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INTEGRATING NANOCARRIERS FOR TARGETED CANCER THERAPY

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ABSTRACT

Cancer is a complex and life-threatening disease, with conventional treatments such as surgery, radiation, and chemotherapy often causing damage to healthy tissues and posing a risk of recurrence due to incomplete tumor removal. In recent years, nanotechnology has emerged as a transformative approach in oncology, offering targeted and efficient cancer diagnosis and treatment. By enabling site-specific drug delivery and controlled release, nanotechnology minimizes side effects and enhances therapeutic outcomes. Advancements in materials science have facilitated the development of nanoscale carriers engineered to selectively target malignant cells. Several of these nanocarriers have already received clinical approval and are showing promise in improving patient outcomes. This review outlines the various types of nanocarriers used in cancer therapy and diagnosis, emphasizing their ability to enhance precision while reducing harm to healthy tissues. Overall, nanotechnology offers a promising avenue for safer and more effective cancer management, marking a significant shift toward personalized and less invasive treatments.

KEYWORDS: Cancer; Nanotechnology; Nanocarriers; Disease diagnostics; Therapy

Nanotechnology involves the manipulation of matter at the nanoscale (1–100 nm). The concept was first proposed by Richard Feynman (Feynman 1959) and the term "nano-technology" was later coined by Norio Taniguchi in 1974 (Taniguchi 1974). The advent of the scanning tunneling microscope enabled visualization at the atomic level, marking the beginning of modern nanotechnology (Filipponi and Sutherland 2013). Nanotechnology now plays a vital role in diagnosing and treating diseases such as cancer, neurological disorders, cardiovascular issues, and infections (Patra *et al.*, 2018). It focuses on engineering nanoparticles or nanomedicines to target diseased cells selectively (Kawadkar *et al.*, 2011; Patra *et al.*, 2018; Soares *et al.*, 2018).

Cancer remains a complex and life-threatening disease due to abnormal cell proliferation and challenges in early detection, management, and therapy have long offered substantial medical obstacles to progress. (Hanash and Taguchi 2010; Srivastava and Ahn 2015; Srivastava *et al.*, 2016b; Srivastava and Lodhi 2022; Srivastava *et al.*, 2023). It can arise from genetic mutations, carcinogens, chromosomal abnormalities, and failure in programmed cell death (Srivastava *et al.*, 2016a; Srivastava *et al.*, 2023). Cancer is a genetic disease marked by two key abnormalities: (i) persistent cell replication driven by genetic mutations from environmental factors or carcinogens (e.g., translocations, gene amplifications), and (ii) disruption of apoptosis mechanisms (Baylin and Jones 2016). This uncontrolled cell division forms clusters of undifferentiated cells that promote angiogenesis, creating abnormal blood vessels that impair the lymphatic system (Lammers *et al.*, 2008; Schroeder *et al.*, 2012; Chapman *et al.*, 2013). These malignant tumors deplete surrounding tissues of nutrients and may metastasize through the bloodstream to other body parts (Mansoori *et al.*, 2007). Tumor vasculature differs from normal vessels, displaying distinct protein markers in the extracellular matrix, pericytes, and endothelium (Ruoslahti 2002). while tumor-associated lymphatic vessels also show unique features (Laakkonen *et al.*, 2002). Additionally, cancer cells exhibit specific molecular alterations, including distinctive surface receptors (Alexis *et al.*, 2008). Current treatments—surgery, radiation, chemotherapy—are often limited by side effects and incomplete tumor removal, raising the need for novel, targeted approaches. Conventional imaging tools (X-ray, CT, MRI, ultrasound, endoscopy) lack sensitivity and specificity in distinguishing benign from malignant tumors.

Nanotechnology offers promising solutions by enabling precise, targeted detection and therapy of cancer cells. Therapeutic nanoparticles can be engineered to bind cancer-specific markers, offering enhanced drug delivery and minimizing damage to healthy tissue (Kairemo *et al.*,

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2010; Mishra and Srivastava 2017; Soares *et al.,* 2018). To address these issues, we discuss the development of nanoparticle-based methods for cancer detection by analyzing the techniques designed for the detection of extracellular cancer biomarkers and the mechanism involved in the use of nanoparticles for cancer therapy. Furthermore, a thorough understanding of the uses of nanocarriers in cancer diagnostic and therapeutic combinations known as theragnostic has been discussed.

UTILIZATION OF NANOPARTICLES IN CANCER MANAGEMENT

Nanomaterials, which can exist in solid or semi-solid forms such as hydrogels and liquid crystals, are defined by their internal structures at the nanometer scale. This nanoscale organization distinguishes them from crystalline, microstructured, and amorphous solids due to their unique dimensional characteristics (Baig *et al.,* 2021). Based on structural dimensions, nanomaterials are typically categorized into three groups: zero-dimensional (all dimensions <100 nm), such as nanoparticles, nanorings, nanoshells, microcapsules, and quantum dots; one-dimensional structures (two dimensions <100 nm), including nanowires, nanotubes, and nanofibers; and two-dimensional forms (one dimension <100 nm), such as thin films, coatings, and layers (Filipponi and Sutherland 2013). Among these, nanoparticles have garnered particular interest due to their remarkable physicochemical properties that emerge at the nanoscale. These include quantum confinement effects, superparamagnetism in magnetic materials, and an exceptionally high surface-area-to-volume ratio. Such features are absent in larger microstructured or bulk materials, making nanoparticles especially useful in precision-targeted applications. Furthermore, nanoparticles can be synthesized from a variety of materials, both inorganic and polymeric, and their surfaces provide a versatile platform for the attachment and assembly of functional molecules (Ajayan 2003; Achilleos and Vamvakaki 2010). In terms of morphology, nanoparticles are most commonly spherical but may also appear in cylindrical, vesicular, or plate-like forms. Many are enclosed within membranes or layered structures, which further enhances their functional adaptability (Kawadkar *et al.,* 2011; Joudeh and Linke 2022). These structural and functional attributes enable their integration across multiple scientific disciplines. As a result, nanomaterials are now foundational in research and development spanning biology, chemistry, physics, medicine, engineering, and materials science, driving innovation in diagnostics, drug delivery, energy storage, and environmental remediation.

Nanocarriers are nanoscale materials or nanomedicines engineered to deliver therapeutic agents or specific ligands with high precision. These nanostructures are at the forefront of nanomedicine due to their dual diagnostic and therapeutic potential. For nanocarriers to function effectively, they must exhibit several critical characteristics: (i) functional versatility, (ii) strong architecture with multiple conjugation sites, (iii) high specificity and binding affinity to target tissues or receptors, (iv) improved pharmacokinetics and biodistribution for enhanced tumor targeting, (v) scalability and reproducibility in production, (vi) controlled and sustained release with optimized drug-release kinetics, (vii) minimal immunogenicity and toxicity, (viii) mechanical stability, (ix) construction from biocompatible and biodegradable polymers or inorganic materials, (x) high uptake efficiency by target cells, (xi) solubility and colloidal stability in physiological environments, and (xii) extended circulation half-life, low aggregation, and long shelf life (Peer *et al.,* 2007; Jaishree and Gupta 2012; Barua and Mitragotri 2014; Wicki *et al.,* 2015). These design principles have enabled the creation of numerous nanoformulations, combinations of nanocarriers with therapeutic or imaging agents, that have demonstrated efficacy in the treatment and diagnosis of various cancers. These nanoformulations allow for the site-specific delivery of anticancer drugs, reducing off-target effects and enhancing therapeutic efficacy (Brannon-Peppas and Blanchette 2004; Ferrari 2005; Zhang *et al.,* 2019b; Chen *et al.,* 2020). One of the most crucial aspects of successful cancer management is early detection, which relies on minimally invasive methods to identify malignancies at their inception. Equally important is monitoring treatment response and tumor dynamics over time, especially to eradicate residual cancer cells (Jain 2001; Sawyers 2004; Kim 2007; Khazaei *et al.,* 2023). Molecular biomarkers—such as altered DNA methylation patterns, oncogene or tumor suppressor gene expression, mutated RNA transcripts, deregulated proteins, and metabolic signatures—provide critical information about the disease state and therapeutic outcomes. Their detection has been significantly improved by nanoscale tools, which enhance sensitivity, specificity, and real-time monitoring capability (Rosi and Mirkin 2005; Couvreur 2013; Savaliya *et al.,* 2015; Khazaei *et al.,* 2023). For instance, gold nanoparticles, quantum dots**,** and magnetic nanoparticles have been developed to amplify signals in biomarker detection platforms, thereby improving the accuracy of early diagnosis and personalized therapy.

Plants produce bioactive compounds like alkaloids, flavonoids, and terpenoids as natural defenses. When combined with nanotechnology, these can be

delivered more effectively through nanoscale systems, enhancing their stability and targeting. This approach improves disease control, boosts immunity, and supports cancer therapy. The synergy has led to emerging fields like nano-phytomedicine and opens promising careers in green nanotechnology, nano-therapeutics, and plant-based healthcare (Srivastava *et al.*, 2018; Kumar *et al.*, 2021; Prakash *et al.*, 2021; Kumar *et al.*, 2022; Srivastava *et al.*, 2024; Srivastava *et al.*, 2025).

The nanomaterials that have been developed are carbon nanotubes, dendrimers, liposomes, nanodiamonds, nanoshells, nanowires, quantum dots, super magnetic nanoparticles, nanosponges, etc. (Rai *et al.*, 2021). These structures are formed to develop the capability to identify distinctive surface characteristics of cancer cells, such as receptors exclusive to tumors that enable the internalization of nanoparticles, biomarkers specific to tumors for cancer detection, proteins with the capacity to target specific tissues or tumors, and enzymes that facilitate the selective absorption by cells or deposition in the microenvironment of malignancy (Jaishree and Gupta 2012; Zhang *et al.*, 2019a). A mechanistic and correlative pathway of cancer progression and its control by the line of treatment based on nanomedicines has been represented in Figure 1.

With ongoing advancements, nanocarrier-based platforms continue to transform the landscape of oncology by offering solutions that integrate diagnosis, targeted therapy, and disease monitoring. These systems also pave the way for future theranostic applications, merging therapy with diagnostics in a single nanoplatform (Xie *et al.*, 2010; Xue *et al.*, 2021).

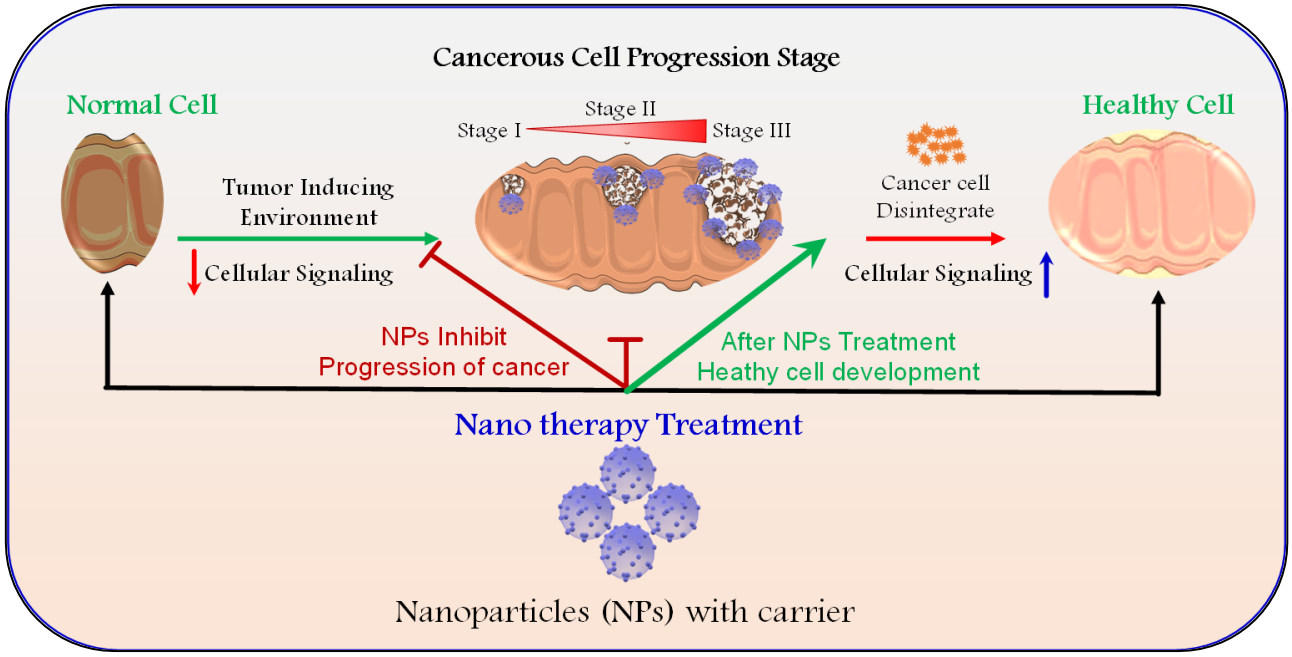

Figure 1: A pathway of cancer progression and its control bypassed by nanomedicine-based theragnostic.

The schematic highlights how nanotechnology-based approaches offer a promising strategy for cancer treatment by targeting specific cellular mechanisms and promoting the regeneration of healthy tissues. The figure illustrates the role of nanotherapy in modulating cancer progression and restoring healthy cell function. It begins with a normal cell exposed to a tumor-inducing environment, which alters cellular signaling pathways and initiates the transformation into a cancerous state. As the disease progresses through different stages (Stage I to Stage III), cellular abnormalities accumulate, leading to the development of malignant cells. The introduction of nanoparticles (NPs), delivered via a carrier system, serves as a targeted therapeutic intervention. These NPs interfere with the cancer-promoting signals, effectively inhibiting further progression of the disease. As a result of nanotherapy, cancer cells disintegrate, and cellular signaling pathways are reestablished toward normalcy. This therapeutic reversal facilitates the development of healthy cells, restoring tissue integrity.

CANCER THERAGNOSTIC

Diagnosis of Cancers

Nanoparticles selectively target cancer biomarkers through cross-linkers like specific antibodies attached to nanoshells, enabling precise recognition of cancer cells such as HER2-positive breast adenocarcinoma and enhancing diagnostic sensitivity

(Loo *et al.,* 2005; Yuan *et al.,* 2013). Since the advent of liposomal drugs, nanomedicine has progressed through gold nanoparticles, fullerenes, polymeric nanoparticles, and quantum dots, leading to approved formulations for chemotherapy and diagnostics. Some nanomaterials also act as imaging agents—gold and iron oxide nanoparticles improve contrast in modalities like MRI, ultrasound, and nuclear imaging(Sharma *et al.,* 2022). Superparamagnetic iron oxide nanoparticles (50–100 nm) offer superior magnetic sensitivity over gadolinium-based agents and effectively detect metastatic breast cancer (Sengupta and Sasisekharan 2007; Singh *et al.,* 2022). Quantum dots, with intense fluorescence, photostability, biocompatibility, and high surface-to-volume ratio, outperform traditional fluorophores and serve in cancer imaging and biomarker detection (Shi *et al.,* 2020).

Nanoparticles are extremely effective at acquiring cancer biomarkers (Rodríguez *et al.,* 2022b). These biomarkers encompass migrating tumor cell DNA, cell-surface proteins, carbohydrates, miRNA and cancer-linked proteins. Cancer-associated proteins and migrating tumor cell DNA are examples of these. Because of their high surface-to-volume ratio, nanoparticles are a superior candidate for screening for cancer than large components of tissue. Because nanoparticles may be coated with immunoglobulin peptides, or aptamers that can interact with and identify cancer-related compounds, Such nanoparticles find optimal utility in the tumor microenvironment, enhancing both sensitivity and specificity. Detection and monitoring of these biomarker levels enable early cancer diagnosis and tracking of recurrences. Among the primary nanoparticle probes for cancer diagnosis, quantum dots (QDs), gold nanoparticles, and polymer dots stand out (Zhang *et al.,* 2019b; Jin *et al.,* 2020). Presently, diverse nanotechnology-based methods for cancer diagnosis are in use. For instance, silica-hybrid nanoparticles (C-dots) combined with peptides are employed for PET imaging in patients with metastatic melanoma or malignant brain tumors (Zhang *et al.,* 2019b). Furthermore, fluorescent C-dots are useful in surgery for lymph node mapping, aiding in identifying cancer-affected lymph nodes (Frangioni *et al.,* 2007). Peptide-based targeting or irradiation-mediated diagnostic imaging using peptide-targeting liposomes offers versatile options for tumor recognition at different phases (Rong *et al.,* 2020). Dendrimers possess a distinct structure that enables them to attach multiple imaging agents and targeting molecules. This characteristic enhances their effectiveness as a valuable tool for diagnosing cancer (Vieira and Gamarra 2016a). Gadolinium-based magnetic resonance contrast compounds require far lower concentrations than iodine-based contrast agents used in CT scans, and they are often directed to particular regions to improve imaging sensitivity (Mahan and Doiron 2018). Carbon nanotubes, resembling cylinders with benzene rings, serve various purposes, such as DNA and protein sensing, distinguishing proteins in serum samples, and carrying proteins, drugs, vaccines, and other constituents (Vieira and Gamarra 2016b). The field of nanotechnology is increasingly focusing on the intriguing properties of single-walled nanotubes (SWNTs), including their application in biosensors and as molecular carriers for drug delivery (Batool *et al.,* 2023). SWNTs' high optical absorbance produces heat when they are subjected to near-infrared laser light, and this heat is efficient in selectively destroying cancer cells that the nanotubes have absorbed. (Zhou *et al.,* 2009).

A type 2 transmembrane protein called prostate-specific membrane antigen (PSMA), which has folate activity and is highly expressed in prostate cancer cells, makes an excellent target for both therapeutic delivery systems and diagnostic imaging (Parsi *et al.,* 2021; He *et al.,* 2022). It is extensively investigated as a possible target for direct vascular cancer targeting and used to create drug-loaded NPs containing a PSMA ligand (Evans *et al.,* 2016; Vit *et al.,* 2021). Transferrin-based MRI contrast agents, Super Paramagnetic Iron Oxide Nanoparticles (SPIONs), improve the diagnostic accuracy of SPIONs (Kola *et al.,* 2023; Mohanty *et al.,* 2023). The cathepsin B-responsive probe can be used to detect and treat cancer using photoacoustic imaging (Shen and Li 2022; Egorova *et al.,* 2023).

Treatment of Cancers

Nanoparticles, as core elements of nano-biomaterials, can be surface-modified with various molecules to evade immune detection and improve targeted delivery. Their small size, high surface-to-volume ratio, specificity, low toxicity, and enhanced bioavailability enable them to overcome biological barriers and effectively target metastatic tumors, offering advantages over traditional drugs (Lammers *et al.,* 2008; Ventola 2012b). Their compactness allows accumulation in tumor tissues via the enhanced permeation and retention (EPR) effect, exploiting leaky vasculature in solid tumors (Peer *et al.,* 2007; Schroeder *et al.,* 2012; Chapman *et al.,* 2013). However, EPR-based targeting is less effective against circulating or micrometastatic tumor cells (Wang *et al.,* 2012; Li *et al.,* 2014). Nanocarriers can be employed to target cancer cells or tissues through two primary strategies: passive targeting and active targeting. Passive targeting leverages the enhanced permeability and retention (EPR) effect, wherein nanoparticles accumulate within tumor tissues due to the leaky vasculature and inefficient lymphatic drainage

characteristic of tumors (Peer *et al.,* 2007; Schroeder *et al.,* 2012; Dadwal *et al.,* 2018; Babu *et al.,* 2019). This phenomenon allows nanocarriers to preferentially localize in tumor sites without the need for specific ligands. The first clinical applications of passively targeted nanocarriers, such as liposomal formulations and polymer–protein conjugates, began in the mid-1980s and led to the approval of several marketed products by the 1990s (Allen and Cullis 2004; Barenholz 2012). In contrast, active targeting involves functionalizing nanocarriers with specific molecules—such as antibodies, peptides, or aptamers—that bind to overexpressed receptors or antigens on cancer cells. This receptor–ligand interaction facilitates receptor-mediated endocytosis, enhancing cellular uptake and therapeutic efficiency while reducing off-target effects (Schroeder *et al.,* 2012; Dadwal *et al.,* 2018; Babu *et al.,* 2019). The integration of both targeting mechanisms has paved the way for the next generation of nanomedicines with improved site-specific delivery and clinical outcomes (Zhao *et al.,* 2020). Various active targeting agents, such as antibodies, aptamers, peptides, or small molecules that identify cancer-specific or cancer-associated antigens, are employed to achieve this. Examples of commonly employed tactics for cancer targeting include nanoparticles coupling maleimide and thiolated antibodies, ethyl-3-(3-dimethyl aminopropyl) carbodiimide (EDC)/N-hydroxysuccinimide (NHS) activation, and subsequent incorporation of the antibody (Petrilli *et al.,* 2021). Another relevant instance of immunoconjugates employed in cancer treatment involves Glucan particles. These are surface proteins found on cells that act as markers, facilitating the uptake of substances through receptors present in phagocytic macrophage cells, which express β-glucan receptors. In this method, nanoparticles are affixed to the surface, serving as carriers for delivering doxorubicin specifically to macrophages. These macrophages then traverse into solid tumors, transporting the cytotoxic agent to the intended tissues. Importantly, the macrophages are resilient to the effects of doxorubicin due to their specialized, nondividing nature (Huang *et al.,* 2020).

The attachment of tumor-specific ligands to the surface of nanoparticles significantly improves active targeting capabilities, thereby increasing specificity and enhancing the efficiency of chemotherapeutic drug delivery directly to cancer cells (Sanna *et al.,* 2014; Yoo *et al.,* 2019; Dutta *et al.,* 2021). Compared to free or unconjugated drugs, nanocarriers provide multiple advantages. These include protecting the therapeutic agents from premature degradation, minimizing undesired interactions with the biological environment, enhancing accumulation in target tissues such as solid tumors, modulating drug pharmacokinetics and biodistribution, and facilitating deeper cellular penetration (Jaishree and Gupta 2012; Ventola 2012b; Ventola 2012a). Several nanocarrier-based formulations have received FDA approval, including chemotherapeutic agents such as acetate, 5-aminolevulinic acid, cytarabine, DM1 (emtansine), doxorubicin, daunorubicin, irinotecan, leuprorelin, paclitaxel, pegaspargase, and vincristine. These formulations specifically target components of the tumor microenvironment or cancer cells, while other agents, such as mifamurtide, are designed to stimulate macrophages, denileukin diftitox targets activated T cells, and Fe_2O_3 nanoparticles show promise in eliminating resistant tumor and stromal cells (Barenholz 2012; Ventola 2012a; Rodríguez *et al.,* 2022b). A wide range of nanocarrier types—including carbon nanotubes, gold and metallic nanoparticles, quantum dots, liposomes, dendrimers, nanoemulsions, nanospheres, nanoshells, polymersomes, peptide nanoparticles, polymer–drug conjugates, and polymeric nanoparticles—have been synthesized and applied in numerous anticancer strategies across different tumor types (Allen and Cullis 2004; Barenholz 2012; Shi *et al.,* 2020; Edis *et al.,* 2021). These advanced nanodelivery systems are summarized in Table 1.

Table 1: Some of the nanocarrier-based anticancer drugs used in different types of cancers

Name of compound	Nanocarrier	Type of Cancer	References
Abraxane/paclitaxel	Albumin-bound paclitaxel	Breast cancer	(Gradishar *et al.,* 2005)
Ameluz/ 5-aminolevulinic acid	Gel containing 5-aminolevulinic acid & various lipoid formulations	Skin cancer	(Rodríguez *et al.,* 2022a)
Bexxar/anti-CD20 conjugated to iodine-131	Radio-immunoconjugate	Non-Hodgkin's lymphoma	(Peer *et al.,* 2007)
Bone-targeting peptide-conjugated	Superparamagnetic iron oxide nanoparticles	Breast cancer and bone metastasis	(Pang *et al.,* 2021)
Caelyx/Doxorubicin	PEG-Liposome	Breast and Ovarian Cancers, multiple myeloma	(Rodríguez *et al.,* 2022a)

Conjugated RNase	Glyco-gold nanoparticles	Cervical cancer	(Zhao *et al.,* 2021)
DaunoXome/daunorubicin	Liposome	Kaposi's sarcoma	(Gabizon 2001)
Doxil/doxorubicin	PEG-Liposome	Kaposi's sarcoma, Breast and ovarian cancers	(Zhao *et al.,* 2021)
Eligard/ Leuprorelin acetate	Poly(lactic-co-glycolic acid), N-Methyl-2- Pyrrolidone; and leuprolide acetate	Prostate cancer	(Ahmad *et al.,* 2021; Rodríguez *et al.,* 2022a)
Folic acid decorated and pH-sensitive	Nickel oxide nanoparticles	Triple-negative breast cancer cells	(Binu *et al.,* 2021)
Kadcyla/ DM1 (or Emtansine)	Protein-Drug Conjugate	HER2+ breast cancer	(Rodríguez *et al.,* 2022a)
Marqibo/Vincristine	Liposome	Acute lymphoid leukemia	(Silverman and Deitcher 2013; Shukla *et al.,* 2023)
Mepact/ Mifamurtide	Liposome	Osteosarcoma	(Rodríguez *et al.,* 2022a)
Myoset/doxorubicin	Liposome	Combinatory action of persistent breast and ovarian cancers	(Gabizon 2001)
NanoTherm/ Fe_2O_3	Superparamagnetic iron oxide coated with amino silane	Glioblastoma, prostate and pancreatic cancers	(Rodríguez *et al.,* 2022a)
Oncaspar/PEG-L-asparaginase	Polymer-protein conjugate	Acute lymphoblastic leukemia	(Pasut and Veronese 2009)
Onivyde/ Irinotecan	Liposome	Pancreatic cancer, Colorectal Cancer	(Rodríguez *et al.,* 2022a)
Ontak/IL-2 fused to diphtheria toxin	Immunotoxic fusion protein	T-cell lymphoma	(Peer *et al.,* 2007)
Oxygen-based (ROS) or nitrogen-based (RNS) reactive species	Silver nanoparticles	Pancreatic cancer	(Wang *et al.,* 2021)
Pazenir/ Paclitaxel	Albumin-bound nanoparticles	Breast cancer, non-small cell lung cancer, Pancreatic cancer	(Rodríguez *et al.,* 2022a)
Photothermal therapy/doxorubicin	Mesoporous platinum nanoparticles	Breast cancer	(Fu *et al.,* 2020)
Styrene maleic anhydride-neocarzinostatin /zinostatin	Polymer-protein conjugate	Hepatocellular carcinoma	(Peer *et al.,* 2007)
Vyxeos/Daunorubicin Cytarabine	Liposome	Acute myeloid leukemia	(Rodríguez *et al.,* 2022a)
Zevalin/anti-CD20 conjugated to yttrium-90	Radio-immunoconjugate	Non-Hodgkin's lymphoma	(Peer *et al.,* 2007)
Zoladex/goserelin acetate	Polymer rods	Prostate cancer	(Tsukagoshi 2002)
Somatostatin analog	CdS/ZnS core-shell type quantum dots	Breast cancer	(Nirmala *et al.,* 2023)
Ferumoxtran-10 (USPIO)	Superparamagnetic nanoparticle	Bladder cancer, prostate cancer	(Nirmala *et al.,* 2023)

REVISITING THE NANOCARRIERS

Nanocarriers are nanoscale delivery systems used to transport drugs, genes, or other therapeutic agents to specific targets within the body, enhance the stability, bioavailability, and controlled release of therapeutics while minimizing side effects inclusively liposomes, polymeric nanoparticles, dendrimers, solid lipid nanoparticles (SLNs), micelles, carbon nanotubes (CNTs), and metallic nanoparticles. Nanocarriers are highly effective in cancer therapy because they can

deliver chemotherapeutic agents directly to tumor cells, reducing toxicity to healthy cells. For example, liposomal formulations like Doxil deliver the chemotherapy drug doxorubicin directly to cancer cells, significantly reducing side effects like cardiotoxicity. Nanocarriers can also be designed to respond to the acidic microenvironment of tumors, ensuring drug release only at the target site. Nanocarriers can be utilized in imaging and diagnostic applications by enhancing the sensitivity and specificity of imaging modalities such as magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and fluorescence imaging.

Liposomes

Liposomes represent a well-established class of nanoparticles that have garnered considerable interest, particularly in biomedicine and targeted drug delivery. Structurally, liposomes are formed through the hydrophobic-hydrophilic interactions between phospholipids and aqueous environments. They consist of a spherical lipid bilayer, where the hydrophilic phosphate heads face outward toward the aqueous environment, and the hydrophobic tails are oriented inward, forming the bilayer's interior. This configuration allows for the encapsulation of both hydrophilic drugs in the aqueous core and hydrophobic drugs within the lipid bilayer (Dianzani *et al.,* 2014). Liposomal nanotherapy in cancer has emerged as a promising approach that facilitates controlled and targeted drug delivery, enhances therapeutic efficacy, and reduces systemic toxicity. Among the earliest and most successful examples of liposomal cancer nanotherapy is Doxil (liposomal doxorubicin), a formulation in which the chemotherapeutic agent doxorubicin is encapsulated within PEGylated liposomes. The addition of polyethylene glycol prolongs the circulation time of the liposomes by preventing rapid recognition and clearance by the mononuclear phagocyte system, thus improving accumulation in tumor tissues through the enhanced permeability and retention (EPR) effect (Barenholz 2012; Xie *et al.,* 2016). It is used in the treatment of various cancers, including ovarian cancer and Kaposi's sarcoma. Doxil's liposomal structure improves drug delivery, reduces cardiotoxicity, and enhances therapeutic efficacy. Onivyde is a liposomal formulation of the chemotherapy drug irinotecan. It is used in combination with other chemotherapy agents to treat metastatic pancreatic cancer (Milano *et al.,* 2022). In comparison to non-liposomal irinotecan, Onivyde has increased exposure and prolonged retention in tumor cells, as well as boosted plasma half-life and other appealing pharmacokinetics attributes (Milano *et al.,* 2022). Another liposomal formulation, Marqibo, consists of the chemotherapy drug vincristine sulfate. It is used for the treatment of a specific type of leukemia called Philadelphia chromosome-negative acute lymphoblastic leukemia (Shukla *et al.,* 2023). Marqibo has fewer side effects and better VCR absorption at the specific tumor location.

Metallic Nanoparticles

Metal nanoparticles have significant prospects in the field of cancer therapy. Due to their distinctive small-scale characteristics, such as a large surface area, adaptable size and structure, and surface plasmon resonance. They are appealing for a variety of applications in cancer diagnosis, imaging, therapy, and drug administration due to their qualities (Hu *et al.,* 2006; Abd Elrahman and Mansour 2019). Presently, numerous anticancer medicines, including doxorubicin, methotrexate, and paclitaxel, have been using metallic nanoparticles as a carrier (Desai *et al.,* 2021). Numerous metal nanoparticles with bases in barium, cerium oxide, copper, calcium, gold, silver, iron and/or iron oxide, nickel, magnesium, zinc, titanium, and bismuth have been reported as cancer treatments. Gold nanoparticles are among the most prominent, followed by silver and magnetic nanoparticles. Table 1 shows the function of certain metal NPs in the treatment of cancer.

Gold Nanoparticles

Gold plays a crucial role in our society and has transcended borders due to its use in medicine as gold nanoparticles. With their physicochemical and electrical characteristics, gold nanoparticles are highly favored and promising carriers for delivering metallic nanoparticles for cancer treatment (Barbosa *et al.,* 2014). Gold nanoparticles come in various shapes like spheres, rods, and tubes, and it's essential to control their morphology because it significantly impacts their physical properties, influencing their effectiveness as therapeutic and imaging tools (Xie *et al.,* 2010; Poon *et al.,* 2021). Notably, gold nanoparticles have a few key properties that make them suitable for medical purposes and a valuable tool for sensing and treating cancer: (i) easy conjugation of antibodies and other bioactive molecules to their surface; (ii) ease of functionalization, and ability to interact with light (plasmon resonance), which make them suitable for targeted drug delivery and photothermal therapy, and (iii) absorption efficiency is much better compared to that of conventional photothermal dyes, which is unaffected by photobleaching (Liu *et al.,* 2023). By absorbing radiation at the right wavelength, gold nanomaterials can be activated, leading to the irreversible thermal destruction of cells, which presents an opening for dealing with tissues in deeper parts (Loo *et al.,* 2004). In Photothermal

therapy, light-absorbing gold nanoparticles are utilized to convert light energy into heat, which can specifically target cancer cells while inflicting minimal injury to healthy tissue (Han and Choi 2021). For example, Aurolase is a Photothermal therapy that utilizes gold nanoparticles for the treatment of solid tumors, including those in the prostate, head and neck, and other areas. AuroLase therapy utilizes gold nanoparticles to absorb the laser energy and convert it into heat, leading to localized hyperthermia and destruction of cancer cells (Han and Choi 2021). Doxil-coated gold Nanoparticles for Drug Delivery are used to enhance the delivery of chemotherapy drugs to cancer cells, leading to improved efficacy and reduced side effects (Choubdar *et al.*, 2022).

Quantum Dots

Quantum dots (QDs) are nanoscale semiconductor particles that possess unique fluorescent properties, allowing them to absorb a broad spectrum of electromagnetic radiation and emit light, particularly in the near-infrared (NIR) region. Common examples include cadmium selenide (CdSe), cadmium telluride (CdTe), zinc selenide (ZnSe), zinc sulfide (ZnS), and zinc telluride (ZnTe), which are widely explored as detection and labeling agents in cancer diagnostics and therapy (Clift and Stone 2012). These QDs typically consist of a metal or metalloid core, which is often coated with biocompatible materials such as ZnS or silica to improve their physiological stability and prevent premature clearance from the body before they accumulate in tumor sites (Jin and Hildebrandt 2012). Due to their unique optical and physicochemical characteristics, including high quantum yield, resistance to photobleaching, and size-tunable fluorescence emission, QDs serve as effective theranostic agents, which enable both tumor imaging and targeted drug delivery (Jin and Hildebrandt 2012). Furthermore, they have shown potential in real-time monitoring of drug delivery via other nanocarriers, as well as in the detection of cancer-specific biomarkers such as proteins, metabolites, and nucleic acids.

Polysaccharide is used to envelop the positively charged, oily core of cadmium telluride (CdTe) quantum dots (QDs), creating nanocapsules with dual functions for cancer therapy and diagnosis. These nanocapsules are additionally packed with the anticancer drugs rapamycin and celecoxib (Dutta Chowdhury *et al.,* 2018). The hydrophobic medicines celecoxib and rapamycin are shown to have increased cytotoxicity in breast cancer cells when co-loaded with highly fluorescent quantum dots linked with gelatin/chondroitin (AbdElhamid *et al.,* 2018). The combined therapy of photothermal implementation and chemotherapy employing the anticancer medication doxorubicin-Graphene quantum dots coated in porous copper sulfide nanoparticles produced a synergistic therapy influence on human breast carcinoma cells with a regulated intracellular release of drugs (Zheng *et al.,* 2020). It has been shown that the doxorubicin-transferrin-carbon quantum dots nano-carrier may be an excellent targeted delivery strategy for breast cancer treatment. This combination is more hazardous than doxorubicin owing to its ability to combat multidrug resistance in breast cancer cells (Mahani *et al.*, 2021).

Carbon Nanotubes

Carbon nanotubes (CNTs) are cylindrical nanostructures formed by rolling sheets of graphene into seamless tubes. These structures possess unique electrical, thermal, and mechanical properties, making them promising candidates for a wide range of biomedical applications such as biosensing, cancer diagnostics, drug delivery, and photothermal therapy (Bianco *et al.,* 2005; Liu *et al.,* 2009; Kumar *et al.,* 2014; Rahamathulla *et al.,* 2021). Single-walled carbon nanotubes (SWCNTs) consist of a single graphene layer rolled into a cylinder, while multi-walled carbon nanotubes (MWCNTs) comprise multiple concentric graphene cylinders. MWCNTs have shown potential in distinguishing between gastric cancer cells (MGC-803) and normal gastric mucosa cells (GES-1) by detecting specific (Zhang *et al.,* 2014). Additionally, CNTs can be functionalized to improve solubility, biocompatibility, and targeting specificity, allowing them to deliver therapeutic agents directly to tumor cells while minimizing off-target effects. Notably, functionalized SWCNTs have been designed to target breast cancer cells, demonstrating their utility in molecular targeting and imaging applications (Madani *et al.,* 2012). Furthermore, studies have shown that CNTs can serve as nanocarriers for chemotherapy drugs, with the capacity to bypass biological barriers and deliver cargo to intracellular targets (Kong *et al.,* 2011).

Composite Nanoparticle

Composite nanoparticles have shown great potential in cancer treatment due to their unique properties and the ability to combine multiple functionalities into a single nanoscale structure. The combination of biocompatible polymer compounds, functioning nanoparticles, and medically triggered proteins enables a path to sensitive, multifunctional engineered composite nanoparticle systems for cancer treatment. Noteworthy research has demonstrated the creation of composite nanoparticles, such as the tamoxifen-loaded magnetite/poly (l-lactic acid) composite, which has exhibited promising in vitro treatment activity against breast cancer (Hu *et al.,* 2006).

Another compelling illustration involves the utilization of composite nanoparticles, in this case, curcumin in conjunction with a tripolymeric composite, for effective drug delivery targeted at HeLa cancer cells (Das *et al.,* 2010).

Dendrimers

Dendrimers are a unique class of synthetic, highly branched, tree-like macromolecules that have garnered substantial attention in nanomedicine, particularly for cancer drug delivery. These nanoscale structures are synthesized through a stepwise, iterative process and are characterized by a central initiator core, multiple interior branching layers (generations), and functional end groups on the surface, which can be chemically modified for drug attachment or targeting (Dutta *et al.,* 2010; Vidal and Guzman 2015; Hsu *et al.,* 2017; Asl *et al.,* 2023). Due to their well-defined architecture and tunable surface functionalities, dendrimers can simultaneously encapsulate hydrophobic drugs within their internal cavities and hydrophilic molecules within their surface branches. This dual drug-loading capacity enhances solubility, bioavailability, and targeted delivery. For instance, generation 5 poly(propylene imine) (PPI) dendrimers have been engineered to carry methotrexate, a hydrophobic chemotherapeutic agent, within the core, while retinoic acid, a hydrophilic molecule with mild anticancer properties, is sequestered within the outer branching clefts (Duncan and Izzo 2005; Tekade *et al.,* 2009; Jain *et al.,* 2010; Madaan *et al.,* 2014). Dendrimers have also demonstrated controlled release, cellular uptake efficiency, and reduced systemic toxicity, making them highly promising nanocarriers in oncological applications (Tekade *et al.,* 2009; Crintea *et al.,* 2023).

Nanofibers

Nanofibers represent a promising class of nanostructures that can be fabricated from inorganic, organic, or hybrid materials, with diameters typically below 1000 nm and lengths ranging from a few micrometers to several tens of nanometers (Yang *et al.,* 2018; Wongkaew 2019). Their large surface area-to-volume ratio, tunable porosity, and mechanical strength make them suitable for targeted drug delivery in cancer therapy (Singh *et al.,* 2021). One innovative approach involves smart hyperthermia nanofibers embedded with magnetic nanoparticles that can be remotely activated using an alternating magnetic field. Upon activation, these nanofibers release doxorubicin, achieving up to 70% tumor cell destruction, as demonstrated in a study involving human cancer cells (Kim *et al.,* 2013; Yang *et al.,* 2018; Sasikala *et al.,* 2019; Wongkaew 2019). Additionally, nanofiber-based systems loaded with paclitaxel have shown great potential for controlled and localized drug release, thereby minimizing systemic toxicity and limiting damage to healthy tissues (Hasanbegloo *et al.,* 2023; Rehman *et al.,* 2025). This localized delivery strategy significantly improves therapeutic efficacy while reducing adverse effects commonly associated with conventional chemotherapy. Despite encouraging results, further in vivo and clinical investigations are required to fully evaluate the therapeutic efficacy, biodegradability, and biosafety of nanofiber-based systems in oncology (Alves *et al.,* 2023).

Additional Nanoparticles

Other types of nanoparticles have garnered considerable attention in cancer research due to their versatility and clinical potential. Nanoemulsions, typically formed through oil-in-water techniques, are particularly useful for delivering poorly water-soluble drugs, significantly enhancing their cellular uptake and bioavailability (Lu and Park 2013). Beyond drug delivery, nanoemulsions have also been employed in bioimaging; for instance, a perfluorocarbon-based nanoemulsion conjugated with a near-infrared (NIR) probe was developed to detect inflammatory sites, aiding in precise diagnostic imaging (Balducci *et al.,* 2013). In terms of therapeutic applications, protein-based nanoparticles such as Abraxane (ABI-007), an albumin-bound formulation of paclitaxel, have been clinically approved for the treatment of metastatic breast cancer (Li *et al.,* 2021). Clinical trials have demonstrated that ABI-007 not only enhances drug delivery but also results in improved efficacy and a lower incidence of grade 4 neutropenia compared to conventional paclitaxel (Gradishar *et al.,* 2005). Moreover, protein nanoparticle-conjugated IgG antibodies have shown significantly prolonged retention in tumor tissues. In one study, these antibodies persisted for up to 120 hours in 4T1 mouse mammary tumors, whereas free IgG lasted only 24 hours, suggesting their superior capability for targeting tumor-specific biomarkers and enhancing therapeutic precision (Wen *et al.,* 2013).

CHALLENGES AND FUTURE DIRECTIONS IN NANOCARRIER USE IN CANCERS

While nanocarriers offer great promise in cancer therapy, several challenges remain. Key concerns include toxicity and biocompatibility, as some nanomaterials may accumulate in organs over time, leading to long-term risks. Developing biodegradable, biocompatible materials (e.g., polymers, lipids) and applying surface modifications like PEGylation can reduce immune detection and improve clearance. Another major hurdle is

controlled drug release. Nanocarriers must remain stable in biological environments and release their payload only at the target site. However, premature drug release remains a concern. Designing stimuli-responsive systems (pH-sensitive, enzyme-sensitive, or temperature-sensitive) and hybrid nanocarriers may improve release control.

Scalability and manufacturing consistency also pose challenges. Nanocarrier synthesis is often costly and complex, complicating large-scale production. Microfluidics and simpler, cost-effective methods using natural polymers may enhance reproducibility and reduce costs. Strict quality control is essential to minimize batch variability. Targeting specificity is limited by tumor heterogeneity and complex microenvironments. Even with targeting ligands, off-target effects occur. Overcoming barriers like the blood-brain barrier (BBB) remains difficult for brain cancer therapies. Solutions include ligand engineering, aptamers, antibodies, and cell-penetrating peptides, as well as personalized nanocarriers tailored to individual tumor profiles.

Regulatory approval is another major barrier. The approval of nanomedicines involves rigorous safety and efficacy testing, with long-term effects still under investigation. Clear regulatory guidelines and standardized testing protocols are needed to streamline this process. Finally, cost and accessibility are significant issues. High production and testing costs limit widespread adoption, especially in low-resource settings. Simplified manufacturing, affordable materials, and public–private collaborations can improve cost-effectiveness. Patient variability, in genetics, metabolism, and immune response, also affects outcomes. Personalized approaches, including biomarker-driven clinical trials, can help optimize nanocarrier-based treatments for better therapeutic precision.

CONCLUSION

Nanotechnology-based cancer therapies offer significant potential for both prevention and treatment, yet several challenges remain. Traditional anticancer drugs often lack specificity, leading to low tumor accumulation, poor treatment response, and drug resistance. Nanocarriers—such as liposomes, niosomes, polymeric, and solid lipid nanoparticles—enable targeted delivery, controlled drug release, and enhanced accumulation in tumor tissues, minimizing damage to healthy cells. A major advantage of nanotherapy is its ability to cross the blood-brain barrier, improving treatment options for brain tumors. Nanocarriers also support the co-delivery of multiple drugs, enhancing therapeutic outcomes and reducing the likelihood of resistance. Personalized nanomedicine, tailored to an individual's tumor profile, may improve treatment efficacy and reduce side effects and healthcare costs. Combining passive and active targeting strategies enhances precision in drug delivery. Exploiting cellular signaling pathways and tumor-specific features allows for more accurate localization of therapeutic agents. Despite promising preclinical and clinical results, large-scale production, regulatory approval, and long-term safety remain key challenges. Future success depends on developing safe, cost-effective, and scalable nanocarrier systems. Continued research and multidisciplinary collaboration are essential to translate nanotechnology into widely accessible cancer treatments, ultimately transforming current oncology practices.

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