Review Article

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Nanotechnology Applications in Cancer Drug Delivery Systems: A Review

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ABSTRACT

Nanotechnology of medicine, particularly therapy, by novel longstanding in drug delivery. Cancer, a complex and multifaceted disease, demands innovative therapeutic approaches capable of addressing its heterogeneity, drug resistance, and adverse effects associated with conventional avenues for nanomaterials, dimensions, large-to-volume ratio, and the ability to be functionalized for specific purposes. Moreover, advancements in nanotechnology have enabled chemotherapeutics, siRNA, to address the multifactorial nature of cancer and overcome drug resistance mechanisms. Advancements, nanotechnology significant challenges. Issues such as scalability in manufacturing, reproducibility, and biocompatibility, hinder cancer and further complicate the design of universally effective nanocarriers, necessitating tailored approaches for different cancer types and patient populations. This review examines the developments driven by cancer highlighting design principles and their impact on improving therapeutic outcomes. It also offers insights into emerging trends and future directions. With continuous innovation and interdisciplinary collaboration, nanotechnology holds immense potential to transform cancer therapy, and targeted, patient-specific treatment modalities.

Keywords: Nanotechnology; Targeted delivery systems; Cancer drug delivery.

1. INTRODUCTION

Chemotherapy, a cornerstone of cancer treatment, is particularly constrained by low therapeutic efficacy, adverse side effects, and poor pharmacokinetics, resulting in a pressing need for more effective and precise treatment modalities. These challenges underscore the demand for innovative solutions that can be safe. Beyond targeted delivery, nanotechnology also offers platforms for controlled therapeutic payload stimuli within elevated temperatures; this spatiotemporal control minimizes premature drug release and enhances. Furthermore, nanotechnology facilitates immunomodulators, tackles multifaceted natural cancer, and combats drug resistance. Theranostic nanoplatforms, which integrate therapeutic and diagnostic capabilities, represent another significant advancement in nanotechnology-based cancer treatment. These systems enable imaging, allowing clinicians to track treatment progress and make informed decisions. Combining therapy with diagnostics, theranostics pave the way for treatment strategies for specific needs. Despite these promising applications, they are not without challenges. Scalability and reproducibility of nanoparticle synthesis remain significant hurdles, particularly when transitioning from laboratory-scale research to clinical production. Biocompatibility safety concerns include the accumulation of nanoparticles in the body, which could lead to unforeseen toxicities. Cancer drug delivery has long been a critical challenge in oncology, as the effectiveness of traditional cancer treatments is often limited by poor drug targeting, low bioavailability, and systemic toxicity. This review explores the various applications of nanotechnology in cancer drug delivery systems, highlighting the advancements made in the field, including the development of novel nanocarriers, drug-loading strategies, and targeting mechanisms. Through a comprehensive analysis, we aim to offer insights into the current state of research and the future potential of nanotechnology in cancer therapy. Additionally, tumors' complex and heterogeneous nature often requires a combination of different nanocarrier systems or the development of hybrid carriers to achieve optimal therapeutic outcomes. Future Directions: Advancements in nanocarrier design continue to address existing limitations, focusing on improving biocompatibility, stability, and targeting efficiency. Emerging approaches, such as hybrid nanocarriers combining different nanomaterials' strengths, are gaining attention. Nanocarrier modalities and biosensors the development of theranostic platforms for personalized medicine. As research progresses, interdisciplinary collaborations will be crucial in overcoming technical and regulatory challenges, paving the way for the widespread clinical adoption of cancer. In summary, nanocarriers offer innovative solutions that are specific and safe. Nanocarriers offer targeted and efficient treatment options. However, their clinical success depends on

addressing toxicity and biocompatibility challenges. By leveraging advanced materials, surface modifications, and innovative delivery strategies, researchers aim to develop nanocarriers that maximize therapeutic benefits while ensuring patient safety. Continued interdisciplinary collaboration and rigorous evaluation of potential nanocarrier cancer therapies.

2. NANOTECHNOLOGY AND CANCER DRUG DELIVERY

Theranostic potential theranostic nanoparticles provide a robust monitoring tool that allows clinicians to optimize drug delivery and helps track tumor progression, enabling more personalized and adaptive cancer treatment strategies. Long-term research and development while significant nanotechnology-based cancer is substantial, much must be done to address the challenges of clinical translation, manufacturing scalability, and regulatory approval. To ensure that nanotechnology-based therapies become widely available to patients. By improving cancer therapies' precision, efficacy, and safety, nanotechnology can provide better treatment options for patients, particularly those with advanced or refractory cancers (Siddiqi *et al*. 2018). Reducing systemic side effects and targeting drugs specifically to tumor sites will enhance the overall therapeutic index. Additionally, integrating combination therapies and theranostic systems into cancer treatment holds promise for more personalized approaches and tailor regimens tumors. This individualized treatment approach will likely lead to better response rates, reduced recurrence, and longer survival times for cancer patients.

2.1 Types of Nanocarriers for Cancer Drug Delivery

Composed as one of the earliest and most extensively studied nanocarriers, liposomes are highly biocompatible and biodegradable, and structural versatility allows for the incorporation of coating to enhance circulation time by evading immune clearance (Adnane and Fahmy, 2022). Additionally, conjugated liposomes are used for targeted drug delivery. Polymeric nanoparticles are particularly advantageous for delivering poorly soluble drugs, protecting them through functionalization active targeting to improve the tumor site. Polymeric nanoparticles are also used in siRNA to combat multidrug resistance (Ahamed *et al*. 2012). Despite their potential, polymeric nanoparticles face challenges, including potential limited scalability and regulatory hurdles. Dendrimers: three-dimensional and architectural shape, chemistry, therapeutic agents on their surface through chemical bonds. Their multivalency enables the simultaneous drug incorporation and imaging agents. Poly(amidoamine) (PAMAM) dendrimers, for example, demonstrate improved drug solubility and targeted delivery (Aljabali *et al.* 2022). However, the synthetic complexity and potential cytotoxicity of dendrimers, particularly at higher generations, challenge their clinical application. Carbon Nanotubes: Carbon nanotubes (CNTs), composed of graphene sheets rolled into cylindrical structures, are unique nanocarriers. Their hollow core enables the loading of significant quantities of drugs, while their functional Zable surface facilitates targeted delivery. CNTs can penetrate cellular membranes, allowing efficient intracellular delivery of anticancer agents (Almatroodi *et al*. 2020). Functionalized CNTs have shown promise in delivering chemotherapeutics, siRNA, and gene therapy agents. Liposomes are ideal for clinical translation due to their established safety profile, while polymeric nanoparticles provide tunable properties for controlled release and co-delivery of multiple agents. Dendrimers offer precise molecular design for multifunctional delivery, and CNTs bring unique properties for advanced therapeutic strategies (Alrushaid *et al.* 2023). However, limitations such as scalability, reproducibility, stability, and potential toxicity remain significant challenges.

2.2 Targeted Cancer Therapy using Nanoparticles

Targeted cancer therapy aims to deliver therapeutic agents, specifically enhancing treatment efficacy. Nanoparticles carry therapeutic payloads, their tuneable physicochemical properties, and their potential for precise Targeting. Targeted delivery using nanoparticles leverages enabling high levels of drug accumulation tumor tissue ligands antibodies into nanoparticle designs has further enhanced the specificity and efficiency of these systems, conventional cancer treatments (Anjum *et al.* 2021). Passive Targeting: unique pathophysiological tumors. The most notable mechanism exploited is tumor tissues, which possess large fenestrations. This phenomenon is tumor site without the need for active cellular Targeting. Passive Targeting is particularly beneficial for solid tumors, where nanoparticles can remain localized for extended periods, ensuring sustained drug release. However, the efficacy of passive Targeting depends on the tumor's vascular structure and interstitial pressure, which can vary significantly among patients and tumor types. Additionally, the EPR effect may not be as effective in metastatic or poorly vascularized tumors, highlighting the need for complementary targeting strategies. Active Targeting: Active Targeting also facilitates receptor-mediated endocytosis, enabling the internalization of intracellular nanoparticles. This mechanism is particularly advantageous for delivering A and DNA, drugs that act on intracellular targets. The design of active targeting systems requires careful consideration of ligand-receptor interactions, as overexpression of target receptors on normal tissues or receptor downregulation in tumors may affect targeting specificity.

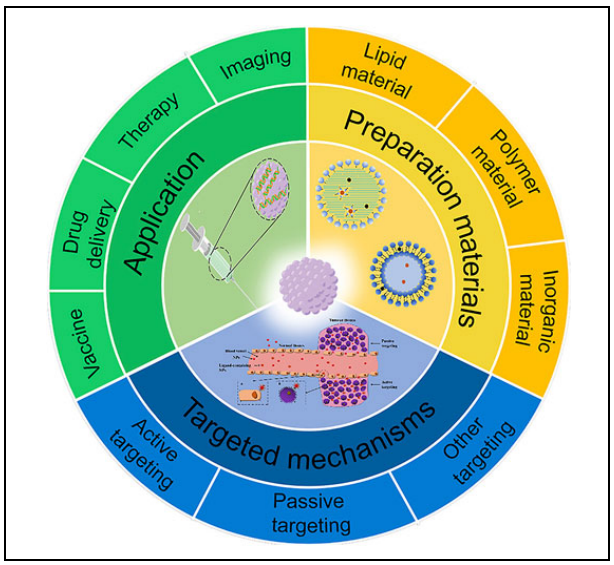


Fig. 1: Application of nanoparticles in tumour targeted drug delivery

2.3 Role of Ligands and Antibodies

Ligands and antibodies active targeting strategies. Monoclonal antibodies, widely used in targeted therapy, offer high specificity and affinity for tumor-associated antigens. Antibody-drug conjugates (ADCs) represent a notable application where cytotoxic drugs are linked to antibodies, allowing targeted delivery to cancer cells. Nanoparticles functionalized with antibodies further enhance targeting capabilities, as seen in trastuzumab-functionalized nanoparticles for HER2-positive cancers or cetuximab-functionalized nanoparticles. Peptides and aptamers are also effective in small, high-specificity synthesis (Asif *et al.* 2023). For example, RGD peptides and integrin vasculature have functionalized nanoparticles for targeted delivery to angiogenic tumors. To offer similar advantages and have been explored in nanoparticle-based targeting systems for cancer therapy. Advantages and Challenges: Targeted cancer therapy using nanoparticles offers several advantages over conventional treatments. Enhanced specificity reduces off-target effects, while increased tumor improvement Nanoparticles also provide a platform for enabling simultaneous Additionally, targeted nanoparticles can be stimuli, ensuring site-specific (Aasyim *et al.* 2023). Furthermore, nanoparticle synthesis's scalability, reproducibility, and cost-effectiveness must be addressed for successful commercialization. Future Perspectives: Advancements in nanotechnology and molecular biology continue to drive the development of next-generation targeted nanoparticles. Emerging strategies include multifunctional nanoparticles combining imaging, diagnosis, and therapy (theranostics) and hybrid nanoparticles integrating multiple targeting ligands for enhanced specificity. Advances in bioengineering also aid nanoparticles with optimized pharmacokinetics and biodistribution. In conclusion, targeted cancer therapy using nanoparticles promises oncology and overcomes the limitations of traditional treatments. By leveraging active and passive targeting strategies and incorporating ligands and antibodies, these systems improve patient outcomes and quality of life. Interdisciplinary will be realizing nanoparticle-based targeted therapies.

2.4 Nanotechnology-based Combination Therapies for Cancer Treatment

Cancer is a complex and multifaceted disease characterized by heterogeneity that evades the immune system, making single-modality treatments often insufficient. Combination therapies, which use powerful targeting of multiple combination cancer therapies, offer platforms that integrate chemotherapy, radiotherapy, photodynamic therapy (PDT), and immunotherapy into a single system. These multifunctional nanoplatforms provide significant advantages, including enhanced efficacy, reduced systemic toxicity, and precise spatiotemporal control over therapeutic delivery. However, they also present challenges related to design, manufacturing, and clinical translation (Baranwal *et al.* 2023). Nanotechnology offers solutions to these issues through the development of chemotherapeutic nanoparticles. These carriers enhance drug solubility, improve pharmacokinetics, and tumor target ligand-functionalized nanocarriers). In combination therapies, nanocarriers allow chemotherapeutics to be used as other therapeutics, enabling and overcoming multidrug resistance (Halanayake *et al.* 2021). For example, nanocarriers loaded with paclitaxel and doxorubicin have shown enhanced therapeutic efficacy in preclinical models. Radiotherapy is a widely used cancer treatment modality that relies on damaged cancer cells. However, its efficacy is often limited by radiation resistance. They act as radiosensitizers, affecting radiation. For instance, in gold nanoparticles and hafnium oxide deposition energy-enhanced therapies, nanoparticles provide a platform for synergistic effects, improving overall treatment outcomes. Nanotechnology also enables the radiosensitizers to ensure that both modalities are delivered simultaneously to the tumor site.

2.5 Photodynamic Therapy (PDT) with Nanotechnology

Nanotechnology has advanced PDT by enhancing the delivery and stability of photosensitizers. Nanoparticles protect photosensitizers from degradation, improve their solubility, and enable targeted tumor delivery. In combination therapies, PDT-paired immunotherapy has synergistic effects. For example, nanoparticles co-loaded with a photosensitizer and a chemotherapeutic agent allow simultaneous ROS generation and drug release, enhancing tumor cell death.

Additionally, nanocarriers enable the use of near-infrared (NIR) light for deeper tissue penetration, expanding the applicability of PDT to a broader range of tumors (Javed *et al*. 2016). Nanoparticles can also serve as adjuvants, enhancing dendritic and T cells' activation. In combination therapies, nanocarriers enable the co-delivery of immunotherapeutics with chemotherapeutics, PDT agents, or radiosensitizers, creating synergistic effects that enhance immune activation and direct tumor cell killing. For instance, nanoparticles co-loaded with a checkpoint inhibitor and a chemotherapeutic agent can suppress immune evasion and induce tumor cell death (Jaya *et al*. 2019). Despite their potential, combining the design and synthesis of multifunctional nanocarriers requires meticulous optimization to ensure stability and biocompatibility. Scalability and reproducibility manufacturing remain significant barriers to clinical translation, as do regulatory hurdles related to safety and efficacy. Tumor heterogeneity and the dynamic tumor microenvironment complicate the design of universally effective nanoplatforms, necessitating personalized approaches (Kapoor *et al.* 2016).

2.6 Nanoparticle-Mediated Delivery of Nucleic Acids for Cancer Gene Therapy

This therapeutic strategy involves delivering RNA, gene-editing tools, inhibiting oncogenes, restoring tumor suppressor genes, or sensitizing tumors to conventional therapies. However, the efficient and safe significant and difficulty in crossing biological barriers. By serving as versatile carriers for nucleic acids, offering protection, stability, and targeted delivery. Due to efficient encapsulation, lipid-based carriers facilitate endosomal escape—polymeric capabilities. Inorganic nanoparticles, including gold and mesoporous silica nanoparticles, provide structural stability and multifunctionality, such as the ability to incorporate imaging agents (Khan *et al.* 2022). The coating enhances nanoparticle stability and circulation time by preventing immune recognition. Peptides, aptamers, and nanoparticles enable active targeting of cancer cells, improving therapeutic specificity. Upon reaching the tumor site, nanoparticles interact with other uptake mechanisms. Once internalized, the nanoparticles facilitate the release of nucleic acids into therapeutic. Strategies to enhance endosomal escape, such as incorporating pH-sensitive materials or fusogenic lipids, are critical for ensuring efficacy. Applications in Cancer Therapy: demonstrated significant potential in various cancer therapy applications. Silencing Oncogenes with siRNA and miRNA are potential tools for silencing oncogenes function Nanoparticles protect these targeted to siRNA lipid nanoparticles used to silence the KRAS oncogene, a typical driver mutation in multiple cancers, showing Similarly, miRNA-based therapies using nanoparticles have demonstrated the ability to modulate gene networks involved in tumor progression and metastasis.

2.7 Restoring Tumor Suppressors with pDNA and mRNA

Plasmid DNA (pDNA) and messenger RNA (mRNA) delivered restore genes lost or downregulated in cancer. For example, p53, a critical tumor suppressor gene, has been a target for gene therapy using nanoparticle-mediated delivery systems. LNPs and polymeric nanoparticles have successfully delivered mRNA encoding functional p53 to tumors, leading to tumor regression. Gene Editing with CRISPR-Cas9: The CRISPR-Cas9 system has revolutionized cancer gene therapy by enabling precise genome editing. Nanoparticles effectively deliver the CRISPR-Cas9 components, including the Cas9 protein and guide RNA (gRNA), to cancer cells (Linima *et al*. 2023). Lipid and gold nanoparticles have been used to deliver CRISPR-Cas9 tools for knockout oncogenes or correction of genetic mutations. These approaches hold great promise for treating cancers with specific genetic alterations. Nanoparticle-mediated nucleic acid delivery can also sensitize tumors to chemotherapy, radiotherapy, or immunotherapy.

2.8 Toxicity and Biocompatibility of Nanocarriers for Cancer Drug Delivery

Nanocarriers have transformed cancer therapy by improving therapeutic efficacy and reducing systemic toxicity. These nanoscale systems enhance solubility, bioavailability, and targeting specificity through drug encapsulation or conjugation. However, concerns remain regarding the toxicity and biocompatibility of nanocarriers. These parameters are critical to ensuring patient safety and minimizing adverse effects associated with nanomaterials. While nanocarriers provide unique benefits, their interaction with biological systems poses risks that must be addressed during development and clinical application. The biocompatibility of nanocarriers is influenced by their surface properties, size, shape, and composition (Li *et al*. 2021). Nanocarriers are typically coated with hydrophilic polymers to reduce immune recognition and extend circulation time, minimizing protein adsorption and macrophage uptake while improving biocompatibility. Other surface modifications include zwitterionic or biomimetic coatings that mimic natural cell membranes, further reducing immunogenicity. Biodegradability: Biodegradability is another critical aspect of biocompatibility.

Biodegradable materials, such as are broken down into that are naturally. In contrast, materials, specifically metal nanoparticles, may accumulate in tissues and cause long-term toxicity. Designing nanocarriers with controlled biodegradability is essential to balance therapeutic efficacy and safety (Küp *et al.* 2020). Different nanomaterials exhibit varying levels of toxicity. For instance, metal-based nanoparticles (e.g.,

gold, silver, or quantum dots) may release ions, inflammation, or DNA.

In contrast, organic nanocarriers like liposomes and polymeric nanoparticles are generally considered less toxic due to their biodegradable and biocompatible nature. However, organic nanocarriers may trigger immune responses or cause accumulation in organs like the liver and spleen. Immune System Activation: Nanocarriers can activate the immune system through complement activation or interactions with immune cells. This activation may result in hypersensitivity reactions, inflammation, or cytokine release syndrome. PEGylated nanoparticles, for example, can induce, reduce their efficacy, and cause immune-related side effects.

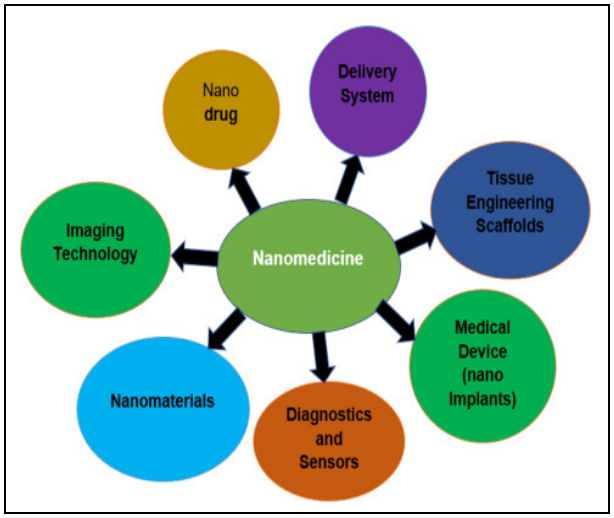


Fig. 2: Application of nanomedicine in cancer drug delivery systems

2.9 Accumulation and Long-term Toxicity

Non-biodegradable nanocarriers, such as specific metal-based nanoparticles and carbon nanotubes, may accumulate in tissues, leading to chronic toxicity. These materials can persist in the body for extended periods, potentially causing inflammation, fibrosis, or organ dysfunction—long-term toxicity safety such materials clinical applications. Modifying nanocarrier surfaces with biocompatible coatings reduces toxicity by minimizing non-specific interactions and immune recognition. Biodegradable Materials: Using biodegradable polymers and lipids ensures that nanocarriers are safely metabolized and eliminated from the body. For example, liposomal formulations of chemotherapeutics, such as doxorubicin (Doxil), have demonstrated reduced cardiotoxicity and improved patient outcomes (Liu *et al*. 2024). Similarly, lipid nanoparticles used in mRNA-based cancer vaccines offer high efficacy with manageable side effects. Regulatory and Clinical Considerations: rigorous nanocarrier safety and efficacy evaluation before approval. Preclinical studies must assess biodistribution, pharmacokinetics, and toxicity profiles while immunogenicity humans. The scalability and reproducibility of nanocarrier synthesis and regulatory approval commercialization. Future Perspectives: Advancements in nanotechnology and material science continue to be safe. Developing hybrid nanocarriers offers new possibilities for reducing toxicity (Nandiyanto *et al.* 2019). Personalized nanocarriers tailored to individual patients' tumor profiles are also being explored to minimize the expected to accelerate the design of safer nanocarriers by optimizing their properties and predicting potential toxicities.

2.10 Clinical Trials and Translational Research in Nanotechnology-based Cancer Drug Delivery

Cancer has transformed oncology by overcoming the limitations of conventional cancer therapies. By enhancing drug solubility, targeting specific cancer cells, and minimizing systemic toxicity, nanocarrier micelles paved the way for translational efficacy and feasibility of these technologies and clinical. Despite significant advancements, the journey from bench to bedside presents unique challenges and opportunities, requiring interdisciplinary collaboration and rigorous validation to ensure successful outcomes (Nawaz, 2024). Current Status of Nanotechnology-Based Cancer Therapies in Clinical Trials: Several nanotechnology-based drug delivery systems have successfully transitioned to clinical trials and, in some cases, received regulatory approval. Clinical trials for nanotechnology-based cancer therapies primarily focus on assessing safety and biocompatibility, which evaluates nanocarriers' toxicity, immunogenicity, and off-target effects. Determining the therapeutic benefits, including tumor regression, progression-free survival, and overall survival. Investigating how nanocarriers distribute, metabolize, and clear from the body (Zhang *et al*. 2021). Translational Research: Bridging the Gap: Translational research is the cornerstone of advancing nanotechnology-based drug delivery from preclinical studies to clinical application. This process involves optimizing nanocarrier design, addressing scalability, and ensuring reproducibility. Preclinical research lays the foundation by testing nanocarriers in cell cultures and animal models. Key parameters evaluated include Stability and maintaining nanocarrier integrity under physiological conditions. Identifying potential toxicities, such as oxidative stress, inflammation, or organ accumulation.

2.11 Scale-up and Manufacturing

Translating nanotechnology-based therapies to clinical use requires scalable and reproducible manufacturing processes. Challenges include maintaining uniform particle size, surface properties, and drug loading during large-scale production. Regulatory requirements demand consistency in formulation, purity, and stability. Advances in microfluidics and automated production systems are helping to address these

challenges. Comprehensive on toxicity, biodistribution, and pharmacokinetics. Collaborative initiatives, such as aiming to streamline regulatory approval by providing standardized protocols and guidelines. Despite their potential, nanotechnology-based cancer therapies face several obstacles in clinical translation. presents a significant barrier to effective nanocarrier delivery (Nguyen *et al*. 2020) Factors such as abnormal vasculature, high interstitial pressure, and stromal barriers hinder nanocarrier penetration and accumulation in tumors. Strategies like TME-modulating agents or combination therapies are being explored to address these challenges. Innovations in material synthesis and automation are needed to reduce costs while maintaining quality (Oh *et al*. 2010). Regulatory and Ethical Concerns: Regulatory approval for nanotechnology-based therapies is often delayed due to a lack of standardized testing methods and long-term safety data. These systems can be tailored to deliver targeted therapies based on individual tumor profiles, maximizing efficacy while minimizing toxicity. Combination Therapies: Nanocarriers offer platforms for co-delivering multiple therapeutic agents, such as chemotherapeutics, immunotherapies, and gene-editing tools.

2.12 Future Directions and Challenges in Nanotechnology-Based Cancer Drug Delivery

These systems enable targeted, controlled tumors, side and improve patient outcomes. However, despite significant advances, several challenges remain, necessitating further innovation. Nanotechnology cancer drug delivery is overcoming these barriers, developing new nanomaterials, and addressing regulatory and safety concerns. This article explores the ongoing offering insights into opportunities and hurdles that lie ahead. Personalized and Precision Medicine Promising Future Directions Drug Delivery Integration of Personalized Medicine. The growing understanding of cancer genomics and molecular profiling allows for nanocarriers patients (Ohnishi *et al.* 2020). By co-delivering chemotherapy drugs, immunotherapies, and radiotherapy agents, nanocarriers can simultaneously target various aspects of cancer biology. This approach is tumor to single-agent therapies. Nanocarriers can also control time, maximizing synergistic effects and minimizing toxicity Nanocarrier-Based Immunotherapy Immunotherapy has become a cornerstone of cancer treatment, and nanotechnology has the potential to revolutionize this approach. Nanocarriers engineered immune modulators, cytokines, and tumor-associated antigens to destroy cancer. Nanoparticles can also deliver cancer vaccines or act as adjuvants to boost the immune response (Zaki *et al*. 2024). The ability of nanocarriers to target the tumor microenvironment and enhance immune cell infiltration into tumors makes them ideal vehicles for improving the effectiveness of immunotherapies.

2.13 Challenges in Nanotechnology-based Cancer Drug Delivery

Nanocarrier design and optimization of cancer remains a critical challenge. The shape and composition profoundly affect their behavior in vivo, including drug loading capacity, stability, pharmacokinetics, and targeting efficiency. Ensuring that nanocarriers are stable in biological environments while remaining capable of releasing their payloads at the tumor site is a delicate balancing act. In addition, optimizing the surface properties to reduce non-specific interactions with healthy tissues and improve targeting specificity is crucial (Vissink *et al*. 2023). Furthermore, the tumor microenvironment, characterized by abnormal vasculature, high interstitial pressure, and an acidic extracellular matrix, poses additional challenges for nanoparticle penetration and accumulation. Based on these issues, future research should focus on developing advanced targeting strategies, such as dual or multi-ligand targeting, to address the complexity of tumor biology better and enhance nanocarrier uptake and distribution. Immunogenicity and biocompatibility Although nanocarriers are designed to be biocompatible, their long-term safety remains a concern. Leading to affect the of therapy. For example, using specific materials, such as metal-based nanoparticles, may provoke inflammation or generate reactive oxygen species (ROS), causing toxicity.

Regulatory agencies, including clinical ones, must be involved in nanocarriers' safety, efficacy, and long-term effects before approval. The lack of standardized testing protocols for nanomaterials further complicates the regulatory process. Moreover, the scalability and reproducibility of nanocarrier production are critical for large-scale clinical applications. The synthesis of nanocarriers with consistent quality, purity, and performance is essential for ensuring their success in clinical settings. Advances in manufacturing technologies, such as microfluidics and automated production systems, are necessary for nanocarriers while maintaining quality control. Cost and Accessibility The cost of developing and manufacturing nanotechnology-based cancer therapies is another significant barrier to their widespread clinical adoption. Continued advancements in materials science, personalized medicine, combination therapies, and theranostics will pave the way for nanotechnology-based cancer. However, addressing these challenges will require sustained investment in research and a commitment to improving the safety and efficacy of these groundbreaking therapies. With ongoing innovation and careful consideration of the difficulties, nanotechnology has significantly transformed cancer in future oncology.

2.14 Comparision of Different Nanocarrier Platforms (Liposomes, Polymeric Nanoparticles, Dendrimers, Etc.)

They offer a controlled and sustained drug release, but their release kinetics can be influenced by the lipid composition, potentially leading to premature leakage. While liposomes have good targeting efficiency through surface modification (e.g., adding ligands or antibodies), their targeting precision can be limited compared to other platforms. Polymeric nanoparticles, made from biodegradable polymers, provide high drug loading capacities, especially for hydrophobic drugs, due to the versatility of their polymer matrix (Paver *et al.* 2020). These nanoparticles can be designed to have tunable release profiles by modifying the polymer's degradation rate, which allows for precise control over drug release. Moreover, polymeric nanoparticles can be engineered for enhanced targeting efficiency using various surface modifications or by exploiting the tumor microenvironment. Dendrimers**,** highly branched, tree-like macromolecules, offer unique advantages in drug loading, with the ability to carry multiple therapeutic agents or imaging agents due to their well-defined, multi-functional surface (Tsvetkova and Ivanova, 2022). In summary, while liposomes are favored for their versatility in drug encapsulation and biocompatibility, polymeric nanoparticles provide flexible release profiles and superior targeting capabilities, and dendrimers excel in multi-drug loading and precise control over release kinetics. Each platform has its own strengths and trade-offs, making the choice of nanocarrier dependent on the specific therapeutic goals and the type of cancer being treated.

2.15 Influence of Nanoparticle Physicochemical Properties on their Biodistribution and Tumor Penetration

The physicochemical properties of nanoparticles play a critical role in determining their biodistribution and tumor penetration, significantly influencing the effectiveness of cancer drug delivery. Size is one of the most crucial factors; nanoparticles typically range from 10 to 200 nm in diameter, as particles within this size range are able to take advantage of the enhanced permeability and retention. Surface charge also plays a significant role in determining nanoparticle interaction with cellular membranes and the immune system. Positively charged nanoparticles tend to have higher cellular uptake but may also experience rapid clearance by the immune system, whereas negatively charged nanoparticles are more likely to evade immune detection but may face challenges in cellular uptake. Shape can further influence nanoparticle biodistribution, with elongated or rod-shaped particles often exhibiting better penetration through tumor tissues compared to spherical particles (Pitakpawasutthi *et al.* 2016). Moreover, biodegradability and surface coatings **(**such as PEGylation) can affect the circulation time of nanoparticles, as hydrophilic coatings can reduce protein adsorption and prevent rapid clearance, extending the nanoparticles' half-life in the bloodstream and promoting more effective tumor accumulation. Collectively, the careful engineering of these physicochemical properties allows for the optimization of nanoparticles for enhanced biodistribution, effective tumor targeting, and deeper tissue penetration, ultimately improving the therapeutic outcome in cancer treatments.

2.16 Interaction Mechanism Between Nanoparticles and the Tumor Microenvironment

The TME is characterized by unique features such as leaky blood vessels, high interstitial pressure, and a slightly acidic pH, all of which can affect how nanoparticles behave within it. Once inside the tumor, nanoparticles may face challenges such as high interstitial fluid pressure, which can limit their penetration into the deeper regions of the tumor. To address these challenges, several strategies have been implemented to enhance nanoparticle accumulation in tumors (Sairam *et al.* 2023). This targeted approach increases the specificity of nanoparticle accumulation at tumor sites, reducing off-target effects on healthy tissues. Another strategy is the use of pH-sensitive materials in nanoparticle design, which enables the release of therapeutic agents in the acidic environment typical of the TME, further enhancing drug delivery efficiency (Selvakumar *et al.* 2024). Additionally, size optimization is a crucial factor in improving tumor penetration; nanoparticles of sizes around 100 nm are most effective at accumulating through the EPR effect while also being small enough to penetrate into the tumor tissue more deeply. Tumor microenvironment-modifying agents**,** such as enzymes or hyaluronidase, have also been incorporated into nanoparticle formulations to degrade the extracellular matrix, reduce interstitial pressure, and improve nanoparticle diffusion and distribution within tumors (Sung *et al*. 2021). Finally, stimuli-responsive nanoparticles, which release their drug payloads in response to specific stimuli in the TME (like low pH or high enzyme activity), further enhance the therapeutic potential of nanoparticles by ensuring that drugs are released specifically within the tumor site, minimizing systemic toxicity. These strategies, either alone or in combination, aim to optimize the interaction between nanoparticles and the tumor microenvironment, improving the accumulation, penetration, and therapeutic effectiveness of cancer nanomedicines.

Table 1. Comparison of different types of nanocarriers for cancer drug delivery

Nanocarrier Type	Drug Loading Capacity	Release Kinetics	Targeting Efficiency	Biocompatibility	Examples
Liposomes	Moderate to High (both hydrophilic and hydrophobic drugs)	Controlled release, depending on lipid composition	Moderate, can be improved by surface functionalization	High, as they are composed of natural phospholipids	Doxil, Marqibo
Polymeric Nanoparticles	High (especially for hydrophobic drugs)	Tunable, based on polymer degradation rate	High, can be modified for specific tumor targeting	Good, biodegradable and biocompatible polymers	PLGA nanoparticles, Polymeric micelles
Dendrimers	Very High (due to highly branched structure)	Highly controlled, release can be engineered	Very high, surface can be functionalized with targeting ligands	Moderate to low, potential for toxicity at high doses	Dendrisome, PAMAM dendrimers
Solid Lipid Nanoparticles (SLNs)	Moderate (hydrophobic drugs)	Slow and sustained release, controlled by lipid matrix	Moderate, functionalization improves targeting efficiency	High, made of biocompatible lipids	Abraxane, SLN-based formulations
Nanostructured Lipid Carriers (NLCs)	High (both hydrophilic and hydrophobic drugs)	Sustained, more controlled compared to SLNs	Moderate, enhanced by surface modification	High, improved compared to SLNs due to better stability	NLC formulations for anticancer drugs
Carbon Nanotubes (CNTs)	High (especially for hydrophobic drugs)	Rapid release unless modified with coatings	High, functionalization allows for selective targeting	Moderate, concerns regarding toxicity and biocompatibility	Carbon nanotube-based drug delivery systems
Gold Nanoparticles	Moderate to High (hydrophobic drugs)	Controlled release, can be tuned with functionalization	High, surface modification allows targeting of cancer cells	High, inert nature but potential for toxicity at high doses	AuroLase, gold nanoparticle-based therapies
Quantum Dots	Moderate (for small molecule drugs)	Controlled, can be influenced by size and coating	Moderate, primarily used for imaging and diagnostics	Moderate to low, concerns with long-term toxicity	QD-based imaging and drug delivery systems
Mesoporous Silica Nanoparticles (MSNs)	High (hydrophobic and hydrophilic drugs)	Tunable, based on mesopore structure and surface coating	Moderate to high, surface functionalization enhances targeting	High, generally biocompatible and biodegradable	MSNs for anticancer drug delivery

2.17 Impact of Nanocarriers on Immune Responses Strategies & Minimize Nanoparticle-induced Toxicity

Nanocarriers can significantly impact immune responses, both positively and negatively, which affects their safety and therapeutic efficacy in cancer treatment. On one hand, nanoparticles can be engineered to stimulate the immune system, promoting antitumor immunity (Sanikop *et al*. 2021). Nanoparticles, especially those with large surface areas or cationic charges, may provoke the activation of the complement system or trigger inflammatory responses, leading to immune cell activation, cytokine release, and potential tissue damage. To minimize nanoparticle-induced toxicity, several strategies have been developed**.** This reduces premature clearance by the MPS and minimizes immune-related toxicity. Additionally, size and charge optimization of nanoparticles can lower the likelihood of nonspecific immune activation, with neutral or slightly negative charges being more biocompatible. Targeted delivery to tumor cells, achieved through surface functionalization with specific ligands, ensures that nanoparticles accumulate primarily at the tumor site, reducing exposure to healthy tissues and minimizing systemic side effects (Thamarai *et al.* 2024). Furthermore, biodegradable nanoparticles, which break down into non-toxic byproducts, are preferred to avoid accumulation and long-term toxicity in the body. Finally, dose control and temporal release mechanisms that regulate nanoparticle exposure can prevent excessive immune activation and reduce the risk of chronic inflammation or toxicity. By carefully tailoring the physicochemical properties and surface characteristics of nanocarriers, researchers aim to balance their therapeutic benefits with minimal adverse immune responses, thereby improving their safety profile in cancer treatments.

2.18 Nanotechnology-based Cancer Drug Delivery Systems

Current status and future prospects: nanotechnology in cancer drug delivery represents transformative developments in oncology. Current Status of nanotechnology-based cancer drug delivery systems: cancer made substantial progress in recent years, with several systems already undergoing clinical trials and some achieving market approval. The most common nanocarriers currently being researched and tested include micelles and dendrimers, such as silica-based particles. These nanocarriers serve as vehicles for various types of therapeutic (DNA, RNA), molecule inhibitors, and immunotherapeutics (Saravanan *et al*. 2021). The potential benefits of using nanotechnology for cancer drug delivery include improved energy, prolonged circulation times, and the ability to achieve selective targeting of cancer cells. Polymeric nanoparticles and micelles formed from biocompatibility gained attention and can provide sustained and controlled drug release. These nanoparticles are highly customizable, allowing for the optimization of properties. Block copolymers are another promising nanocarrier system. Micelles are ideal and poorly soluble. Several polymeric nanoparticle formulations are currently being evaluated in clinical trials, and early results have shown. Dendrimers, highly branched, tree-like macromolecules, offer high surface areas and a precise structure, which makes them ideal for both Dendrimers easily and therapeutic molecules, allowing for more efficiency.

2.19 Future Prospects of Nanotechnology-based Cancer Drug Delivery Systems

While the current status of cancer treatment is promising, the future depends on addressing several technical, biological, and regulatory challenges. Researchers are exploring innovative approaches to efficacy nanocarriers. Targeted and Controlled Drug Release One of the most significant areas of future development is improving targeting strategies (Selvakumar *et al*. 2024). These carriers could offer tumor specificity. Combination Therapies also enable combination therapies. Combining chemotherapy with targeted therapies, immunotherapy, gene therapy, or radiation therapy can enhance overall treatment efficacy and help overcome tumor resistance to single-agent therapies. For instance, the co-delivery of chemotherapy drugs with immune checkpoint inhibitors or siRNA-targeting oncogenes could potentiate the effects of both therapies. Nanocarriers can also encapsulate multiple drugs within a single particle risk. This multi-modal treatment approach, facilitated by nanotechnology, represents a significant frontier in cancer therapy. Integrating Diagnosis and Treatment therapeutic diagnostic, a nanocarrier, is an avenue for future cancer therapies.

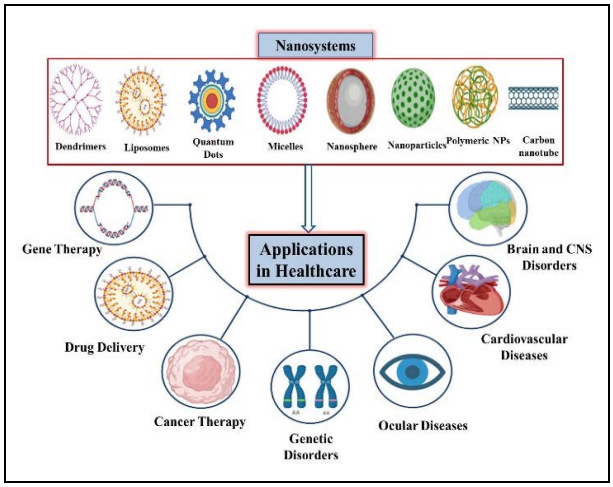


Fig 3. Applications of nanotechnology in healthcare systems

Developing theranostic nanoparticles is critical in improving the personalization of cancer therapy and optimizing patient outcomes. Regulatory and Safety Considerations As cancer progresses through preclinical and clinical trials, safety and regulatory concerns remain significant. The nanomaterials were thoroughly investigated before widespread clinical adoption. Issues with system activation and unintended side must be addressed. Standardized regulatory guidelines are also necessary to ensure that nanotechnology-based therapies meet safety and efficacy requirements. Agencies like the FDA are working to streamline the regulatory processes for nanomedicines. Still, a lack of uniformity in testing methods and data requirements has slowed the approval of many promising formulations (Sherin *et al.* 2020). Manufacturing and Scalability Another critical challenge lies in the large-scale manufacturing of nanocarriers. More efficient targeting strategies, personalized therapies, and the development of new nanomaterials. Regulatory, safety, and manufacturing concerns also cause widespread adoption of nanotechnology-based therapies. Despite these hurdles, nanotechnology treatment is highly promising, and continued innovation and collaboration will cure cancer worldwide.

2.20 Nanotechnology Applications in Cancer Drug Delivery Systems

The ability to engineer nanoscale materials with high precision has led to platforms' non-selective distribution, poor bioavailability, and systemic toxicity. These systems enable pharmacokinetics, making cancer treatment more effective. The key points of nanotechnology application systems discuss the potential impact on patient outcomes and explore future directions for advancing this field. Nanotechnology Platforms Nanotechnology nanoparticles, inorganic nanoparticles, were developed to improve the delivery of anticancer drugs.

Furthermore, active targeting strategies using molecules are incorporated into nanocarriers to achieve even greater specificity for cancer cells. This cancer directly enhances the index, minimizing surrounding and improving the overall safety profile of the treatment. Combination Therapies and Nanocarriers gene therapy can be co-delivered in a single nanocarrier. This combination approach is particularly beneficial in overcoming drug resistance and enhancing synergistic effects (Sun *et al.* 2012). Nanocarriers can also simultaneously deliver chemotherapeutic agents and immunomodulatory molecules, boosting fight multi-modal treatment strategies and therapy of multiple aspects of tumor biology simultaneously. Theranostic nanoparticles theranostics, which combines nanoparticles exciting emerging Nanocarriers designed for theranostic applications, can carry drugs while incorporating radioactive isotopes. It allows clinicians therapeutic responses to improve treatment's personalization (Shin *et al*. 2010). Theranostic nanoparticles provide a comprehensive approach to cancer management by enabling the treatment and monitoring of disease progression in a single therapeutic strategy.

Regulatory and manufacturing challenges: Obtaining regulatory approval for nanotechnology-based cancer therapies is complicated due to the intricate nature of nanomaterials. Extensive testing is required to ensure their safety and effectiveness. Regulatory and EMA are working to develop guidelines for nanomedicines, but current testing protocols are not fully standardized. Moreover, producing nanocarriers in sufficient quantities for clinical use requires robust manufacturing processes that ensure consistency, quality, and scalability. Minimizing side effects using nanocarriers drug, the reduction of nanotechnology helps to limit the adverse effects commonly observed in cancer treatment, such as nausea, fatigue, and organ damage.

2.21 Limitations of Conventional Cancer Therapies and their Challenges

One of the primary challenges is the lack of specificity in targeting cancer cells, which leads to the destruction of healthy tissues and severe side effects. Additionally, many chemotherapeutic drugs suffer from poor bioavailability, meaning they are not efficiently absorbed or distributed to the tumor site. This can result in inadequate drug concentrations at the tumor, reducing the overall efficacy of the treatment. Furthermore, conventional therapies often develop resistance over time, complicating treatment protocols and limiting long-term success. Nanotechnology addresses these challenges by offering a more precise and targeted approach to drug delivery. The small size and high surface area of nanoparticles allow them to penetrate tumor tissues more effectively, overcoming barriers that limit drug distribution in conventional therapies. Moreover, nanotechnology enables the controlled release of drugs, improving their bioavailability and ensuring a sustained therapeutic effect at the tumor site. By utilizing targeting strategies, such as ligand-receptor interactions or the unique properties of the tumor microenvironment, nanocarriers can selectively release their payload at the cancer site, enhancing the drug's potency while reducing systemic toxicity. These advancements make nanotechnology a promising solution to the major limitations of conventional cancer therapies.

3. CONCLUSION

Nanotechnology offers a potential solution to many challenges by enabling highly specific, enhanced efficacy, improved drug solubility, minimized technological advancement transforming landscape cancer new patient side effects, and more personalized therapies. Another significant advancement in nanotechnology is functions into nanoparticles, often referred to as theranostics. Theranostic nanoparticles combine drug delivery with imaging capabilities, enabling tracking efficacy and early detection of therapeutic failure. By incorporating diagnostic fluorescence, MRI, or radioactive isotopes, theranostic nanoparticles would allow clinicians to visualize the tumor and assess the therapeutic response, thus improving treatment decision-making. Tumors in real-time also optimize treatment regimens, ensuring that the most effective therapies are delivered to the patient. Theranostic systems represent an up-and-coming innovation that combines therapy with personalized care. This advancement is particularly valuable in the context of the molecular profile of an individual. Challenges and Barriers to Clinical Translation: Despite the numerous advantages of nanotechnology-based drug delivery systems, significant challenges in translating these systems' microenvironments, varied blood supply, and different molecular profiles can complicate the targeting and delivery of nanocarriers. Tumors are often surrounded by a dense extracellular matrix, which can hinder the penetration of nanoparticles and limit their therapeutic effectiveness. Moreover, the variability of tumor-associated biomarkers and the inability of some nanocarriers to achieve selective targeting mean that not all nanoparticles can effectively deliver drugs to the intended cancer cells.

Additionally, long-term safety concerns, such as the potential accumulation of nanoparticles in vital organs, must be addressed to ensure the biocompatibility of nanomaterials. The possibility of immune responses against nanoparticles or their accumulation in non-target tissues raises concerns regarding systemic toxicity and clearance of these materials. Careful biocompatibility testing, long-term animal studies, and clinical trials will be crucial for understanding nanomaterials and ensuring human safety. Several areas are likely to shape the future of nanotechnology. Personalized and Precision Medicine

The development of personalized medicine will optimize nanocarrier tumor markers, treatments incorporating patient-specific tumor genetic and molecular data, nanoparticle-based therapies can be designed therapeutic combination personalized medicine with nanotechnology could significantly enhance the clinical outcomes of cancer patients, making treatment more effective and less toxic. Combination Therapy Combination therapies using nanocarriers are another crucial area of future research. By co-delivering multiple in a single nanoparticle platform, it is possible to overcome drug resistance and achieve a synergistic therapeutic effect. As these technologies mature and overcome current challenges, nanotechnology-based cancer drug delivery systems may become a cornerstone of cancer treatment, offering new hope to patients worldwide.

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CONFLICT OF INTEREST

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