, and cell-penetrating peptides enhances

selective cellular internalization and targeting efficiency. Once internalized, nanocarriers are trafficked through intracellular compartments such as endosomes and lysosomes, where therapeutic agents may undergo degradation[27]. To overcome this limitation, advanced nanocarriers are engineered with endosomal escape strategies, including proton sponge polymers, pH-sensitive lipids, and membrane-disruptive materials, enabling efficient cytoplasmic drug release before lysosomal degradation.

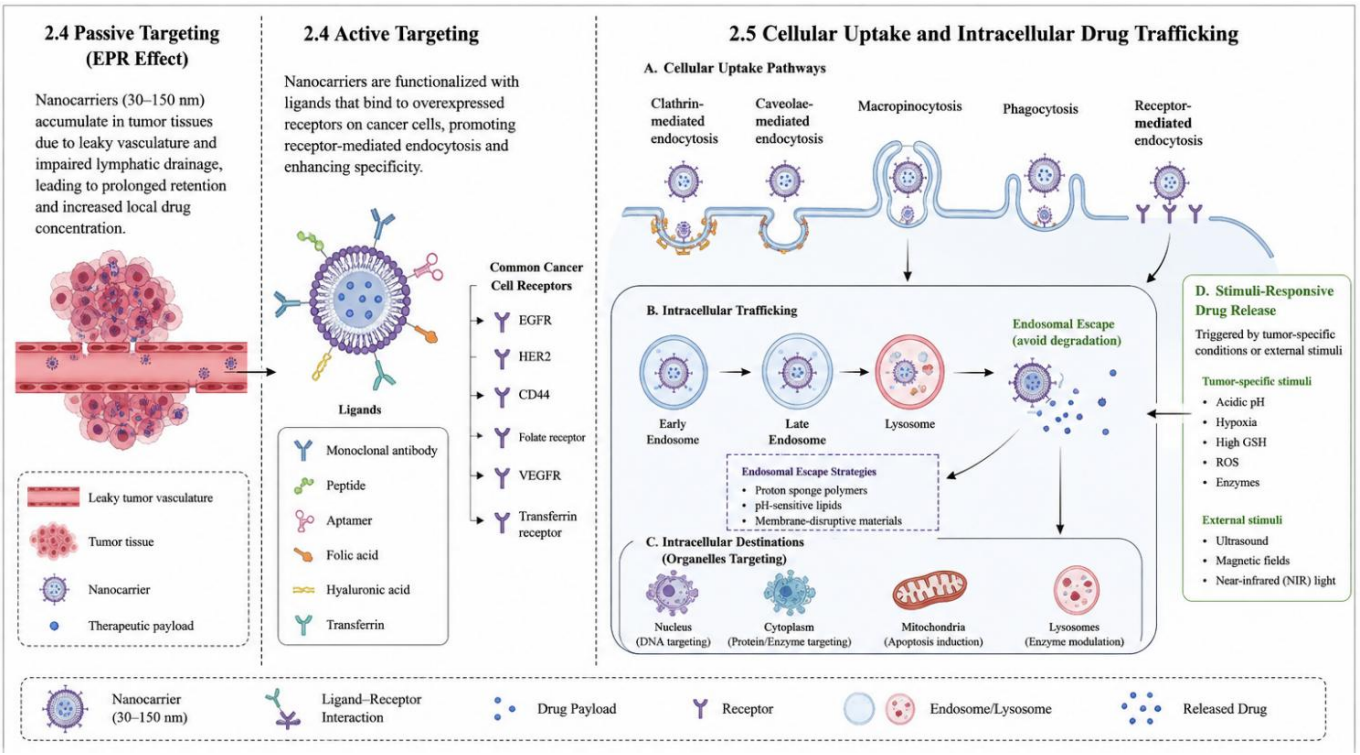


**Figure 1.** Passive and active targeting mechanisms, cellular uptake pathways, intracellular trafficking, and stimuli-responsive drug release of nanocarrier-based cancer therapeutics.

Depending on the therapeutic payload, drugs may subsequently target the nucleus, cytoplasm, mitochondria, or lysosomes to exert their biological effects. The integration of receptor-mediated uptake, efficient intracellular trafficking, organelle-specific targeting, and stimuli-responsive drug release has significantly improved the precision and effectiveness of nanocarrier-based cancer therapy, supporting the development of next-generation nanomedicines[28].

## 3. TYPES OF ADVANCED NANOCARRIERS

Advanced nanocarriers have significantly transformed cancer therapy by enabling targeted drug delivery, improving pharmacokinetics, enhancing therapeutic efficacy, and minimizing systemic toxicity. Based on their composition and functional properties, nanocarriers are broadly classified into lipid-based, polymeric, inorganic, carbon-based, protein- and biomimetic-based, and hybrid nanocarriers. Each class possesses unique physicochemical characteristics that determine its suitability for delivering chemotherapeutic agents, nucleic acids, proteins, and imaging probes. Recent advances in nanotechnology have further facilitated the development of multifunctional nanocarriers capable of combining targeted drug delivery, controlled drug release, molecular imaging, and immunotherapy within a single platform[29].

### 3.1 Lipid-Based Nanocarriers (Liposomes, Solid Lipid Nanoparticles, Nanostructured Lipid Carriers)

Lipid-based nanocarriers are among the most clinically established drug delivery systems owing to their excellent biocompatibility, biodegradability, and ability to encapsulate both hydrophilic and hydrophobic therapeutic agents. Liposomes, composed of phospholipid bilayers surrounding an aqueous core, have demonstrated remarkable success in improving drug stability, reducing systemic toxicity, and prolonging circulation time. Solid lipid nanoparticles (SLNs) provide enhanced physical stability and controlled drug release by utilizing solid lipid matrices, whereas nanostructured lipid carriers (NLCs) incorporate both solid and liquid lipids to improve drug loading capacity and minimize drug leakage. These nanocarriers are widely employed for the delivery of chemotherapeutic drugs, nucleic acids, and immunotherapeutic agents and have shown significant clinical success in targeted cancer therapy[30].

### 3.2 Polymeric Nanocarriers (Polymeric Nanoparticles, Polymeric Micelles, Dendrimers)

Polymeric nanocarriers are fabricated using biodegradable natural or synthetic polymers such as PLGA, PEG, chitosan, and polycaprolactone, offering excellent stability, controlled drug release, and flexible

surface functionalization. Polymeric nanoparticles effectively protect therapeutic agents from degradation while allowing sustained drug release. Polymeric micelles possess hydrophobic cores that efficiently encapsulate poorly water-soluble anticancer drugs, thereby enhancing their solubility and bioavailability. Dendrimers are highly branched macromolecules with numerous surface functional groups that enable high drug loading, ligand conjugation, and gene delivery. Owing to their tunable architecture and excellent biocompatibility, polymeric nanocarriers are extensively investigated for targeted chemotherapy, gene therapy, and combination treatment strategies[31].

### 3.3 Inorganic Nanocarriers (Gold, Silver, Silica, Iron Oxide Nanoparticles)

Inorganic nanocarriers possess unique optical, magnetic, electrical, and catalytic properties that make them highly attractive for cancer diagnosis and therapy. Gold nanoparticles exhibit excellent photothermal conversion efficiency and are widely used in photothermal therapy, biosensing, and targeted drug delivery. Silver nanoparticles possess strong antimicrobial and anticancer properties, largely attributed to reactive oxygen species generation and apoptosis induction. Mesoporous silica nanoparticles offer exceptionally high surface area and pore volume, enabling efficient drug encapsulation and controlled release. Iron oxide nanoparticles exhibit superparamagnetic properties that facilitate magnetic resonance imaging (MRI), magnetic targeting, and hyperthermia-based cancer therapy[32]. These multifunctional characteristics have established inorganic nanoparticles as important components of modern theranostic platforms.

### 3.4 Carbon-Based Nanomaterials (Carbon Nanotubes, Graphene, Fullerenes)

Carbon-based nanomaterials have gained considerable attention because of their exceptional mechanical strength, electrical conductivity, thermal stability, and large surface area. Carbon nanotubes (CNTs) efficiently transport drugs, nucleic acids, and proteins into cancer cells owing to their needle-like morphology and membrane-penetrating capability. Graphene and graphene oxide possess extensive surface functional groups that facilitate high drug loading, photothermal therapy, and biosensing applications. Fullerenes exhibit potent antioxidant properties and can generate reactive oxygen species upon light activation, making them suitable photosensitizers for photodynamic therapy. Although carbon-based nanomaterials demonstrate enormous therapeutic potential, concerns regarding long-term toxicity and biodegradability remain important challenges for their clinical translation[33].

### 3.5 Protein- and Biomimetic-Based Nanocarriers

Protein- and biomimetic-based nanocarriers have emerged as highly promising drug delivery systems due to their superior biocompatibility, biodegradability, and ability to evade immune recognition. Albumin nanoparticles, gelatin nanoparticles, and ferritin nanocages provide natural carriers for hydrophobic drugs while improving circulation time and reducing toxicity. Biomimetic nanocarriers, including exosomes and cell membrane-coated nanoparticles, mimic natural biological systems by retaining membrane proteins responsible for immune evasion and cell-specific targeting. These carriers exhibit prolonged circulation, enhanced tumor accumulation, and improved intracellular delivery of chemotherapeutics, nucleic acids, and immunotherapeutic agents, making them attractive candidates for precision oncology[34].

### 3.6 Hybrid and Multifunctional Nanocarriers

Hybrid nanocarriers combine two or more nanomaterials to integrate their complementary advantages within a single delivery platform. Examples include lipid–polymer hybrid nanoparticles, polymer–inorganic composites, and biomimetic hybrid systems, which provide enhanced structural stability, high drug loading, controlled drug release, and efficient tumor targeting. Multifunctional nanocarriers can simultaneously incorporate therapeutic agents, imaging probes, targeting ligands, and stimuli-responsive components, enabling combined chemotherapy, gene therapy, immunotherapy, photothermal therapy, and molecular imaging. These intelligent nanoplatforms respond to internal stimuli such as acidic pH, enzymes, and reactive oxygen species or external stimuli including light, ultrasound, magnetic fields, and heat, thereby improving therapeutic precision and minimizing systemic toxicity. Consequently, hybrid and multifunctional nanocarriers represent one of the most promising directions for the future development of personalized cancer nanomedicine[35].

Overall, the continuous evolution of advanced nanocarriers has significantly expanded the possibilities for targeted cancer therapy by overcoming many limitations associated with conventional treatment modalities. Each nanocarrier system offers distinct advantages in terms of drug loading, targeting specificity, controlled release, and multifunctionality, enabling more precise and effective therapeutic interventions. Ongoing advances in material science, nanotechnology, and molecular engineering are expected to accelerate the clinical translation of these platforms, paving the way for safer, smarter, and personalized nanomedicines that improve patient outcomes in cancer management.

## 4. RECENT DEVELOPMENTS IN NANOCARRIER-BASED CANCER THERAPIES

Recent advances in nanotechnology have revolutionized cancer treatment by enabling the development of multifunctional nanocarriers capable of improving therapeutic efficacy, reducing systemic toxicity, and overcoming biological barriers associated with conventional therapies. Modern nanocarrier platforms integrate targeted drug delivery, controlled drug release, gene therapy, immunotherapy, molecular imaging, and artificial intelligence (AI)-guided design, paving the way for precision oncology. The following sections discuss the latest developments that are

shaping the future of nanocarrier-based cancer therapeutics[36-37].

### 4.1 Targeted Drug Delivery Systems

Targeted drug delivery systems are designed to selectively transport therapeutic agents to tumor tissues while minimizing exposure to healthy cells. Recent developments include ligand-functionalized nanoparticles, antibody-drug conjugates, peptide-based targeting systems, aptamer-conjugated nanocarriers, and receptor-specific nanoparticles that improve tumor accumulation and cellular uptake. These systems enhance therapeutic efficacy, reduce systemic toxicity, and overcome multidrug resistance, making them an essential component of modern cancer nanomedicine.

### 4.2 Stimuli-Responsive (Smart) Nanocarriers

Stimuli-responsive or smart nanocarriers have emerged as advanced drug delivery systems capable of releasing therapeutic agents in response to specific internal or external stimuli. Internal triggers include acidic tumor pH, hypoxia, reactive oxygen species (ROS), glutathione (GSH), and tumor-associated enzymes, whereas external stimuli include magnetic fields, ultrasound, temperature, electric fields, and near-infrared (NIR) light. These intelligent nanocarriers provide precise spatiotemporal drug release, thereby improving therapeutic outcomes while minimizing adverse effects[38-39].

### 4.3 Co-delivery of Therapeutic Agents

Co-delivery nanocarriers enable the simultaneous transport of multiple therapeutic agents, such as chemotherapeutic drugs, nucleic acids, proteins, immunotherapeutics, or photosensitizers, within a single delivery platform. This strategy improves synergistic therapeutic effects, reduces multidrug resistance, lowers required drug dosages, and enhances treatment efficacy. Recent research has focused on optimizing co-delivery systems for combination chemotherapy, chemo-immunotherapy, chemo-gene therapy, and photothermal-chemotherapy combinations.

### 4.4 Gene and Nucleic Acid Delivery

Nanocarrier-mediated gene delivery has become an important strategy for precision cancer therapy by enabling the safe and efficient transport of genetic materials such as siRNA, miRNA, mRNA, plasmid DNA, antisense oligonucleotides, and CRISPR-Cas gene-editing components. Lipid nanoparticles, polymeric nanoparticles, dendrimers, and biomimetic nanocarriers protect nucleic acids from enzymatic degradation while facilitating targeted intracellular delivery. These technologies hold significant promise for gene silencing, genome editing, and personalized cancer treatment[40].

### 4.5 Nanocarriers for Cancer Immunotherapy

Nanocarriers have significantly advanced cancer immunotherapy by improving the delivery of immune checkpoint inhibitors, cytokines, cancer vaccines, tumor-associated antigens, adjuvants, and immune-modulating agents. Targeted nanocarriers enhance antigen presentation, stimulate cytotoxic T-cell activation, reprogram tumor-associated macrophages, and overcome the immunosuppressive tumor microenvironment. The integration of nanotechnology with immunotherapy has opened new opportunities for durable and highly specific anticancer immune responses[41].

### 4.6 Theranostic Nanoplatforms

Theranostic nanoplatforms combine therapeutic and diagnostic capabilities within a single multifunctional system, enabling simultaneous drug delivery, molecular imaging, and treatment monitoring. These platforms commonly integrate imaging agents with chemotherapeutic drugs, photosensitizers, or gene therapeutics, allowing real-time assessment of drug biodistribution and therapeutic response. Theranostic nanomedicine represents an important step toward personalized and image-guided cancer treatment.

### 4.7 Artificial Intelligence and Personalized Nanomedicine

Artificial intelligence (AI) is increasingly transforming nanomedicine by accelerating nanoparticle design, formulation optimization, toxicity prediction, patient stratification, and treatment planning. Machine learning algorithms can analyze large biological datasets to predict nanoparticle behavior, optimize drug release profiles, and identify suitable nanocarrier formulations for individual patients. The integration of AI with nanotechnology is expected to facilitate personalized cancer therapy, improve clinical decision-making, and accelerate the translation of next-generation nanomedicines into routine clinical practice.

Recent developments in nanocarrier-based cancer therapies have significantly improved the precision, safety, and efficacy of anticancer treatments through innovations in targeted delivery, smart drug release, combination therapy, gene delivery, immunotherapy, theranostics, and AI-driven nanomedicine. As these technologies continue to evolve, they are expected to overcome current therapeutic limitations and play a central role in the development of personalized and clinically translatable cancer treatment strategies[42-43].

## 5. THERAPEUTIC APPLICATIONS OF ADVANCED NANOCARRIERS

Advanced nanocarriers have revolutionized cancer treatment by enabling the precise and controlled delivery of therapeutic agents to tumor tissues while minimizing systemic toxicity. Unlike conventional drug formulations, nanocarriers can improve the pharmacokinetic profile, enhance drug solubility, prolong circulation time, and facilitate selective accumulation within tumors through passive and active targeting mechanisms. Furthermore, multifunctional nanocarriers can integrate therapeutic and diagnostic capabilities, allowing real-time monitoring of treatment responses while simultaneously delivering multiple therapeutic agents. Their ability to overcome biological barriers, including the tumor microenvironment and multidrug resistance mechanisms, has expanded their

applications across diverse therapeutic modalities such as chemotherapy, photothermal therapy, photodynamic therapy, radiotherapy, immunotherapy, and combination therapies. Recent advances in biomaterials, surface engineering, and stimuli-responsive systems have further enhanced the efficacy of nanocarrier-based interventions, paving the way for personalized and precision oncology. This section discusses the major therapeutic applications of advanced nanocarriers and highlights their role in improving cancer treatment outcomes[44-45].

### 5.1 Chemotherapy

Chemotherapy remains one of the primary treatment modalities for both solid and hematological malignancies. However, conventional chemotherapeutic agents often exhibit poor water solubility, rapid systemic clearance, nonspecific biodistribution, dose-limiting toxicity, and the development of multidrug resistance (MDR). Advanced nanocarriers have emerged as an effective strategy to overcome these limitations by enhancing targeted drug delivery and improving therapeutic efficacy. Various nanocarrier systems—including liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles, nanostructured lipid carriers, mesoporous silica nanoparticles, and metallic nanoparticles—have been extensively investigated for chemotherapeutic drug delivery. These nanocarriers encapsulate anticancer drugs such as doxorubicin, paclitaxel, cisplatin, docetaxel, temozolomide, and gemcitabine, protecting them from premature degradation while enhancing their bioavailability. Surface modification with polyethylene glycol (PEG) prolongs circulation time by reducing recognition by the reticuloendothelial system (RES), whereas ligand conjugation with antibodies, peptides, folic acid, transferrin, hyaluronic acid, or aptamers enables active targeting toward tumor-specific receptors[46].

Nanocarriers also exploit the enhanced permeability and retention (EPR) effect, facilitating preferential accumulation within tumor tissues due to abnormal tumor vasculature. Once internalized by cancer cells through receptor-mediated endocytosis, stimuli-responsive nanocarriers can release drugs in response to acidic pH, elevated glutathione levels, reactive oxygen species (ROS), enzymes, or external stimuli such as heat and ultrasound. Such controlled drug release increases intracellular drug concentration while minimizing exposure to healthy tissues. Moreover, nanocarrier-mediated chemotherapy has demonstrated significant potential in overcoming MDR by bypassing efflux pumps such as P-glycoprotein, co-delivering efflux pump inhibitors, or delivering small interfering RNA (siRNA) to silence resistance-related genes. Several clinically approved nanoformulations, including liposomal doxorubicin and albumin-bound paclitaxel, have validated the clinical utility of nanotechnology in chemotherapy by improving therapeutic indices and reducing adverse effects[47-48].

### 5.2 Photothermal Therapy (PTT)

Photothermal therapy is a minimally invasive treatment modality that utilizes photothermal agents capable of converting near-infrared (NIR) light into localized heat, inducing irreversible thermal damage to tumor cells. Compared with conventional thermal ablation techniques, nanocarrier-assisted PTT offers superior spatial precision, reduced collateral damage, and enhanced treatment specificity. A wide range of nanomaterials—including gold nanoparticles, gold nanorods, graphene oxide, carbon nanotubes, copper sulfide nanoparticles, iron oxide nanoparticles, and semiconducting polymer nanoparticles—have demonstrated remarkable photothermal conversion efficiencies. Upon NIR irradiation, these nanocarriers generate localized temperatures exceeding 45–50°C, leading to protein denaturation, membrane disruption, mitochondrial dysfunction, DNA damage, and apoptosis or necrosis of cancer cells[49-50].

Surface functionalization further enhances tumor specificity by incorporating targeting ligands that selectively recognize overexpressed receptors on malignant cells. Additionally, stimuli-responsive photothermal nanocarriers can simultaneously release encapsulated chemotherapeutic drugs during laser irradiation, thereby integrating chemotherapy with thermal ablation for synergistic anticancer effects. Recent developments have focused on biodegradable photothermal nanomaterials, second near-infrared (NIR-II) responsive systems with deeper tissue penetration, and multifunctional theranostic platforms capable of simultaneous imaging and therapy. These innovations significantly improve treatment precision while reducing systemic toxicity.

### 5.3 Photodynamic Therapy (PDT)

Photodynamic therapy employs photosensitizing agents that generate reactive oxygen species (ROS) upon activation by light of a specific wavelength. The generated singlet oxygen and free radicals induce oxidative damage to cellular membranes, proteins, mitochondria, and nucleic acids, ultimately triggering apoptosis, necrosis, or autophagy in tumor cells. Despite its clinical promise, conventional PDT is limited by poor photosensitizer solubility, inadequate tumor accumulation, rapid clearance, and tumor hypoxia. Nanocarriers effectively overcome these challenges by encapsulating hydrophobic photosensitizers, improving their pharmacokinetic properties, and facilitating targeted delivery to tumors[51].

Liposomes, polymeric nanoparticles, mesoporous silica nanoparticles, metal-organic frameworks (MOFs), and upconversion nanoparticles are commonly employed for PDT. Upconversion nanoparticles are particularly advantageous because they convert deeply penetrating near-infrared light into visible light capable of activating photosensitizers within deep-seated tumors. Modern nanoplatforms incorporate oxygen-generating components such as catalase or manganese dioxide nanoparticles to alleviate tumor hypoxia, thereby enhancing ROS production and therapeutic efficacy.

Additionally, combined photodynamic and immunotherapeutic approaches have demonstrated promising results by inducing immunogenic cell death and stimulating systemic antitumor immune responses capable of eliminating metastatic lesions[52].

### 5.4 Radiotherapy Enhancement

Radiotherapy is widely employed in cancer management but is often constrained by radioresistance and damage to surrounding healthy tissues. Advanced nanocarriers serve as radiosensitizers that selectively amplify radiation-induced damage within tumors while protecting normal tissues. High atomic number (high-Z) nanoparticles, including gold, hafnium oxide, bismuth, platinum, and gadolinium nanoparticles, efficiently absorb ionizing radiation and produce secondary electrons that enhance localized DNA damage and oxidative stress. This phenomenon significantly increases radiation dose deposition within tumor tissues without increasing external radiation exposure. Nanocarriers also deliver radiosensitizing drugs, DNA repair inhibitors, hypoxia-modifying agents, or oxygen-generating compounds that improve tumor oxygenation and reduce radioresistance. Stimuli-responsive systems can release therapeutic payloads specifically after radiation exposure, thereby maximizing treatment efficiency.

Furthermore, multifunctional nanocarriers integrating imaging modalities such as MRI, CT, or PET facilitate image-guided radiotherapy by improving tumor localization, treatment planning, and response monitoring. These theranostic systems contribute to highly personalized radiation treatment strategies with enhanced therapeutic precision.

### 5.5 Immunotherapy

Cancer immunotherapy harnesses the patient's immune system to recognize and eliminate malignant cells. However, immunotherapeutic efficacy is frequently compromised by immunosuppressive tumor microenvironments, poor antigen presentation, limited immune cell infiltration, and systemic immune-related toxicities. Nanocarriers have emerged as versatile platforms for delivering immune checkpoint inhibitors, tumor-associated antigens, cytokines, adjuvants, messenger RNA (mRNA), and immune-modulating agents directly to immune cells or tumor tissues. Lipid nanoparticles have gained particular importance following their successful application in nucleic acid delivery technologies.

Nanocarrier-based immunotherapy enhances dendritic cell maturation, promotes efficient antigen presentation, stimulates cytotoxic $CD8^+$ T-cell activation, modulates tumor-associated macrophages from M2 to M1 phenotypes, and reduces regulatory T-cell-mediated immunosuppression. Furthermore, nanocarriers improve the pharmacokinetic properties of immune checkpoint inhibitors targeting PD-1, PD-L1, and CTLA-4 pathways while reducing systemic adverse events. Emerging nanoplatforms capable of co-delivering immune modulators and chemotherapeutic agents induce immunogenic cell death, transforming immunologically "cold" tumors into "hot" tumors that exhibit stronger immune responses and improved sensitivity to checkpoint blockade therapy[53-54].

### 5.6 Combination Cancer Therapy

Cancer is a highly heterogeneous disease involving multiple dysregulated signaling pathways, making single-agent therapies insufficient in many cases. Combination therapy has therefore become an important strategy to achieve synergistic therapeutic effects while reducing drug resistance and minimizing toxicity. Advanced nanocarriers provide an ideal platform for co-delivering multiple therapeutic agents with synchronized pharmacokinetics and controlled release profiles. These systems can simultaneously transport chemotherapeutic drugs, nucleic acids, photosensitizers, immune modulators, or molecular inhibitors within a single nanoparticle.

Combination approaches include chemotherapy-photothermal therapy, chemotherapy-photodynamic therapy, chemotherapy-immunotherapy, radiotherapy-immunotherapy, gene therapy-chemotherapy, and photothermal-photodynamic therapy. Multifunctional nanocarriers ensure precise drug ratios, sequential drug release, and targeted accumulation within tumors, thereby maximizing synergistic interactions while minimizing systemic toxicity. Recent intelligent nanoplatforms incorporate stimuli-responsive mechanisms that release individual therapeutic agents in response to tumor-specific triggers, enabling personalized and highly efficient multimodal treatment strategies capable of overcoming tumor heterogeneity and therapeutic resistance[55-56].

### 5.7 Cancer Stem Cell-Targeted Therapy

Cancer stem cells (CSCs) constitute a small but highly tumorigenic subpopulation capable of self-renewal, differentiation, metastasis, therapeutic resistance, and tumor recurrence. Conventional therapies frequently fail to eradicate CSCs, allowing tumor relapse even after initial treatment success. Advanced nanocarriers offer promising strategies for selectively targeting CSCs by delivering therapeutic agents directly to stem cell-associated biomarkers such as CD44, CD133, EpCAM, ALDH, and integrins. Surface modification with antibodies, peptides, aptamers, or hyaluronic acid enhances selective uptake by CSC populations while minimizing toxicity to normal stem cells. Nanocarriers have been employed to deliver chemotherapeutic drugs, siRNA, microRNA, CRISPR/Cas gene-editing systems, differentiation-inducing agents, and signaling pathway inhibitors targeting Wnt/β-catenin, Notch, Hedgehog, PI3K/Akt, and STAT3 pathways. These interventions effectively suppress CSC self-renewal, inhibit epithelial-mesenchymal transition (EMT), reduce metastatic potential, and enhance treatment sensitivity[57-58].

Emerging multifunctional nanoplatforms combining CSC-targeted therapy with conventional chemotherapy or immunotherapy have shown remarkable potential for preventing tumor recurrence and improving long-term survival. Continued advancements in biomarker

identification and precision nanomedicine are expected to further enhance CSC-directed therapeutic strategies.

Advanced nanocarriers have significantly expanded the therapeutic landscape of modern oncology by improving drug delivery, enhancing treatment specificity, and enabling multimodal cancer therapy. Their applications now extend beyond conventional chemotherapy to include photothermal therapy, photodynamic therapy, radiotherapy enhancement, immunotherapy, combination treatment strategies, and selective targeting of cancer stem cells. Through precise tumor targeting, controlled and stimuli-responsive drug release, improved pharmacokinetics, and the integration of therapeutic and diagnostic functions, advanced nanocarriers effectively address many limitations associated with traditional cancer therapies[59]. Future advances in biomaterials, artificial intelligence-assisted nanomedicine design, precision oncology, and personalized therapeutic approaches are expected to further optimize nanocarrier performance, ultimately improving survival outcomes and quality of life for patients with cancer.

## 6. CURRENT CHALLENGES, LIMITATIONS, AND FUTURE PERSPECTIVES

Despite remarkable progress in the development of advanced nanocarriers for cancer therapy, several scientific, technological, and regulatory challenges continue to hinder their widespread clinical implementation. While nanocarriers have demonstrated superior tumor targeting, improved pharmacokinetics, and reduced systemic toxicity in numerous preclinical and clinical studies, their successful translation from laboratory research to routine clinical practice remains limited. The complexity of the tumor microenvironment, biological variability among patients, concerns regarding long-term biosafety, manufacturing inconsistencies, and stringent regulatory requirements represent major barriers to commercialization. Furthermore, achieving reproducible large-scale production while maintaining product quality and therapeutic performance remains technically demanding[60]. Addressing these limitations through interdisciplinary collaboration, standardized evaluation protocols, and technological innovations is essential for realizing the full potential of nanomedicine in precision oncology. This section discusses the major challenges associated with advanced nanocarriers and highlights emerging strategies that may shape the future of cancer nanotherapeutics.

### 6.1 Biological and Therapeutic Challenges

The biological complexity of cancer remains one of the greatest obstacles to effective nanocarrier-mediated drug delivery. Tumor heterogeneity, characterized by variations in genetic mutations, cellular phenotypes, metabolic activity, and receptor expression both within and between tumors, significantly influences nanoparticle accumulation and therapeutic response. Moreover, abnormal tumor vasculature, elevated interstitial fluid pressure, dense extracellular matrix components, hypoxic regions, and acidic tumor microenvironments restrict deep nanoparticle penetration, leading to heterogeneous drug distribution. The enhanced permeability and retention (EPR) effect, although widely exploited for passive targeting, varies considerably among tumor types and individual patients, limiting its clinical reliability[61].

In addition to biological barriers, therapeutic challenges remain substantial. Efficient drug loading without compromising nanoparticle stability, preventing premature drug leakage during circulation, and achieving controlled and site-specific drug release continue to be difficult. Multidrug resistance (MDR), overexpression of drug efflux transporters, and intracellular drug sequestration further reduce treatment efficacy. Although stimuli-responsive nanocarriers have shown considerable promise in addressing these issues, achieving precise and reproducible drug release under complex physiological conditions remains an ongoing challenge. Future research should focus on developing intelligent, biomimetic, and personalized nanocarrier systems capable of adapting to the dynamic tumor microenvironment and improving therapeutic precision[62].

### 6.2 Safety, Manufacturing, and Translational Limitations

Ensuring the long-term safety of nanocarrier systems remains a critical prerequisite for their successful clinical application. While many nanomaterials exhibit excellent biocompatibility in laboratory studies, comprehensive data regarding their long-term biodistribution, biodegradation, metabolism, clearance, and chronic toxicity in humans are still limited. Certain inorganic nanoparticles may accumulate in organs such as the liver, spleen, kidneys, or lungs, potentially inducing oxidative stress, inflammation, immune dysregulation, or organ-specific toxicity following repeated administration. Consequently, extensive toxicological evaluations and long-term clinical studies are necessary to establish their safety profiles[63-64].

From a manufacturing perspective, translating laboratory-scale nanocarriers into commercially viable products presents significant challenges. Producing nanoparticles with consistent particle size, morphology, surface charge, drug encapsulation efficiency, and release characteristics requires highly standardized and reproducible manufacturing processes. Even minor variations during synthesis can alter biological behavior and therapeutic performance. Furthermore, multifunctional nanocarriers often involve complex fabrication procedures, expensive raw materials, and sophisticated quality-control measures, increasing production costs and limiting commercial scalability. Addressing these translational barriers will require advances in scalable manufacturing technologies, automation, standardized characterization methods, and internationally accepted quality assurance guidelines.

### 6.3 Regulatory Considerations and Future Perspectives

The regulatory approval of nanomedicines remains considerably more complex than that of conventional pharmaceuticals due to their unique physicochemical characteristics and multifunctional properties. Existing regulatory frameworks are often insufficient to comprehensively evaluate nanoparticle quality, pharmacokinetics, biodistribution, immunogenicity, biodegradation, and long-term safety. Differences in regulatory requirements among international agencies further complicate product development and global commercialization. Consequently, despite thousands of promising preclinical studies, only a limited number of nanocarrier-based formulations have successfully reached routine clinical practice. Looking ahead, continuous advances in nanotechnology are expected to overcome many of these limitations. Emerging strategies include biomimetic nanocarriers, artificial intelligence-assisted nanoparticle design, personalized nanomedicine, stimuli-responsive drug delivery systems, gene-editing nanoplatforms, extracellular vesicle-based therapeutics, multifunctional theranostic nanoparticles, and nano-immunotherapeutic platforms. Integration of multi-omics technologies, precision oncology, and machine learning is anticipated to facilitate patient-specific treatment selection and optimize therapeutic outcomes[65].

Advanced nanocarriers represent one of the most promising innovations in modern cancer therapy; however, their widespread clinical adoption continues to face significant biological, technological, manufacturing, and regulatory challenges. Overcoming tumor heterogeneity, improving drug delivery efficiency, ensuring long-term biosafety, achieving reproducible large-scale production, and establishing globally harmonized regulatory frameworks remain critical priorities. Continued progress in biomaterials engineering, intelligent nanoplatform design, precision medicine, artificial intelligence, and translational research is expected to address many of these limitations. With sustained interdisciplinary collaboration and rigorous clinical validation, next-generation nanocarrier systems have the potential to transform personalized cancer treatment by providing safer, more effective, and highly targeted therapeutic strategies that ultimately improve patient survival and quality of life[66-68].

## CONCLUSION

Advanced nanocarriers have transformed the landscape of cancer therapeutics by addressing many of the limitations associated with conventional treatment modalities, including poor drug solubility, nonspecific biodistribution, systemic toxicity, multidrug resistance, and inadequate tumor selectivity. Recent developments in nanotechnology have led to the design of sophisticated nanocarrier platforms-such as liposomes, polymeric nanoparticles, dendrimers, micelles, solid lipid nanoparticles, nanostructured lipid carriers, inorganic nanoparticles, biomimetic nanocarriers, and hybrid nanoplatforms—that enable targeted drug delivery, controlled and stimuli-responsive drug release, prolonged circulation, and enhanced therapeutic efficacy. In addition to improving chemotherapy, advanced nanocarriers have significantly expanded the scope of cancer treatment by facilitating photothermal therapy, photodynamic therapy, radiotherapy enhancement, immunotherapy, gene therapy, and multimodal combination therapies. The incorporation of diagnostic imaging agents into these multifunctional systems has further promoted the development of theranostic nanomedicine, enabling simultaneous disease diagnosis, treatment, and therapeutic monitoring. Despite these remarkable advances, the successful clinical translation of advanced nanocarriers remains challenging. Biological barriers such as tumor heterogeneity, the complexity of the tumor microenvironment, variability of the enhanced permeability and retention (EPR) effect, and immune system interactions continue to limit therapeutic outcomes. Furthermore, concerns regarding long-term biosafety, nanoparticle biodegradation, large-scale manufacturing, batch-to-batch reproducibility, quality control, regulatory standardization, and cost-effective commercialization must be addressed before widespread clinical implementation can be achieved. Although several nanomedicine formulations have received regulatory approval and demonstrated improved clinical outcomes, many promising nanocarrier systems remain confined to preclinical research due to these translational limitations. Future research should focus on developing intelligent, biomimetic, and personalized nanocarrier systems capable of overcoming biological barriers while adapting to the dynamic characteristics of individual tumors. Emerging technologies—including artificial intelligence-assisted nanomedicine design, machine learning-based formulation optimization, CRISPR/Cas-mediated gene editing, messenger RNA (mRNA)-loaded nanoparticles, extracellular vesicle-inspired nanocarriers, and multifunctional theranostic platforms—are expected to further enhance the precision and effectiveness of cancer treatment. Additionally, integrating nanotechnology with precision oncology, multi-omics approaches, and patient-specific biomarkers will facilitate individualized therapeutic strategies and improve clinical decision-making.

## LIST OF ABBREVIATIONS

**AI:** Artificial Intelligence; **ALDH:** Aldehyde dehydrogenase; **CD44:** Cluster of differentiation **44;** CD133: Cluster of differentiation 133; CD8: Cluster of differentiation 8; **CNTs:** Carbon nanotubes; CRISPR/Cas: Clustered regularly interspaced short palindromic repeats/CRISPR-associated protein; **CSCs:** Cancer stem cells; CT: Computed tomography; CTLA-4: Cytotoxic T-lymphocyte-associated protein 4; **ECM:** Extracellular matrix; EGFR: Epidermal growth factor receptor; EMT: Epithelial–mesenchymal transition; EpCAM: Epithelial cell adhesion molecule; EPR: Enhanced permeability and retention; GSH: Glutathione; HER2: Human epidermal growth factor receptor 2; LNPs: Lipid nanoparticles; MDR: Multidrug resistance; miRNA: MicroRNA; MOFs: Metal–organic frameworks; MPS:

Mononuclear phagocyte system; MRI: Magnetic resonance imaging; mRNA: Messenger RNA; NIR: Near-infrared; NIR-II: Second near-infrared window; NLCs: Nanostructured lipid carriers; PD-1: Programmed cell death protein 1; PD-L1: Programmed death-ligand 1; PDT: Photodynamic therapy; PEG: Polyethylene glycol; PET: Positron emission tomography; PI3K/Akt: Phosphoinositide 3-kinase/protein kinase B signaling pathway; PLGA: Poly(lactic-co-glycolic acid); PTT: Photothermal therapy; RES: Reticuloendothelial system; ROS: Reactive oxygen species; siRNA: Small interfering RNA; SLNs: Solid lipid nanoparticles; STAT3: Signal transducer and activator of transcription 3; TME: Tumor microenvironment; VEGFR: Vascular endothelial growth factor receptor.

**Ethical Approval:** Not applicable.

**Consent for Publication:** Not applicable.

**Human and Animal Ethical Right:** Not applicable.

**Conflict of Interest:** The authors declare no conflict of interest, and no funding was required to conduct these review data.

**Acknowledgments:** The corresponding authors would like to thank, all involved members and faculty staff for their collaboration.

**Availability of Data and Materials:** The data supporting this study's findings will be available in the cited references.

**Funding:** The research received no external funding.

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