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Review Article

Customized multifunctional nanocarriers for cancer therapy: Integrating targeting, imaging, and combination treatment for diverse patient needs

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ABSTRACT

Multifunctional nanocarriers have emerged as a transformative approach in cancer therapy by overcoming traditional limitations such as systemic toxicity, poor tumor selectivity, and multidrug resistance. This review highlights recent advances in the design and application of customizable nanocarrier systems that integrate targeting, imaging, and combination drug delivery for more personalized and population-specific treatments. We examine major nanocarrier platforms, including lipid-based, polymeric, inorganic, and hybrid systems, with particular emphasis on their tunable physicochemical properties and modular architectures that facilitate adaptation to diverse patient populations, including elderly patients and those with treatment-resistant conditions. Functionalization strategies, such as ligand-mediated targeting and stimuli-responsive release, are discussed in the context of improving site-specific delivery and minimizing off-target effects. The integration of imaging agents enables theranostic functionality for real-time treatment monitoring. We also explore co-delivery systems for synergistic therapies combining chemotherapy, immunomodulation, and phototherapy. Clinical progress, regulatory challenges, and future trends including AI-driven design and bioinspired materials are discussed. This review underscores the pivotal role of multifunctional nanocarriers in advancing precision and inclusive oncology.

Keywords:
Multifunctional nanocarriers; Cancer therapy; Targeted drug delivery; Theranostics; Co-delivery systems; Personalized nanomedicine; Stimuli-responsive systems

1. INTRODUCTION

1.1. Challenges in traditional cancer therapies

The effectiveness and patient outcomes of traditional cancer therapies, such as radiation and chemotherapy, are limited by issues like toxicity, resistance, and non-specificity. Poor tissue penetration and off-target toxicities, which are made worse by the medications' instability and poor solubility in the bloodstream, frequently cause serious adverse effects from these treatments [1]. Furthermore, the emergence of intrinsic

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or acquired drug resistance is a significant obstacle since cancer cells adapt through intricate signaling pathways, which results in treatment evasion and spread. This resistance is made worse by tumor heterogeneity and the shifting characteristics of the tumor microenvironment, which can alter the efficacy of drugs [2]. Traditional medicines' lack of specificity frequently harms both healthy and malignant cells, causing patients to endure severe physical and mental suffering [3]. To address these issues, it is becoming increasingly crucial to create tailored drugs and advanced drug delivery methods, such as those based on nanotechnology. These strategies seek to improve drug specificity, solubility, and bioavailability to lessen side effects and overcome resistance mechanisms [4]. Together with precision medicine and immunotherapies, these developments present encouraging opportunities to enhance treatment results and patient quality of life. To guarantee equal healthcare advancements, however, the high costs and accessibility of these innovative drugs continue to be major obstacles that must be overcome [2].

Furthermore, the development of drug resistance makes treatment plans more difficult and calls for the formation of more specialized treatments [5]. In low-resource contexts, patients frequently turn to established, traditional, complementary, and alternative medicine (TCAM) due to the high cost and ineffectiveness of established therapies, which can lead to unmonitored drug interactions and adverse effects. Furthermore, many patients do not tell healthcare practitioners that they take TCAM, which increases these dangers due to the absence of defined practices and regulatory control. In general, resolving these complex issues is essential to enhancing patient safety and the effectiveness of cancer treatment [6].

1.2. Overview of multifunctional nanocarriers and their transformative potential

Multifunctional nanocarriers are a groundbreaking advancement in nanobiotechnology that hold great potential for a variety of biomedical applications, including environmental sustainability, cancer treatment, and targeted medication delivery. Because of their distinct physiological characteristics, these nanocarriers make it possible to combine several therapeutic modalities onto a single platform, improving the effectiveness and specificity of treatment [7]. To overcome issues like solubility and biological barriers, hybrid nanoparticles can be designed for precise targeting and controlled release [8]. Additionally, by demonstrating synergistic effects in the treatment of cancer and bacterial infections, multifunctional nanoparticles have demonstrated their versatility and effectiveness when compared to traditional medications. The development of these cutting-edge nanocarriers is anticipated to transform healthcare as research advances, enabling individualized therapy and enhancing therapeutic results [7].

1.3. Objectives and scope of review

Enhancing therapeutic efficacy, reducing systemic toxicity, and increasing selectivity towards disease locations are the main goals of multifunctional nanocarriers in targeted drug delivery systems. These nanocarriers, which include peptide-mediated systems, liposomes, and dendrimers, use special qualities to concentrate drugs at specific places, like tumors or infection sites, while minimizing exposure to healthy tissues [9]. These systems can accomplish targeted drug release by utilizing both passive and active targeting mechanisms, which is essential for addressing problems such as antibiotic resistance and improving cancer treatments. Additionally, these multipurpose systems' efficacy and adaptability in clinical contexts are improved by the incorporation of diagnostics and responsive delivery capabilities [10]. All things considered, the development of these sophisticated nanocarriers addresses the shortcomings of traditional drug delivery techniques and marks a substantial breakthrough in precision medicine [10].

The use of multifunctional nanocarriers in targeted drug delivery systems is very promising, particularly for the treatment of cancer and infectious disorders. The capacity of hybrid nanocarriers to co-deliver various therapies is gaining popularity since it improves patient outcomes in difficult cases like pancreatic cancer and increases efficacy against multidrug-resistant tumors [11]. Furthermore, the special qualities of nanoparticles, such liposomes and dendrimers, allow for accurate drug delivery targeting, reducing systemic toxicity and optimizing therapeutic concentration at tumor locations [9]. Additionally, by delivering drugs straight to infection areas, multifunctional nanoparticles might combine responsive drug release mechanisms with diagnostic capabilities to address problems like antibacterial resistance. The successful deployment of these cutting-edge drug delivery systems will depend on resolving issues with scalability and biocompatibility as research advances [12].

2. TYPES AND DESIGN OF MULTIFUNCTIONAL NANOCARRIERS

2.1. Lipid based systems

Because of their exceptional capacity to encapsulate both hydrophilic and lipophilic drugs, liposomes multifunctional nanocarriers have become a crucial element in the field of drug delivery, improving

bioavailability and lowering toxicity [13, 14]. The biocompatibility, biodegradability, and nonimmunogenic characteristics of these lipid-based nanocarriers make them very beneficial for a variety of therapeutic applications. Liposomes' adaptable surface further increases their versatility by enabling functionalization with a variety of ligands, including peptides, antibodies, and aptamers, which enhances therapeutic efficacy and targeting specificity. This functionalization is crucial for overcoming challenges like inadequate encapsulation and improper cellular internalization, thereby extending circulation time and enhancing site-specific drug delivery [14]. Moreover, liposomes are being integrated with other nanostructures, such as quantum dots and metallic nanoparticles, to create theranostic systems that combine therapeutic and diagnostic capabilities, offering real-time treatment monitoring [15]. In the realm of natural product delivery, liposomes address issues of low solubility and stability, facilitating targeted delivery and reducing side effects associated with multi-targeting. The development of sophisticated liposomal formulations, such as stimuli-responsive and hybrid nanocarriers, keeps pushing the limits of drug delivery methods and holds out the promise of better disease detection and treatment results. All things considered, liposomes' versatility makes them a viable option for upcoming pharmaceutical advancements, especially in the treatment of complicated and chronic illnesses like cancer [13].

In drug delivery systems, solid lipid nanoparticles (SLNs) are becoming multipurpose nanocarriers because of their biocompatibility, biodegradability, and capacity to improve drug stability and bioavailability. They are appropriate for a range of therapeutic uses, including the treatment of cancer, because they efficiently carry both hydrophilic and lipophilic drugs. Because SLNs may avoid the liver and spleen, they can deliver drugs more precisely and with greater therapeutic efficacy [16]. Their preparation methods, such as high shear homogenization and microemulsion techniques, contribute to their scalability and versatility [16, 17]. Furthermore, the development of nanostructured lipid carriers (NLCs) has increased the stability and drug loading capacity of lipid-based systems, increasing their potential uses in clinical medicine and cosmetics. All things considered, SLNs are a promising method in nanomedicine that enable accurate and effective drug delivery [17]. Figure 1 illustrates the pictorial representation of multifunctional nanocarrier.

2.2. Polymeric systems

Polymeric systems that employ polyethylene glycol (PEG) as multifunctional nanocarriers have become essential instruments in cutting-edge drug delivery applications, especially when it comes to treating difficult diseases like cancer and brain tumors. These systems, like the PEG and poly (ε-caprolactone) dual-responsive nanoparticles, show the capacity to release therapeutic compounds in response to redox conditions and near-infrared light, improving the effectiveness of localized treatment [18]. Furthermore, Fe_3O_4/PLA-PEG and other multifunctional nanocarriers have been developed for simultaneous drug delivery, magnetic resonance imaging (MRI), and hyperthermia, demonstrating their adaptability in the treatment of cancer. The integration of PEG with other polymers,

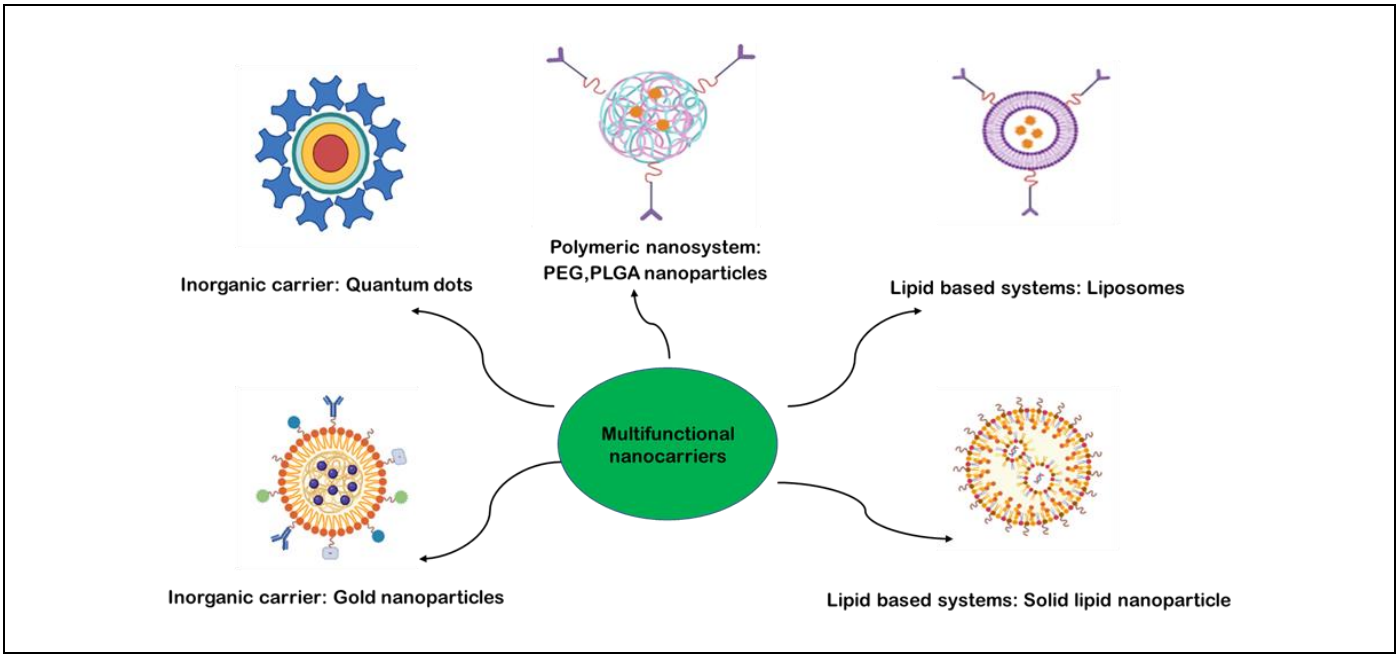

Figure 1. Diagrammatic representation of different multifunctional nanocarriers.

such as PMPC, has also been explored to improve biocompatibility and reduce protein absorption, facilitating theranostic applications [19]. Overall, these multifunctional polymeric systems not only improve drug delivery precision but also address the complexities of biological barriers, particularly in the context of brain tumors. Particularly in drug delivery systems aimed at cancer treatment, poly (lactic-co-glycolic acid) (PLGA) has become a versatile material for multifunctional nanocarriers. Because of their advantageous qualities, including biocompatibility, biodegradability, and low toxicity, PLGA nanoparticles (NPs) have been approved for clinical usage [20]. Recent research has shown that they can improve the solubility and bioavailability of a range of medicinal drugs by encapsulating them, including chemotherapeutics and organic substances like resveratrol and curcumin [21]. Furthermore, PLGA NPs can be functionalized to enhance targeting and lessen adverse effects linked to traditional treatments, especially in difficult-to-treat diseases like triple-negative breast cancer. Innovative approaches, such as co-encapsulation of drugs and the use of hybrid nanoparticles, have shown synergistic effects in enhancing therapeutic efficacy. Overall, PLGA-based multifunctional nanocarriers represent a promising strategy for improving cancer treatment outcomes through targeted and efficient drug delivery.

A major development in drug delivery systems, drug polymer conjugates in multifunctional nanocarriers improve therapeutic efficacy and safety. By enabling targeted distribution, controlled release, and enhanced stability through the covalent attachment of pharmaceuticals to polymers, these conjugates help to overcome issues including early drug release and low bioavailability [22]. Recent developments have integrated smart polymers that respond to biological stimuli, allowing for tailored drug release profiles and enhanced targeting capabilities. Additionally, the emergence of polymer-drug conjugates as theranostic agents enables simultaneous diagnosis and treatment, providing real-time tracking of drug distribution within the body. The versatility of these nanocarriers is further exemplified by their application in various therapeutic areas, including cancer treatment and gene delivery, showcasing their potential to revolutionize clinical practices [23].

2.3. Inorganic carriers

Because of their special physicochemical characteristics, such as stability, biocompatibility, and strong localized surface plasmon resonance (LSPR), gold nanoparticles (AuNPs) have become multifunctional nanocarriers that improve their uses in drug administration and diagnostics. They are appropriate for targeted therapies, such as the delivery of biomolecules like transferrin and antimiR-135b and chemotherapeutic drugs like paclitaxel in the treatment of cancer, because of their high surface-to-volume ratio, which enables effective drug loading [24]. As shown in folate-functionalized systems, AuNPs can be functionalized with a variety of ligands, such as vitamins and folic acid, to enhance targeting and therapeutic efficacy. Additionally, their optical properties facilitate bioimaging and photothermal therapies, further broadening their utility in theranostics. The ongoing development of environmentally friendly synthesis methods also highlights their potential for sustainable biomedical applications [25]. Overall, AuNPs represent a versatile platform for advancing nanomedicine.

Because of their distinct optical and electrical characteristics, which are impacted by their size and composition, quantum dots (QDs) are useful multifunctional nanocarriers in biological applications. Their high surface-to-volume ratio improves drug delivery efficiency by enabling efficient drug loading through both covalent and non-covalent interactions [26]. QDs exhibit excellent photostability and brightness, making them ideal for bioimaging and diagnostics, as they can provide real-time tracking of therapeutic agents within biological systems. Additionally, the integration of QDs with liposomes creates hybrid systems that improve biocompatibility and stability, particularly for challenging applications like brain tumor targeting. These advancements position QDs as promising candidates for next-generation nanomedicine, facilitating simultaneous imaging and therapeutic functions [27].

2.4. Hybrid systems combining multiple materials for enhanced functionality

Multifunctional nanocarriers in particular, hybrid systems are becoming increasingly popular in cancer treatment because of their capacity to improve therapeutic efficacy and drug delivery while reducing side effects. Mesoporous silica nanoparticles and biomimetic magnetic nanoparticles are two examples of nanocarriers that can be functionalized for targeted delivery. This enables the co-delivery of multiple chemotherapeutics, which can address issues like multidrug resistance and have synergistic effects against tumors [28]. Furthermore, hybrid nanoparticles can incorporate diagnostic properties, allowing for real-time therapy response monitoring and supporting customized medicine strategies. Multifunctional nanoparticles can also have antibacterial qualities, according to recent research, which expands their use in treating cancer patients' co-occurring infections [29]. All things considered; these developments demonstrate the promise of hybrid nanocarriers as adaptable instruments in contemporary cancer treatment.

3. FUNCTIONALIZATION FOR TARGETING AND IMAGING

Drugs or other therapeutic substances can be transported via nanocarriers, which are tiny particles. Lipids, polymers, and inorganic elements like gold or silica can all be used to create these carriers. Multifunctional nanocarriers are designed to serve a variety of purposes, such as delivering drugs while encasing and safeguarding therapeutic ingredients [30]. Focusing on and modifying the surface to enable precise binding to target tissues or cells. Utilizing imaging chemicals (such as MRI contrast agents and fluorescent dyes) for diagnostic reasons. Controlled release is the process of designing the carriers to release drugs in a predetermined manner in response to outside stimuli (such pH or temperature) [31].

3.1. Active targeting with ligands, antibodies and aptamers

An interesting and developing area of nanomedicine is active targeting, which combines multifunctional nanocarriers with ligands, antibodies, and aptamers. Enhancing the distribution of drugs to specific cells or tissues while minimizing adverse effects and off-target effects is the goal. Active targeting is the use of certain substances that can selectively bind to receptors or antigens expressed on the target cells. These molecules, which include ligands, antibodies, and aptamers, are frequently coupled to the surface of nanocarriers [32].

Small chemicals called ligands attach themselves precisely to receptors on the cell surface. Drugs can be precisely administered to target cells that express the corresponding receptors via ligands attached to nanocarriers. Folate is a common ligand that targets the overexpressed folate receptors found in many cancer cells. Certain pathogens or cancer indicators can be targeted with peptides or small compounds. Vitamin ligands that target certain receptors include biotin and vitamin B_{12} [33].

Monoclonal antibodies have a high degree of specificity for the antigens produced on the surface of target cells, such as cancer cells or pathogenic organisms. To accomplish targeted delivery, antibodies can be coupled with nanocarriers. Antibodies used in cancer therapy that target tumor-specific antigens (such as EGFR and HER2) are common applications. Immune-modulatory medications can be targeted to specific immune cell types using immune cell targeting [34]. Aptamers are short, single-stranded oligonucleotides (DNA or RNA) that have a high affinity for specific target molecules. They can be designed and selected to bind to a wide range of targets, including proteins, cells, and small molecules. Aptamers are superior than antibodies in that they are non-immunogenic, easy to manufacture and modify, and have great specificity and affinity [33]. The mechanism of action involves surface modification, whereby ligands, antibodies, or aptamers are chemically linked to the nanocarriers' surface. Numerous techniques, including covalent bonding and electrostatic interactions, can be used to accomplish this conjugation. Following their attachment to the target receptor on the cell surface, the nanocarriers go through a process known as receptor-mediated endocytosis. This enables the cell to ingest the therapeutic payload. The nanocarriers can either release their payload in a controlled or stimulus-responsive manner after entering the cell. Changes in the internal environment (pH, enzymes, etc.) or external stimuli (light, magnetic fields, etc.) may cause the release [35].

3.2. Stimuli responsive systems

3.2.1. pH-sensitive nanocarriers

At the forefront of precision delivery of drugs are stimuli-responsive systems, especially those that make use of pH-sensitive and enzyme-responsive multifunctional nanocarriers. In reaction to physiological or pathological triggers, like as pH shifts or the presence of particular enzymes, these systems are made to release their therapeutic payloads. This feature reduces adverse effects and increases treatment efficacy by enabling the focused and controlled delivery of drugs [36]. By engineering stimuli-responsive nanocarriers to react to different internal or external signals, encapsulated medicinal substances can be released in a regulated manner. Changes in pH (pH-sensitive), the presence of particular enzymes (enzyme-responsive), temperature changes (thermo-responsive), exposure to light (photo-responsive), magnetic fields (magneto-responsive), and redox potential (redox-responsive) can all activate these systems [37].

pH-sensitive nanocarriers take advantage of the differences in pH between normal tissues and disease environments, such as tumors or inflamed tissues [38]. Tumor tissues typically exhibit a lower pH (around 6.5-7.0) compared to healthy tissues (pH around 7.4). The drug can be released from the nanocarrier by taking advantage of this acidic environment. Likewise, several internal compartments (including lysosomes and endosomes) have a pH that is lower than the external pH, which makes them perfect for initiating drug release [38]. pH-sensitive nanocarriers are often made from polymers or lipids that undergo a conformational or solubility change in response to pH variations. Some common strategies for designing pH-sensitive nanocarriers include ionizable groups includes polymers containing amine, carboxyl, or imidazole groups can be protonated or deprotonated at different

pH levels, causing the nanocarrier to either swell, collapse, or degrade. Polymer crosslinking networks can be designed to break under acidic conditions, releasing the encapsulated drug. Examples include polymeric micelles have amphiphilic properties that allow them to assemble at neutral pH but disassemble or release the drug in acidic environments. Liposomes or lipid-based nanocarriers can be modified with pH-sensitive linkers to release their payload in acidic conditions [39].

3.2.2. Enzyme-responsive nanocarriers

When certain enzymes are overexpressed in disease situations like cancer, infection, or inflammation, enzyme-responsive nanocarriers are made to release their payload. It is possible to customize enzyme-responsive systems to identify the enzymes found in the intended tissue or organ. These enzymes could be proteases that break down proteins (e.g., matrix metalloproteinases (MMPs), cathepsins) are overexpressed in many cancerous tissues and inflammatory sites. Kinases or phosphatases Enzymes that modify proteins through phosphorylation or dephosphorylation processes may be overactive in specific diseases. Lipases enzymes that break down lipids may be useful for drug release in lipophilic drug formulations [40].

Enzyme-responsive nanocarriers are usually constructed using biodegradable polymers or materials that can be cleaved by specific enzymes. The drug can be encapsulated in a shell or bonded to the carrier via enzyme-sensitive linkers. Peptide linkers is a commonly used strategy to conjugate therapeutic agents to nanocarriers using peptide sequences that are cleaved by disease-specific enzymes. The presence of the enzyme causes the bond to break, releasing the drug. Enzyme-sensitive polymers can be designed to degrade upon enzymatic cleavage, releasing the payload in a controlled manner (41). Examples include nanoparticles with enzyme-degradable peptides are cleaved by overexpressed enzymes in certain tissues (e.g., MMP-sensitive nanoparticles for tumor therapy). Enzyme-sensitive liposome coatings could be composed of a polymeric substance that breaks down in the presence of a particular enzyme, releasing the therapeutic payload [40].

3.2.3. Multifunctional nanocarriers with pH and enzyme responsiveness

Multifunctional nanocarriers that react to pH and enzyme stimuli can be developed to improve therapeutic efficacy and targeting accuracy. By combining the benefits of several responsive system types, these nanocarriers enable more regulated and customized medication release [40].

It may be possible to develop a dual-responsive nanocarrier that would release its payload in reaction to the presence of a particular enzyme as well as an acidic environment. pH-sensitive polymeric nanocarriers could respond to the acidic TME, while simultaneously being sensitive to proteases like MMPs that are abundant in tumor tissues. Combination of pH-sensitive liposomes and enzyme-degradable polymers to ensure drug release at the optimal site of action, both in the acidic microenvironment and upon exposure to tissue-specific enzymes. Examples of pH-sensitive nanoparticles conjugated with enzyme-degradable peptides could be designed to release drugs at a tumor site where the acidic environment and high protease activity trigger both the disassembly of the carrier and the cleavage of the peptide linkers [42].

3.3. Imaging capabilities

Multifunctional nanocarriers have become vital tools for improving imaging capabilities in a variety of modalities, such as fluorescence, MRI, and PET. These nanocarriers, like PLGA-based nanocapsules, can incorporate several imaging agents without sacrificing their therapeutic payload or structural integrity, allowing for simultaneous tracking by fluorescence, PET, and MRI imaging [43]. For example, a new graphene quantum dots-cobalt ferrite platform showed good bimodal imaging using MRI and fluorescence, which improved therapeutic efficacy and made drug delivery monitoring easier. Furthermore, it has been demonstrated that combining nuclear and optical imaging methods enhances biodistribution measurement, with PET offering higher accuracy in deep tissue imaging than fluorescence [44]. These developments highlight the promise of multifunctional nanocarriers in theranostic applications, providing enhanced therapeutic results in clinical settings as well as sensitivity and specificity [45].

3.4. Theranostic: Combining diagnostic and therapy in one platform

By integrating therapeutic and diagnostic capabilities into a single platform, theranostics are revolutionizing individualized medicine, particularly in the treatment of cancer. Multifunctional nanocarriers, which offer enhanced targeting, biodegradability, and real-time monitoring capabilities, are at the forefront of this research. Lipid-based and biomimetic nanoparticles are two examples of these [46]. By enabling the tracking of medication release and therapeutic efficacy, these nanocarriers enable the simultaneous detection and treatment of diseases, which is essential for improving patient outcomes [47]. Numerous nanoscale materials, such as magnetic nanoparticles and quantum dots, have

demonstrated great promise in theranostic applications, tackling issues including tumor immune evasion and enhancing immunotherapy efficacy. To improve these technologies in clinical settings, however, the sector must work together to overcome obstacles including high costs and regulatory concerns [48].

4. APPLICATIONS IN COMBINATION CANCER THERAPIES

4.1. Synergistic approaches: Chemotherapy, immunotherapy, and gene therapy

Multifunctional nanocarriers play a pivotal role in enhancing combination cancer therapies by enabling co-delivery of therapeutic agents for improved efficacy. These carriers utilize active targeting and stimuli-responsive release mechanisms to overcome drug resistance, contributing to advancements in precision oncology and personalized medicine [49]. Table 1 highlights the potential of multifunctional nanocarriers to enhance therapeutic efficacy, improve targeting, and reduce side effects compared to conventional cancer therapies.

Nanoparticles facilitate targeted drug delivery, improving therapeutic efficiency while minimizing side effects. SPIONs contribute to cancer diagnostics through enhanced imaging contrast, targeted tumor detection, and multimodal imaging. Their multifunctionality allows their use as drug carriers, hyperthermia agents, and synergistic components in combination treatments. Functionalized SPIONs can deliver chemotherapy drugs, photosensitizers, or radiosensitizers for precise and effective therapy [55]. Hezarjaribi et al. [52] investigated SPION-based silica nanoparticles loaded with 5-fluorouracil (5-FU), oxaliplatin (OX), and metformin (MET) for colorectal cancer treatment. These nanocarriers integrated pH-responsive AuNPs for controlled drug release, PEGylation for prolonged circulation, and folic acid (FA) for targeted therapy. Tumor suppression efficacy was assessed in tumor-bearing mice, with size measurements recorded every other day. FA-PEG-Au-NPs@5-FU-MET and FA-PEG-Au-NPs@OX-MET demonstrated significant anticancer activity, particularly with radiation therapy. The radio-sensitizing effect of MET and precise targeting by FA contributed to enhanced therapeutic outcomes, underscoring the potential of integrating nanocarriers with radiation therapy for superior tumor reduction.

Nanoparticle-based drug delivery enables precise cancer targeting by utilizing tumor-specific biochemical cues. Calcium carbonate nanoparticles, which are pH-sensitive, dissolve in acidic tumor environments, releasing therapeutic agents while also disrupting calcium balance. This dual action induces tumor calcification, inhibits growth, and allows imaging-based therapy monitoring [56].

Martin et al. [53] developed a calcium carbonate nanoparticle-based system for targeted breast cancer therapy. Loaded with doxorubicin (DOX), these nanoparticles induce cancer cell death through tumor calcification and DNA damage. A layer-by-layer coating with hyaluronic acid and poly-L-lysine (PLL) enhances targeting and stability. Their effects on cell viability, proliferation, Ca^{2+} overload, and calcification were assessed in Hs578T cancer spheroids and HMF fibroblasts [53]. The proliferative capacity of Hs578T cancer spheroids was assessed by measuring Ki-67 expression, a marker for cell proliferation. Hs578T spheroids showed significantly higher Ki-67 expression than HMF spheroids, indicating more aggressive tumor growth. After 1 day of nanoparticles treatment, no significant change in Ki-67 expression was observed. By day 3, untreated Hs578T spheroids showed active cell division, while nanoparticle -treated spheroids had reduced Ki-67 expression, suggesting slower proliferation. This slower rate may result from metabolic and signaling adjustments to cope with Ca2+ burst and DOX toxicity. NP treatment did not affect the proliferative capacity of HMF spheroids.

Reda et al. developed a nanoparticle-based immunotherapeutic platform, termed ARAC (Antigen Release Agent and Checkpoint Inhibitor), co-delivering the PLK1 inhibitor volasertib and a PD-L1 antibody to enhance immune-mediated tumor suppression. Experiment design demonstrated in in Figure 2a. As illustrated in Figure 2b, ARAC significantly inhibited the growth of local tumors compared with nanoparticles carrying either PD-L1 antibody (p-NP) or volasertib (iPLK1-NP) alone. Moreover, ARAC delayed the onset of distant untreated tumors (Figure 2c) and significantly improved overall survival (Figure 2d), indicating the induction of a systemic antitumor immune response. Immune profiling further demonstrated reduced PD-L1 expression in both immune and tumor cell populations (Figure 2e), enhanced proliferation of effector CD8+ T cells in tumor-draining lymph nodes (Figure 2f), and increased infiltration of immune cells along with a higher CD8+/Treg ratio within tumors (Figure 2g).

These findings demonstrate the potential of ARAC to synergistically combine targeted cytotoxicity and immune checkpoint blockade. However, the relatively low doses of volasertib and PD-L1 antibody used in the study make it difficult to directly compare its efficacy with conventional monotherapies, and further investigations are needed to assess long-term immune memory, systemic safety, and clinical translatability [57].

Autophagy in the tumor microenvironment has a complex role, influencing tumor growth by regulating immune cell functions. It supports the survival of T cells,

Table 1. Multifunctional nanocarriers for cancer diagnosis and therapy.

Type of cancer	Nanoparticle composition	Physicochemical properties	Mechanism	Findings	Advantages	References
Abdominal pelvic tumors	Self-assembled gambogic acid (GA) and metformin (Met) nanoparticles (GA/Met NPs).	Particle size:268.9 nm; polydispersity index: 0.215; zeta potential: 10.8 mV	GA inhibits HSP-90 to enhance apoptosis, Met clears extracellular matrix components for better penetration, and HIPEC induces immunogenic cell death, activating anti-tumor immunity.	Significant tumor suppression, prolonged survival, increased CD8+ T cells, NK cells, M1 macrophages, and reduced immunosuppressive cells.	Enhanced HIPEC efficacy, improved tumor penetration, stronger immune activation, reduced toxicity, and high clinical potential.	(50)
Breast cancer	Polyethyleneimine-oleic acid nanoparticles loaded with paclitaxel, chloroquine (CQ), ovalbumin, CpG, and anti-PD-L1 antibody	Particle size:131.52 nm; polydispersity index: 0.144; Zeta potential: -20.9 mV	Targeted delivery via PD-L1 and CD44 interaction, Inhibition of autophagy with CQ, Induction of strong immune memory and T-cell response	Significant reduction in tumor size, prevention of lung metastasis, enhanced CD8+ and CD4+ T cell infiltration	Multifunctional approach (chemotherapy + immunotherapy), autophagy inhibition enhances immune response, long-lasting immune memory	(51)
Colorectal cancer	SPION@MSNs loaded with 5-fluorouracil (5-FU) or oxaliplatin (OX), and metformin (MET) functionalized with PEG and folic acid for targeted delivery	Particle size: 79.8 nm (5-FU), 85.2 nm (OX); Zeta potential: -21 mV (5-FU), -22 mV (OX)	Targeted drug delivery via folate receptor; pH-responsive drug release	5-FU-MET and OX-MET nanocarriers with radiation therapy maximized antitumor effects with minimal side effects, ensuring precise tumor targeting.	Enhanced tumor localization and reduced side effects; improved therapeutic efficacy.	(52)
Breast cancer	Calcium carbonate nanoparticles loaded with doxorubicin (DOX); coated with poly-L-lysine (PLL) and hyaluronic acid	Particle size:447 nm; polydispersity index: 0.182; Zeta potential: -12 mV	Targeted delivery via CD44 and RHAMM receptors, synergistic mechanism combining Ca2+ overload and DOX-induced DNA damage	PLL-coated NPs showed reduced cytotoxicity to healthy cells, significant reduction in tumor cell viability in 3D spheroid models	Enhanced targeting capacity, reduced side effects on healthy cells, sustained drug release in acidic environments	(53)
Breast cancer	Mesoporous polydopamine (MPDA) nanoparticles co-loaded with DOX and imiquimod (R837)	Particle size of MPDA: 186.93 ± 32.50 nm; zeta potential: 35 ± 0.44 mV	Synergistic photothermal therapy and chemotherapy, enhanced immune response via dendritic cell activation	Significant cytotoxicity against 4T1 cells under NIR laser irradiation, enhanced cellular uptake in both tumor and immune cells	Multifunctional platform integrating chemotherapy, photothermal therapy, and immunotherapy, reduced side effects and improved therapeutic efficacy	(54)

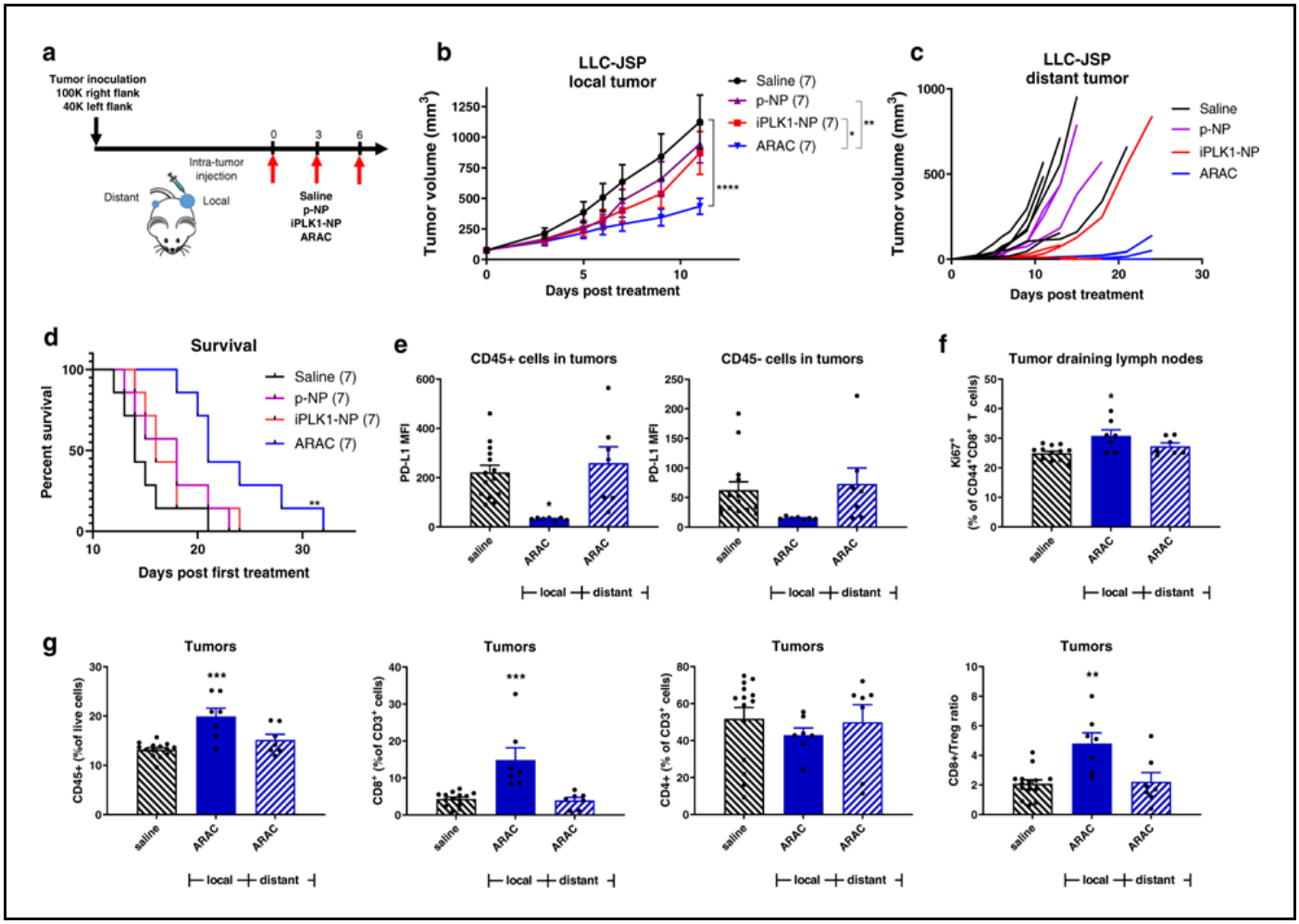

Figure 2. Antitumor immune responses induced by the ARAC nanoplatform: (a) experimental design showing bilateral tumor establishment in C57BL/6 mice by inoculating 100,000 LLC-JSP cells into the right flank and 40,000 cells into the left flank, (b) growth kinetics of locally treated tumors following different nanoparticle treatments, (c) progression of distant, untreated tumors, demonstrating delayed tumor development in mice receiving ARAC therapy, (d) Kaplan–Meier survival analysis, with animals euthanized when the combined tumor burden reached 2000 mm³, (e) quantification of PD-L1 expression levels in hematopoietic ($CD45^+$) and non-hematopoietic ($CD45^-$) cell populations, (f) proliferative activity of effector $CD8^+$ T cells ($Ki67^+CD44^+CD8^+$) within tumor-draining lymph nodes, (g) tumor immune microenvironment analysis showing the proportions of total immune cells ($CD45^+$), $CD8^+$ and $CD4^+$ T lymphocytes, and the $CD8^+$/regulatory T-cell (Treg) ratio, indicative of enhanced antitumor immunity following ARAC treatment. Adapted with permission from [57], Under CC BY.

but elevated lactic acid in tumors can impair this process. Additionally, the absence of autophagy in regulatory T cells can increase tumor resistance. Targeting autophagy may help overcome immune suppression in the tumor microenvironment, promoting immune cell infiltration and enhancing T cell activity. Chloroquine (CQ), an autophagy inhibitor, has shown potential when combined with immune checkpoint inhibitors [58]. Combining autophagy inhibition and chemotherapy using MNPs could improve treatment efficacy but requires careful design to minimize side effects. Cheg et al. [51] introduced a rapid and efficient self-assembly method for creating a multilayered nanoplatform designed for targeted delivery to tumors and lymph nodes, enhancing long-term antitumor immunity. The developed MNPs were loaded with a combination of chemotherapeutic agents (paclitaxel-PTX and chloroquine-CQ), an antigen (ovalbumin), an immunostimulant (CpG), and an immune checkpoint inhibitor (atezolizumab, an anti-PD-L1 antibody). In a subcutaneous 4T1 breast cancer model in Balb/c mice, different formulations were tested for their antitumor effects. On day 5 post-injection, the mice were treated with various MNPs formulations, including CpG+OVA+PTX-S, CpG+OVA+PTX-N, CpG+OVA+PTX+CQ-N, and CpG+OVA+CQ+PTX-N/A, on days 5 and 10. A more pronounced suppressive effect was seen in the CpG+OVA+PTX-N group, indicating that the MNPs effectively targeted the tumor. On the other hand, the combination of CpG+OVA+CQ+PTX-N/A significantly slowed tumor progression, highlighting the advantageous synergistic effect of combining chemotherapy with immune checkpoint blockade therapy. The combination of chemotherapy and immune checkpoint blockade therapy (CpG+OVA+CQ+PTX-N/A) achieved the most

significant tumor suppression, with tumors weighing less than 0.3g and the highest survival rate [51]. This approach also induced severe tumor cell damage. No significant changes in mouse body weight indicated the safety of the MNPs, highlighting the superior efficacy of combined treatments.

Recognizing the tumor-suppressive role of miR-200c-3p in breast cancer, Cano et al. developed hyaluronic acid-functionalized mesoporous silica nanoparticles (MSN-PEI-miR200c-HA) to achieve targeted and efficient microRNA delivery. The nanoplatform demonstrated favorable biocompatibility, effective endosomal escape, and inhibition of tumor cell proliferation, migration, and invasion *in vitro.* In an orthotopic breast cancer model, Figure 3 shows that treatment with MSN-PEI-miR200c-HA significantly reduced tumor growth and suppressed lung metastasis compared with control groups. Histological and Ki-67 analyses confirmed decreased tumor cell proliferation, while increased miR-200c-3p expression and reduced ZEB1 and ZEB2 levels verified successful *in vivo* delivery and biological activity of the microRNA. Importantly, the treatment achieved these therapeutic benefits without detectable systemic toxicity [59].

These findings demonstrate the potential of mesoporous silica nanoparticles as a safe and effective platform for tumor-targeted microRNA therapy. Nevertheless, further studies are needed to assess long-term biodistribution, immune responses, and clinical scalability before translation into human applications [59].

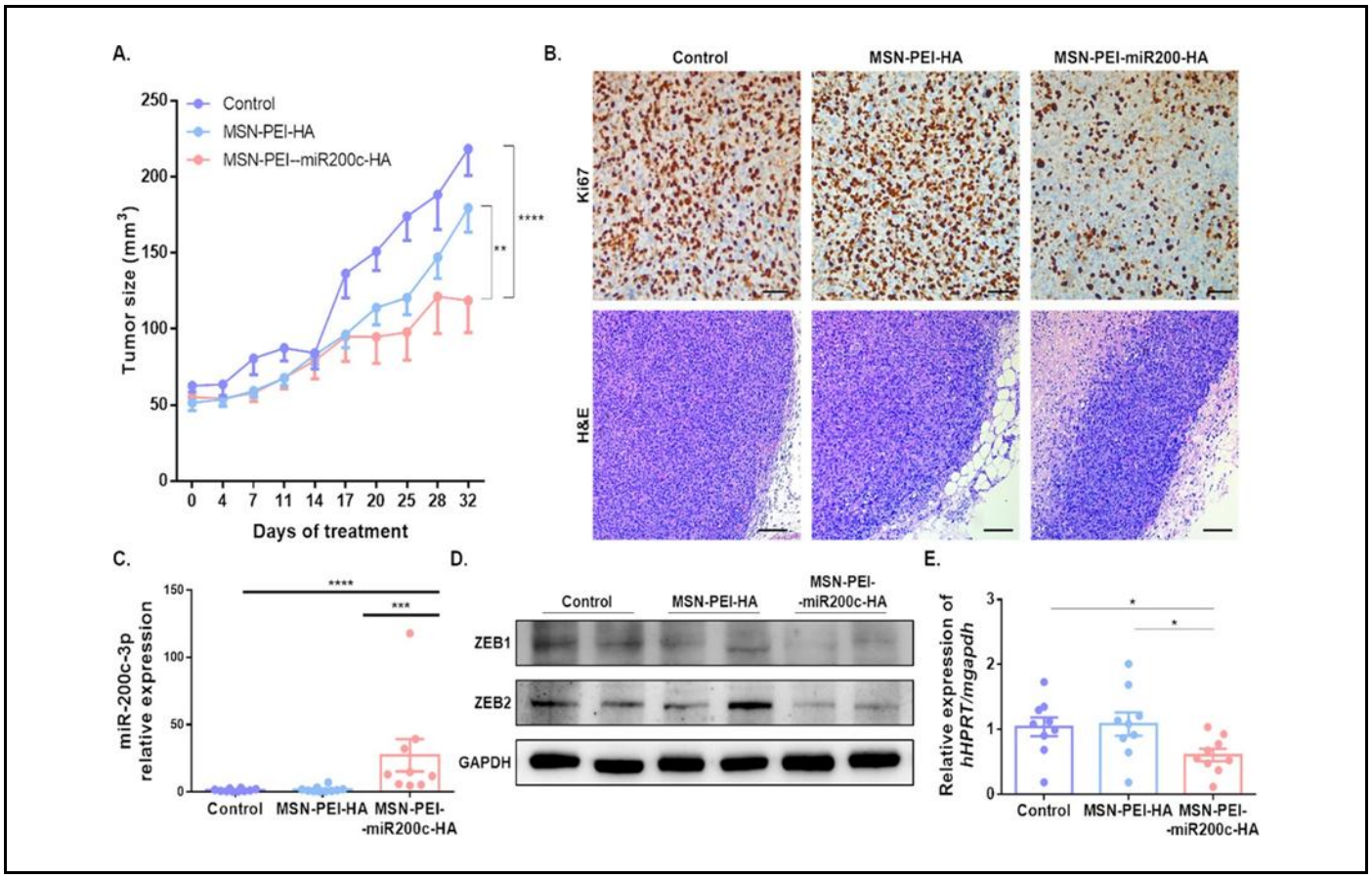

Figure 3. *In vivo* antitumor efficacy of miR-200c-3p-loaded mesoporous silica nanoparticles (MSN-PEI-miR200c-HA): (A) tumor growth profiles of mice receiving PBS, MSN-PEI-HA, or MSN-PEI-miR200c-HA treatment, (B) representative H&E and Ki-67-stained tumor sections demonstrating histological changes and reduced cellular proliferation following treatment, (C) quantitative analysis of miR-200c-3p expression in excised tumors by qRT-PCR, (D) expression levels of the miR-200c-3p target proteins ZEB1 and ZEB2 in tumor tissues, with GAPDH used as the loading control, (E) relative expression of human HPRT (hHPRT) in lung tissues, normalized to mouse GAPDH (mGAPDH), as an indicator of metastatic burden. Adapted with permission from [59], Under CC BY 4.0.

4.2. Photo-based therapies: Photothermal and photodynamic therapies

Recent studies highlight the potential of advanced therapies, including photothermal therapy (PTT), sonodynamic therapy, photodynamic therapy, and immunotherapy, in cancer treatment. However, the complex nature of the tumor microenvironment can reduce the effectiveness of individual therapies. A multimodal approach that combines multiple treatment strategies may enhance therapeutic benefits while minimizing adverse effects (60). Toll-like receptor 7/8 (TLR7/8), highly expressed in dendritic cells (DCs), plays a key role in immune activation and DC

maturation. Its agonists enhance antigen presentation and cytokine release, making them promising for cancer immunotherapy. R837, a potent TLR7 agonist, strengthens DC function [61].

Building on this concept, Wu et al. [54] designed mesoporous polydopamine (MPDA) with photothermal properties for the simultaneous delivery of DOX and the immune adjuvant imiquimod (R837) to treat breast cancer. The combined therapy was termed as multifunctional nanoplatforms (MDR). Intratumoral injection followed by NIR irradiation increased tumor temperatures to 45.46 ± 2.17 °C (MPDA + NIR) and 49.76 ± 2.33 °C (MDR + NIR), with MDR exhibiting stronger photothermal effects. This led to effective PTT-mediated tumor ablation. Tumor size and weight were significantly lower in the DOX, MPDA + NIR, and MDR + NIR groups compared to the control [54].

Notably, MDR + NIR resulted in near-complete tumor elimination, highlighting its effectiveness due to the synergy of PTT, chemotherapy, and immunotherapy. This study confirms that MPDA-based synergistic therapy enhances drug delivery, photothermal performance, and immune activation. The acidic tumor environment boosts DOX and R837 release, amplifying antitumor effects. This approach effectively eliminates primary tumors while potentially preventing metastasis and recurrence.

Traditional chemotherapy for abdominal pelvic tumors is often hindered by systemic toxicity and ineffective drug delivery. Hyperthermic intraperitoneal chemotherapy (HIPEC) offers localized treatment with heated drug infusion but struggles with heat shock protein activation and a dense tumor matrix. In response, Fang et al. [50] developed a carrier-free nanomedicine platform by self-assembling gambogic acid (GA) and metformin (Met) into GA/Met nanoparticles for hyperthermic intraperitoneal chemotherapy (HIPEC). GA not only inhibits heat shock proteins and acts as a chemotherapeutic agent but also works in synergy with metformin, which breaks down the tumor extracellular matrix to enhance drug penetration. This combined approach triggers immunogenic cell death, boosting both innate and adaptive immune responses. These results demonstrate that MH+GA/Met-7 NPs enhance HIPEC efficacy by improving drug penetration, inhibiting heat-induced resistance, and stimulating anti-tumor immunity.

Park et al. developed doxorubicin (DOX)-loaded liposomal iron oxide nanoparticles (Lipo-IONP/DOX) using the thin-film evaporation method and evaluated their potential for combined chemo-photothermal cancer therapy. The nanoparticles formed globular aggregates with an average size of approximately 240 nm. As shown in Figure 4A, free DOX produced minimal tumor suppression, whereas Lipo-IONP/DOX significantly inhibited tumor growth. The therapeutic efficacy was further improved by magnetic targeting (Lipo-IONP/DOX + MAG), while the addition of photothermal therapy (Lipo-IONP/DOX + MAG + PTT) resulted in the greatest tumor growth inhibition (84%) (Figure 4B). Histopathological examination (Figure 4C) revealed substantial tumor cell depletion and tissue damage in the combination treatment group. Similarly, TUNEL staining (Figure 4D) demonstrated a markedly higher level of apoptosis in tumors treated with Lipo-IONP/DOX + MAG + PTT compared to the other groups [62].

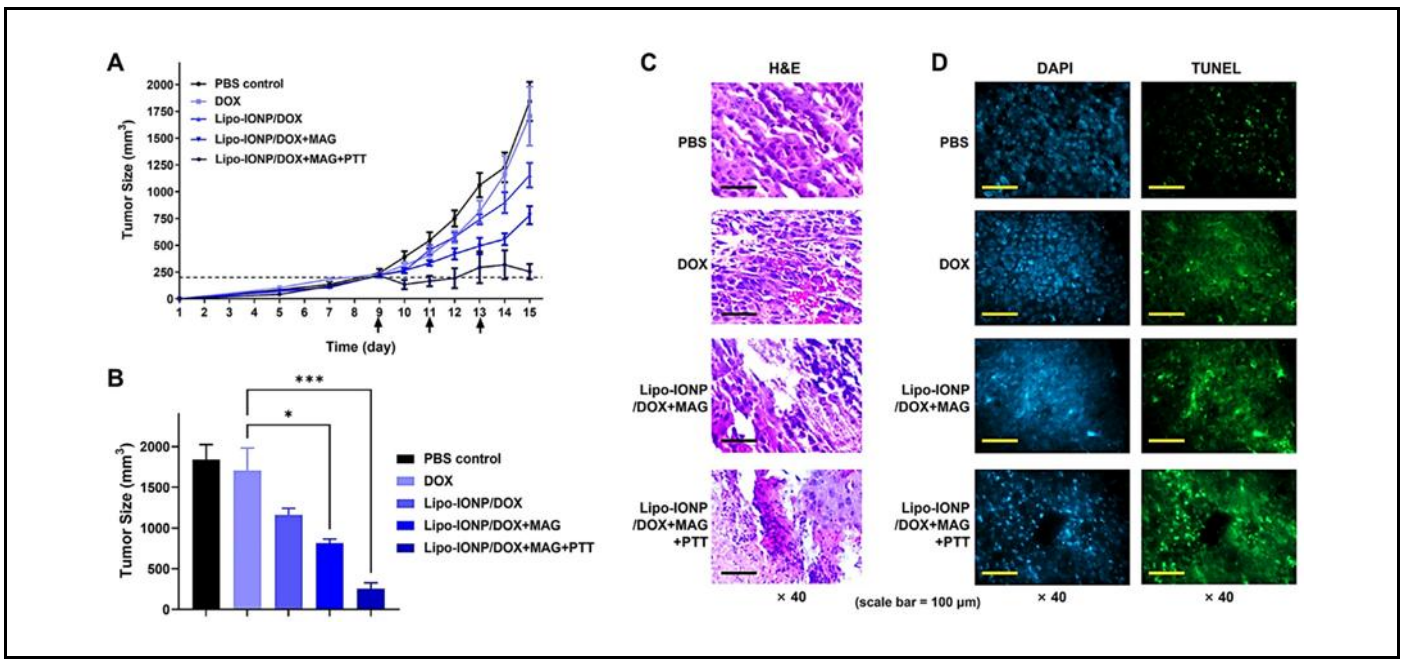

Figure 4. Study of the combined liposomes-IONP/DOX chemo-photothermal therapy in a B16F10 s.c. allograft tumor mouse model: (A) tumor growth temporal profile, (B) day 15 tumor sizes when the experiment was concluded, (C) histological study, (D) TUNEL assay of tumor tissues (green stain of TUNEL with blue DAPI nuclear counterstain). Adapted with permission from (62), Under CC BY.

These findings highlight the synergistic benefits of integrating chemotherapy, magnetic targeting, and photothermal therapy within a single nanoplatform. However, further studies are required to evaluate long-term safety, biodistribution, and translational feasibility before clinical application.

4.3. Co-delivery systems for simultaneous treatment and diagnostic monitoring

In recent years, cancer treatment has evolved significantly with the advent of theranostic, which integrates both diagnostic and therapeutic functions. Multifunctional nanocarriers, designed to simultaneously deliver imaging and therapeutic agents, present notable advantages over traditional nanomedicines. Hybrid nanocarriers, including lipid-polymer, inorganic, metal-organic, and carbon-based types, enhance cancer diagnosis and therapy with improved cargo encapsulation, stability, and targeting. Studies highlight their potential in breast cancer imaging, photothermal and photodynamic therapy, chemotherapy, gene therapy, and combination treatments [63].

These systems allow for real-time tracking of nanocarrier accumulation at the disease site before drug administration, aiding in patient selection for targeted therapies. They also enable real-time monitoring, improve imaging efficiency through high agent-loading capacity, and can be activated on demand using biological triggers or external energy sources. Additionally, nanotheranostic platforms can indicate drug release, enhancing precision in cancer therapy [64]. By facilitating non-invasive monitoring of nanocarrier distribution, nanotheranostics enable personalized treatment approaches while improving the targeted delivery of therapeutic and imaging agents. Unlike conventional molecular agents, these platforms provide benefits such as patient stratification and externally controlled activation [65]. Examples include iron oxide-based nanocubes for MRI-assisted magnetic hyperthermia, nanoparticles with heavy metals for enhanced radiation therapy, and luminescent nanocarriers that aid in surgical navigation. Moreover, some multifunctional nanocarriers transport luminescent nanoparticles and chemotherapy agents via passive diffusion, while iron oxide-loaded carriers release anticancer drugs upon exposure to high-intensity focused ultrasound [66].

Clinical research underscores the impact of nanotheranostics, with polymeric gadolinium complexes (AGuIX) demonstrating MRI-detectable accumulation in brain metastases, correlating with positive treatment outcomes. Additionally, nanotheranostics functionalized with tumor-targeting agents offer valuable insights for surgical precision and tumor margin identification, further advancing the effectiveness of cancer diagnostics and therapy [67]. Ultrasound-driven piezocatalysis using tetragonal barium titanate (T-BTO) enables diagnostic and therapeutic applications by generating reactive oxygen species (ROS) for tumor therapy with deep penetration and biosafety [68]. Li et al. designed a GSH-responsive theranostic nanoparticle (DHP) for dual-modal imaging and combination therapy. Comprising hydroxyethyl starch-paclitaxel (HES-SS-PTX) and near-infrared fluorophore DiR, DHP enables controlled drug release and fluorescence recovery upon intracellular activation. This system facilitates real-time monitoring, supports fluorescence and photoacoustic imaging, and enhances chemo-photothermal tumor therapy, offering a clinically viable approach [69].

Guo et al. [70] developed CS-AuNR hybrid nanospheres using a counterion complexation method and incorporated cisplatin for cancer treatment. These nanocarriers support real-time imaging, enable NIR-triggered photothermal therapy, and enhance drug delivery, offering a versatile approach for simultaneous cancer diagnosis and therapy.

Refining theranostic materials to achieve a precise equilibrium between diagnostic imaging and therapeutic effects is crucial for addressing technical hurdles. Meanwhile, modern regulatory strategies, such as repurposing existing nanomedicines and employing AI are accelerating clinical trial development. Ultimately, integrating nanotheranostics into standard cancer care could transform personalized treatment by enabling highly tailored interventions.

5. CLINICAL PROGRESS AND CHALLENGES

Multifunctional nanocarriers have emerged as a revolutionary paradigm in oncological therapy, providing a spectrum of functionalities that include precise drug delivery, diagnostic imaging, and the enhancement of integrated therapeutic strategies. Notwithstanding their promising capabilities, the clinical translation of these nanocarriers encounters numerous impediments. This review undertakes an examination of the extant clinical advancements regarding multifunctional nanocarriers, evaluates the challenges obstructing their mass production and regulatory endorsement, and contemplates issues pertaining to financial implications, accessibility, and the long-term biocompatibility of these systems.

5.1. Current multifunctional nanocarriers in clinical trials and FDA approvals

The assimilation of multifunctional nanocarriers into clinical methodologies has progressed incrementally. According to the latest statistics, more than 45 nanocarrier-derived formulations have attained

authorization from the U.S. Food and Drug Administration (FDA), while over 80 supplementary formulations are currently in the process of clinical evaluation. A noteworthy entry in this domain is Doxil®, a liposomal formulation of DOX that received regulatory approval in 1995, representing a pivotal advancement in the field of nanomedicine through its ability to improve drug bioavailability while simultaneously mitigating systemic toxicity [71].

Another notable progression in the medical field is the formulation of mRNA-4157/V940, an mRNA-based oncological vaccine encapsulated within lipid nanoparticles [72]. This individualized vaccine, engineered to elicit tumor-specific antigens, has demonstrated promising efficacy in conjunction with pembrolizumab for the treatment of resected high-risk melanoma.

Notwithstanding these advancements, the clinical application of multifunctional nanocarriers continues to be constrained. The intricacies involved in the design of nanocarriers capable of concurrently delivering therapeutic agents, enabling imaging, and targeting specific neoplastic sites present considerable challenges. This intricacy frequently results in complex manufacturing protocols and potential safety issues, which may hinder clinical advancement.

5.2. Barriers to large-scale production, regulatory approval, and safety

Despite the promising potential of multifunctional nanocarriers in oncological therapy, significant challenges persist in their large-scale production, regulatory approval, and safety assessment. A primary challenge in large-scale manufacturing is the maintenance of batch-to-batch consistency while ensuring the uniformity of the physicochemical properties of NPs [73]. Minor discrepancies in size, charge, and surface chemistry can profoundly affect biological behavior, resulting in variability in therapeutic efficacy and toxicity. Scalable and reproducible fabrication methodologies, such as microfluidic synthesis, are currently being investigated to address these challenges [73].

Regulatory endorsement constitutes a significant obstacle owing to the intricate characteristics inherent to nanomedicines. In contrast to traditional pharmaceuticals, nanocarriers necessitate comprehensive characterization to fulfill the regulatory criteria established by the FDA and EMA. The absence of uniform evaluation protocols for therapeutics based on nanoparticles exacerbates the complexities associated with the approval procedure. Regulatory bodies underscore the necessity for thorough preclinical evaluations, encompassing pharmacokinetics, biodistribution, and immunogenicity investigations, which frequently demand sophisticated analytical methodologies and extended timeframes [74].

One of the major issues in relation to translational medicine involving multifunctional nanocarriers is the process of their regulatory evaluation which proves to be significantly more challenging in comparison with regular liposomal formulations. Contrary to single-component nanodrugs, multifunctional nanocarriers tend to combine a drug cargo, targeting ligands, imaging molecules, and responsive structures. This poses additional difficulties in terms of physiochemical characterization and quality control processes. In terms of regulation, FDA and EMA impose strict demands regarding Chemistry, Manufacturing, and Controls (CMC) documentation which requires thorough examination of parameters like particle size distribution, surface characteristics, drug loading and release dynamics, stability and manufacturing reproducibility [75].

Moreover, multifunctional nanocarriers are categorized by FDA as combination products due to their ability to serve both for therapy and diagnosis; therefore, there should also be an evaluation of individual components and integrated performance of the system. There also remains a lack of standardized guidelines for evaluation of theranostic and multifunctional nanosystems which poses yet another issue in regard to clinical development of such materials. Finally, thorough investigations into biodistribution, immunological behavior, accumulation and interaction of individual nanoparticles *in vivo* should be carried out to receive a proper approval from regulatory authorities [76].

Safety apprehensions significantly impede the clinical applicability of multifunctional nanocarriers. The potential for toxicity is attributed to factors such as prolonged bioaccumulation, degradation byproducts, and unintended off-target effects. Although surface modifications, including PEGylation, may improve biocompatibility, issues pertaining to immune responses, complement system activation, and unanticipated toxicities continue to pose significant concerns. Consequently, comprehensive *in vitro* and *in vivo* investigations are imperative to ascertain potential risks prior to clinical implementation [77].

5.3. Addressing cost, accessibility, and long-term biocompatibility concerns

Notwithstanding the considerable promise exhibited by multifunctional nanocarriers in oncological therapeutics, their transition into clinical practice continues to be obstructed by issues related to cost, accessibility, and long-term biocompatibility. The elevated expenses associated with the synthesis of nanoparticles, their functionalization, and the large-scale production processes significantly restrict their extensive utilization in settings characterized by limited resources [78]. Innovative fabrication methodologies,

including microfluidics and scalable self-assembly approaches, present auspicious alternatives by enhancing both reproducibility and cost-effectiveness. Furthermore, the incorporation of biodegradable and naturally sourced materials, such as lipid-based and polymeric nanoparticles, has the potential to mitigate costs while preserving therapeutic effectiveness. Accessibility continues to pose a considerable obstacle, especially within low- and middle-income nations. The inequity in healthcare infrastructure constrains the accessibility of advanced nanomedicine-based interventions [79].

Long-term biocompatibility and safety apprehensions represent significant obstacles to the clinical translation of nanotechnology. The accumulation of inorganic nanoparticles, including quantum dots and certain metallic nanocarriers, has the potential to elicit cytotoxic effects and organ-specific toxicity over prolonged durations [80]. The advancement of biodegradable nanocarriers that can achieve complete biocompatibility through systemic clearance is imperative to alleviate the risk of potential long-term adverse effects. Recent investigations into stimuli-responsive, enzyme-degradable, and biomimetic nanocarriers present promising methodologies for enhancing biocompatibility while simultaneously ensuring targeted delivery and controlled pharmacological release [80].

6. EMERGING TRENDS AND FUTURE PERSPECTIVES: AI-DRIVEN DESIGN AND OPTIMIZATION OF MULTIFUNCTIONAL NANOCARRIERS

The future of multifunctional nanocarriers in cancer therapy is poised for groundbreaking advancements, with emerging trends in AI-driven design, bioinspired nanocarriers, personalized medicine, and metastasis-targeted therapies reshaping the landscape of oncology. AI-driven design is revolutionizing the development of nanocarriers by leveraging machine learning algorithms to optimize nanoparticle composition, size, surface chemistry, and targeting efficiency, enabling rapid screening and prediction of therapeutic efficacy with unparalleled precision [81]. AI-guided drug delivery platforms can analyze vast datasets, refine nanoformulations, and predict biodistribution patterns to enhance therapeutic outcomes while minimizing systemic toxicity. Furthermore, bioinspired nanocarriers designed to mimic natural biological entities such as exosomes, lipoproteins, or viral particles offer enhanced biocompatibility, immune evasion, and precise tumor targeting, opening new frontiers in cancer treatment. These bioengineered nanoparticles can efficiently navigate the tumor microenvironment, overcome biological barriers, and facilitate targeted drug release, significantly improving treatment specificity and efficacy [82]. Personalized medicine and adaptive cancer treatments using nanotechnology are becoming a reality, as nanocarriers enable patient-specific treatment regimens tailored to tumor genetic profiles, real-time disease monitoring, and dynamic therapy adjustments. The integration of liquid biopsy-derived biomarkers with nanotechnology allows for continuous assessment of treatment response and early detection of resistance, ensuring optimal therapeutic interventions [83]. Additionally, smart nanocarriers incorporating stimuli-responsive mechanisms, such as pH-sensitive, redox-responsive, or enzyme-triggered drug release systems, can adaptively modulate drug delivery based on tumor-specific cues, maximizing efficacy while reducing off-target effects. Future directions in metastasis-targeted and precision oncology therapies will focus on tackling the most aggressive and treatment-resistant cancer phenotypes, where multifunctional nanocarriers offer unprecedented opportunities. Strategies targeting metastatic niches such as the pre-metastatic microenvironment, circulating tumor cells (CTCs), and tumor-derived extracellular vehicles are emerging as powerful tools in precision oncology. Nanoparticles functionalized with ligands against metastatic markers can selectively bind and neutralize CTCs, preventing secondary tumor formation and disease progression. Additionally, the combination of imaging-guided nanotherapies with immunomodulatory approaches, such as nanoparticle-mediated immune checkpoint inhibition and tumor vaccine delivery, holds immense potential for transforming metastatic cancer management [84]. The convergence of nanomedicine with cutting-edge technologies, including CRISPR-based gene editing, RNA therapeutics, and theranostic platforms, will further refine the precision of cancer treatments, allowing for highly selective gene silencing, epigenetic reprogramming, and real-time tumor visualization. As nanocarrier platforms continue to evolve, interdisciplinary collaborations among oncologists, material scientists, bioengineers, and data scientists will be crucial in translating these innovations from bench to bedside [29]. Regulatory frameworks and large-scale clinical trials will play a pivotal role in ensuring the safety, scalability, and efficacy of next-generation nanomedicines, paving the way for a future where cancer therapies are not only more effective but also highly individualized, minimally invasive, and seamlessly integrated with real-time diagnostics. While significant challenges remain including addressing nanoparticle clearance, optimizing delivery to heterogeneous tumors, and overcoming multidrug resistance continued advancements in nanotechnology, AI, and bioengineering will undoubtedly shape the next era of cancer treatment, bringing us closer to the goal of precision oncology and long-term disease eradication.

By enabling data-driven prediction of physicochemical attributes and biological performance, artificial intelligence (AI) and machine learning (ML) are progressively revolutionizing the design and optimization of multifunctional nanocarriers. Large datasets can be analyzed by ML algorithms to find correlations between nanoparticle composition, size, surface charge, ligand density, and therapeutic outcomes, whereas traditional nanocarrier development frequently depends on labor-intensive trial-and-error testing [85]. Formulation development has been accelerated by using supervised learning models to predict drug loading efficiency, cellular absorption, biodistribution, and toxicity profiles. Optimizing nanoparticle designs for improved tumor penetration and targeted delivery can be further aided by deep learning techniques. Additionally, AI-driven platforms facilitate virtual material screening, protein corona formation prediction, and optimal targeted ligand selection, all of which shorten development times and lower experimental expenses [86]. In precision oncology, combining AI-guided nanocarrier design with patient-specific genomic, proteomic, and imaging data may help create customized nanomedicine approaches based on unique tumor features. AI-assisted nanotechnology is anticipated to be crucial in developing next-generation multifunctional nanocarriers with enhanced efficacy, safety, and clinical translatability as computer power and biological datasets continue to grow [87].

7. CONCLUSION

Multifunctional nanocarriers have emerged as a transformative paradigm in the realm of cancer therapy, effectively addressing pivotal shortcomings associated with traditional treatment modalities, including lack of specificity, inherent toxicity, and the phenomenon of drug resistance. By amalgamating targeted drug delivery systems, sophisticated imaging techniques, and integrative therapeutic approaches within a singular framework, these nanocarriers provide unparalleled accuracy and effectiveness in the field of oncology. Various types of nanocarriers, including lipid-based, polymeric, inorganic, and hybrid formulations, have exhibited exceptional promise in augmenting drug bioavailability, curtailing systemic adverse effects, and facilitating real-time assessment of therapeutic efficacy. The implementation of functionalization methodologies, such as ligand-mediated active targeting, stimuli-responsive drug release mechanisms, and theranostic functionalities, further enhances the precision and versatility of these nanocarriers, thereby fostering the development of highly effective, individualized treatment regimens. The synergistic integration of chemotherapy, immunotherapy, gene therapy, and phototherapy within multifunctional nanocarriers has demonstrated significant potential in surmounting tumor heterogeneity and resistance, thereby amplifying therapeutic efficacy while mitigating negative side effects. Notwithstanding the considerable advancements achieved, obstacles persist in the clinical translation of these technologies, including challenges related to large-scale manufacturing, regulatory compliance, long-term biocompatibility assessments, and economic viability. Nevertheless, emerging paradigms such as artificial intelligence-driven design of nanocarriers, bioinspired delivery systems, and precision oncology methodologies are poised to expedite progress within this domain. The advent of personalized nanomedicine, which is capable of dynamically adjusting to distinct tumor characteristics and treatment responses, is anticipated to revolutionize cancer management strategies in the forthcoming years. Moreover, therapies aimed at metastasis and innovative approaches to counteract tumor evolution will be instrumental in enhancing survival rates and improving patient outcomes. As interdisciplinary collaborations persist in fostering innovation, the forthcoming generation of multifunctional nanocarriers holds tremendous potential to revolutionize cancer treatment, providing safer, more effective, and patient-centered therapeutic options. Addressing prevailing challenges through technological advancements and regulatory improvements will be essential for fully leveraging the capabilities of nanomedicine, ultimately propelling us closer to the aspirational goals of precision oncology and enduring cancer eradication.

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Author contribution

Devesh U. Kapoor: Writing – original draft, Methodology, Investigation, Data curation. Anil Pareek: Methodology, Data curation. Jigal Hirawala: Methodology, Data curation. Bhupendra G. Prajapati: Writing – original draft, Supervision, Project administration,Methodology, Data curation, Conceptualization. Kasitpong Thanawuth: Writing – review & editing, Methodology. Pornsak Sriamornsak: Writing – review & editing, Visualization, Supervision, Methodology, Funding acquisition, Data curation, Conceptualization.

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Conflicts of interest
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Ethics approval
Not applicable.

Declaration of generative AI in scientific writing:
During the preparation of this work, the authors used QuillBot and ChatGPT in order to improve the language and readability of the manuscript. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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REFERENCES

1. Sharma A, Sharma L, Nandy SK, Payal N, Yadav S, Vargas-De-La-Cruz C, et al. Molecular aspects and therapeutic implications of herbal compounds targeting different types of cancer. Molecules. 2023;28(2):750.
2. Mutebi I. Renewed insight into cancer mechanism and therapy: Advances, challenges, and future directions. Res Output J Public Health Med. 2024;4(1):8-12.
3. Liu B, Zhou H, Tan L, Siu KTH, Guan X-Y. Exploring treatment options in cancer: tumor treatment strategies. Signal Transduct Target Ther. 2024;9(1):175.
4. Nagaraju GP, Kamal MA. Challenges in the discovery of novel therapeutic agents for cancer treatment (Part IV). Curr Drug Metab. 2020;21(3):165-6.
5. Nikolaou M, Pavlopoulou A, Georgakilas AG, Kyrodimos E. The challenge of drug resistance in cancer treatment: A current overview. Clin Exp Metastasis. 2018;35(4):309-18.
6. Sapio L, Naviglio S. Innovation through tradition: the current challenges in cancer treatment. Cancers (Basel). 2022;14(21):5296.
7. Karnwal A, Sharma V, Kumar G, Jassim AY, Dohroo A, Sivanesan I. Transforming medicine with nanobiotechnology: Nanocarriers and their biomedical applications. Pharmaceutics. 2024;16(9):1114.
8. Hashim A, Fatima F. Exploring the transformative potential of hybrid nanoparticles in biomedical applications: relevance of hybrid nanoparticles. In: Technological applications of nano-hybrid composites. Hershey (PA): IGI Global; 2024. p. 226-46.
9. Nankya W. Nanotechnology in cancer treatment: Targeted drug delivery. Res Output J Public Health Med. 2024;4(2):38-42.
10. Pandey V, Pandey T. Chitosan-functionalized nanobubbles for precision oncology: Advances in targeted cancer therapeutics. J Mater Chem B. 2024;12:11076-88.
11. Erebor JO, Agboluaje EO, Perkins AM, Krishnakumar M, Ngwuluka N. Targeted hybrid nanocarriers as co-delivery systems for enhanced cancer therapy. Adv Pharm Bull. 2024;14(3):558-73.
12. Talwar A, Nayyar A, Anand S, Zahera M, Fatima F. A futuristic approach on the multifunctionality of nanomaterials: relevance of nanoparticles. In: Technological applications of nano-hybrid composites. Hershey (PA): IGI Global Scientific Publishing; 2024. p. 1-36.
13. Chudasma MP, Shah SA, Qureshi MHN, Shah N, Shah D, Trivedi R, et al. Brief insight on nanovesicular liposomes as drug-delivery carriers for medical applications. J Explor Res Pharmacol. 2023;8(3):222-36.
14. Misra SK, Pathak K. Functionalized liposomes: a nanovesicular system. In: Systems of nanovesicular drug delivery. Amsterdam: Elsevier; 2022. p. 83-101.
15. Mehrarya M, Gharehchelou B, Kabarkouhi Z, Ataei S, Esfahani FN, Wintrasiri MN, et al. Functionalized nanostructured bioactive carriers: Nanoliposomes, quantum dots, tocosome, and theranostic approach. Curr Drug Deliv. 2022;19(10):1001-11.
16. Jana M, Biswas UK, Patra CS, Debnath B, Sharma S, Naskar S. Solid lipid nanoparticles: A review of their biomedical applications and preparation. Pharm Nanotechnol. 2025;13(4):758-74.
17. Waghmare S, Palekar R, Potey L, Khedekar P, Sabale P, Sabale V. Solid lipid nanoparticles as an innovative lipidic drug delivery system. Pharm Nanotechnol. 2025;13(1):22-40.
18. Ferrentino N, Behroozi Kohlan T, Mehrtashfar S, Finne-Wistrand A, Pappalardo D. Dual-responsive nanoparticles for smart drug delivery: A NIR light-sensitive and redox-reactive PEG-PCL-based system. Biomacromolecules. 2024;25(12):7660-73.
19. Chen N, Li S, Li X, Long L, Yuan X, Hou X, et al. Functionalization of PEG-PMPC-based polymers for potential theranostic applications. Front Mater Sci. 2021;15(2):280-90.
20. Marecki EK, Oh KW, Knight PR, Davidson BA. Poly(lactic-co-glycolic acid) nanoparticle fabrication, functionalization, and biological considerations for drug delivery. Biomicrofluidics. 2024;18(5):051503.
21. Pandey P, Verma M, Lakhanpal S, Pandey S, Kumar MR, Bhat M, et al. An updated review summarizing the anticancer potential of poly(lactic-co-glycolic acid) (PLGA)-based curcumin, epigallocatechin gallate, and resveratrol nanocarriers. Biopolymers. 2025; 116(1):e23637.
22. Manandhar S, Sjöholm E, Bobacka J, Rosenholm JM, Bansal KK. Polymer-drug conjugates as nanotheranostic agents. J Nanotheranostics. 2021;2(1):63-81.
23. Oner E, Ilhan M, Gultekin HE, Karpuz M. Nanoconjugate formulations for enhanced drug delivery. In: Nayak AK, Hasnain MS, Laha B, Maiti S, editors. Advanced and modern approaches for drug delivery. Amsterdam: Elsevier; 2023. p. 441-91.
24. Pourali P, Neuhoferova E, Dzmitruk V, Svoboda M, Stodulkova E, Flieger M, et al. Bioproduced nanoparticles deliver multiple cargoes via targeted tumor therapy *in vivo*. ACS Omega. 2024;9(31):33789-804.
25. Duman H, Akdaşci E, Eker F, Bechelany M, Karav S. Gold nanoparticles: multifunctional properties, synthesis, and future prospects. Nanomaterials (Basel). 2024;14(22):1805.
26. Mondal S, Pan A. Quantum dots in biosensing, bioimaging, and drug delivery. In: Pan A, editor. Application of quantum dots in biology and medicine: recent advances. Singapore: Springer; 2022. p. 165-90.
27. Ali MK, Javaid S, Afzal H, Zafar I, Fayyaz K, ul Ain Q, et al. Exploring the multifunctional roles of quantum dots for unlocking the future of biology and medicine. Environ Res. 2023;232:116290.
28. Curcio F, Sanguedolce M, Filice L, Testa F, Catapano G, Giordano F, et al. Hybrid nanoparticles based on mesoporous silica and functionalized biopolymers as drug carriers for chemotherapeutic agents. Materials (Basel). 2024;17(15):3877.
29. Mengyuan H, Aixue L, Yongwei G, Qingqing C, Huanhuan C, Xiaoyan L, et al. Biomimetic nanocarriers in cancer therapy: Based on intercellular and cell-tumor microenvironment communication. J Nanobiotechnology. 2024;22(1):604.
30. Siddique S, Chow JC. Recent advances in functionalized nanoparticles in cancer theranostics. Nanomaterials (Basel). 2022;12(16):2826.

31. Zhang L, Jin D, Stenzel MH. Polymer-functionalized upconversion nanoparticles for light/imaging-guided drug delivery. Biomacromolecules. 2021;22(8):3168-201.
32. Khan N, Dhritlahre RK, Saneja A. Recent advances in dual-ligand targeted nanocarriers for cancer therapy. Drug Discov Today. 2022;27(8):2288-99.
33. Omidi Y, Barar J, Vandghanooni S, Eskandani M, Omidian H. Aptamers as smart ligands for the development of cancer-targeting nanocarriers. In: Kesharwani P, editor. Aptamers engineered nanocarriers for cancer therapy. Amsterdam: Elsevier; 2023. p. 103-39.
34. Onzi G, Guterres SS, Pohlmann AR, Frank LA. Active targeting of nanocarriers. In: Talevi A, editor. The ADME encyclopedia: a comprehensive guide on biopharmacy and pharmacokinetics. Cham: Springer; 2021. p. 1-13.
35. Sahu BP, Baishya R, Hatiboruah JL, Laloo D, Biswas N. A comprehensive review on different approaches for tumor targeting using nanocarriers and recent developments with special focus on multifunctional approaches. J Pharm Investig. 2022;52(5):539-85.
36. Majumder J, Minko T. Multifunctional and stimuli-responsive nanocarriers for targeted therapeutic delivery. Expert Opin Drug Deliv. 2021;18(2):205-27.
37. Kaushik N, Borkar SB, Nandanwar SK, Panda PK, Choi EH, Kaushik NK. Nanocarrier cancer therapeutics with functional stimuli-responsive mechanisms. J Nanobiotechnology. 2022;20(1):152.
38. AlSawaftah NM, Awad NS, Pitt WG, Husseini GA. pH-responsive nanocarriers in cancer therapy. Polymers (Basel). 2022;14(5):936.
39. Zarrabi A, Zarepour A, Khosravi A, Alimohammadi Z, Thakur VK. Synthesis of curcumin-loaded smart pH-responsive stealth liposome as a novel nanocarrier for cancer treatment. Fibers. 2021;9(3):19.
40. Kapalatiya H, Madav Y, Tambe VS, Wairkar S. Enzyme-responsive smart nanocarriers for targeted chemotherapy: An overview. Drug Deliv Transl Res. 2022;12(6):1293-305.
41. Zhao N, Zhu L, Liu M, He L, Xu H, Jia J. Enzyme-responsive lignin nanocarriers for triggered delivery of abamectin to control plant root-knot nematodes (*Meloidogyne incognita*). J Agric Food Chem. 2023;71(8):3790-9.
42. Song SJ, Choi JS. Enzyme-responsive amphiphilic peptide nanoparticles for biocompatible and efficient drug delivery. Pharmaceutics. 2022;14(1):143.
43. Zhang Y, García-Gabilondo M, Grayston A, Feiner IV, Anton-Sales I, Loiola RA, et al. PLGA protein nanocarriers with tailor-made fluorescence/MRI/PET imaging modalities. Nanoscale. 2020;12(8):4988-5002.
44. Deng H, Konopka CJ, Cross TWL, Swanson KS, Dobrucki LW, Smith AM. Multimodal nanocarrier probes reveal superior biodistribution quantification by isotopic analysis over fluorescence. ACS Nano. 2020;14(1):509-23.
45. Fernandes DA, Fernandes DD, Malik A, Gomes GNW, Appak-Baskoy S, Berndl E, et al. Multifunctional nanoparticles as theranostic agents for therapy and imaging of breast cancer. J Photochem Photobiol B. 2021;218:112110.
46. Calatayud DG, Neophytou S, Nicodemou E, Giuffrida SG, Ge H, Pascu SI. Nano-theranostics for the sensing, imaging and therapy of prostate cancers. Front Chem. 2022;10:830133.
47. Parveen S, Abira R, Paikray S, Sahoo L, Tripathy NS, Dilnawaz F. Recent advancement of nanotheranostics in cancer applications. Curr Drug Deliv. 2025;22(8):1073-91.
48. Priyadarshni N, Singh R, Mishra MK. Nanodiamonds: Next generation nano-theranostics for cancer therapy. Cancer Lett. 2024;587:216710.
49. Abrishami A, Bahrami AR, Saljooghi AS, Matin MM. Enhanced theranostic efficacy of epirubicin-loaded SPION@MSN through co-delivery of an anti-miR-21-expressing plasmid and ZIF-8 hybridization to target colon adenocarcinoma. Nanoscale. 2024;16(12):6215-40.
50. Fang H, Zhang L, Wu Y, Chen L, Deng Z, Zheng Z, et al. Carrier-free multifunctional nanomedicine for enhanced hyperthermic intraperitoneal chemotherapy against abdominal pelvic tumors. Chem Eng J. 2024;498:155781.
51. Cheng Y, Wang C, Wang H, Zhang Z, Yang X, Dong Y, et al. Combination of an autophagy inhibitor with immunoadjuvants and an anti-PD-L1 antibody in multifunctional nanoparticles for enhanced breast cancer immunotherapy. BMC Med. 2022;20(1):411.
52. Khalili-Hezarjaribi H, Bahrami AR, Saljooghi AS, Matin MM. Modified mesoporous silica nanocarriers containing superparamagnetic iron oxide nanoparticle, 5-fluorouracil or oxaliplatin, and metformin as a radiosensitizer significantly impact colorectal cancer radiation therapy. Int J Pharm. 2024;666:124838.
53. Martins SA, Costa RR, Brito A, Reis RL, Alves NM, Pashkuleva I, et al. Multifunctional calcium-based nanocarriers for synergistic treatment of triple-negative breast cancer. J Colloid Interface Sci. 2024;674:500-12.
54. Wu S, Chen Y, Wang K, Huang M, Yang L, Yang J, et al. Multifunctional mesoporous polydopamine nanoplatforms for synergistic photothermal-chemotherapy and enhanced immunotherapy in breast cancer treatment. Colloids Surf B Biointerfaces. 2025;248:114483.
55. Kaushik S, Thomas J, Panwar V, Ali H, Chopra V, Sharma A, et al. *In situ* biosynthesized superparamagnetic iron oxide nanoparticles (SPIONs) induce efficient hyperthermia in cancer cells. ACS Appl Bio Mater. 2020;3(2):779-88.
56. Zhang M, Song R, Liu Y, Yi Z, Meng X, Zhang J, et al. Calcium-overload-mediated tumor therapy by calcium peroxide nanoparticles. Chem. 2019;5(8):2171-82.
57. Reda M, Ngamcherdtrakul W, Nelson MA, Siriwon N, Wang R, Zaidan HY, et al. Development of a nanoparticle-based immunotherapy targeting PD-L1 and PLK1 for lung cancer treatment. Nat Commun. 2022;13(1):4261.
58. Maycotte P, Aryal S, Cummings CT, Thorburn J, Morgan MJ, Thorburn A. Chloroquine sensitizes breast cancer cells to chemotherapy independent of autophagy. Autophagy. 2012;8(2):200-12.
59. Garrido-Cano I, Adam-Artigues A, Lameirinhas A, Blandez JF, Candela-Noguera V, Lluch A, et al. Delivery of miR-200c-3p using tumor-targeted mesoporous silica nanoparticles for breast cancer therapy. ACS Appl Mater Interfaces. 2023;15(32):38323-34.
60. Tang H, Wang X, He L, Yuan Z, Han L. An injectable composite hydrogel containing polydopamine-coated curcumin nanoparticles and indoximod for the enhanced combinational chemo-photothermal-immunotherapy of breast tumors. Colloids Surf B Biointerfaces. 2024;244:114130.
61. Rodell CB, Arlauckas SP, Cuccarese MF, Garris CS, Li R, Ahmed MS, et al. TLR7/8-agonist-loaded nanoparticles promote the polarization of tumour-associated macrophages to enhance cancer immunotherapy. Nat Biomed Eng. 2018;2(8):578-88.
62. Park T, Amatya R, Min KA, Shin MC. Liposomal iron oxide nanoparticles loaded with doxorubicin for combined chemo-photothermal cancer therapy. Pharmaceutics. 2023;15(1):292.
63. Rajana N, Mounika A, Chary PS, Bhavana V, Urati A, Khatri D, et al. Multifunctional hybrid nanoparticles in diagnosis and therapy of breast cancer. J Control Release. 2022;352:1024-47.
64. Al-Thani AN, Jan AG, Abbas M, Geetha M, Sadasivuni KK. Nanoparticles in cancer theranostic and drug delivery: A comprehensive review. Life Sci. 2024;352:122899.
65. Gupta D, Roy P, Sharma R, Kasana R, Rathore P, Gupta TK. Recent nanotheranostic approaches in cancer research. Clin Exp Med. 2024;24(1):8.

66. Bilynsky C, Millot N, Papa A-L. Radiation nanosensitizers in cancer therapy: From preclinical discoveries to the outcomes of early clinical trials. Bioeng Transl Med. 2022;7(1):e10256.
67. Rashidi N, Davidson M, Apostolopoulos V, Nurgali K. Nanoparticles in cancer diagnosis and treatment: Progress, challenges, and opportunities. J Drug Deliv Sci Technol. 2024;95:105599.
68. Edis Z, Wang J, Waqas MK, Ijaz M, Ijaz M. Nanocarriers-mediated drug delivery systems for anticancer agents: An overview and perspectives. Int J Nanomedicine. 2021;16:1313-30.
69. Li Y, Wu Y, Chen J, Wan J, Xiao C, Guan J, et al. A simple glutathione-responsive turn-on theranostic nanoparticle for dual-modal imaging and chemo-photothermal combination therapy. Nano Lett. 2019;19(8):5806-17.
70. Guo R, Zhang L, Qian H, Li R, Jiang X, Liu B. Multifunctional nanocarriers for cell imaging, drug delivery, and near-IR photothermal therapy. Langmuir. 2010;26(8):5428-34.
71. Giri PM, Banerjee A, Layek B. A recent review on cancer nanomedicine. Cancers (Basel). 2023;15(8):2256.
72. Jacob EM, Huang J, Chen M. Lipid nanoparticle-based mRNA vaccines: a new frontier in precision oncology. Precis Clin Med. 2024;7(3):pbae017.
73. Bezelya A, Küçüktürkmen B, Bozkır A. Microfluidic devices for precision nanoparticle production. Micro (Basel). 2023;3(4):822-66.
74. Becker SJ, Curry JF. Testing the effects of peer socialization versus selection on alcohol and marijuana use among treated adolescents. Subst Use Misuse. 2014;49(3):234-42.
75. Csóka I, Ismail R, Jójárt-Laczkovich O, Pallagi E. Regulatory considerations, challenges and risk-based approach in nanomedicine development. Curr Med Chem. 2021;28(36):7461-76.
76. Foulkes R, Man E, Thind J, Yeung S, Joy A, Hoskins C. The regulation of nanomaterials and nanomedicines for clinical application: current and future perspectives. Biomater Sci. 2020;8(17):4653-64.
77. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2021;20(2):101-24.
78. Aflori M. Smart nanomaterials for biomedical applications: a review. Nanomaterials (Basel). 2021;11(2):396.
79. Xu X, Ho W, Zhang X, Bertrand N, Farokhzad O. Cancer nanomedicine: from targeted delivery to combination therapy. Trends Mol Med. 2015;21(4):223-32.
80. Thu HE, Haider M, Khan S, Sohail M, Hussain Z. Nanotoxicity induced by nanomaterials: A review of factors affecting nanotoxicity and possible adaptations. OpenNano. 2023;14:100190.
81. Shirzad M, Salahvarzi A, Razzaq S, Javid-Naderi MJ, Rahdar A, Fathi-Karkan S, et al. Revolutionizing prostate cancer therapy: Artificial intelligence-based nanocarriers for precision diagnosis and treatment. Crit Rev Oncol Hematol. 2025;208:104653.
82. Tripathi D, Hajra K, Maity D. Recent advancement of bio-inspired nanoparticles in cancer theragnostic. J Nanotheranostics. 2023;4(3):299-322.
83. Krzyszczyk P, Acevedo A, Davidoff EJ, Timmins LM, Marrero-Berrios I, Patel M, et al. The growing role of precision and personalized medicine for cancer treatment. Technology (Singap World Sci). 2018;6(3-4):79-100.
84. Fan D, Cao Y, Cao M, Wang Y, Cao Y, Gong T. Nanomedicine in cancer therapy. Signal Transduct Target Ther. 2023;8(1):293.
85. Cheng CH, Shi SS. Artificial intelligence in cancer: applications, challenges, and future perspectives. Mol Cancer. 2025;24(1):274.
86. Agrahari V, Choonara YE, Mosharraf M, Patel SK, Zhang F. The role of artificial intelligence and machine learning in accelerating the discovery and development of nanomedicine. Pharm Res. 2024;41(12):2289-97.
87. Dave P, Gandhi A, Dudhat K. Artificial intelligence in drug discovery and pharmaceutical development: machine learning approaches for molecular design, nanomedicine, and precision therapeutics. J Pharm Innov. 2026;21:392.