



Metal grafted graphene-based nanomaterials towards cancer theranostic efficacy

Prashant H. Gohil , Gopal Avashthi* 

School of Sciences, P P Savani University, Dhamdod, Kosamba, Surat 394125, Gujarat, India

***Correspondence:** Gopal Avashthi, School of Sciences, P P Savani University, NH 8, Dhamdod, Kosamba, Surat 394125, Gujarat, India. gopalavashthi@gmail.com

Academic Editor: Javier Reguera, University of Valladolid, Spain

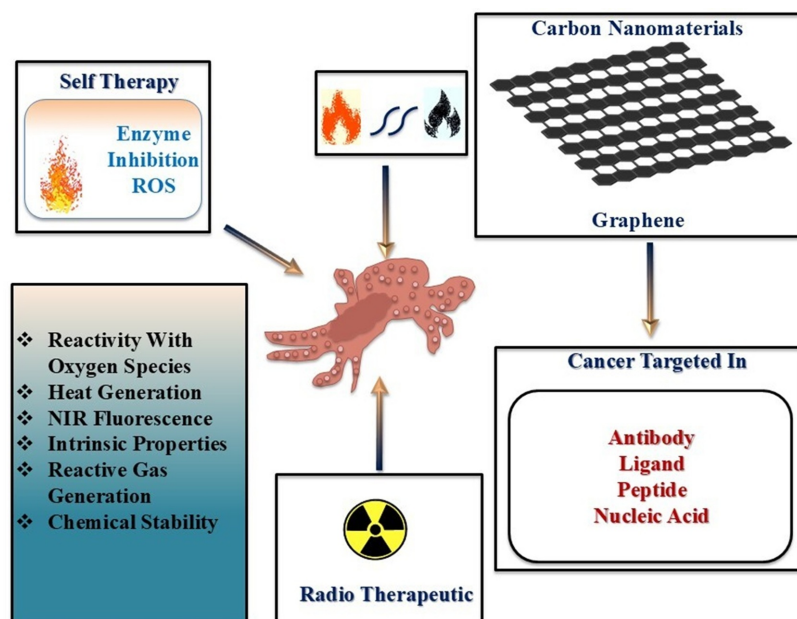
Received: June 27, 2025 **Accepted:** October 20, 2025 **Published:** November 10, 2025

Cite this article: Gohil PH, Avashthi G. Metal grafted graphene-based nanomaterials towards cancer theranostic efficacy. *Explor Target Antitumor Ther.* 2025;6:1002346. <https://doi.org/10.37349/etat.2025.1002346>

Abstract

Cancer is one of the leading global causes of mortality and morbidity, so it needs early diagnosis and therapies. Traditional diagnostic and therapeutic strategies are inadequate due to several limitations, such as poor specificity, systemic toxicity, and delays, while metal-grafted Gr nanostructures have emerged as promising theranostic platforms due to their unique electronic, optical, and structural properties. Metals such as Fe_3O_4 , Au, Ag, TiO_2 , Pd, Pt, Bi, ZnO, and Cu grafted onto the Gr surface impart electronic modulation, enhance surface area, flexibility, conductivity, reactivity, biomolecular interactions, and biosensing, thereby enabling precise biomarker detection, targeted drug delivery, imaging, and photothermal/photodynamic therapy (PTT/PDT). Eco-friendly synthesis using plant extracts and microbes offers a sustainable and biocompatible alternative to conventional chemical synthesis. However, challenges remain, such as homogenous doping, synthetic complexity, long-term safety, and clinical scalability. Innovations such as scalable, cost-effective, biocompatible nanofibers, nanopapers, microfluidic, and wearable biosensors are being explored by incorporating AI and advanced diagnostic tools for advanced biomedical devices. In vitro, half maximum inhibitory concentrations (IC_{50}) studies show that size- and dose-dependent nanohybrids such as Fe_3O_4 -Gr, $\gamma\text{-Fe}_2\text{O}_3$ -Gr, Au-Gr, and Bi-Gr exhibited safer responses at lower concentrations 10–200 $\mu\text{g}/\text{mL}$ across HBE, MCF-7, HeLa B, and LNCaP cell lines. Bi-Gr was tested on human liver cancer (HepG2) cell line, which exhibits higher reactivity despite a safer profile of Bi at $\sim 53\text{--}88 \mu\text{g}/\text{mL}$. Pd-Gr and Pt-Gr significantly reduced viability in prostate and ovarian cancer cells at 10–50 $\mu\text{g}/\text{mL}$, while ZnO-Gr, Ag-Gr, and Cu-Gr showed safer activity at lower concentrations on MCF-7. In vivo studies remain limited; median lethal dose (LD_{50}) values for Fe_3O_4 -Gr and $\gamma\text{-Fe}_2\text{O}_3$ -Gr were determined to be associated with rapid lethal biodistribution observed in the liver, lungs, and spleen. Metal-grafted Gr nanohybrids demonstrate immense potential for multifunctional cancer theranostics, though systematic in vivo toxicity studies still need to be explored by the intravenously administered route to lower the LD_{50} of nanohybrids for their clinical translation.





Graphical abstract. Multifaceted graphene-based nanomaterials for cancer therapy. ROS: reactive oxygen species; NIR: near-infrared.

Keywords

metal-grafted graphene nanohybrids, cancer theranostics, targeted drug delivery, reactive oxygen species (ROS)

Introduction

Cancer is a multifaceted disease characterized by the uncontrolled growth of abnormal cells [1]. WHO projected global cancer incidence statistics of 29.5 million new cases and 16.4 million deaths by 2040 [2]. The three most common cancers worldwide are breast, lung, and prostate cancers. Early diagnosis is crucial for improving treatment efficacy and patient survival [3, 4]. Conventional diagnostic methods, including X-rays, mammography, magnetic resonance imaging (MRI), CT scans, endoscopy, and Pap smears, are commonly employed but suffer from notable drawbacks such as lengthy procedures and high expenses. So, there is a need for specialized expertise, particularly in preventive early-stage cancer detection [5–8] (Figure 1). The discussions are focused notably on designing, properties, advantages, disadvantages, applications, and toxicity study of carbon-based materials like graphene oxide (GO), reduced GO (rGO), Gr quantum dots, carbon nanotubes (CNTs), and metal-grafted Gr-based nanomaterials for improving the cancer theranostics. Size and time-dependent cell viability studies of Au-Gr, Fe₃O₄-Gr, ZnO-Gr, Pd-Gr, Pt-Gr, Bi-Gr, Cu-Gr, and Ag-Gr, along with their mechanisms in cancer treatment, have strengthened the study. Au-Gr composites improve photothermal therapy (PTT) by converting near-infrared (NIR) light into heat to kill cancerous cells, while Fe₃O₄-Gr nanohybrids provide MRI and magnetically guided drug delivery. Additional systems, such as rGO-TiO₂, enable efficient reactive oxygen species (ROS) production for photodynamic therapy (PDT). Grafting several metals onto the Gr surface suggests multifunctional platforms for integrated cancer diagnosis and treatment simultaneously. Also, complex and scalable structural synthesis may create complications for achieving homogenous doped nanohybrids. However, their toxicity results at the laboratory scale may not be directly translated into clinical outcomes. Study highlights the rapidly growing interest of researchers in the field of Gr and its uses for cancer therapy, focusing on its primary applications in drug delivery, optical photothermal (PT) and photodynamic (PD) theranostics efficacy, which help to treat cancerous cells with real-time diagnosis [9]. However, the Gr-based materials have numerous potentials; several drawbacks persist. Its poor solubility, dispersibility, and low bioavailability in physiological media, unpredictable metabolization and drug elimination from the body, non-specific

selectivity, and side effects on normal tissues are drawbacks of these composites. These fundamental issues hinder its uniform distribution throughout the body and compromise its stability and presenting a key challenge to its successful clinical application. Moreover, there is a need to reframe the discussion of challenges, including cytotoxicity, synthesis scalability, and barriers to clinical translation. So, this ensures that the reported argument for the continued investigation of metal-grafted graphene-based nanomaterials is vibrant, compelling, and aligned with current scientific discourse. Improved performance of graphene-based nanocomposites is directly associated with their synergistic physicochemical properties, such as high surface area, excellent electron mobility, and inherent biocompatibility, which make it highly suitable for drug delivery and biosensing for efficient electrochemical sensors, catalytic, and therapeutic applications. $V_{3.6}Mo_{2.6}O_{16}$ -chitosan (Mv-CHT) nanostructure provides abundant electroactive sites and high electron mobility, in which CHT ensures colloidal stability and biocompatibility, thereby lowering the detection limit to the nanomolar range [10]. Similarly, the anti-cancer efficacy of $NiCO_2O_4/NiO$ nanoparticles (NPs) is primarily attributed to their ability to generate ROS, which induce mitochondrial dysfunction and apoptosis in breast cancer cells [11]. Cobalt oxide (CO_3O_4) NPs, on the other hand, act as catalyzers in the Fenton-like reaction, accelerating the decomposition of H_2O_2 into ($\cdot OH$) for improving tumor cell killing efficacy. The factors such as particle size, surface charge, doping consistency, and reproducibility influence biodistribution and cellular uptake through eco-friendly synthesis. Synergistic effects of metals-graphene interactions and their comparative analysis of systems (Au-Gr, Fe_3O_4 -Gr, ZnO-Gr, Pd-Gr, Pt-Gr, Bi-Gr, Cu-Gr, and Ag-Gr) have been included to contextualize clinical suitability.

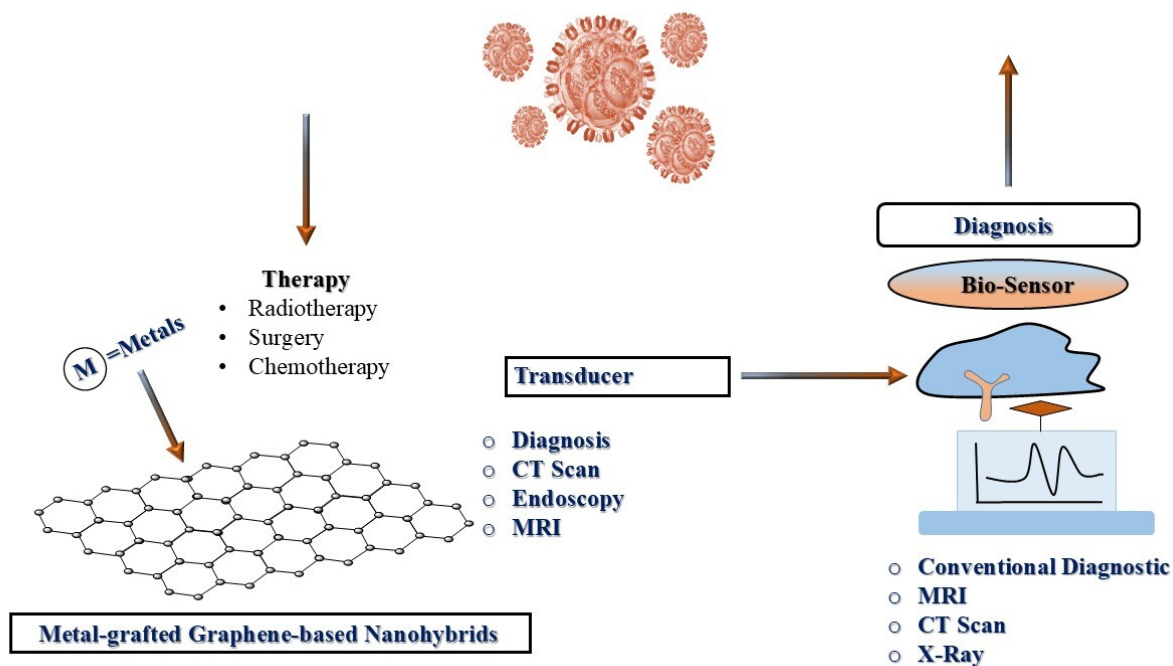


Figure 1. Graphene nanohybrids as multifunctional platforms for cancer diagnosis and therapy. MRI: magnetic resonance imaging.

Alternatively, biosensors have emerged as innovative diagnostic tools capable of accurately identifying cancer biomarkers. It incorporates a bio-recognition element that specifically interacts with a target biomarker and a transducer that is responsible for biological interaction as a detectable signal. Successful early diagnosis often depends on detecting tumor-specific biomarkers, including peptides, enzymes, proteins, nucleic acids, and antibodies, present in biological fluids like blood, urine, or sweat [12–16]. Their advantages include low cost, rapid response, sensitivity, and minimal sample requirements. Cancer treatment strategies include chemotherapy, radiotherapy, surgical interventions, or multimodal therapies [17–19]. Radiotherapy utilizes ionizing radiation to induce DNA damage in cancer cells and is delivered

externally through external beam radiotherapy (EBRT) or internally via brachytherapy and radionuclide injections [20, 21]. Although EBRT is widely used and effective, it lacks specificity and often affects surrounding healthy tissues. Brachytherapy, on the other hand, provides more localized treatment but depends on precise tumor targeting [22]. Despite being a fundamental component of cancer treatment and the non-selective nature of ionizing radiation poses a risk of collateral damage to normal cells. A cornerstone of ionizing radiation of cancer therapy primarily exerts its effects by generating ROS, which induce DNA damage such as single-strand breaks (SSBs) and, more critically, double-strand breaks (DSBs) that can lead to apoptosis if unrepaired [23–25]. However, its non-specific mechanism of action often results in collateral damage to healthy tissues. EBRT delivers radiation from an external source that directly affects both cancerous and surrounding normal cells, so this highlights the need for more targeted approaches. Despite advances in medical treatments, cancer remains the second leading cause of death globally, accounting for one in six deaths, with more than 70% of fatalities occurring in low- and middle-income countries. Risk factors include tobacco use, obesity, unhealthy diets, sedentary lifestyles, and alcohol consumption. The complexity of cancer is further amplified by its genetic heterogeneity, multidrug resistance, and tendency for recurrence. Its development is driven by numerous mutations often affecting tumor suppressor genes such as p53, which normally plays a crucial role in regulating apoptosis [26, 27]. Malignant cells often evade apoptotic mechanisms and proliferate rapidly, infiltrating surrounding tissues. Due to the diversity of genetic mutations, pinpointing a single causative mutation per cancer type is exceedingly difficult. Biosensors are classified based on their bio-receptor type: catalytic biosensors employ enzymes, while biosensors with affinity use antibodies, nucleic acids, or proteins [28, 29]. Used transducers in these devices act through optical, electrochemical, piezoelectric, or calorimetric mechanisms [30–32]. Enhancing biosensor performance involves metal-grafting using precursors such as Au-TiO₂, Ag-ZnO, Fe₃O₄, CuO, CeO₂, MnO₂, and MoS₂. It is investigated that several factors like synergistic mechanism, morphology control, phase transformations, and surface functionalization, show a critical role for enhancing biosensor performance. Hydrothermally engineered Cu₅V₂O₁₀ nanostructures delivered ultra-low detection limits for mefenamic acid due to optimized crystallinity and high surface area [33]. Such a method has been applied first time to synthesize such nanomaterials, which enables accurate control over their properties to make them highly selective for efficient sensing efficacy. Similarly, integrating chitosan with metal oxide nanostructures improved biosensing selectivity and stability in biological media [10]. Conventional analytical methods are effective, but they have disadvantages due to sluggishness, high cost, and complex action mechanisms for clinical trials. Several electrochemical sensors deliver an improved option because of their high sensitivity, rapid response, and low cost. Standard carbon paste electrodes (CPEs) have limitations of low sensitivity and slow electron transfer rates. So, there is a necessity for the incorporation of modifier materials compatible with the initial functionalities. Although transition metal oxides (such as TiO₂ and MoO₃) have been widely explored for excellent energy storage and electrochemical sensing efficacy, they have significant limitations for poor electrical conductivity and instability for electrochemical applications. These limitations have been resolved through new advanced approaches by replacing single metal oxides with hybrid oxide materials. Though another method has been applied to develop more complex materials, such as molybdenum vanadium oxide (M-V-O) by introducing vanadium into MoO₃ lattices. Such a type of structurally engineered material has superior electronic properties. However, there are major challenges in controlling the size, morphology, and phase transformations of these nanomaterials. But the research demonstrates a paradigm shift towards the broad concept by using metal oxides for designing and architecting multi-metal nanostructures. These materials improve electron transfer rates, surface reactivity, and signal amplification [34]. So, in this regard, Gr-based metal-grafted nanohybrids [35] have emerged as highly promising materials owing to their outstanding physicochemical properties [36–38]. Gr and its derivatives GO, rGO, and pristine Gr offer large surface area, high electrical conductivity, and versatile surface chemistry [39, 40]. This leads to significant improvement in their biomedical capabilities after grafting with metal oxides or noble metals. For example, GO-Au is used for plasmonic sensing and PTT, while rGO-TiO₂ is effective in ROS generation and imaging [41, 42]. GO-ZnO enables fluorescence-based detection, rGO-Fe₃O₄ supports magnetic targeting, Gr-CuO facilitates PDT, and rGO-CeO₂ offers antioxidant and enzyme-like functionalities [43]. Further have summarized data in Table 1.

These nanohybrids not only enhance the sensitivity and specificity of biosensors but also aid in targeted drug delivery and tumor-specific accumulation. The integration of nanotechnology further refines cancer treatment via synergistic platforms. Synthesis methods play a critical role in determining nanostructure morphology, stability, and biological efficacy in cancer treatment [11, 44]. Several studies have shown that synthetic routes such as sol-gel, hydrothermal, and chemical reduction methods control particle size and crystallinity precisely. However, the green synthesis approach using plant or biological extracts improves the eco-friendliness and biocompatibility of NPs though sometimes it may be expensive due to low reproducibility [45, 46]. Recently, green synthesis of magnetic NiCo₂O₄/NiO NPs from *Dactylopius coccus* extract and TbFeO₃/g-C₃N₄ nanocomposites using grape juice illustrates the relevance as capping and reducing agents for their significant influences on cytotoxicity outcomes at cancer cell lines because of the overlayer surface and functional groups modulation of nanocomposites. Co₃O₄ NPs show inclusive biomedical potential due to their antimicrobial, antioxidant, anticancer, and magnetic properties for their advantageous imaging therapy. *Crataegus microphylla* extract-capped silver NPs (CME@Ag-NPs) are synthesized for a capping agent using *Crataegus microphylla* extract as a green precursor, which demonstrates significant antibacterial activity and anticancer activity against multidrug-resistant strains and cytotoxicity in MCF-7 and AGS cancer cell lines, respectively. So, such metal NPs may extend their properties with Gr for improving their biological efficacy towards cancer theranostics because of synergizing the surface activity and functionalities of hybrid nanomaterials [47, 48]. Experimental methods like sol-gel and hydrothermal routes are efficient because of their important parameters, such as calcination, quality, and molar concentration of chelating ligands and cross-linker, pH buffer, reaction time, and biogenic reducing/capping agents and water-to-feedstock ratio (W/B ratio) help to increase the yield of reactions. A 10% polymeric matrix concentration of Mv-CHT provided optimum dispersibility and electrochemical performance. pH, AgNO₃ concentration, and reaction temperature may affect the size, morphology, and yield of Mv-CHT-Gr-based nanomaterial synthesis. Furthermore, the concept of architectural synthesis uses a sacrificial template as a novel approach to precisely control size, morphology, and phase of the resulting nano-electrocatalyst. These optimized parameters (such as temperature, pH, concentration, and solvent selectivity) are vital for achieving the desired properties of higher yield and uniform morphology, along with improved functionality like the structural integrity, surface area, stability, and biological activity which can be considered to measure the improved synthetic efficiency successfully. Integration of metals such as Au, Ag, Fe₃O₄, TiO₂, Pt, Pd, Cu, Bi, and ZnO onto graphene's edges not only enhances electrical conductivity, surface reactivity, and biosensing efficacy but also significantly improves and imparts optical, magnetic, catalytic, and biological properties to the less biologically available pristine graphene. Multifunctionalities not only improve PT and PD therapeutic efficacy but also enable multimodal imaging, biosensing, and controlled drug release. Such an integrated and synergized system creates a multifunctional theranostic platform capable of real-time diagnosis, precise tumor targeting, and simultaneous therapy. To overcome the limitations of conventional cancer treatments, researchers are emphasizing the synergy between metals and graphene for its transformative potential in advancing personalized and minimally invasive oncology. NPs exploit the enhanced permeability and retention (EPR) effect to facilitate passive tumor targeting. Surface engineering allows these particles to evade immune detection, carry therapeutic payloads, and release drugs in a controlled manner. Recent advances of such nanohybrids have illustrated the fundamental mechanisms, innovations, and their significance for cancer theranostics. Metal-grafted Gr-based nanomaterials have emerged as highly versatile single platforms for cancer theranostics, integrating multiple therapeutic and diagnostic functions. The multifaceted advantages of metal-grafted Gr-based nanomaterials make it a promising candidate for addressing major challenges of cancer therapy like low specificity, systemic toxicity, and drug resistance. However, an AI-based study highlights the revolution in breast cancer care through the synergy of AI and metal-grafted Gr-based nanomaterials. AI improves diagnostic accuracy with predictive modeling and improved imaging, while metal-grafted Gr-based nanomaterials ensure precise drug delivery with reduced toxicity. This synergy enables personalized treatments but faces challenges like data quality and model interpretability. Overcoming these challenges through multidisciplinary collaboration promises to significantly improve therapeutic efficacy and clinical outcomes. Gr-metal nanocomposites are especially effective in synergizing

multiple therapeutic approaches, including chemotherapy, gene therapy (GT), PTT, PDT, and radiotherapy [49–51]. These therapies yield better tumor targeting, reduce side effects, and improve treatment outcomes compared to monotherapies [52–54]. Brachytherapy, which involves radioactive seed implantation directly into the tumor, limits off-target effects but is restricted to accessible sites. Internal radiotherapy offers a solution by using radionuclide-labeled compounds that localize within tumors, delivering targeted irradiation. Therapeutic radionuclides are categorized based on emission types, primarily alpha (α) and beta-minus (β^-) particles [55, 56]. α particles, composed of helium nuclei, exhibit high linear energy transfer (LET) and a short penetration depth (28–100 μm), making them ideal for destroying hypoxic tumors [57–59]. They cause direct DNA DSBs that are independent of oxygen levels. β^- particles have longer penetration (2–10 mm) and lower LET, acting through ROS-mediated indirect DNA damage [60, 61]. Their ability to affect nearby cells enhances therapeutic reach towards cancer progression, which is driven by the accumulation of genetic mutations that provide malignant cells with an advantageous growth over normal cells [62]. Their resistance to apoptosis, coupled with invasive behavior, promotes metastasis, the spread of cancer to distant sites. In response to early and accurate detection, recent technological advancements have led to the development of Gr-based biosensors. Recent studies have reported significant progress in graphene-assisted phototherapies like gas-facilitated PTT, NIR laser-triggered photo-immunotherapy, and multifunctional hydrogel-based phototherapy [63, 64]. These developments demonstrate the versatility of graphene-based metal nanohybrids as integrated platforms that enable precise, light-triggered cancer therapy by simultaneously supporting multimodal diagnostics and real-time monitoring. PTT combination with nitric oxide gas therapy, PDT, chemotherapy, and immunotherapy has led to innovative multimodal nanoplatforms that enhance therapeutic efficacy by minimizing side effects [65]. Additionally, novel nanostructures such as antibody-conjugated carbon dots and hydrogel composites (AuNPs-CuCCDs@Gel), incorporating copper carbon dots (CuCCDs) and Au, have shown excellent PT and PD antibacterial performance. In particular, graphene-based electrochemical biosensors have shown great promise for oral cancer detection through salivary biomarkers. These sensors offer high sensitivity, specificity, and potential integration with AI and microfluidic platforms for personalized healthcare. Collectively, these advancements highlight that graphene-based systems and emerging phototherapy strategies are converging to drive the next generation of cancer theranostics [66, 67]. These devices integrate with a bio-receptor that specifically identifies cancer biomarkers with a transducer that converts this recognition into a measurable signal. The “seed and soil” theory suggests that metastatic cells colonize microenvironments conducive to their survival, while Ewing’s theory emphasizes anatomical pathways like blood vessels and lymphatics [68, 69]. Immune system surveillance and cellular traits influence metastasis, which remains incompletely understood. Surface functionalization of the transducer is critical to enhancing bio-recognition efficiency and is commonly achieved through covalent bonding, adsorption, or encapsulation techniques. However, it is prone to aggregation and instability in colloidal systems. To mitigate these issues, researchers have explored grafting metals and metal oxides onto Gr to enhance its performance.

Table 1. Examples of metal-grafted graphene nanocomposites.

Serial number	Metal-grafted graphene	Efficacy	Samples	Site of action	References
1	Silver-grafted graphene (Ag-Gr)	Enhances conductivity and plasmonic sensitivity for optical biosensing.	Plasma, urine, serum, and stool.	Biofluids or tissues.	[70, 71]
2	Gold-grafted graphene (Au-Gr)	Provides biocompatibility and facilitates biomolecule attachment.	Blood, serum, saliva, urine, cerebrospinal fluid, and tissue biopsies.	Blood vessels, tumor microenvironments, neural tissues, and implant surfaces.	[72]
3	Zinc oxide-grafted graphene (ZnO-Gr)	Offers high electron mobility and photocatalytic activity for electrochemical sensing.	Blood, plasma, urine, saliva, sweat, and tissue extracts.	Tumor tissues, blood vessels, and skin surfaces.	[73, 74]

Table 1. Examples of metal-grafted graphene nanocomposites. (continued)

Serial number	Metal-grafted graphene	Efficacy	Samples	Site of action	References
4	Iron oxide-graphene (Fe ₂ O ₃ -Gr or Fe ₃ O ₄ -Gr)	Adds magnetic properties for targeted detection and imaging.	Blood, plasma, serum, saliva, urine, cerebrospinal fluid, and biopsies.	Tumor tissues, lymph nodes, liver, and spleen.	[75]
5	Manganese dioxide-graphene (MnO ₂ -Gr)	Improves charge transfer and sensing efficiency.	Blood, plasma, serum, cerebrospinal fluid, saliva, urine, and biopsies.	Tumor tissues, neural tissues, implanted sensor interfaces, and blood vessels.	[76, 77]
6	Titanium dioxide-graphene (TiO ₂ -Gr)	Delivers stability and enhanced electron transport for biosensing.	Blood, plasma, serum, saliva, and urine.	Tumor microenvironments, blood vessels, skin surfaces, and implanted medical devices.	[78–80]
7	Cobalt oxide-graphene (Co ₃ O ₄ -Gr)	Provides strong redox properties for signal enhancement.	Blood, plasma, serum, saliva, biopsies, and urine.	Tumor tissues, neural tissues, implanted sensor locations, and blood vessels.	[81, 82]
8	Nickel oxide-graphene (NiO-Gr)	Displays high electrocatalytic activity for non-enzymatic sensors.	Blood, plasma, serum, urine, and saliva.	Blood vessels, skin surfaces, and tumor tissues.	[83, 84]
9	Zirconium dioxide-graphene (ZrO ₂ -Gr)	Known for chemical stability and effective biomolecule immobilization.	Plasma, blood, urine, serum, tissues, biopsies, and saliva.	Bone surfaces, blood vessels, and tumor tissues.	[85–87]
10	Copper oxide-graphene (CuO-Gr)	Boosts catalytic and conductive properties for fast signal generation.	Urine, serum, tissues, biopsies, plasma, saliva, and blood.	Wound sites, blood vessels, and tumor tissues.	[88–90]

These Gr-based hybrids enhance biosensor performance by increasing sensitivity, providing effective bio-receptor binding surfaces, and supporting multifunctional detection platforms. Their unique physicochemical properties, derived from both Gr and the grafted metal/oxide, enable more accurate, reliable, and efficient cancer diagnostics. By synergizing superior sensing capabilities with enhanced therapeutic delivery systems, these nanohybrids contribute significantly to early diagnosis, improved treatment outcomes, and the reduction of cancer-related mortality.

Multifaceted carbon nanomaterials for cancer nanomedicine

Carbon-based nanomaterials like fullerenes, CNTs, Gr, and Gr-derivatives have gained considerable attention in nanomedicine due to their NIR fluorescence activity, high chemical stability, and ease of functionalization [91–93]. These materials are focused on their role in nanomedicine. Therapeutic applications discussed targeted include chemotherapy, PTT/PDT, and multimodal cancer treatments. Diagnostic efficacies are emphasized in biosensing, biomarker detection, and advanced imaging techniques. In this context, theranostics show dual-function nanoplatfroms that combine therapy and diagnosis, including emerging AI-driven precision in oncology. Additionally, biocompatibility and toxicity of nanocomposites are considered as the key challenges and future perspectives for clinical trials. Recent advancements in the radiolabeling of carbon nanomaterials offer potential in cancer therapy extending beyond drug delivery to include targeted tumor destruction with minimal harm to healthy tissues [94, 95]. Their nano size enables conjugation with ligands, nucleic acids, peptides, or antibodies for selective targeting. Additionally, their intrinsic properties, such as ROS and the generation of heat or in situ reactive species, make them promising for direct therapeutic uses. Self-therapeutic nanomaterials have been effectively used to eliminate cancer cells with mechanisms involving ROS production and enzyme growth inhibition. For example, boron-containing materials are used in neutron capture therapy [96, 97]. Fullerenes (C₆₀) were discovered by Kroto et al. [98] in 1985. C₆₀ and bulkier forms of fullerenes like C₇₀ are spherical carbon nanostructures that are encapsulated with metals forming metallofullerenes [99]. These nanostructures can be radiolabeled and functionalized through known organic molecules [100]. CNTs are formed by rolling Gr sheets as single-walled CNTs (SWCNTs) or multi-walled CNTs (MWCNTs). Hence, their

large surface area and modifiability make them suitable with agents like polydopamine and polyethylene glycol, enhancing therapeutic efficacy for a long time [101, 102] (Figure 2).

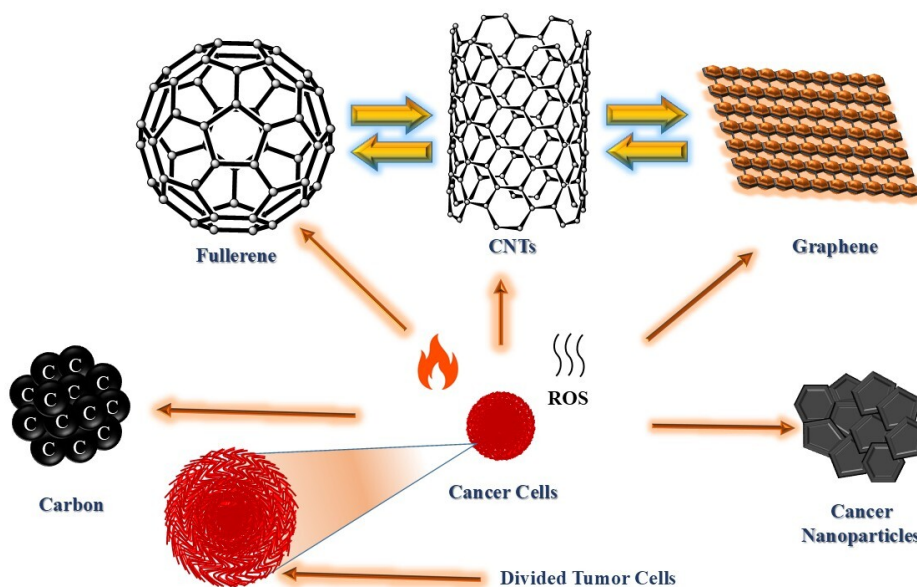


Figure 2. Carbon nanostructures for therapeutic uses by targeting tumor cells. CNTs: carbon nanotubes; ROS: reactive oxygen species.

Multifaceted metal grafted graphene for cancer therapeutics and diagnostics

Carbon-based nanostructures such as Gr, GO, rGO, and graphene quantum dots (GQDs) offer exceptional properties for biomedical applications [103–106]. These materials exhibit excellent mechanical strength, thermal stability, electrical conductivity, and tunable optical features, making them ideal for cancer therapy, biosensing, and imaging [107]. Gr is a single-layered hexagonal lattice of carbon atoms, which is synthesized using either top-down or bottom-up methods. Top-down techniques comprise mechanical exfoliation, liquid-phase dispersion, and electrochemical reduction, which break down bulk graphite into a number of single-layered graphene [108–110]. Bottom-up approaches comprise chemical vapor deposition (CVD), epitaxial growth, and molecular synthesis, assembling Gr from smaller chemical units [108, 111]. GO is synthesized through the most effective oxidative process using Hummer and Tour methods. So, the Tour method is considered safer and more eco-friendly [112, 113]. This method introduces oxygen-containing functional groups (hydroxyl, epoxy, carbonyl, and carboxyl) that enhance hydrophilicity and reactivity. However, these functional groups reduce electrical conductivity, which is restored by reducing GO into rGO using thermal, chemical, or electrochemical processes [114]. CVD allows the formation of uniform Gr films but requires sophisticated equipment and may also release toxic by-products. Alternatively, sustainable biosynthesis uses of biological agents like bacteria, fungi, or plant extracts to produce NPs under milder conditions [115, 116]. These biosynthesized nanomaterials are biocompatible and biodegradable, suitable for drug delivery, GT, imaging, and antibacterial applications [117, 118]. Further, inorganic metal grafting onto the surface of Gr also plays a significant role in cancer treatment. Platinum-based drugs (cisplatin, carboplatin, oxaliplatin), ruthenium complexes (NAMI-A, KP1019), and gold agents (auranofin) [119–121] are schematic highlights of an innovative and promising approach for cancer therapy using metal-functionalized Gr nanocomposites. Therapeutic efficacy of Gr is enhanced through the incorporation of metals such as ruthenium (Ru), gold (Au), platinum (Pt), and palladium (Pd), which significantly elevate its biomedical performance via a synergistic effect [122]. In vitro half maximum inhibitory concentrations (IC_{50}) studies indicate that the toxicity of Fe_3O_4 -Gr [123], γ - Fe_2O_3 -Gr, Au-Gr [124], and Bi-Gr [125] is dose and time-dependent. Studies on HBE, MCF-7, HeLa B, and LNCaP cell lines observed at variable concentrations of 10–200 μ g/mL, considering lower concentrations safer for cell viability studies [126]. Au-

Gr demonstrates possible selectivity against breast cancer, while Bi-Gr was tested on human liver cancer (HepG2) cell line, which exhibits higher reactivity despite safer consideration of Bi at ~53–88 µg/mL [125]. Pd-Gr and Pt-Gr composites show high reduction in cell viability on LNCaP prostate adenocarcinoma and human ovarian cancer cell lines, respectively, at doses of 10–50 µg/mL [126]. However, a 50% reduction of cell viability and proliferation has been observed at a higher concentration of 100 µg/mL of Pt-Gr [126]. Cell viability studies of ZnO-Gr at three different concentrations of 12.5 µg/mL, 25 µg/mL, 50 µg/mL [127], Ag-Gr at 2 µg/mL [128], and Cu-Gr at 50 µg/mL [129] have been reported with identifying the lower concentrations as safer for the breast cancer cell line MCF-7. In vivo toxicity studies for metal-grafted Gr-based materials are inadequate and often extrapolated from studies on specific Gr-based nanomaterials. The median lethal dose (LD₅₀) values for Fe₃O₄-Gr and γ-Fe₂O₃-Gr are under investigation [130]; while injected Fe₃O₄ nanomaterials exhibit an LD₅₀ of ~163.6 mg/kg in mice, and death is caused by fast circulation of nanomaterials in the liver, lung, and spleen. However, the associated proteins are denatured. Cell death is observed in the cardiac muscle along with kidney failure. Surface coatings of nanomaterials help mitigate these effects. Intravenously injected Pt NPs have established short-duration safety in rats at therapeutic doses of 10–20 mg/kg without detectable organ damage, while death is caused by the accumulation of Pt nanomaterials in the liver, spleen, kidney, and heart [131]. Au-Gr remains less studied, while Au NPs show size-dependent toxicity on mice, with 8–37 nm being most toxic [132]. Bi-Gr of ~33–38 nm size is usually considered cytotoxic on NRK52E and HepG2 cells, whereas Pd-Gr may induce dose-dependent cytotoxicity [125]. 20 nm ZnO, 8–20 nm Ag, and 23.5 nm Cu NPs characteristically exhibit a higher toxicity (LD₅₀) at 5–2,000 mg/kg, 413 mg/kg, and 5,000 mg/kg, respectively [131, 133, 134]. So, the toxicity of NPs depends on their doses and particle size, which causes mice death due to accumulation in the liver, kidney, spleen, and heart. So, there are several future in vivo opportunities that still need to be explored for the toxicity study by grafting of metal NPs with Gr by intravenously administered route to minimize the LD₅₀ of NPs. These modifications improve the Gr's drug-loading capacity, biological compatibility, and targeted delivery efficiency [135]. Once therapeutic agents are loaded, the resulting nanocarriers can be administered through oral or injectable routes, offering flexibility and patient-friendly treatment options. Upon targeting the tumor site, the nanocomposite effectively delivers the drug payload, enabling precise and controlled cancer cell elimination. This advanced system maximizes therapeutic outcomes while minimizing side effects, offering a powerful and efficient strategy for safe, targeted, and personalized cancer treatment [136]. Lab-scale studies and patient use primarily arise from the differences between experimental models and real physiological environments. While in vitro and in vivo studies are typically tested on specific cell lines or animal models. These conditions do not fully replicate the complexity of the human body, including metabolism alteration, immune responses, and other physiological functions. So, the obtained results at the laboratory scale may not directly translate into clinical outcomes. Therefore, there is a need to highlight the extensive preclinical and clinical studies before patient use (Figure 3).

These show promise in targeted drug delivery, PDT, and imaging due to their ROS-generating capability and high surface reactivity. There is a rapidly growing interest among researchers in the use of conjugate graphene-based nanomaterials for cancer treatment and diagnosis (theranostics). However, the graphene field is lacking in research from the oncophysics point of view. The primary application so far has been discovered for drug and gene delivery (73%), followed by PTT (32%), PDT (10%), and imaging (31%). Metal grafted graphene-based nanomaterials focus on these therapeutic techniques to treat the cancerous cells with minimal harm to healthy cells. Its potential lies in revolutionizing medicine's ability to diagnose and treat cancer simultaneously. However, oncophysics encompasses numerous onco-techniques, such as fluorescence, electron-beam imaging, and ultrasonography, which can be synergized with one or more therapeutic modalities. The synergize technology of Gr-based nanomaterials and onco-techniques may significantly enhance their opportunity to develop a real revolution in the field of medical therapy if conjugate diagnosis and therapy are simultaneously. Gr-based nanomaterials have achieved improved targeting ability, reduced side effects, and controlled release profiles [137]. GQDs, below 100 nm, possess strong fluorescence and a large surface area [138, 139]. Their surface can be easily functionalized with

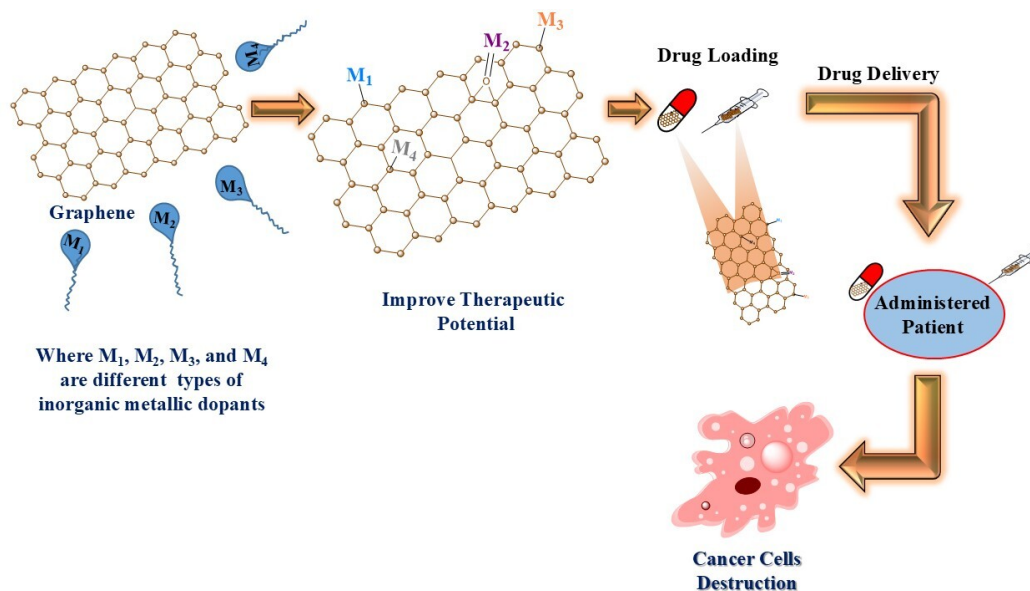


Figure 3. Catalyst-driven graphene functionalization for a smart drug delivery system.

biomolecules for selective recognition of cancer biomarkers. GQDs enable sensitive detection, early diagnosis, and therapeutic monitoring, positioning them as cutting-edge tools for on-site cancer diagnostics [140]. So, metal-grafted Gr is expected to enable highly reactive cancer treatments (Table 2), as well as improved diagnostic tools for early detection and continuous monitoring, ultimately leading to better therapeutic outcomes.

Metal-grafted graphene as a nanocarrier for targeted chemotherapy

The origin of chemotherapy traces back to the discovery that sulfur mustard gas irreversibly damaged bone marrow and produced unnecessary cell growth [141]. This observation raised concern for researchers to investigate similar types of compounds for targeting fast-growing cancerous cells. So, this effort led to the development of non-cytotoxic drugs that remain vital for cancer treatment. These medications are primarily intended to attack rapidly multiplying cancerous cells. However, it also harms healthy cells, which may cause to divide cells of hair follicles, bone marrow, and gastrointestinal tract resulting in side effects like fatigue, nausea, hair loss, and infertility [142] (Figure 4).

Alkylating agents are one of the earliest chemotherapeutic classes, disrupting the DNA into a number of divided cells, resulting in cell death [143, 144]. Another class of chemotherapeutic agents is microtubule stabilizers that interfere with cell division by preventing microtubule breakdown [145]. Such a type of supportive therapy helps manage these side effects, and most symptoms lessen after the end of treatment. Despite side effects of chemotherapy, it remains highly effective against testicular cancer, survival rate of up to 95%. So, nanotechnology-based drug delivery systems have been developed to make efficient, targeted, and reduced side effects therapy. Hyaluronic acid (HA)-hybrid NPs are targeted to breast cancerous stem cells through cluster of differentiation 44 (CD44) receptor interaction [146, 147]. These NPs are synthesized by binding of lipids with poly(lactide-co-glycolic acid) (PLGA), resulting in superior cellular uptake [148, 149]. Fluorescence microscopy and confocal imaging confirmed that HA-hybrid NPs had a 72% higher uptake than PLGA NPs and showed specificity due to CD44 binding [25, 150, 151]. Gr doped with metals like Au, Ag, and Fe_3O_4 enhances drug delivery and cancer therapeutic efficiency [152]. Au-Gr improves PTT by converting NIR light into heat, selectively destroying tumor cells [153–155]. AgNPs grafted onto Gr possess cytocompatibility and antimicrobial properties, increasing the effectiveness of chemotherapy while reducing infection risks during treatment [156–158]. Similarly, Fe_3O_4 -Gr composites offer dual functionality as drug carriers and magnetic agents for targeted therapy and imaging [159–162]. The integration of chemotherapy with cutting-edge nanotechnology and metal-grafted Gr-based materials holds a significant role for advancing personalized cancer treatment [163, 164]. Approaching studies are

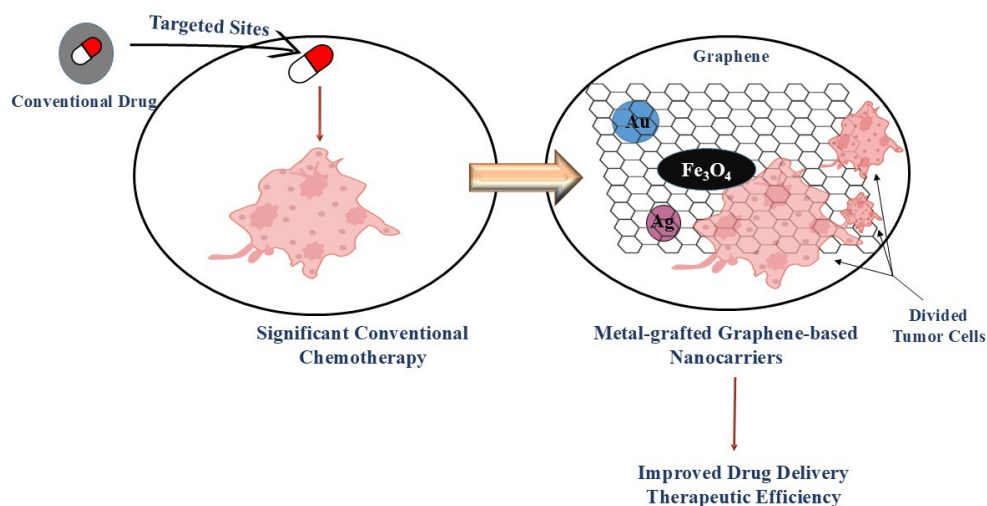


Figure 4. Improved drug targeting and tumor reduction using metal-grafted graphene.

likely to emphasize the creation of versatile nanocarriers that have the capability of delivering therapeutic agents with exceptional precision while simultaneously enabling real-time diagnosis and treatment monitoring. Ongoing investigations with Gr composites and metal-integrated nanostructures may lead to the development of intelligent environment-responsive drug delivery platforms tailored to the unique characteristics of tumor tissues [165]. Additionally, optimizing biocompatibility, minimizing adverse systemic effects, and ensuring scalable, cost-effective production will be essential for their transition into clinical settings. As these multidisciplinary innovations progress, they are poised to redefine cancer management by reducing harmful side effects, addressing drug resistance, and enhancing overall patient outcomes and longevity.

Metal-grafted graphene from targeted delivery to precision diagnostics

Cancer endures to claim millions of lives annually, making it one of the deadliest diseases worldwide. Over the past two decades, cancer research has grown rapidly and particularly with the emergence of NPs and their innovative applications. Numerous cancer types exist, including breast, lung, colorectal, and prostate cancers [166]. According to the American Cancer Society, breast, lung (non-small cell), prostate, colorectal, and melanoma are the most prevalent across U.S. states recently [167]. Metal-grafted Gr nanocomposites exhibit exceptional biomedical sensing and therapeutic applications. These are typically fabricated through techniques like electrochemical deposition, chemical reduction, sonication, microwave-assisted methods, and photo-induced reduction [168, 169]. A popular route involves the simultaneous reduction of metal precursors and oxidation of Gr, often stabilized using surfactants or co-ligands to prevent NP aggregation and improve dispersion [170]. In breast cancer therapy, conventional chemotherapeutics have progressed, but nonspecific toxicity toward healthy cells remains a significant challenge. To overcome this, cyclodextrin (CD)-functionalized polyurethane (PU)-based magnetic NPs were synthesized [171]. Initially, a dipodal silane carbamate-functionalized alkoxy silane (ECA) was formed by reacting 3-aminopropyltriethoxysilane and γ -glycidoxypropyltrimethoxysilane in dimethyl sulfoxide under nitrogen to avoid moisture [172]. Fe₃O₄ NPs were prepared via the coprecipitation method using ferric and ferrous chlorides with ammonium hydroxide at pH 11 [173–175]. Then, these were coated with ECA and combined with PU to form Fe₃O₄-ECA-PU-CD nanocomposites [171, 172]. The resulting system has been demonstrated to enhance targeted and reduced off-target toxicity in breast cancer therapy. Furthermore, arginine-glycine-aspartic acid (RGD)-doxorubicin (DOX) loaded solid lipid NPs (SLNPs) showed 5.58-fold higher plasma exposure, indicating improved drug delivery efficiency [25, 176, 177]. Among plasmonic NPs, AuNPs are widely used due to their resistance to oxidation with a strong surface reactivity and biocompatibility [178]. So, rGO-Au composites were synthesized via a hydrothermal method, which were used in electrochemical sensors for

detecting prostate-specific antigen (PSA) with a detection limit of 50 pg/mL [179–181]. Additionally, doping of Fe₃O₄ and ZnO with Gr enhances both magnetic targeting and ROS-mediated cancer cell apoptosis [182, 183]. These multifunctional nanocomposites serve as promising platforms for drug delivery, imaging, and PTT or oxidative therapy. Thereby, these improve therapeutic precision and efficacy. However, an AI-based study highlights the revolution in breast cancer care through the synergy of AI and metal-grafted Gr-based nanomaterials. AI improves diagnostic accuracy with predictive modeling and improved imaging, while metal-grafted Gr-based nanomaterials ensure precise drug delivery with reduced toxicity [184]. This synergy enables personalized treatments, but it has challenges like data quality and model interpretability. Overcoming these challenges through multidisciplinary collaboration promises to significantly improve therapeutic efficacy and clinical outcomes. Researchers are focusing on the development of intelligent stimuli-responsive nanomaterials that are capable of performing real-time tumor detection, monitoring, and therapy [185]. Functionalization of Gr-based nanostructures with targeting moieties and immunomodulatory agents offers promising avenues for advancing individualized cancer care. Continued efforts to enhance their biocompatibility, minimize adverse effects, and ensure reproducibility are critical for clinical translation. Regulatory validation and extensive clinical testing will be essentially required to transition these advanced nanotherapeutics from laboratory research to standard medical applications, ultimately improving patient outcomes and survival rates.

Metal-grafted graphene for cancer theranostics and biosensing

The integration of metallic elements onto Gr structures substantially elevates their performance across diverse domains such as biosensing, energy storage, and electronic devices. Also, these composites substantially enhance the efficacy of cancer imaging and treatment strategies. Gr integrated with iron oxide improves MRI precision diagnosis, while Au nanorods on Gr surface increase photoacoustic responses [186]. Au and Bi-doped Gr enhance CT scan resolution, while the ZnO and CuO onto the Gr surface facilitate fluorescence-based tracking of cancer cells [178, 187, 188]. These nanocarriers are functionalized with specific ligands, such as antibodies and folic acid (FA), to achieve targeted drug delivery to tumor sites in therapeutic applications [189, 190]. Au- and Ag-coated Gr absorbs near infrared light and converts it into localized heat for cancer cell ablation (removal of dead tissues) in PTT [155, 191]. Also, metal oxides on the Gr surface generate ROS light exposure, leading to cancer cell apoptosis in PDT [192]. These multifunctional systems also enable dual action approaches by combining drug release and light-triggered therapies, thereby enhancing treatment precision, reducing toxicity, and improving therapeutic outcomes.

Metal-grafted Gr frameworks substantially boost electrochemical biosensing efficacy by optimizing charge transfer and catalytic performance [193]. This advancement facilitates recognition of highly sensitive markers of cancer targets like proteins [PSA, human epidermal growth factor receptor 2 (HER2), and cancer antigen 125 (CA-125)], genetic materials (DNA and miRNA), and extracellular components such as exosomes and circulating tumor cells [194, 195]. Au-GO hybrid sensor equipped with aptamers can detect PSA at exceptionally low (femtomolar) concentrations [196]. Au-Gr strengthens surface plasmon effects, thereby enabling accurate label-free detection for optical biosensing efficacy [197]. Light-sensitive metal-grafted Gr improves fluorescence detection precision [198]. Additionally, Ag-Gr nanocomposites show sensing ability for enzymes to improve colorimetric assays that visually identify cancer biomarkers [197]. Furthermore, metal-grafted Gr nanohybrid nanostructures are being integrated as rapid diagnostic tools offering immediate, non-invasive, and on-site monitoring of cancer markers, which is an essential feature for timely diagnosis and therapeutic evaluation [199]. Metal-grafted Gr provides dual functionality to enable both therapeutic and diagnostic capabilities within a single platform as an ideal configuration for advanced cancer theranostics. Their extensive surface area supports the effective attachment of biomolecules such as enzymes, DNA, or antibodies, which is crucial for selective targeting and biosensing ability [200]. Chemical surface properties of Gr are readily modifiable to improve its biocompatibility. These nanohybrids also exhibit responsiveness to external stimuli during pH and temperature variations, light exposure, thereby facilitating controlled therapeutic delivery and adaptable diagnostic responses [201].

Metal-grafted Gr nanocomposites demonstrate significant potential in cancer diagnosis and treatment, but several key challenges persist that require attention. Issues such as potential long-term toxicity and limited biocompatibility of certain formulations remain a concern [202]. Furthermore, consistent synthesis with higher stability and reproducibility presents difficulties in large-scale production and clinical approval, which endures a significant hurdle [203]. However, there is a strong authoritative process for advanced multifunctional platforms of precisely controlled drug delivery. Crucially, thorough *in vivo* evaluations and rigorous clinical trials will be essentially required to facilitate their safe and successful integration into real-world medical applications. Future studies should prioritize the development of environmentally sustainable and scalable manufacturing approaches.

Biocompatible metal-grafted graphene for targeted cancer drug delivery

Conventional chemotherapy is often constrained by widespread toxicity, suboptimal target sites, and the emergence of resistance. To overcome these challenges, metal-grafted Gr has analysed advanced solutions for site-specific delivery as anticancer agents. Among these, Gr-based nanostructures have gained significant attention owing to their exceptional physical and chemical properties [204]. The incorporation of biocompatible metals onto the Gr surface further expands its therapeutic potential by drug loading efficiency, which enables controlled drug release, supporting imaging applications, and facilitating selective accumulation in tumor tissues [205].

Gr derivatives such as GO, rGO, and GQDs are well-suited for drug delivery owing to their extensive surface area, ability to interact with aromatic compounds, tunable surface chemistry, and robust mechanical properties [92]. Pristine Gr has less biocompatibility, while it has numerous reactive groups for its surface modifications. However, oxidation, reduction, and metal-grafting are performed to augment its biomedical functionality [206]. Metals are grafted onto the Gr surface via chemical reduction, electrochemical methods, or green synthesis using natural agents [207]. Metals incorporation confers distinct therapeutic advantages. Au mediates PTT, imaging diagnostic, which also enhances biocompatibility along with antimicrobial properties and ROS generation. Pt facilitates dual-action chemotherapy. Fe₃O₄ enables magnetic and MRI-based imaging. ZnO promotes pH-triggered drug release and induces cell apoptosis. Cu aids PDT and inhibits tumor angiogenesis [43, 161]. These functional enhancements confirm metal-grafted Gr as a versatile platform for targeted and multimodal cancer treatment.

Metal-functionalized Gr platforms support both passive target through the EPR effect and active target via ligands such as FA, HA, antibodies, aptamers, and peptides that specifically recognize receptors of cancer cells, thereby improving delivery precision [208]. These nanocarriers exhibit excellent drug-loading capacity and enable stimulus-responsive drug release triggered by acidic pH, thermal energy (photothermal effect), redox environments, or external magnetic fields, allowing for localized therapy with minimal adverse effects [209].

Integrating chemotherapy with additional treatment modalities like PTT (utilizing Au or Cu), PDT (with ZnO or CuO), or magnetically assisted therapy significantly improves therapeutic efficacy, which promotes cancer cell apoptosis and mitigates drug resistance [210]. Experimental results demonstrate biocompatibility with normal cells, efficient uptake by tumor cells, prolonged and controlled drug release, substantial tumor growth inhibition, and support for non-invasive imaging techniques. Notable metal includes Au-GO-DOX and Gr-Fe₃O₄-FA-Cisplatin systems [211].

Realizing the future necessitates clinical translation of these nanoplatforms make efforts to focus on sustainable and scalable production using natural templates or plant-derived materials. This leads to the development of advanced multifunctional systems enabling controlled drug delivery, imaging treatment, and comprehensive *in vivo* testing across diverse cancer models. For this, the implementation of regulatory-compliant strategies for safety, toxicity, and pharmacokinetic assessment is essentially required [212].

Metal-grafted graphene precision oncology for smart cancer detection and therapy

Inorganic metal-grafted Gr nanocomposites have emerged as multifunctional platforms in the field of precision oncology, which offer dual functions for cancer detection as well as treatment within a single engineered nanosystem [53]. Integration of metals such as Au, Ag, Pd, and Fe₃O₄ or γ-Fe₂O₃ onto Gr shows high electrical conductivity, large surface area, and functional tunability with the unique optical, magnetic, and catalytic properties [213, 214]. Au-Gr and Ag-Gr nanocomposites enable ultra-sensitive detection of cancer biomarkers through chemical sensing mechanisms that enhance optical and electrochemical signals [215, 216]. Also, catalysts such as Pt and Pd improve signal transduction in electrochemical assays [217]. Additionally, superparamagnetic metal oxide Fe₃O₄ NPs serve as MRI contrasting agents, which facilitate early tumor localization [218]. Upon successful identification and accumulation in malignant tissues, the homogeneous and heterogeneous metal-grafted Gr platform can initiate targeted therapy through photothermal ablation, magnetic hyperthermia, or stimuli-responsive drug release, triggered by environmental prompts such as pH, redox gradients, or external fields [219]. Functionalization with ligands like FA or monoclonal antibodies enhances tumor selectivity to ensure precise delivery and minimize systemic toxicity [220]. Furthermore, real-time imaging efficacy of nanostructures allows for dynamic treatment monitoring, which enables adaptive therapeutic strategies. This convergence of sensitive diagnostics and localized therapy within a single system exemplifies the core principles of cancer theranostics, paving the way for more effective, tailored, and minimally invasive clinical interventions.

Table 2. Comparison between Metal-grafted graphene as a nanocarrier for targeted chemotherapy and Metal-grafted graphene precision oncology for smart cancer detection and therapy.

Serial number	Metal-grafted graphene	Application in cancer theranostics	References
1	Au-Gr	Chemotherapeutic drugs	[155, 156, 159]
2	Fe ₃ O ₄ -Gr	Detecting biomarkers (PSA)	[178, 183, 187, 188]
3	Ag-Gr	Imaging (CT) biosensing	[43, 156, 161]
4	ZnO-Gr	Biocompatible non-toxic nanocarrier	[161, 182, 188]
5	Pd-Gr	Ultra-sensitive and real-time monitoring	[212, 216]
6	Bi-Gr	MRI	[178, 187, 188]
7	Cu-Gr	Photodynamic	[209]
8	γ-Fe ₂ O ₄ -Gr	Photothermal	[213]
9	Pt-Gr	Dual-action chemotherapy	[216, 217]

PSA: prostate-specific antigen; MRI: magnetic resonance imaging.

Conclusions

Metal-grafted graphene nanohybrids synergize progression in cancer theranostics by diagnostic precision with therapeutic efficacy. Several mono-metallic graphene-based nanomaterials, such as Fe₃O₄-Gr, γ-Fe₂O₃-Gr, Au-Gr, Bi-Gr, Pd-Gr, Pt-Gr, ZnO-Gr, and Cu-Gr, have been studied for their cancer theranostics efficacy, but many are still being explored. However, new opportunities are emerging for the synthesis of bimetallic/trimetallic graphene-based nanomaterials for pursuing their unexplained efficacy. Additionally, these nanocomposites are being explored for in vitro and in vivo toxicity testing to justify their cancer theranostics efficacy. Mono-metallic graphene-based nanomaterials have shown positive in vitro anticancer responses with measured IC₅₀ values at lower concentrations. However, in most cases, in vivo assessments with measured LD₅₀ cause death of the organisms even after the nanomaterials have been successfully delivered into the cells. These nanohybrids offer multiple theranostic capabilities, including real-time biosensing, targeted drug delivery, multimodal imaging, and therapeutic modalities such as PT, PD, and immunotherapy. Their large surface area, tunable electronic properties, and enhanced catalytic or plasmonic activity make them strong candidates for next-generation nanomedicine as minimally invasive and personalized cancer treatments. Environment-friendly biogenic synthetic methods further strengthen their ecological and clinical applicability. Future studies must focus on a systematic in vivo analysis of biodistribution and clearance, the development of scalable and eco-friendly synthetic methods, and the

integration of these nanohybrids with AI, microfluidics, and wearable devices for real-time monitoring and adaptive therapies. AI and metal-grafted graphene nanomaterials are synergistically transforming breast cancer therapy by enhancing diagnostic accuracy, enabling personalized treatment, and supporting targeted drug delivery with reduced toxicity and real-time monitoring. While challenges in data accessibility, manufacturing scalability, and lengthy clinical trials persist, a multidisciplinary, collaborative approach is essential for advancing oncology therapy. Furthermore, improved tumor cell selectivity through functionalization and targeted drug release, along with synergistic use with immunotherapy, can further enhance efficacy, reduce systemic toxicity, and decrease the overall patient burden.

Abbreviations

CD: cyclodextrin

CD44: cluster of differentiation 44

CNTs: carbon nanotubes

CVD: chemical vapor deposition

DOX: doxorubicin

DSBs: double-strand breaks

EBRT: external beam radiotherapy

ECA: carbamate-functionalized alkoxy silane

EPR: enhanced permeability and retention

FA: folic acid

GO: graphene oxide

GQDs: graphene quantum dots

GT: gene therapy

HA: hyaluronic acid

HepG2: human liver cancer

IC₅₀: half maximum inhibitory concentrations

LD₅₀: median lethal dose

LET: linear energy transfer

MRI: magnetic resonance imaging

Mv-CHT: V_{3.6}Mo_{2.6}O₁₆-chitosan

NIR: near-infrared

NPs: nanoparticles

PD: photodynamic

PDT: photodynamic therapy

PLGA: poly(lactic-co-glycolic acid)

PSA: prostate-specific antigen

PT: photothermal

PTT: photothermal therapy

PU: polyurethane

rGO: reduced graphene oxide

ROS: reactive oxygen species

Declarations

Author contributions

PHG: Conceptualization, Data curation, Writing—original draft. GA: Conceptualization, Supervision, Validation, Writing—review & editing. Both authors read and approved the submitted version.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

Copyright

© The Author(s) 2025.

Publisher's note

Open Exploration maintains a neutral stance on jurisdictional claims in published institutional affiliations and maps. All opinions expressed in this article are the personal views of the author(s) and do not represent the stance of the editorial team or the publisher.

References

1. Nenclares P, Harrington KJ. The biology of cancer. *Medicine*. 2020;48:67–72. [DOI]
2. Parham GP, Mathieu KM, YouYou TG, Hicks ML, Henry-Tillman R, Mutombo A, et al. Establishing women's cancer care services in a fragile, conflict and violence affected ecosystem in Africa. *Ecancermedicalscience*. 2021;15:1231. [DOI] [PubMed] [PMC]
3. Zhang C, Zhang C, Wang Q, Li Z, Lin J, Wang H. Differences in Stage of Cancer at Diagnosis, Treatment, and Survival by Race and Ethnicity Among Leading Cancer Types. *JAMA Netw Open*. 2020;3:e202950. [DOI] [PubMed] [PMC]
4. Hamilton W, Walter FM, Rubin G, Neal RD. Improving early diagnosis of symptomatic cancer. *Nat Rev Clin Oncol*. 2016;13:740–9. [DOI] [PubMed]
5. Fass L. Imaging and cancer: a review. *Mol Oncol*. 2008;2:115–52. [DOI] [PubMed] [PMC]
6. Pulumati A, Pulumati A, Dwarakanath BS, Verma A, Papineni RVL. Technological advancements in cancer diagnostics: Improvements and limitations. *Cancer Rep (Hoboken)*. 2023;6:e1764. [DOI] [PubMed] [PMC]

7. Hussain S, Mubeen I, Ullah N, Shah SSUD, Khan BA, Zahoor M, et al. Modern Diagnostic Imaging Technique Applications and Risk Factors in the Medical Field: A Review. *Biomed Res Int.* 2022;2022: 5164970. [DOI] [PubMed] [PMC]
8. Jaglan P, Dass R, Duhan M. Breast Cancer Detection Techniques: Issues and Challenges. *J Inst Eng India Ser B.* 2019;100:379–86. [DOI]
9. Fernandez-Fernandez A, Manchanda R, McGoron AJ. Theranostic applications of nanomaterials in cancer: drug delivery, image-guided therapy, and multifunctional platforms. *Appl Biochem Biotechnol.* 2011;165:1628–51. [DOI] [PubMed] [PMC]
10. Monsef R, Salavati-Niasari M. Electrochemical sensor based on a chitosan-molybdenum vanadate nanocomposite for detection of hydroxychloroquine in biological samples. *J Colloid Interface Sci.* 2022;613:1–14. [DOI] [PubMed]
11. Goudarzi M, Salavati-Niasari M, Amiri M. Effective induction of death in breast cancer cells with magnetite NiCo₂O₄/NiO nanocomposite. *Composites, Part B.* 2019;166:457–63. [DOI]
12. Broza YY, Zhou X, Yuan M, Qu D, Zheng Y, Vishinkin R, et al. Disease Detection with Molecular Biomarkers: From Chemistry of Body Fluids to Nature-Inspired Chemical Sensors. *Chem Rev.* 2019; 119:11761–817. [DOI] [PubMed]
13. Maruvada P, Wang W, Wagner PD, Srivastava S. Biomarkers in molecular medicine: cancer detection and diagnosis. *Biotechniques.* 2005;38:9–15. [DOI] [PubMed]
14. Sarhadi VK, Armengol G. Molecular Biomarkers in Cancer. *Biomolecules.* 2022;12:1021. [DOI] [PubMed] [PMC]
15. Das S, Dey MK, Devireddy R, Gartia MR. Biomarkers in Cancer Detection, Diagnosis, and Prognosis. *Sensors (Basel).* 2023;24:37. [DOI] [PubMed] [PMC]
16. Hanash SM, Baik CS, Kallioniemi O. Emerging molecular biomarkers–blood-based strategies to detect and monitor cancer. *Nat Rev Clin Oncol.* 2011;8:142–50. [DOI] [PubMed]
17. Cancer chemotherapy, immunotherapy, and biotherapy: principles and practice. In: Chabner BA, Longo DL, editors. 6th ed. Philadelphia: Wolters Kluwer; 2019.
18. Abbas Z, Rehman S. An Overview of Cancer Treatment Modalities. In: Shahzad HN, editor. *Neoplasm.* London: IntechOpen; 2018. [DOI]
19. Surwade SP, Smirnov SN, Vlassioux IV, Unocic RR, Veith GM, Dai S, et al. Water desalination using nanoporous single-layer graphene. *Nat Nanotechnol.* 2015;10:459–64. [DOI] [PubMed]
20. Sadeghi M, Enferadi M, Shirazi A. External and internal radiation therapy: past and future directions. *J Cancer Res Ther.* 2010;6:239–48. [DOI] [PubMed]
21. Koka K, Verma A, Dwarakanath BS, Papineni RVL. Technological Advancements in External Beam Radiation Therapy (EBRT): An Indispensable Tool for Cancer Treatment. *Cancer Manag Res.* 2022; 14:1421–9. [DOI] [PubMed] [PMC]
22. Xue H, Qiu B, Wang H, Jiang P, Sukocheva O, Fan R, et al. Stereotactic Ablative Brachytherapy: Recent Advances in Optimization of Radiobiological Cancer Therapy. *Cancers (Basel).* 2021;13:3493. [DOI] [PubMed] [PMC]
23. Olive PL. The role of DNA single- and double-strand breaks in cell killing by ionizing radiation. *Radiat Res.* 1998;150:S42–51. [PubMed]
24. Saini S, Gurung P. A comprehensive review of sensors of radiation-induced damage, radiation-induced proximal events, and cell death. *Immunol Rev.* 2025;329:e13409. [DOI] [PubMed] [PMC]
25. Bajpai S, Tiwary SK, Sonker M, Joshi A, Gupta V, Kumar Y, et al. Recent Advances in Nanoparticle-Based Cancer Treatment: A Review. *ACS Appl Nano Mater.* 2021;4:6441–70. [DOI]
26. Muñoz-Fontela C, Mandinova A, Aaronson SA, Lee SW. Emerging roles of p53 and other tumour-suppressor genes in immune regulation. *Nat Rev Immunol.* 2016;16:741–50. [DOI] [PubMed] [PMC]
27. Kirsch DG, Kastan MB. Tumor-suppressor p53: implications for tumor development and prognosis. *J Clin Oncol.* 1998;16:3158–68. [DOI] [PubMed]

28. Nangare SN, Patil PO. Affinity-Based Nanoarchitected Biotransducer for Sensitivity Enhancement of Surface Plasmon Resonance Sensors for *In Vitro* Diagnosis: A Review. *ACS Biomater Sci Eng*. 2021; 7:2–30. [DOI] [PubMed]
29. Leech D. Affinity biosensors. *Chem Soc Rev*. 1994;23:205–13. [DOI]
30. Roy SS, Raj D. Sensors and modern transducers. In: McLaughlin J, Mathur A, Tauseef SM, editors. *Emerging Sensors for Environmental Monitoring*. Elsevier; 2025. pp. 43–55. [DOI]
31. Piezoelectric Transducers and Applications. In: Vives AA, editor. 2nd ed. Springer Berlin, Heidelberg; 2008. [DOI]
32. Yadav S, Saini A, Devi R, Lata S. Transducers in Biosensors. In: Kumar P, Dash SK, Ray S, Parween S, editors. *Biomaterials-Based Sensors: Recent Advances and Applications*. Singapore: Springer Nature Singapore; 2023. pp. 101–25. [DOI]
33. Monsef R, Salavati-Niasari M. Hydrothermal architecture of $\text{Cu}_5\text{V}_2\text{O}_{10}$ nanostructures as new electro-sensing catalysts for voltammetric quantification of mefenamic acid in pharmaceuticals and biological samples. *Biosens Bioelectron*. 2021;178:113017. [DOI] [PubMed]
34. Krishnan SK, Singh E, Singh P, Meyyappan M, Nalwa HS. A review on graphene-based nanocomposites for electrochemical and fluorescent biosensors. *RSC Adv*. 2019;9:8778–881. [DOI] [PubMed] [PMC]
35. Geim AK, Novoselov KS. The rise of graphene. *Nat Mater*. 2007;6:183–91. [DOI] [PubMed]
36. Nanotemplating: Engineering nanocomposite materials for the future. In: Yiu HHP, editor. 1st ed. Jenny Stanford Publishing; 2024.
37. Nasrollahzadeh M, Sajjadi M, Soufi GJ, Iravani S, Varma RS. Nanomaterials and Nanotechnology-Associated Innovations against Viral Infections with a Focus on Coronaviruses. *Nanomaterials (Basel)*. 2020;10:1072. [DOI] [PubMed] [PMC]
38. Fernandes DM. POM -based Electrocatalysts for Inorganic Water Contaminants and Hydrogen Peroxide Reduction. In: Fernandes DM, editor. *Applied Polyoxometalate-based Electrocatalysis*. John Wiley & Sons, Ltd; 2025. pp. 123–59. [DOI]
39. Razaq A, Bibi F, Zheng X, Papadakis R, Jafri SHM, Li H. Review on Graphene-, Graphene Oxide-, Reduced Graphene Oxide-Based Flexible Composites: From Fabrication to Applications. *Materials (Basel)*. 2022;15:1012. [DOI] [PubMed] [PMC]
40. Singh RK, Kumar R, Singh DP. Graphene oxide: strategies for synthesis, reduction and frontier applications. *RSC Adv*. 2016;6:64993–5011. [DOI]
41. Zhao Y, Sang L, Wang C. Thermoplasmonics effect of Au-rGO/TiO₂ photoelectrode in solar-hydrogen conversion. *Sol Energy Mater Sol Cells*. 2023;255:112306. [DOI]
42. Safavipour M, Kharaziha M, Amjadi E, Karimzadeh F, Allafchian A. TiO₂ nanotubes/reduced GO nanoparticles for sensitive detection of breast cancer cells and photothermal performance. *Talanta*. 2020;208:120369. [DOI] [PubMed]
43. Ko YC, Fang HY, Chen DH. Fabrication of Ag/ZnO/reduced graphene oxide nanocomposite for SERS detection and multiway killing of bacteria. *J Alloys Compd*. 2017;695:1145–53. [DOI]
44. Baladi M, Amiri M, Amirinezhad M, Abdulsahib WK, Pishgouii F, Golshani Z, et al. Green synthesis and characterization of terbium orthoferrite nanoparticles decorated with *g*-C₃N₄ for antiproliferative activity against human cancer cell lines (Glioblastoma, and Neuroblastoma). *Arabian J Chem*. 2023; 16:104841. [DOI]
45. Bayati-Komitaki N, Ganduh SH, Alzaidy AH, Salavati-Niasari M. A comprehensive review of Co₃O₄ nanostructures in cancer: Synthesis, characterization, reactive oxygen species mechanisms, and therapeutic applications. *Biomed Pharmacother*. 2024;180:117457. [DOI] [PubMed]
46. Rahimkhoei V, Alzaidy AH, Abed MJ, Rashki S, Salavati-Niasari M. Advances in inorganic nanoparticles-based drug delivery in targeted breast cancer theranostics. *Adv Colloid Interface Sci*. 2024;329:103204. [DOI] [PubMed]

47. Mortazavi-Derazkola S, Ebrahimzadeh MA, Amiri O, Goli HR, Rafiei A, Kardan M, et al. Facile green synthesis and characterization of *Crataegus microphylla* extract-capped silver nanoparticles (CME@Ag-NPs) and its potential antibacterial and anticancer activities against AGS and MCF-7 human cancer cells. *J Alloys Compd.* 2020;820:153186. [DOI]
48. Rahimkhoei V, Akbari A, Jassim AY, Hussein UA, Salavati-Niasari M. Recent advances in targeting cancer stem cells by using nanomaterials. *Int J Pharm.* 2025;673:125381. [DOI] [PubMed]
49. Wang Y, Li J, Li X, Shi J, Jiang Z, Zhang CY. Graphene-based nanomaterials for cancer therapy and anti-infections. *Bioact Mater.* 2022;14:335–49. [DOI] [PubMed] [PMC]
50. Younis MR, He G, Lin J, Huang P. Graphene-semiconductor nanocomposites for cancer phototherapy. *Biomed Mater.* 2021;16:022007. [DOI] [PubMed]
51. Al-Ani LA, AlSaadi MA, Kadir FA, Hashim NM, Julkapli NM, Yehye WA. Graphene- gold based nanocomposites applications in cancer diseases; Efficient detection and therapeutic tools. *Eur J Med Chem.* 2017;139:349–66. [DOI] [PubMed]
52. Liu B, Zhou H, Tan L, Siu KTH, Guan X. Exploring treatment options in cancer: Tumor treatment strategies. *Signal Transduct Target Ther.* 2024;9:175. [DOI] [PubMed] [PMC]
53. Chehelgerdi M, Chehelgerdi M, Allela OQB, Pecho RDC, Jayasankar N, Rao DP, et al. Progressing nanotechnology to improve targeted cancer treatment: overcoming hurdles in its clinical implementation. *Mol Cancer.* 2023;22:169. [DOI] [PubMed] [PMC]
54. Zhao W, Wang L, Zhang M, Liu Z, Wu C, Pan X, et al. Photodynamic therapy for cancer: mechanisms, photosensitizers, nanocarriers, and clinical studies. *MedComm (2020).* 2024;5:e603. [DOI] [PubMed] [PMC]
55. Sharma S, Pandey MK. Radiometals in Imaging and Therapy: Highlighting Two Decades of Research. *Pharmaceuticals (Basel).* 2023;16:1460. [DOI] [PubMed] [PMC]
56. Stokke C, Kvasheim M, Blakkisrud J. Radionuclides for Targeted Therapy: Physical Properties. *Molecules.* 2022;27:5429. [DOI] [PubMed] [PMC]
57. Maucksch U, Runge R, Oehme L, Kotzerke J, Freudenberg R. Radiotoxicity of alpha particles versus high and low energy electrons in hypoxic cancer cells. *Nuklearmedizin.* 2018;57:56–63. [DOI] [PubMed]
58. Pouget J, Constanzo J. Revisiting the Radiobiology of Targeted Alpha Therapy. *Front Med (Lausanne).* 2021;8:692436. [DOI] [PubMed] [PMC]
59. Tafreshi NK, Doligalski ML, Tichacek CJ, Pandya DN, Budzevich MM, El-Haddad G, et al. Development of Targeted Alpha Particle Therapy for Solid Tumors. *Molecules.* 2019;24:4314. [DOI] [PubMed] [PMC]
60. Sridharan DM, Asaithamby A, Bailey SM, Costes SV, Doetsch PW, Dynan WS, et al. Understanding cancer development processes after HZE-particle exposure: roles of ROS, DNA damage repair and inflammation. *Radiat Res.* 2015;183:1–26. [DOI] [PubMed]
61. Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, et al. Oxidative Stress: Harms and Benefits for Human Health. *Oxid Med Cell Longev.* 2017;2017:8416763. [DOI] [PubMed] [PMC]
62. Adeel M, Duzagac F, Canzonieri V, Rizzolio F. Self-Therapeutic Nanomaterials for Cancer Therapy: A Review. *ACS Appl Nano Mater.* 2020;3:4962–71. [DOI]
63. Li M, Yin B, Gao C, Guo J, Zhao C, Jia C, et al. Graphene: Preparation, tailoring, and modification. *Exploration (Beijing).* 2023;3:20210233. [DOI] [PubMed] [PMC]
64. Mahalakshmi D, Nandhini J, Meenaloshini G, Karthikeyan E, Karthik KK, Sujaritha J, et al. Graphene nanomaterial-based electrochemical biosensors for salivary biomarker detection: A translational approach to oral cancer diagnostics. *Nano TransMed.* 2025;4:100073. [DOI]
65. Liang S, Liu Y, Zhu H, Liao G, Zhu W, Zhang L. Emerging nitric oxide gas-assisted cancer photothermal treatment. *Exploration (Beijing).* 2024;4:20230163. [DOI] [PubMed] [PMC]

66. Fan Y, Zhang R, Shi J, Tian F, Zhang Y, Zhang L, et al. Mild near-infrared laser-triggered photo-immunotherapy potentiates immune checkpoint blockade via an all-in-one theranostic nanoplatform. *J Colloid Interface Sci.* 2025;678:1088–103. [DOI] [PubMed]
67. Lv J, Qiu Y, Pan L, Zhang X, Li M, Yin X. Photothermal/photodynamic antibacterial hydrogel embedded with copper carbon dots and Au nanoparticles. *Nano TransMed.* 2024;3:100034. [DOI]
68. Piris A, Mihm MC Jr. Mechanisms of metastasis: seed and soil. *Cancer Treat Res.* 2007;135:119–27. [DOI] [PubMed]
69. Arvelo F, Sojo F, Cotte C. Cancer and the metastatic substrate. *Ecancermedicalsecience.* 2016;10:701. [DOI] [PubMed] [PMC]
70. Francis R, Joy N, Aparna EP, Vijayan R. Polymer Grafted Inorganic Nanoparticles, Preparation, Properties, and Applications: A Review. *Polym Rev.* 2014;54:268–347. [DOI]
71. Bhattacharjee S, George M, Shim Y, Bernaurdshaw N, Das J. Electropotential-Inspired Star-Shaped Gold Nanoconfined Multiwalled Carbon Nanotubes: A Proof-of-Concept Electrosensing Interface for Lung Metastasis Biomarkers. *ACS Appl Bio Mater.* 2022;5:5567–81. [DOI] [PubMed]
72. Cacheux J, Bancaud A, Leichlé T, Cordelier P. Technological Challenges and Future Issues for the Detection of Circulating MicroRNAs in Patients With Cancer. *Front Chem.* 2019;7:815. [DOI] [PubMed] [PMC]
73. Afshari Babazad M, Foroozandeh A, Abdouss M, SalarAmoli H, Afshari Babazad R, Hasanzadeh M. Recent progress and challenges in biosensing of carcinoembryonic antigen. *Trends Analyt Chem.* 2024;180:117964. [DOI]
74. Ghanbari SM, Kerahrodi ZR, Kolvari E, Koukabi N, Dashtian K. Graphene-Based Photocatalysts in Sensing, Energy, and Therapeutic Applications. In: Johan MR, Naseer MN, Ikram M, Zaidi AA, Abdul Wahab Y, editors. *Graphene-Based Photocatalysts: From Fundamentals to Applications.* Cham: Springer Nature Switzerland; 2024. pp. 611–42. [DOI]
75. Rahman M. Magnetic Resonance Imaging and Iron-oxide Nanoparticles in the era of Personalized Medicine. *Nanotheranostics.* 2023;7:424–49. [DOI] [PubMed] [PMC]
76. Xia HY, Li BY, Zhao Y, Han YH, Wang SB, Chen AZ, et al. Nanoarchitected manganese dioxide (MnO₂)-based assemblies for biomedicine. *Coord Chem Rev.* 2022;464:214540. [DOI]
77. Handbook on Nanobiomaterials for Therapeutics and Diagnostic Applications. In: Anand K, Saravanan M, Chandrasekaran B, Kanchi S, Panchu SJ, Chen Q, editors. Elsevier; 2021. [DOI]
78. Jafari S, Mahyad B, Hashemzadeh H, Janfaza S, Gholikhani T, Tayebi L. Biomedical Applications of TiO₂ Nanostructures: Recent Advances. *Int J Nanomedicine.* 2020;15:3447–70. [DOI] [PubMed] [PMC]
79. Wu S, Weng Z, Liu X, Yeung KWK, Chu PK. Functionalized TiO₂ Based Nanomaterials for Biomedical Applications. *Adv Funct Mater.* 2014;24:5464–81. [DOI]
80. Kumar N, Chauhan NS, Mittal A, Sharma S. TiO₂ and its composites as promising biomaterials: a review. *Biomaterials.* 2018;31:147–59. [DOI] [PubMed]
81. Amu-Darko JNO. Advancing Breath Biomarker Detection with Chemiresistive Metal Oxide Nanostructures: A Pathway to Next-Generation Diagnostic Tools. *Anal Sens.* 2025;5:e202400111. [DOI]
82. Rayappan JBB, Nesakumar N, Ramachandra Bhat L, Gumpu MB, Babu KJ, Jayalatha JBB A. Electrochemical Biosensors with Nanointerface for Food, Water Quality, and Healthcare Applications. In: *Bioelectrochemical Interface Engineering.* John Wiley & Sons, Ltd; 2019. pp. 431–68. [DOI]
83. Akter R, Saha P, Shah SS, Shaikh MN, Aziz MA, Ahammad AJS. Nanostructured Nickel-based Non-enzymatic Electrochemical Glucose Sensors. *Chem Asian J.* 2022;17:e202200897. [DOI] [PubMed]

84. Kaur G, Singh NK, Gupta K. Enzymatic Biosensor Platforms for Non-infectious Diseases: Diagnosis of Metabolic Disorders. In: Patra S, Kundu D, Gogoi M, editors. *Enzyme-based Biosensors: Recent Advances and Applications in Healthcare*. Singapore: Springer Nature Singapore; 2023. pp. 173–215. [DOI]
85. Teymourian H, Salimi A, Firoozi S, Korani A, Soltanian S. One-pot hydrothermal synthesis of zirconium dioxide nanoparticles decorated reduced graphene oxide composite as high performance electrochemical sensing and biosensing platform. *Electrochim Acta*. 2014;143:196–206. [DOI]
86. Patil NA, Kandasubramanian B. Biological and mechanical enhancement of zirconium dioxide for medical applications. *Ceram Int*. 2020;46:4041–57. [DOI]
87. Bannunah AM. Biomedical Applications of Zirconia-Based Nanomaterials: Challenges and Future Perspectives. *Molecules*. 2023;28:5428. [DOI] [PubMed] [PMC]
88. Zomorodian Esfahani M, Soroush E, Mohammadnejad S, Helli M, Malek Khachatourian A, Toprak MS, et al. Copper oxide/graphene-based composites: Synthesis methods, appliances and recent advancements. *FlatChem*. 2024;47:100716. [DOI]
89. Zhou R, Zheng Y, Hulicova-Jurcakovic D, Qiao SZ. Enhanced electrochemical catalytic activity by copper oxide grown on nitrogen-doped reduced graphene oxide. *J Mater Chem A Mater*. 2013;1:13179–85. [DOI]
90. Zhang L, Loh XJ, Ruan J. Photoelectrochemical nanosensors: An emerging technique for tumor liquid biopsy. *J Photochem Photobiol A Chem*. 2022;429:113942. [DOI]
91. Liu W, Speranza G. Functionalization of Carbon Nanomaterials for Biomedical Applications. *C*. 2019;5:72. [DOI]
92. Patel KD, Singh RK, Kim HW. Carbon-based nanomaterials as an emerging platform for theranostics. *Mater Horiz*. 2019;6:434–69. [DOI]
93. Lemaître TA, Burgoyne AR, Ooms M, Parac-Vogt TN, Cardinaels T. Inorganic Radiolabeled Nanomaterials in Cancer Therapy: A Review. *ACS Appl Nano Mater*. 2022;5:8680–709. [DOI]
94. Saleem J, Wang L, Chen C. Carbon-Based Nanomaterials for Cancer Therapy via Targeting Tumor Microenvironment. *Adv Healthc Mater*. 2018;7:e1800525. [DOI] [PubMed]
95. Chen D, Dougherty CA, Zhu K, Hong H. Theranostic applications of carbon nanomaterials in cancer: Focus on imaging and cargo delivery. *J Control Release*. 2015;210:230–45. [DOI] [PubMed]
96. Hu K, Yang Z, Zhang L, Xie L, Wang L, Xu H, et al. Boron agents for neutron capture therapy. *Coord Chem Rev*. 2020;405:213139. [DOI]
97. Barth RF, Mi P, Yang W. Boron delivery agents for neutron capture therapy of cancer. *Cancer Commun (Lond)*. 2018;38:35. [DOI] [PubMed] [PMC]
98. The Fullerenes. In: Kroto HW, Fischer JE, Cox DE, editors. Pergamon; 1993. [DOI]
99. Panda J, Patra T, Panda PK, Sahu R, Tripathy BC, Biswal A. Fullerenes: Synthesis and Applications. In: *New Forms of Carbon*. 1st ed. Apple Academic Press; 2024.
100. Li Z, Conti PS. Radiopharmaceutical chemistry for positron emission tomography. *Adv Drug Deliv Rev*. 2010;62:1031–51. [DOI] [PubMed]
101. Li Z, Liu Z, Sun H, Gao C. Superstructured Assembly of Nanocarbons: Fullerenes, Nanotubes, and Graphene. *Chem Rev*. 2015;115:7046–117. [DOI] [PubMed]
102. Alfei S, Reggio C, Zuccari G. Carbon Nanotubes as Excellent Adjuvants for Anticancer Therapeutics and Cancer Diagnosis: A Plethora of Laboratory Studies Versus Few Clinical Trials. *Cells*. 2025;14:1052. [DOI] [PubMed] [PMC]
103. Gaur M, Misra C, Yadav AB, Swaroop S, Maolmhuaidh FÓ, Bechelany M, et al. Biomedical Applications of Carbon Nanomaterials: Fullerenes, Quantum Dots, Nanotubes, Nanofibers, and Graphene. *Materials (Basel)*. 2021;14:5978. [DOI] [PubMed] [PMC]
104. Maiti D, Tong X, Mou X, Yang K. Carbon-Based Nanomaterials for Biomedical Applications: A Recent Study. *Front Pharmacol*. 2019;9:1401. [DOI] [PubMed] [PMC]

105. Innocenzi P, Stagi L. Carbon-based antiviral nanomaterials: graphene, C-dots, and fullerenes. A perspective. *Chem Sci*. 2020;11:6606–22. [DOI] [PubMed] [PMC]
106. Maktedar SS, Mehetre SS, Avashthi G, Singh M. *In situ* sonochemical reduction and direct functionalization of graphene oxide: A robust approach with thermal and biomedical applications. *Ultrason Sonochem*. 2017;34:67–77. [DOI] [PubMed]
107. Kim CH, Lee SY, Rhee KY, Park SJ. Carbon-based composites in biomedical applications: a comprehensive review of properties, applications, and future directions. *Adv Compos Hybrid Mater*. 2024;7:55. [DOI]
108. Gutiérrez-Cruz A, Ruiz-Hernández AR, Vega-Clemente JF, Luna-Gazcón DG, Campos-Delgado J. A review of top-down and bottom-up synthesis methods for the production of graphene, graphene oxide and reduced graphene oxide. *J Mater Sci*. 2022;57:14543–78. [DOI]
109. Sumdani MG, Islam MR, Yahaya ANA, Safie SI. Recent advances of the graphite exfoliation processes and structural modification of graphene: a review. *J Nanopart Res*. 2021;23:253. [DOI]
110. Agrawal A. Top-down strategies for achieving high-quality graphene: Recent advancements. *J Ind Eng Chem*. 2025;142:103–26.
111. Zhou X, Yu G. Preparation Engineering of Two-Dimensional Heterostructures *via* Bottom-Up Growth for Device Applications. *ACS Nano*. 2021;15:11040–65. [DOI] [PubMed]
112. Zhu Y, James DK, Tour JM. New routes to graphene, graphene oxide and their related applications. *Adv Mater*. 2012;24:4924–55. [DOI] [PubMed]
113. Deemer EM, Paul PK, Manciu FS, Botez CE, Hodges DR, Landis Z, et al. Consequence of oxidation method on graphene oxide produced with different size graphite precursors. *Mater Sci Eng B Solid State Mater Adv Technol*. 2017;224:150–7. [DOI]
114. Zhang P, Li Z, Zhang S, Shao G. Recent Advances in Effective Reduction of Graphene Oxide for Highly Improved Performance Toward Electrochemical Energy Storage. *Energy Environ Mater*. 2018;1:5–12. [DOI]
115. Gupta D, Boora A, Thakur A, Gupta TK. Green and sustainable synthesis of nanomaterials: Recent advancements and limitations. *Environ Res*. 2023;231:116316. [DOI] [PubMed]
116. Pandit C, Roy A, Ghotekar S, Khusro A, Islam MN, Emran TB, et al. Biological agents for synthesis of nanoparticles and their applications. *J King Saud Univ Sci*. 2022;34:101869. [DOI]
117. Harish V, Tewari D, Gaur M, Yadav AB, Swaroop S, Bechelany M, et al. Review on Nanoparticles and Nanostructured Materials: Bioimaging, Biosensing, Drug Delivery, Tissue Engineering, Antimicrobial, and Agro-Food Applications. *Nanomaterials (Basel)*. 2022;12:457. [DOI] [PubMed] [PMC]
118. Pourmadadi M, Ahmadi I, Taromi P, Rahdar A, Fathikarkan S, Bradley Z, et al. Review—Cancer Biosensing Using Plasmonic Metal Doped Graphene-Based Materials. *ECS Sens Plus*. 2025;4:011602. [DOI]
119. Bernal G, Aquea G, Ramírez-Rivera S. Metal-based molecules in the treatment of cancer: From bench to bedside. *Oncol Res*. 2025;33:759–79. [DOI] [PubMed] [PMC]
120. Simpson PV, Desai NM, Casari I, Massi M, Falasca M. Metal-based antitumor compounds: beyond cisplatin. *Future Med Chem*. 2019;11:119–35. [DOI] [PubMed]
121. Ferraro MG, Piccolo M, Misso G, Santamaria R, Irace C. Bioactivity and Development of Small Non-Platinum Metal-Based Chemotherapeutics. *Pharmaceutics*. 2022;14:954. [DOI] [PubMed] [PMC]
122. He S, Yang L, Lin M, Balasubramanian P, Peng H, Kuang Y, et al. Platinum group element-based nanozymes for biomedical applications: an overview. *Biomed Mater*. 2021;16:032001. [DOI] [PubMed]
123. Zhang Y, Zhang Y, Yang Z, Fan Y, Chen M, Zhao M, et al. Cytotoxicity Effect of Iron Oxide (Fe₃O₄)/Graphene Oxide (GO) Nanosheets in Cultured HBE Cells. *Front Chem*. 2022;10:888033. [DOI] [PubMed] [PMC]

124. Yang A, Wen T, Hao B, Meng Y, Zhang X, Wang T, et al. Biodistribution and Toxicological Effects of Ultra-Small Pt Nanoparticles Deposited on Au Nanorods (Au@Pt NRs) in Mice with Intravenous Injection. *Int J Nanomedicine*. 2022;17:5339–51. [DOI] [PubMed] [PMC]
125. Lateef R, Ahmad I, Mahdi AA, Lohia N, Alhadlaq HA, Akhtar MJ, et al. Toxic Effects of Synthesized Bismuth Oxide/Reduced Graphene Oxide (Bi₂O₃/RGO) Nanocomposites in Two Distinct Mammalian Cell Lines: Role Oxidative Stress and Apoptosis. *Int J Nanomedicine*. 2024;19:12655–74. [DOI] [PubMed] [PMC]
126. Kutwin M, Sawosz E, Jaworski S, Wierzbicki M, Strojny B, Grodzik M, et al. Nanocomplexes of Graphene Oxide and Platinum Nanoparticles against Colorectal Cancer Colo205, HT-29, HTC-116, SW480, Liver Cancer HepG2, Human Breast Cancer MCF-7, and Adenocarcinoma LNCaP and Human Cervical Hela B Cell Lines. *Materials (Basel)*. 2019;12:909. [DOI] [PubMed] [PMC]
127. Madeo LF, Schirmer C, Cirillo G, Asha AN, Ghunaim R, Froeschke S, et al. ZnO–Graphene Oxide Nanocomposite for Paclitaxel Delivery and Enhanced Toxicity in Breast Cancer Cells. *Molecules*. 2024;29:3770. [DOI] [PubMed] [PMC]
128. Choi Y, Gurunathan S, Kim J. Graphene Oxide–Silver Nanocomposite Enhances Cytotoxic and Apoptotic Potential of Salinomycin in Human Ovarian Cancer Stem Cells (OvCSCs): A Novel Approach for Cancer Therapy. *Int J Mol Sci*. 2018;19:710. [DOI] [PubMed] [PMC]
129. Biswas K, Mohanta YK, Mishra AK, Al-Sehemi AG, Pannipara M, Sett A, et al. Wet chemical development of CuO/GO nanocomposites: its augmented antimicrobial, antioxidant, and anticancerous activity. *J Mater Sci Mater Med*. 2021;32:151. [DOI] [PubMed] [PMC]
130. Zhao S, Lin X, Zhang L, Sun L, Li J, Yang W, et al. The *In Vivo* Investigation of Fe₃O₄-Nanoparticles Acute Toxicity in Mice. *Biomed Eng Appl Basis Commun*. 2012;24:229–35. [DOI]
131. Brown AL, Kai MP, DuRoss AN, Sahay G, Sun C. Biodistribution and Toxicity of Micellar Platinum Nanoparticles in Mice via Intravenous Administration. *Nanomaterials (Basel)*. 2018;8:410. [DOI] [PubMed] [PMC]
132. Chen Y, Hung Y, Liao I, Huang GS. Assessment of the *In Vivo* Toxicity of Gold Nanoparticles. *Nanoscale Res Lett*. 2009;4:858–64. [DOI] [PubMed] [PMC]
133. Adeyemi OS, Adewumi I. Biochemical Evaluation of Silver Nanoparticles in Wistar Rats. *Int Sch Res Notices*. 2014;2014:196091. [DOI] [PubMed] [PMC]
134. García-Torra V, Cano A, Espina M, Ettcheto M, Camins A, Barroso E, et al. State of the Art on Toxicological Mechanisms of Metal and Metal Oxide Nanoparticles and Strategies to Reduce Toxicological Risks. *Toxics*. 2021;9:195. [DOI] [PubMed] [PMC]
135. Karki N, Tiwari H, Tewari C, Rana A, Pandey N, Basak S, et al. Functionalized graphene oxide as a vehicle for targeted drug delivery and bioimaging applications. *J Mater Chem B*. 2020;8:8116–48. [DOI] [PubMed]
136. Du W, Elemento O. Cancer systems biology: embracing complexity to develop better anticancer therapeutic strategies. *Oncogene*. 2015;34:3215–25. [DOI] [PubMed]
137. Gu Z, Zhu S, Yan L, Zhao F, Zhao Y. Graphene-Based Smart Platforms for Combined Cancer Therapy. *Adv Mater*. 2019;31:e1800662. [DOI] [PubMed]
138. Tian P, Tang L, Teng KS, Lau SP. Graphene quantum dots from chemistry to applications. *Mater Today Chem*. 2018;10:221–58. [DOI]
139. Zheng P, Wu N. Fluorescence and Sensing Applications of Graphene Oxide and Graphene Quantum Dots: A Review. *Chem Asian J*. 2017;12:2343–53. [DOI] [PubMed] [PMC]
140. Ehtesabi H, Amirfazli M, Massah F, Bagheri Z. Application of functionalized carbon dots in detection, diagnostic, disease treatment, and desalination: a review. *Adv Nat Sci: Nanosci Nanotechnol*. 2020; 11:025017. [DOI]
141. Chemotherapy drugs. In: *The War on Cancer: An Anatomy of Failure, A Blueprint for the Future*. Dordrecht: Springer Netherlands; 2005. pp. 69–83. [DOI]

142. Anand U, Dey A, Chandel AKS, Sanyal R, Mishra A, Pandey DK, et al. Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics. *Genes Dis.* 2022;10:1367–401. [DOI] [PubMed] [PMC]
143. Sun Y, Liu Y, Ma X, Hu H. The Influence of Cell Cycle Regulation on Chemotherapy. *Int J Mol Sci.* 2021; 22:6923. [DOI] [PubMed] [PMC]
144. Grant CH, Gourley C. Relevant Cancer Diagnoses, Commonly Used Chemotherapy Agents and Their Biochemical Mechanisms of Action. In: Anderson RA, Spears N, editors. *Cancer Treatment and the Ovary.* Boston: Academic Press; 2015. pp. 21–33. [DOI]
145. Albahde MAH, Abdrakhimov B, Li G, Zhou X, Zhou D, Xu H, et al. The Role of Microtubules in Pancreatic Cancer: Therapeutic Progress. *Front Oncol.* 2021;11:640863. [DOI] [PubMed] [PMC]
146. Yang Z, Sun N, Cheng R, Zhao C, Liu J, Tian Z. Hybrid nanoparticles coated with hyaluronic acid lipid for targeted co-delivery of paclitaxel and curcumin to synergistically eliminate breast cancer stem cells. *J Mater Chem B.* 2017;5:6762–75. [DOI] [PubMed]
147. Espinosa-Cano E, Huerta-Madroñal M, Cámara-Sánchez P, Seras-Franzoso J, Schwartz S Jr, Abasolo I, et al. Hyaluronic acid (HA)-coated naproxen-nanoparticles selectively target breast cancer stem cells through COX-independent pathways. *Mater Sci Eng C Mater Biol Appl.* 2021;124:112024. [DOI] [PubMed]
148. Rezvantalab S, Drude NI, Moraveji MK, Güvener N, Koons EK, Shi Y, et al. PLGA-Based Nanoparticles in Cancer Treatment. *Front Pharmacol.* 2018;9:1260. [DOI] [PubMed] [PMC]
149. Perinelli DR, Cespi M, Bonacucina G, Palmieri GF. PEGylated polylactide (PLA) and poly (lactic-co-glycolic acid) (PLGA) copolymers for the design of drug delivery systems. *J Pharm Investig.* 2019;49: 443–58. [DOI]
150. Glasgow MDK, Chougule MB. Recent Developments in Active Tumor Targeted Multifunctional Nanoparticles for Combination Chemotherapy in Cancer Treatment and Imaging. *J Biomed Nanotechnol.* 2015;11:1859–98. [DOI] [PubMed] [PMC]
151. Miao T, Wang J, Zeng Y, Liu G, Chen X. Polysaccharide-Based Controlled Release Systems for Therapeutics Delivery and Tissue Engineering: From Bench to Bedside. *Adv Sci (Weinh).* 2018;5: 1700513. [DOI] [PubMed] [PMC]
152. Khan AAP, Khan A, Asiri AM, Ashraf GM, Alhogbia BG. Graphene Oxide Based Metallic Nanoparticles and their Some Biological and Environmental Application. *Curr Drug Metab.* 2017;18:1020–9. [DOI] [PubMed]
153. Gao S, Zhang L, Wang G, Yang K, Chen M, Tian R, et al. Hybrid graphene/Au activatable theranostic agent for multimodalities imaging guided enhanced photothermal therapy. *Biomaterials.* 2016;79: 36–45. [DOI] [PubMed]
154. Abadeer NS, Murphy CJ. Recent Progress in Cancer Thermal Therapy Using Gold Nanoparticles. In: *Nanomaterials and Neoplasms.* 1st ed. Jenny Stanford Publishing; 2021. [DOI]
155. Li J, Zhang W, Ji W, Wang J, Wang N, Wu W, et al. Near infrared photothermal conversion materials: mechanism, preparation, and photothermal cancer therapy applications. *J Mater Chem B.* 2021;9: 7909–26. [DOI] [PubMed]
156. Liao C, Li Y, Tjong SC. Antibacterial Activities of Aliphatic Polyester Nanocomposites with Silver Nanoparticles and/or Graphene Oxide Sheets. *Nanomaterials (Basel).* 2019;9:1102. [DOI] [PubMed] [PMC]
157. Habiba K, Encarnacion-Rosado J, Garcia-Pabon K, Villalobos-Santos JC, Makarov VI, Avalos JA, et al. Improving cytotoxicity against cancer cells by chemo-photodynamic combined modalities using silver-graphene quantum dots nanocomposites. *Int J Nanomedicine.* 2015;11:107–19. [DOI] [PubMed] [PMC]
158. Kumar P, Huo P, Zhang R, Liu B. Antibacterial Properties of Graphene-Based Nanomaterials. *Nanomaterials (Basel).* 2019;9:737. [DOI] [PubMed] [PMC]

159. Li D, Deng M, Yu Z, Liu W, Zhou G, Li W, et al. Biocompatible and Stable GO-Coated Fe₃O₄ Nanocomposite: A Robust Drug Delivery Carrier for Simultaneous Tumor MR Imaging and Targeted Therapy. *ACS Biomater Sci Eng.* 2018;4:2143–54. [DOI] [PubMed]
160. Karthika V, AlSalhi MS, Devanesan S, Gopinath K, Arumugam A, Govindarajan M. Chitosan overlaid Fe₃O₄/rGO nanocomposite for targeted drug delivery, imaging, and biomedical applications. *Sci Rep.* 2020;10:18912. [DOI] [PubMed] [PMC]
161. Shen L, Li B, Qiao Y. Fe₃O₄ Nanoparticles in Targeted Drug/Gene Delivery Systems. *Materials (Basel).* 2018;11:324. [DOI] [PubMed] [PMC]
162. Hooshmand S, Hayat SMG, Ghorbani A, Khatami M, Pakravanan K, Darroudi M. Preparation and Applications of Superparamagnetic Iron Oxide Nanoparticles in Novel Drug Delivery Systems: An Overview. *Curr Med Chem.* 2021;28:777–99. [DOI] [PubMed]
163. Huang C, Wu J, Jiang W, Liu R, Li Z, Luan Y. Amphiphilic prodrug-decorated graphene oxide as a multi-functional drug delivery system for efficient cancer therapy. *Mater Sci Eng C Mater Biol Appl.* 2018;89:15–24. [DOI] [PubMed]
164. Liu L, Ma Q, Cao J, Gao Y, Han S, Liang Y, et al. Recent progress of graphene oxide-based multifunctional nanomaterials for cancer treatment. *Cancer Nano.* 2021;12:18. [DOI]
165. He Q, Chen J, Yan J, Cai S, Xiong H, Liu Y, et al. Tumor microenvironment responsive drug delivery systems. *Asian J Pharm Sci.* 2020;15:416–48. [DOI] [PubMed] [PMC]
166. Koul B. Types of Cancer. In: *Herbs for Cancer Treatment.* Singapore: Springer Singapore; 2019. pp. 53–150. [DOI]
167. Zavala VA, Bracci PM, Carethers JM, Carvajal-Carmona L, Coggins NB, Cruz-Correa MR, et al. Cancer health disparities in racial/ethnic minorities in the United States. *Br J Cancer.* 2021;124:315–32. [DOI] [PubMed] [PMC]
168. Baig N, Kammakakam I, Falath W. Nanomaterials: a review of synthesis methods, properties, recent progress, and challenges. *Mater Adv.* 2021;2:1821–71. [DOI]
169. De B, Karak N. Recent progress in carbon dot–metal based nanohybrids for photochemical and electrochemical applications. *J Mater Chem A.* 2017;5:1826–59. [DOI]
170. Abdolmaleki H, Kidmose P, Agarwala S. Droplet-Based Techniques for Printing of Functional Inks for Flexible Physical Sensors. *Adv Mater.* 2021;33:e2006792. [DOI] [PubMed]
171. Nasiri S, Alizadeh N. Hydroxypropyl-β-cyclodextrin-polyurethane/graphene oxide magnetic nanoconjugates as effective adsorbent for chromium and lead ions. *Carbohydr Polym.* 2021;259:117731. [DOI] [PubMed]
172. Jafari S, Soleimani M, Salehi R. Nanotechnology-based combinational drug delivery systems for breast cancer treatment. *Int J Polym Mater Polym Biomater.* 2018;68:859–69. [DOI]
173. Ayed SB, Sbihi H, Azam M, Al-Resayes S, Ayadi M, Ayari F. Local iron ore identification: comparison to synthesized Fe₃O₄ nanoparticles obtained by ultrasonic assisted reverse co-precipitation method for Auramine O dye adsorption. *Desalin Water Treat.* 2021;220:446–58. [DOI]
174. Rani S, Varma G. Superparamagnetism and metamagnetic transition in Fe₃O₄ nanoparticles synthesized via co-precipitation method at different pH. *Physica B: Condensed Matter.* 2015;472:66–77. [DOI]
175. Khalil MI. Co-precipitation in aqueous solution synthesis of magnetite nanoparticles using iron(III) salts as precursors. *Arabian J Chem.* 2015;8:279–84. [DOI]
176. Zheng G, Zheng M, Yang B, Fu H, Li Y. Improving breast cancer therapy using doxorubicin loaded solid lipid nanoparticles: Synthesis of a novel arginine-glycine-aspartic tripeptide conjugated, pH sensitive lipid and evaluation of the nanomedicine *in vitro* and *in vivo*. *Biomed Pharmacother.* 2019;116:109006. [DOI] [PubMed]
177. Wei Q, Xu Y, Lau ATY. Recent Progress of Nanocarrier-Based Therapy for Solid Malignancies. *Cancers (Basel).* 2020;12:2783. [DOI] [PubMed] [PMC]

178. Craciun AM, Focsan M, Magyari K, Vulpoi A, Pap Z. Surface Plasmon Resonance or Biocompatibility—Key Properties for Determining the Applicability of Noble Metal Nanoparticles. *Materials (Basel)*. 2017;10:836. [DOI] [PubMed] [PMC]
179. Assari P, Rafati AA, Feizollahi A, Joghani RA. An electrochemical immunosensor for the prostate specific antigen based on the use of reduced graphene oxide decorated with gold nanoparticles. *Mikrochim Acta*. 2019;186:484. [DOI] [PubMed]
180. Saeidi tabar F, pourmadadi m, Yazdian F, Rashedi H. Design of a Novel Electrochemical Nanobiosensor for the Detection of Prostate Cancer by Measurement of PSA Using Graphene-based Materials. *AUT J Electr Eng*. 2021;53:213–22. [DOI]
181. Tran HL, Darmanto W, Doong R. Electrochemical immunosensor for ultra-sensitive detection of attomolar prostate specific antigen with sulfur-doped graphene quantum dot@gold nanostar as the probe. *Electrochimica Acta*. 2021;389:138700. [DOI]
182. Liu X, Yan B, Li Y, Ma X, Jiao W, Shi K, et al. Graphene Oxide-Grafted Magnetic Nanorings Mediated Magnetothermodynamic Therapy Favoring Reactive Oxygen Species-Related Immune Response for Enhanced Antitumor Efficacy. *ACS Nano*. 2020;14:1936–50. [DOI] [PubMed]
183. Yuan R, Xu H, Liu X, Tian Y, Li C, Chen X, et al. Zinc-Doped Copper Oxide Nanocomposites Inhibit the Growth of Human Cancer Cells through Reactive Oxygen Species-Mediated NF-κB Activations. *ACS Appl Mater Interfaces*. 2016;8:31806–12. [DOI] [PubMed]
184. Shirzad M, Shaban M, Mohammadzadeh V, Rahdar A, Fathi-karkan S, Hoseini ZS, et al. Artificial Intelligence-Assisted Design of Nanomedicines for Breast Cancer Diagnosis and Therapy: Advances, Challenges, and Future Directions. *BioNanoSci*. 2025;15:354. [DOI]
185. Karimi M, Ghasemi A, Zangabad PS, Rahighi R, Basri SMM, Mirshekari H, et al. Smart micro/nanoparticles in stimulus-responsive drug/gene delivery systems. *Chem Soc Rev*. 2016;45:1457–501. [DOI] [PubMed] [PMC]
186. Reguera J, Jiménez de Aberasturi D, Henriksen-Lacey M, Langer J, Espinosa A, Szczupak B, et al. Janus plasmonic-magnetic gold-iron oxide nanoparticles as contrast agents for multimodal imaging. *Nanoscale*. 2017;9:9467–80. [DOI] [PubMed]
187. Zafar N, Madni A, Khalid A, Khan T, Kousar R, Naz SS, et al. Pharmaceutical and Biomedical Applications of Green Synthesized Metal and Metal Oxide Nanoparticles. *Curr Pharm Des*. 2020;26:5844–65. [DOI] [PubMed]
188. Yan L, Li Y, Gu Z. Imaging Techniques in Nanotoxicology Research. In: *Toxicology of Nanomaterials*. John Wiley & Sons, Ltd; 2016. pp. 121–49. [DOI]
189. Narmani A, Rezvani M, Farhood B, Darkhor P, Mohammadnejad J, Amini B, et al. Folic acid functionalized nanoparticles as pharmaceutical carriers in drug delivery systems. *Drug Dev Res*. 2019;80:404–24. [DOI] [PubMed]
190. Jurczyk M, Jelonek K, Musiał-Kulik M, Beberok A, Wrześniok D, Kasperczyk J. Single- versus Dual-Targeted Nanoparticles with Folic Acid and Biotin for Anticancer Drug Delivery. *Pharmaceutics*. 2021;13:326. [DOI] [PubMed] [PMC]
191. Noh MS, Lee S, Kang H, Yang J, Lee H, Hwang D, et al. Target-specific near-IR induced drug release and photothermal therapy with accumulated Au/Ag hollow nanoshells on pulmonary cancer cell membranes. *Biomaterials*. 2015;45:81–92. [DOI] [PubMed]
192. Zhou Z, Song J, Nie L, Chen X. Reactive oxygen species generating systems meeting challenges of photodynamic cancer therapy. *Chem Soc Rev*. 2016;45:6597–626. [DOI] [PubMed] [PMC]
193. Xu J, Wang Y, Hu S. Nanocomposites of graphene and graphene oxides: Synthesis, molecular functionalization and application in electrochemical sensors and biosensors. A review. *Microchim Acta*. 2016;184:1–44. [DOI]

194. Ingenito F, Roscigno G, Affinito A, Nuzzo S, Scognamiglio I, Quintavalle C, et al. The Role of Exo-miRNAs in Cancer: A Focus on Therapeutic and Diagnostic Applications. *Int J Mol Sci.* 2019;20:4687. [DOI] [PubMed] [PMC]
195. Xiong H, Huang Z, Yang Z, Lin Q, Yang B, Fang X, et al. Recent Progress in Detection and Profiling of Cancer Cell-Derived Exosomes. *Small.* 2021;17:e2007971. [DOI] [PubMed]
196. Drug Targets in Cellular Processes of Cancer: From Nonclinical to Preclinical Models. In: Tuli HS, editor. 1st ed. Springer Singapore; 2020. [DOI]
197. Soni DK, Ahmad R, Dubey SK. Biosensor for the detection of *Listeria monocytogenes*: emerging trends. *Crit Rev Microbiol.* 2018;44:590–608. [DOI] [PubMed]
198. Malik P, Gupta R, Malik V, Ameta RK. Emerging nanomaterials for improved biosensing. *Measurement: Sensors.* 2021;16:100050. [DOI]
199. Aljabali AA, Obeid MA, Amawi HA, Rezigue MM, Hamzat Y, Satija S, et al. Application of Nanomaterials in the Diagnosis and Treatment of Genetic Disorders. In: Khan FA, editor. *Applications of Nanomaterials in Human Health.* Singapore: Springer Singapore; 2020. pp. 125–46. [DOI]
200. Yoon J, Shin M, Lee T, Choi J. Highly Sensitive Biosensors Based on Biomolecules and Functional Nanomaterials Depending on the Types of Nanomaterials: A Perspective Review. *Materials (Basel).* 2020;13:299. [DOI] [PubMed] [PMC]
201. Nguyen KT, Zhao Y. Engineered Hybrid Nanoparticles for On-Demand Diagnostics and Therapeutics. *Acc Chem Res.* 2015;48:3016–25. [DOI] [PubMed]
202. Williams DF. Assessing the triad of biocompatibility, medical device functionality and biological safety. *Med Devices Sens.* 2021;4:e10150. [DOI]
203. Krska SW, DiRocco DA, Dreher SD, Shevlin M. The Evolution of Chemical High-Throughput Experimentation To Address Challenging Problems in Pharmaceutical Synthesis. *Acc Chem Res.* 2017;50:2976–85. [DOI] [PubMed]
204. Rezapour MR, Myung CW, Yun J, Ghassami A, Li N, Yu SU, et al. Graphene and Graphene Analogs toward Optical, Electronic, Spintronic, Green-Chemical, Energy-Material, Sensing, and Medical Applications. *ACS Appl Mater Interfaces.* 2017;9:24393–406. [DOI] [PubMed]
205. Song S, Shen H, Wang Y, Chu X, Xie J, Zhou N, et al. Biomedical application of graphene: From drug delivery, tumor therapy, to theranostics. *Colloids Surf B Biointerfaces.* 2020;185:110596. [DOI] [PubMed]
206. Rizwan M, Alias R, Zaidi UZ, Mahmoodian R, Hamdi M. Surface modification of valve metals using plasma electrolytic oxidation for antibacterial applications: A review. *J Biomed Mater Res A.* 2018; 106:590–605. [DOI] [PubMed]
207. Thakur S, Karak N. Alternative methods and nature-based reagents for the reduction of graphene oxide: A review. *Carbon.* 2015;94:224–42. [DOI]
208. Mahri S, Villa R, Shiau Y, Tang M, Racacho KJ, Zong Q, et al. Nanomedicine Approaches for Autophagy Modulation in Cancer Therapy. *Small Sci.* 2025;5:2400607. [DOI] [PubMed] [PMC]
209. Mi P. Stimuli-responsive nanocarriers for drug delivery, tumor imaging, therapy and theranostics. *Theranostics.* 2020;10:4557–88. [DOI] [PubMed] [PMC]
210. Xu W, Guan G, Yue R, Dong Z, Lei L, Kang H, et al. Chemical Design of Magnetic Nanomaterials for Imaging and Ferroptosis-Based Cancer Therapy. *Chem Rev.* 2025;125:1897–961. [DOI] [PubMed]
211. Ndagi U, Mhlongo N, Soliman ME. Metal complexes in cancer therapy - an update from drug design perspective. *Drug Des Devel Ther.* 2017;11:599–616. [DOI] [PubMed] [PMC]
212. Desai N, Rana D, Patel M, Bajwa N, Prasad R, Vora LK. Nanoparticle Therapeutics in Clinical Perspective: Classification, Marketed Products, and Regulatory Landscape. *Small.* 2025;21: e2502315. [DOI] [PubMed] [PMC]
213. Pourmadadi M, Ahmadi MJ, Dinani HS, Ajalli N, Dorkoosh F. Theranostic Applications of Stimulus-Responsive Systems based on Fe₂O₃. *Pharm Nanotechnol.* 2022;10:90–112. [DOI] [PubMed]

214. Follmann HDM, Naves AF, Araujo RA, Dubovoy V, Huang X, Asefa T, et al. Hybrid Materials and Nanocomposites as Multifunctional Biomaterials. *Curr Pharm Des.* 2017;23:3794–813. [DOI] [PubMed]
215. Chen C, Wang K, Luo L. AuNPs and 2D functional nanomaterial-assisted SPR development for the cancer detection: a critical review. *Cancer Nano.* 2022;13:29. [DOI]
216. Alsharabi RM, Rai S, Mohammed HY, Farea MA, Srinivasan S, Saxena PS, et al. A comprehensive review on graphene-based materials as biosensors for cancer detection. *Oxford Open Mater Sci.* 2023;3:itac013. [DOI]
217. Wang J. Electrochemical biosensing based on noble metal nanoparticles. *Microchim Acta.* 2012;177:245–70. [DOI]
218. Li Y, Zhang H. Fe₃O₄-based nanotheranostics for magnetic resonance imaging-synergized multifunctional cancer management. *Nanomedicine (Lond).* 2019;14:1493–512. [DOI] [PubMed]
219. Gulzar A, Gai S, Yang P, Li C, Ansari MB, Lin J. Stimuli responsive drug delivery application of polymer and silica in biomedicine. *J Mater Chem B.* 2015;3:8599–622. [DOI] [PubMed]
220. Abd Ellah NH, Abouelmagd SA. Surface functionalization of polymeric nanoparticles for tumor drug delivery: approaches and challenges. *Expert Opin Drug Deliv.* 2017;14:201–14. [DOI] [PubMed]