









# A review on nanotechnology in drug delivery systems for cancer therapy

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## Abstract

**Background:** Nanotechnology has introduced several clinically validated drug-delivery platforms that have improved pharmacokinetic profiles and reduced selected toxicities in specific cancer indications.

**Materials and methods:** This review was conducted by searching search engines such as Google Scholar, PubMed, and ScienceDirect using several keywords, such as “nanomedicine,” “lipid-based carriers,” “polymeric nanoparticles,” “dendrimers,” and “precision medicine.” The articles on precision medicine related to targeted therapy and gene therapy, artificial intelligence, and related large language models were excluded, and publications with unreliable, unverifiable, or inaccessible data, including non-peer-reviewed sources, were also excluded.

**Results:** Recent advancements have also enabled the integration of diagnostic and therapeutic functions within a single nanocarrier, paving the way for theranostic applications and real-time treatment monitoring. Despite these significant achievements, challenges such as large-scale manufacturing, stability, immunogenicity, and long-term safety remain substantial barriers to clinical translation.

**Conclusion:** Continuous efforts to develop biocompatible, cost-effective, and personalized nanomedicine platforms are essential to transform nanotechnology-based drug delivery from an experimental concept into a reliable clinical reality that has demonstrated improved pharmacokinetics, tolerability, or clinical outcomes in selected indications, such as liposomal formulations including CPX-351 and pegylated liposomal doxorubicin.

## Keywords

Dendrimers, nanomedicine, precision medicine, tissue distribution

## Introduction

Cancer is the leading cause of death around the world. In Europe, the incidence of cancer is increasing. For example, in a Bulgarian study, cancer incidence increased from 1968 to 2017 (Hristova et al. 1997). This increases the need for targeted anticancer treatment with low side effects, which in turn increases focus on nanoparticles and precision-oriented anticancer treatment strategies, such as proton therapy (Dimitrova et al. 2024a). However, nanotechnology has emerged as a promising approach to improve anticancer therapies (Dessale et al. 2022). The peculiar properties of nanometric materials permit easy set-up and control of tumor targeting, pharmacokinetics, and diagnosis or imaging-guided therapy (Chehelgerdi et al. 2023). One main objective is to increase drug concentration at the tumor site through the enhancement of the extravasation process, followed by better tissue penetration and a longer retention time (Malik et al. 2023). Thus, drug biodistribution across the body at different concentrations will reduce drug safety problems (Li et al. 2021).

Simple procedures prepare anticancer nanocarriers for the encapsulation of cargoes with appropriate physicochemical properties. Co-delivery of cytotoxic drugs with either radiosensitizers and immunomodulatory agents or chemotherapeutics can lead to synergistic effects, reducing toxicity while maintaining or enhancing the anticancer efficacy of the single treatments *in vivo* (Chatterjee and Kumar 2022). Preclinical studies have also focused on the guided administration of organized combined treatments by means of nanocarrier imaging capabilities (Mosleh-Shirazi et al. 2022). Therapeutic efficacy has been determined not only from tumor growth and animal survival data but also by assessing reductions in off-target toxicity and improvements in drug pharmacokinetics (Kemp and Kwon 2021). A minority of conventional cancer therapeutics reaches tumors because of heterogeneous and poorly perfused vasculature (Al-husaini et al. 2025).

Conventional cancer therapeutics are administered systemically, increasing the cancer-cell kill rate but also the potential for serious side effects (Al-Tameemi et al. 2025). The blood-enhanced permeability and retention effect is exploited for passive targeting, ensuring that small particles tend to accumulate in solid tumors and sites of chronic inflammation. Tumor-associated ligands also enable active targeting (Daoud et al. 2025). However, advanced tumor structures, including dense stroma and poor perfusion, impede delivery (Abdulla et al. 2025). Nanocarriers have therefore been designed to penetrate and normalize tumor vasculature, actively modulate local pH, and address other barriers (Hassan et al. 2025). The most widely used nanocarriers consist of lipids, polymers, inorganics, and dendrimers. Integrating imaging into nanoparticle formulations permits imaging-guided therapy or theranostic applications. Consequently, the notion of precisely designed nanocarriers for the effective delivery of chemotherapeutics to tumors was increasingly questioned (Pan-

dey et al. 2025). The challenge remains to convincingly demonstrate that these advanced drug delivery systems (DDS) truly improve the pharmacokinetic and pharmacodynamic properties of the incorporated drugs by enabling higher tumor drug concentrations or reduced off-target toxicity, either individually or combined (Salgueiro and Zubillaga 2025).

## Materials and methods

### Search strategy

This review was conducted by searching scientific databases, such as the EU Clinical Trials Register, ClinicalTrials.gov, Google Scholar, PubMed, and ScienceDirect, covering publications from 2020 to 2025. The search strategy incorporated combinations of relevant keywords related to the article, using several keywords such as “nanomedicine,” “lipid-based carriers,” “nanotechnology drug delivery,” “polymeric nanoparticles,” “dendrimers,” and “precision medicine.” A structured screening process inspired by PRISMA principles was conducted. Only English-language peer-reviewed studies focusing on nanotechnology-based drug delivery for cancer were included. Articles in languages other than English, formulations addressing diseases other than cancer, and formulations above 250 nm in size were excluded.

### PRISMA screening results

The initial database search yielded 1,286 records. After removing duplicate publications ( $n = 214$ ), 1,072 unique articles were screened based on titles and abstracts, as illustrated in Fig. 1.

Finally, 112 studies were included in the qualitative synthesis of this review.

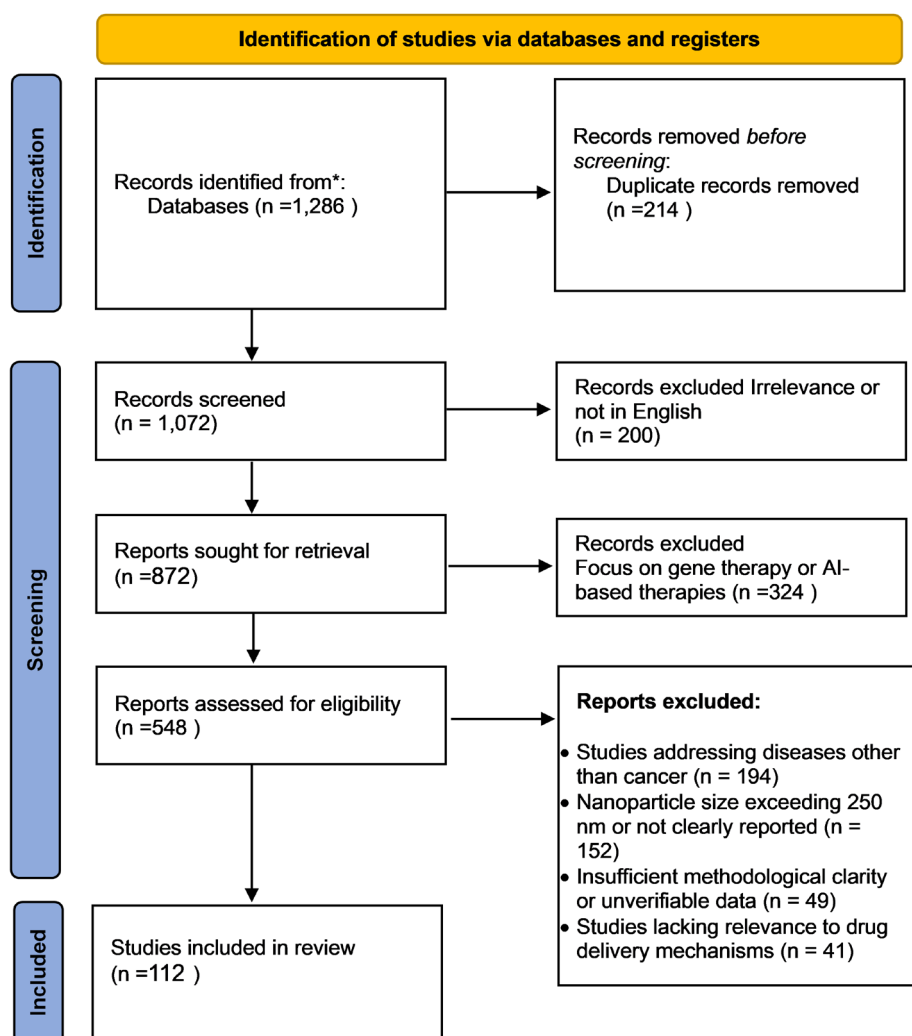
Additionally, clinical trial registry screening identified 67 nanotechnology-based cancer therapeutic trials, which were analyzed separately to provide translational and clinical context.

### Inclusion criteria

1. The articles should focus on nanotechnology-based drug delivery systems used in cancer therapy.
2. Published in peer-reviewed journals.
3. Studies published related to several experimental, clinical, or review data on lipid-based carriers, polymeric nanoparticles, nanomedicine, or dendrimers.

### Exclusion criteria

1. Publications with unreliable, unverifiable, or inaccessible data, including non-peer-reviewed sources, were excluded.
2. Studies with unrealistic or scientifically unsupported claims.



**Figure 1.** PRISMA flow diagram for selection criteria for articles.

## Review results

### Nanocarrier platforms for cancer therapy

Several factors determine the choice of a particular nanocarrier system and whether and how the various targeting strategies will optimize biodistribution and pharmacokinetics. A failure of most conventional drug formulation strategies is that, after administration, the drugs eventually distribute to almost all organs in the body (Smadja and Lellouch 2025). Many of the most common side effects of chemotherapy can be attributed at least in part to the action of these drugs in nontumor-associated tissues (Ebrahim et al. 2025).

### Lipid-based nanocarriers

Liposomes, solid lipid nanoparticles, and lipid–drug formulations constitute the main classes of lipid-based nanocarriers. Liposomes, the pioneering nanocarrier system among the lipid-based candidates, consist entirely of phospholipid bilayers. They are spherical vesicles composed of one to several concentric layers, with an inner aqueous compartment capable of delivering both hydrophilic and

hydrophobic drug (Tantray et al. 2025). Liposomes have been domesticated for use in parenteral formulations of encapsulated drugs and antineoplastic combinations, as well as for localized delivery. Several liposomal formulations are now marketed, with more under investigation in clinical trials (Bhange and Telange 2025).

Solid lipid nanoparticles (SLNs) are colloidal carriers formed from solid lipids dispersed in aqueous surfactant. They contain a solid lipid core and surfactant-stabilized lipophilic drug molecules in or on the particle (Gugleva and Andonova 2023).

### Polymeric nanoparticles

Polymeric nanoparticles are excellent nanocarriers for drug delivery, supported by years of clinical and preclinical data using biodegradable polymers. Biodegradable polymers are commonly used to prepare polymeric nanoparticles due to their regional depot effect and sustained drug-release kinetics (Zhu et al. 2025). Surface modification of polymeric nanoparticles, which alters their physicochemical properties and enables active targeting or stimuli-responsive release, is also employed in various applications.

The two most important types of polymeric nanoparticles are defined as polymeric micelles and nanocapsules with a drug-containing aqueous core (Selvakumar et al. 2024).

## Inorganic nanoparticles

Key among the inorganic nanocarriers are gold nanoparticles, silica nanoparticles, magnetic nanoparticles, and quantum dots. For example, gold nanoparticles can be used for both imaging and therapeutic purposes in cancer therapy; in such applications, they can serve as anticancer drug carriers, imaging agents, photothermal agents, or radiation enhancers. Image-guided cancer therapy can be achieved through silica-core gold-shell nanoparticles, which have strong X-ray absorption properties and thus act as contrast agents for computed tomography imaging. Silica nanoparticles can also be functionalized with nanolayers of gadolinium oxide and iron oxide for multimodal imaging (Sivasubramanian et al. 2022). Silica-based nanoparticles play a major role in the latest developments in cancer biology, targeting of tumors, monitoring drug delivery processes, and supporting hyperthermia-induced therapy. Another interesting class of inorganic carrier materials involves magnetic nanoparticles (MNPs), which consist of a core composed of iron oxide or cobalt and a polymer-based shell. MNPs can be guided *in vivo* toward diseased tissues by means of an external magnetic field, and thus, their biodistribution strongly differs from that of other carriers (Kumar and Mangla 2025). They also provide contrast for magnetic resonance imaging, and if they are made from very small constituent particles (core size < 10 nm), they can also act as photothermal agents. Hybrid magnetic-Au nanoparticles with a very small iron oxide core that can provide MRI contrast have recently been designed (Ahmad et al. 2025).

These types of carriers can be easily biofunctionalized using a variety of polymeric coating agents for delivery to specific tissues, cellular compartments, or other targets (Seliverstov et al. 2024; Mahmoud and Deambrogi 2025).

## Dendrimers and mesoporous silica nanoparticles

Dendrimers and mesoporous silica nanoparticles (MSNs) are two notable categories of nanocarriers characterized by specific features. Dendrimers have been used as drug carriers for methotrexate, doxorubicin, and gemcitabine, among others. At present, the most clinically advanced dendrimers are Radiogel, a polymeric nanoparticle containing iodine, and Cpar, a doxorubicin–polyethylene glycol hyaluronic acid hybrid for liver cancer treatment (Al-Hussaniy et al. 2023; Nankya 2024).

Mesoporous silica nanoparticles (MSNs) are inorganic nanoparticles decorated with nanopores between 2 and 50 nm. These pores provide large surface areas that can be further functionalized with targeting groups or stimuli-sensitive polymers to regulate the release of loaded drugs. MSNs exhibit unique advantages, including a biocompatible silica backbone that permits fast kidney clearance (Chattopadhyay et al. 2025) (see Table 1; Fig. 2).

## Targeting strategies and biodistribution

The relevance of the selected platform for delivery efficiency and off-target risks, as well as a close examination of targeting strategies previously discussed, is underscored by the ensuing sections on drug loading, release, and

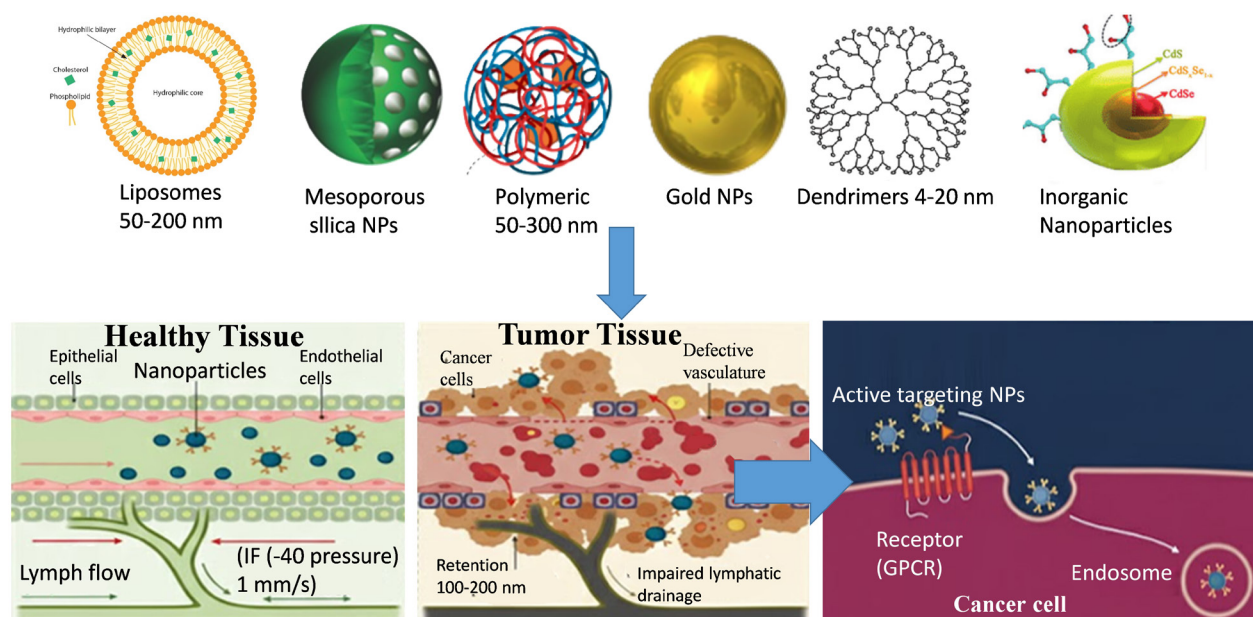
**Table 1.** Comparative major nanocarriers used in cancer therapy.

Platform	Size range (nm)	Loading strategy	Release trigger	Circulation/clearance trends	Key advantages	Regulatory status (US/EU/clinical)
Liposomes	60–200	Encapsulation in an aqueous core or lipid bilayer	pH, temperature, passive diffusion	Long circulation when PEGylated <sup>**</sup> ; hepatic/splenic uptake	Biocompatible, clinically validated	FDA/EMA-approved: Doxil <sup>®</sup> , Vyxeos <sup>®</sup>   Investigational: ThermoDox <sup>®</sup> (Phase III)
Polymeric nanoparticles (PLGA, micelles)	20–150	Encapsulation or polymer–drug conjugates	pH, redox, enzyme, temperature	Controlled release; renal or hepatic clearance	Tunable pharmacokinetics; stimuli responsiveness	Regionally approved: Genexol-PM <sup>®</sup> (South Korea)   Investigational: BIND-014 (Phase II, discontinued)
Solid lipid nanoparticles (SLN)	80–200	Drug in a solid lipid matrix	pH, enzymatic	Rapid RES uptake unless modified	Good stability, scalable	No FDA/EMA-approved anticancer products; multiple early-phase clinical trials
Inorganic nanoparticles (gold, silica, MNPs)	5–100	Surface adsorption, pore loading (MSNs)	Light, magnetic field, pH	RES uptake; possible long-term retention	Imaging and therapy, high stability	Investigational (oncology): AuroLase <sup>®</sup> (photothermal, clinical trials)   Approved (non-therapeutic): iron-oxide agents for MRI
Dendrimers	3–15	Multibranch encapsulation; surface conjugation	pH, enzyme	Renal clearance is < 6 nm; hepatic if larger	High-precision functionalization	Radiogel <sup>®</sup> , Cpar (investigational) No approved anticancer dendrimer drugs;
Mesoporous silica nanoparticles (MSNs)	20–200	Adsorption into pores	pH, redox	Moderate circulation; RES uptake	High loading capacity; tunable pores	No FDA/EMA approvals; Phase I/II clinical candidates

MNPs: magnetic nanocarrier; PLGA: poly (lactic-co-glycolic acid); SLN: solid lipid nanoparticles; MSNs: mesoporous silica nanoparticles; <sup>\*\*</sup>PEG chains attached to the liposome surface. Regulatory status reflects publicly available FDA and EMA records as of March 2025. “Investigational” refers to products evaluated in registered clinical trials without marketing authorization.

- FDA-authorized: approved by the United States Food and Drug Administration.
- EMA-authorized: approved by the European Medicines Agency.
- Regionally approved: approved by national regulatory agencies outside the US/EU.
- Investigational: evaluated in registered clinical trials without marketing authorization.



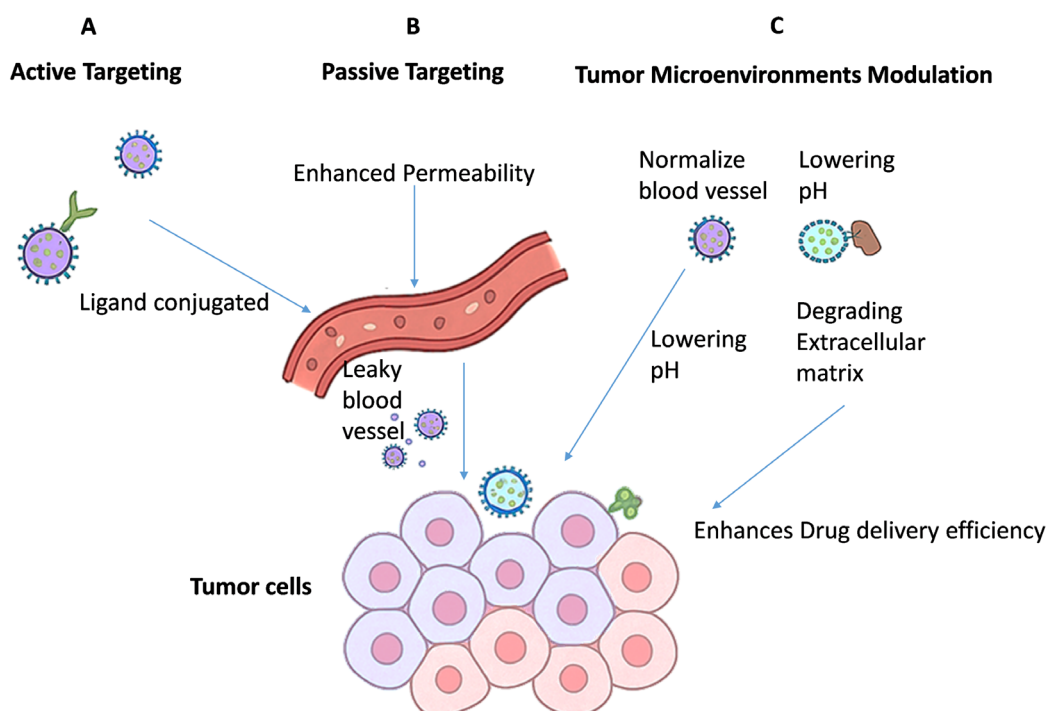


**Figure 2.** Schematic representation of major nanocarrier platforms used in cancer therapy, including lipid-based, polymeric, inorganic, and dendrimer/mesoporous silica nanoparticles, illustrating their role in targeted drug delivery to tumor tissues.

pharmacokinetics. The performance of all tested nanocarriers has strongly benefited from passive targeting via the enhanced permeability and retention (EPR) effect. Cancer cells' unique molecular signatures are now also being utilized actively to improve delivery through a variety of ligand–receptor interactions (Iqbal et al. 2024) (see Fig. 3).

### Passive targeting and enhanced permeability and retention (EPR) effect

Until recently, the heterogeneous architecture of most cancers was viewed as a major barrier for the effective delivery of drugs and imaging agents and the application



**Figure 3.** Overview of tumor-targeting strategies in nanotechnology-based drug delivery systems. The diagram illustrates three principal mechanisms: (A) active targeting, achieved by conjugating ligands to nanocarrier surfaces to recognize and bind specific tumor cell receptors; (B) passive targeting through the enhanced permeability and retention (EPR) effect, allowing nanocarriers to accumulate in tumor tissue via leaky vasculature; and (C) tumor microenvironment modulation, which enhances delivery efficiency by normalizing abnormal blood vessels, reducing extracellular matrix density, and adjusting local pH. Together, these mechanisms improve selective drug accumulation and therapeutic efficacy while minimizing off-target toxicity.

of the “one-size-fits-all” concept. Now, the prominent vascularization in the tumor region and the quiescent state of cancer-associated fibroblasts are exploited to enhance accumulation through passive targeting using appropriate liposome or nanoparticle formulations. These different methods are based on the enhanced permeability and retention (EPR) effect. The rapid proliferation of tumor cells induces the formation of a leaky tumor vessel system with poor lymph drainage, leading to an increased abundance of sub-200 nm-sized carriers in the tumor interstitium. The nanoparticles are retained in the tumor region for a longer time than in normal tissue due to the differences in interstitial fluid pressure and pore size; hence, the distribution is biased toward the tumor for the appropriate size and surface property. Systematic investigations suggest that the EPR effect is more significant for pirarubicin- and paclitaxel-loaded pegylated liposomes than for pegylated liposomes. Other applications also support this effect (Al-Hussaniy and Al-Zobaidy 2024).

## Active targeting: ligand–receptor interactions

Active targeting exploits the specific interactions between tumor-associated antigens or receptors and corresponding ligands conjugated to nanocarrier surfaces. Tumor-specific or overexpressed receptors act as natural traps for such ligand-decorated nanocarriers, which at least temporarily increase accumulation and enhance knowledge of their pharmacokinetics and biodistribution (Schorr et al. 2025). Many successful active-targeting strategies have been reported, with commonly used receptors and ligands listed in Table 2. The general principles of conjugation chemistry, including linker chemistry, surface density, and choice of coupling site, apply, and specific considerations on conjugation strategies may be found in numerous studies (Dong et al. 2023). The efficacy of active targeting may, however, vary tremendously owing to tumor-specific receptor expression levels, heterogeneous expression within individual tumors, modulation of expression levels by the local tumor microenvironment, and rapid internalization of the conjugated constructs once taken up by the tumor cells (Pandey and Pandey 2024).

**Table 2.** Common ligand–receptor pairs used for active targeting in cancer nanomedicine.

Receptor (target)	Ligand/binding moiety	Nanocarrier type	Application/notes
Folate receptor (FR- $\alpha$ )	Folate	Liposomes, polymeric nanoparticles	Overexpressed in ovarian, breast, and lung cancers
Transferrin receptor (TfR)	Transferrin	Liposomes, gold nanoparticles	Enhanced uptake in leukemia and brain tumors
HER2/ErbB2	Trastuzumab, anti-HER2 peptides	Liposomes, dendrimers	Breast cancer targeting; clinically validated mAbs
EGFR	EGF, anti-EGFR antibodies	Polymeric nanoparticles, gold nanoparticles	Internalization in solid tumors
Integrins ( $\alpha v\beta 3$ )	RGD peptides	Liposomes, mesoporous silica nanoparticles	Targeting tumor vasculature and angiogenesis
CD44	Hyaluronic acid (HA)	Polymeric nanoparticles	Highly expressed in breast, lung, and liver cancers
PSMA	PSMA-targeted peptides	Liposomes, polymeric nanoparticles	Prostate cancer targeting
LDL receptor	ApoB, ApoE mimetics	Solid lipid nanoparticles	Tumor and liver targeting
CD123	Anti-CD123 antibodies	Polymer–drug conjugates	Relevant to AML targeting mechanisms
TfR1	T7 peptide	Gold nanoparticles, polymeric nanoparticles	Glioma and brain targeting
VCAM-1/ICAM-1	sLeX, antibodies	Liposomes	Inflammation and metastasis-associated targeting

FR- $\alpha$ : folate receptor alpha; TfR/TfR1: transferrin receptor; HER2/ErbB2 and EGFR: epidermal growth factor receptors;  $\alpha v\beta 3$ : angiogenesis-associated integrin; CD44, CD123, and PSMA: tumor-associated surface antigens; LDL receptor: lipid uptake receptor; VCAM-1/ICAM-1: adhesion molecules involved in inflammation and metastasis.

## Tumor microenvironment modulation

The pH within solid tumors is acidic because of the aberrant physiological function of the tumor microvasculature and a high glycolytic rate. Low pH within tumors can induce premature drug release from carriers with acid-sensitive links, such as those for pH-responsive micelles, core–shell nanoparticles, or poly( $\beta$ -amino ester)-based nanogels. Dendritic polypeptide and poly( $\beta$ -amino ester)-based nanoparticles released 5,3-dichlorobenzoxazine–SRF-078, a potent thrombospondin-1 analog, more rapidly at pH 5.4 and pH 7.4, with consequent cytotoxicity to the neovascular endothelial cells that express the appropriate receptor.

The high deposition of collagen I, III, and IV within the extracellular matrix (ECM) of tumors is responsible for the dense stroma that surrounds and infiltrates most tumors. Multimicelle carriers injectable via fine needles, as with those based on pH-modulating poly(amino ester) copolymers, modulated the pH around tumors and normalized the collagen I-rich ECM (Cassani et al. 2025). The resultant normalization of the ECM promoted the extravasation of small-molecule chemotherapeutics and enhanced the antitumor effects of doxorubicin, irinotecan, or cisplatin (He et al. 2023).

## Drug loading, release mechanisms, and pharmacokinetics

### Encapsulation and conjugation methods

Drug loading in nanocarriers can be via physical encapsulation or covalent/linker-based conjugation methods. Physically encapsulated drugs release at a speed relative to the sensing environment. As such, careful design ensures controlled release that is not only sustained for a longer time but also fast for better responses. Covalent/linker conjugation stabilizes the drug in nanocarriers, enabling controlled release; however, due to cleavage degradation, release becomes erratic because of the hindering agent environment. Therefore, for controlled release profile selection, physical encapsulation is best, whereas linker-based conjugation is preferable for stimuli-driven release (Butt and Tabassum 2026).

## Stimuli-responsive release

Stimuli-responsive release relies on pH-, redox-, temperature-, or enzyme-triggered drug release. The chemical microenvironment of the tumor allows for prolonged systemic stability of nanocarriers before drug release; however, stimulation at the diseased site expedites release. Selectively pH-responsive carriers release drugs more rapidly from the acidic tumor microenvironment than from blood (pH 7.4) with its normal physiological pH. Tumors with overexpressed  $H_2O_2$  facilitate faster release of redox-sensitive carriers than non-pathological tissues. Such carriers are further combined with temperature-responsive polymers to achieve tumor-triggered and conscious deliveries. Enzyme-sensitive carriers enable fast drug release through the action of enzymes upregulated in tumors (Tiwari et al. 2025). These integrated stimulus-responsive nanocarriers utilize tumor-specific microenvironments to ensure release at the disease site (Cao et al. 2025).

## Theranostics and multimodal approaches

### Imaging-guided therapy

Imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and optical imaging allow three-dimensional visualization of tumors and their microenvironments (Bandyopadhyay et al. 2023). The development of imaging-guided therapy has facilitated real-time monitoring of drug delivery, response evaluation, and dose adjustment during treatment (Zeng et al. 2021). By combining diagnostic and therapeutic functions, imaging-guided therapy provides the ability to visualize the biodistribution of drugs or other agents in real time, allowing clinicians to adjust doses accordingly (Zhang et al. 2025).

### Combination therapies and synergy

Therapeutic windows are commonly much larger than the half-lives of substances within the body, providing suitable conditions for the effect of both nanocarriers with therapeutic effects and other agents. Co-delivery of drugs, radiosensitizers, thermal agents, immune modulators, and other substances able to intervene in distinctive ways with the tumor microenvironment is common to provide a collective effect that gives rise, for example, to synergistic enhancement of therapeutic efficacy and reduction of undesirable side effects (Kurungottu et al. 2025). Among the different types of compounds used together with nanocarriers, special emphasis has been given to the association between chemotherapeutics, radiosensitizers, thermosensitizers, photothermal agents, and immune adjuvants (Hu et al. 2025).

Realization of any form of hybrid therapy must obey the package stability conferred by one of the biodegradable

nanoplatfroms. Hybrid therapy may be based on the functionality of the two types of therapeutic agents as long as they share the same or compatible biological mechanism or pathway or exert an antagonistic effect at the micro- or macroscopic levels. In many instances, two or more nanocarrier platforms are involved, one for each type of therapeutic agent, as seen in the award-winning hybrid therapy that involved human epidermal growth factor receptor 2 (HER2)-specific antibody–drug conjugates for targeted delivery of a CD137 agonist into the tumors (Geraldes 2024).

## Safety, toxicology, and regulatory considerations

Safety and long-term toxicological studies are critical for the successful transition of nanoparticulate carriers from preclinical to clinical use. Nanocarriers may elicit immune responses, but the extent and nature of these reactions vary widely depending on physicochemical attributes such as particle size, surface charge, morphology, surface chemistry, protein corona composition, dose, and dosing frequency. Following *in vivo* administration, certain nanocarriers can trigger the formation of antibodies—particularly anti-PEG antibodies in the case of PEGylated systems—which may accelerate blood clearance or alter biodistribution. Importantly, these responses are not unique but are influenced by prior exposure, immunogenic epitopes, and patient-specific factors. However, although hydrophilicity is preferred for preventing the opsonization of agents and interaction with the complement system, the use of a highly hydrophilic carrier may cause its rapid removal from the systemic circulation via the kidneys or spleen. In many cases, long-term safety studies for nanoparticles are not yet available (Iraqi 2024). Therefore, long-term studies should be performed to evaluate any undesirable effects during chronic administration (Beshna et al. 2022).

Nanocarriers should undergo safety studies to meet clinical use regulations. For example, the rapid preclinical-to-clinical translation of pegylated liposomes requires the application of a comprehensive safety evaluation before entering Phase III clinical trials. Immune reaction problems are generally observed after multiple administrations of lipid nanoparticles, leading to a reduction in drug-loaded nanoparticles during therapy. The problem becomes even worse with liposomes containing high doses of cholesterol. Preclinical toxicology studies have further shown that stable lipid nanoparticles made from polysorbate 80 are safe for clinical use, having been observed to produce no inflammation, hemostasis impairment, or hepatic injury. Regulatory agencies such as the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) require long-term toxicity studies before market approval, including assessment of potential age-specific vulnerabilities. Tracking agents within the body following administration during clinical trials can also inform immunocompatibility considerations (Al-Samydai et al. 2025).

## Clinical translation and case studies

### Clinical trials landscape

A variety of clinical trial repositories, trial sponsors, and investigative groups regularly compile information on ongoing and recently completed clinical trials involving various types of nanoparticle-based platforms. The currently active records in the EU Clinical Trials Register list over 60 nanotechnology-based compounds that are being actively investigated within the European Union, with indications ranging from vaccination adjuvants to combination therapies with radiation, chemotherapy, and other non-drug treatments (Dri et al. 2023). Importantly, nearly 40% of these records indicate the use of polymeric-based nanoparticles (Zielińska et al. 2020).

For lipid-based nanomedicine, the clinically validated comparator is CPX-351 (Vyxeos®), a true dual-drug liposomal formulation co-encapsulating cytarabine and daunorubicin at a fixed 5:1 molar ratio. CPX-351—developed originally by Celator Pharmaceuticals—was evaluated in a Phase III trial (NCT01696084) enrolling 309 adults with high-risk or secondary acute myeloid leukemia (AML). Patients received 100 units/m<sup>2</sup> IV on days 1, 3, and 5, with primary endpoints including overall survival (OS) and complete remission rates compared with 7+3 chemotherapy. The trial demonstrated a significant OS improvement (9.6 vs. 5.9 months), leading to FDA approval in 2017. CPX-351 represents one of the few nanocarriers to demonstrate a clear clinical advantage over standard chemotherapy (Agnihotram et al. 2024). Furthermore, the United States National Institutes of Health Clinical Trials database lists over 260 distinct nanoparticle-based trials conducted in the United States and abroad, with more than one-third employing liposome-based systems (Shaaban et al. 2023).

### Representative case analyses

Despite the promise revealed in preclinical studies, only 66 of the 171 cancer nanomedicines in the Nanotechnology Characterization Lab database are currently undergoing clinical trials, with the majority in phases 1 and 2 (Yadav et al. 2025). As yet, clinical outcomes associated with these candidates remain limited, but several interesting advances have recently been reported in the field (Mitrakas et al. 2025). A selection of representative case analyses below captures both the successes and shortcomings of nanocarrier systems in relation to clinical applications (Meng et al. 2024). SL-401, tagraxofusp, is a CD123-directed IL-3-diphtheria-toxin fusion protein (Stemline/ELZONRIS) approved for BPDCN, while Celator is associated with CPX-351 (Vyxeos), the dual-drug liposome for AML (Su et al. 2025). In an investigation staged at the Moffitt Cancer Center, the Phase I clinical trial adopted a pooled cohort accelerated design, with patients receiving SL-401 intravenous infusion at 1/5 of the model-derived maximum tolerated dose (Gao et al. 2024).

### Clinical importance and application to the European population

Nanotechnology-based drugs have a significant clinical outcome in European countries due to several points, such as high cancer incidence, an aging population, and increased need for targeted therapy (Ivanova et al. 2024). If the prevalence of cancer in India and Europe is compared, it is approximately 100.4 per 100,000 in India (Sathishkumar et al. 2022), and according to GLOBOCAN 2022, it is approximately ASR 280 per 100,000 in Europe (Elmadani et al. 2025). Many cancers with rising prevalence in Europe, such as breast, colorectal, and ovarian cancer, can benefit from nanocarrier-enhanced targeting, reduced systemic toxicity, and improved pharmacokinetics (Dimitrova et al. 2024b). The clinical importance of these systems is already evident in several nanomedicines approved for use across Europe, such as Doxil® (pegylated liposomal doxorubicin), Abraxane® (albumin-bound paclitaxel), Myocet® (non-pegylated liposomal doxorubicin), Onivyde® (liposomal irinotecan), and Vyxeos® (CPX-351 liposomal daunorubicin/cytarabine) (Alven et al. 2024). These agents demonstrated context-dependent improvements in tolerability and selected clinical endpoints compared with conventional formulations in specific indications, such as the tolerability and response rate compared to traditional chemotherapies in European clinical trials (Al-Kuraishy et al. 2022).

### Limitations and future directions

Overcoming significant challenges is critical for the commercialization and clinical implementation of nanotechnology-based drug delivery systems. Three key requirements that still await resolution are the manufacturability and scale-up of nanocarriers for actual patients. First, as most components and designs for nanocarriers are irrelevant to commercial production and clinical translation, those based on optimized and simplified formulations with detailed quality assurance and control provisions are most likely to succeed. Second, a shift in focus to patients is essential, through stratification based on relevant clinical, biological, and physicochemical parameters, to predict treatment outcomes based on indications derived from biomarker-associated studies. Finally, the future direction of nanocarrier research may culminate in the development of multifunctional sensors that can detect tumor-associated signals, including abnormal pH, overexpressed enzymes, and overproduced metabolites, while demonstrating satisfactory biocompatibility and minimizing the risk of unwanted toxicities during release (Mangla et al. 2024).

### Personalized nanomedicine and precision oncology

Although personalized nanomedicine with nanocarriers capable of reconciling both the hallmarks and new characteristics of cancer has opened up new avenues, the com-



mercialization of personalized therapy is still quite limited. The practical implementation of personalized nanomedicine lies in patient selection based on biomarkers corresponding to key functions (Karahmet Sher et al. 2024). For example, tumor vascular permeability may be positively correlated with the therapeutic efficacy of nanoparticles, thus allowing for patient stratification; highly vascularized tumors with greater elusiveness and increased radiation sensitivity may be appropriate for liposome–radiation therapy. The selection of an appropriate biomarker is thus essential for determining the candidates of personalized therapy for any specific nanocarrier (Aziz 2024).

Precision oncology seeks to provide patients with targeted medications adapted to the characteristics and development of their own tumors. With the aid of nanotechnology, the specific requirements of these targeted drugs in terms of membrane permeability, targeting, release properties, and the associated inhibitory effect on drug-resistant tumors can now be met as well (Mazumdar et al. 2025).

## Emerging technologies and next-generation nanocarriers

Synthesis of new nanocarriers and a move toward personalized nanomedicine are objectives for cutting-edge research and development. Optical/NIR imaging combined with self-reporting biosensors and theranostic nanocarriers, termed multimodal sensors, is anticipated to be superior to existing platforms in the early detection of cancers. These sensors integrate biocompatibility, tumor response, and pH or biorelease capability for biomarker detection with dual-modal imaging (Subasinghe et al. 2022). Future explorations in the field are likely to focus on multifunctional-targeted sensors equipped with such capabilities. Nanoparticles can be prepared with multiple types of contrast agents in a single NIR fluorescence-CT or NIR fluorescence-MRI nanoprobe for cancer multimodal imaging (Jiang et al. 2023). Further studies of NIR nanohydrogels composed of dense photoactive conjugated polymers incorporated with therapeutics are warranted to expand photothermal imaging-guided cancer therapy (Rahman et al. 2024).

The design of nanoscale drug delivery vehicles that respond accurately to the complicated tumor microenvironment for protein/mRNA/virus release shows promise (Forenzo et al. 2025). Nanocarriers combining the advantages of passive, active, and stimuli-responsive targeting are also possible in conjunction with co-encapsulation or co-delivery of actives, such as chemotherapeutics, radiosensitizers, immunomodulators, or other drugs (Dey et al. 2024).

## Conclusion

Nanotechnology-based drug delivery systems have made substantial progress in preclinical studies aimed at enhancing anticancer efficacy and reducing systemic toxicity. Investigations continue exploring multiple aspects of delivery systems to optimize effectiveness,

safety, and applicability in personalized nanomedicine. Ongoing and completed clinical trials of nearly 60 nanodrugs indicate that several approved nanomedicines, including liposomal and albumin-bound formulations, have demonstrated context-dependent improvements in toxicity profiles or therapeutic outcomes depending on cancer type and clinical indication. Nevertheless, numerous technological, regulatory, and clinical challenges persist in making nanotechnology-based delivery systems a routine aspect of cancer therapy.

Consequently, it is essential to recognize the existence of a generational divide within clinical nanomedicine. While many researchers remain focused exclusively on fundamental nanosystem design for strictly preclinical applications, the clinical market has started consolidating around a more mature set of nanocarrier platforms. These highly studied constructs are proven safe in humans and are the eventual target of nearly every preclinical nanodelivery system developed today. Several nanocarrier platforms have reached clinical use; however, their long-term impact on routine oncology practice remains limited and indication-specific. Human trial results reinforce the idea that others will likely be given more time for fine-tuning, but considerable room exists for multiple types of nanosystems to safely cross the patient line and become commercially available options as soon as it makes sense from a safety and efficiency perspective.

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## Additional information

### Conflict of interest

The authors have declared that no competing interests exist.

### Ethical statements

The authors declared that no clinical trials were used in the present study.

The authors declared that no experiments on humans or human tissues were performed for the present study.

The authors declared that no informed consent was obtained from the humans, donors or donors' representatives participating in the study.

The authors declared that no experiments on animals were performed for the present study.

The authors declared that no commercially available immortalised human and animal cell lines were used in the present study.

### Artificial Intelligence (AI) use

The authors accept full responsibility for the content of the manuscript, including the disclosure of any use of AI.

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- ## Data availability
- All of the data that support the findings of this study are available in the main text.
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