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Review Article

The role of nanoparticles and nanomaterials in cancer diagnosis and treatment: a comprehensive review

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Abstract: Cancer's pathological processes are complex and present several challenges for current chemotherapy methods. These challenges include cytotoxicity, multidrug resistance, the proliferation of cancer stem cells, and a lack of specificity. To address these issues, researchers have turned to nanomaterials, which possess distinct optical, magnetic, and electrical properties due to their size range of 1-100 nm. Nanomaterials have been engineered to improve cancer treatment by mitigating cytotoxicity, enhancing specificity, increasing drug payload capacity, and improving drug bioavailability. Despite a growing corpus of research on this subject, there has been limited progress in permitting nanodrugs for medical use. The advent of nanotechnology, particularly advances in intelligent nanomaterials, has transformed the field of cancer diagnosis and therapy. Nanoparticles' large surface area allows them to successfully encapsulate a large number of molecules. Nanoparticles can be functionalized with various bio-based substrates like RNA, DNA, aptamers, and antibodies, enhancing their theranostic capabilities. Biologically derived nanomaterials offer economical, easily producible, and less toxic alternatives to conventionally manufactured ones. This review offers a comprehensive overview of cancer theranostics methodologies, focusing on intelligent nanomaterials such as metal, polymeric, and carbon-based nanoparticles. I have also critically discussed their benefits and challenges in cancer therapy and diagnostics. Utilizing intelligent nanomaterials holds promise for advancing cancer theranostics, and improving tumor detection and treatment. Further research should optimize nanocarriers for targeted drug delivery and explore enhanced permeability, cytotoxicity, and retention effects.

Keywords: Cancer diagnosis, treatment, nanocarriers, polymeric nanoparticles, metal nanoparticles

Introduction

Despite significant advancements in medicine and technology, the current repertoire of efficacious strategies for completely eradicating cancer remains limited. Metastasis and cancer recurrence are prominent contributors to disability and mortality, yet there remains a dearth of knowledge regarding the underlying mechanisms [1]. Cancer is predominantly attributed to DNA mutations [2]. In the year 2022, it is projected that there will be a total of 1,918,030 newly diagnosed cases of cancer and 609,360 deaths caused by cancer in the United States. Among these deaths, approximately 350 individuals will succumb to lung cancer each day, currently recognized as the primary cause of cancer-related mortality [3]. According to the projections made by the Global Cancer Observatory (GCO), it is anticipated that by 2030, approximately 30 million individuals will succumb to cancer yearly [4]. As a result of the elevated mortality rate linked to cancer, the economic burden on families and society is substantial. Hence, it is imperative to prioritize the prevention, screening, diagnosis, and treatment of cancer.

Nanoparticles exhibit a size distribution from 10 nm to 100 nm, thereby possessing a substantial surface area, rendering them highly appealing for utilization in biological contexts. The nanomaterials exhibit high mobility within the human body, facilitating organ translocation and efficient penetration into specific tissues. Nanoparticles can form conjugates with

drug molecules, thereby facilitating the particular targeting of afflicted tissues, such as cancer cells, for diagnostics. Nanoparticles exhibit dimensions that are smaller in scale compared to blood cells, and they possess a size approximately equivalent to DNA [5]. This facilitates enhancing their performance and endows them with distinctive physical, chemical, and optical characteristics that render them suitable for utilization in the medical domain for cancer treatment and diagnosis. In addition to being utilized for the development of innovative methodologies, they possess the capability to augment traditional techniques.

Medical nanotechnology makes use of materials of nanoscale dimensions, typically ranging from 1 to 100 nanometers. These materials are employed in the development and manufacture of pharmaceuticals and medical devices [6]. Nanomaterials have different optical, magnetic, and electrical properties that distinguish them from typical macromolecules at the nanoscale. Nanomaterials have a high surface area to volume ratio, increased electrical conductivity, super paramagnetic capabilities, a change in optical absorption spectra, and different fluorescence properties. Nanoparticles have the potential to be employed in medicine for pharmaceutical delivery and controlled release. Notable properties include increased permeability for crossing biological barriers and improved biocompatibility. Nanomaterials' unique properties suggest that they might be employed in cancer therapy. Because of their high surface-to-volume ratio, nanoparticles may bind to biomolecules or residues, improving the selectivity of chemical drug complexes in targeted treatment. This, in turn, improves the efficacy of nanomaterial-based treatments while reducing their toxicity to normal cells [7].

Various forms of nanoparticles, including magnetic, carbon nanomaterials, polymeric micelles, and other nanomaterials, have been used in cancer detection and imaging due to their diverse biological uses. Due to their distinct characteristics, these nanoparticles have been used in several medicinal applications. The distinctive chemical, optical, magnetic, and chemical characteristics of nanomaterials enable the creation of imaging probes that possess enhanced contrast, heightened sensitivity, regulated biodistribution, and improved spatial imaging in PET, MRI, SPECT, and ultrasound methods [8]. Microbubbles, a kind of nanomaterial, serve as molecular imaging agents and are used in ultrasonic imaging. In a particular investigation, vascular endothelial growth factor receptor 2 and αvβ3-targeted microbubbles were used for molecular ultrasound imaging. The study successfully showed the accurate attachment of these microbubbles to angiogenic tumour blood capillaries. Efficiently identifying tumours and malignancies at an early stage continues to be a difficult task in clinical diagnostics. Advanced nanomaterials have great potential in the field of early cancer detection, diagnosis, and imaging. Metal nanoclusters have potential use in both cancer detection and therapy. Furthermore, scientists are investigating methods to mitigate the toxicity caused by nanoparticles, as well as strategies for manufacturing nanoparticles that are both safe and effective for human ingestion [9].

Nanoparticles are a superior option for cancer therapy in comparison to microparticles due to their higher biodegradability. Nanoparticles are unable to infiltrate regular blood arteries due to the presence of a compact extracellular matrix. The growth of the tumour hindered the lymphatic drainage due to the presence of underdeveloped blood vessels formed as a result of tumor-induced angiogenesis. The inhibited flow of lymphatic fluid enables nanoparticles to infiltrate specific cells. The phenomenon referred to as "enhanced permeability and retention effect" (EPR) is responsible for the passive targeting of nanoparticles, which relies heavily on this effect [10].

In this review, we discussed several types of nanoparticles and nanomaterials, including magnetic nanoparticles, carbon nanotubes, graphene-based materials, metal nanoparticles, polymeric micelles, and other carbon-based materials, have been utilized in cancer detection, imaging, and treatment due to their diverse biological applications. Due to their distinctive characteristics, these nanomaterials have been employed in various medical applications. Nanomaterials' distinct chemical, ma gnetic, optical, and chemical characteristics facilitate the creation of imaging probes for diagnosis and drug materials for cancer treatment. The advancement of sophisticated nanomaterials represents a highly promising strate-

gy for early cancer detection, diagnosis, and treatment. Lastly, we have given a future outlook for researchers to find new research gaps in the latest research studies.

Nanoparticles: a crucial tool for cancer diagnosis

Detect breast, colon, and cervical malignancies using magnetic, quantum dots, polymeric, metallic, fullerene, liposomes, graphene, carbon nanotubes, or dendrimers. They are also crucial to imaging. After crossing biological barriers like cell membranes, nanoparticles spend a lot of time floating in the blood before engaging with various biological systems. To improve tumour binding and detection, nanoparticles may be combined with cancer-specific antibodies. Nanoparticles and sensors may improve cancer detection and diagnosis, according to recent studies [9]. Methylation patterns and mutation detection have been described as markers for cancer diagnosis. Circulating tumor cells, cell-free RNA, and extracellular vesicles have all been proposed for clinical diagnosis [11], but additional research is needed. (-Mercaptopropyl) trimethoxysilane has been employed as a stabilizing agent for fluorescent gold nanoclusters or superparamagnetic. Conjugation of the produced GNCs@MPS onto the surface of "Fe_3O_4@SiO_2 nanoparticles" was followed by the incorporation of "poly ethylene glycol dimethacrylate" to create Fe_3O_4/GNCs nanoprobes. HL60 cancer cells have been shown to be receptive to absorption of [9].

Nanoparticles as diagnostic imaging agents

Medical imaging is critical in the diagnosis and treatment of malignant tumours. Iron oxide nanoparticles are only one kind of nanoparticle that might be employed to enhance imaging methods by improving optical, magnetic, acoustic, and structural capabilities. Several studies have shown that introducing nanoparticles into certain tissues improves tumour diagnostics and surgical operations by increasing image contrast [12]. In cryosurgery, nanoparticles have been shown to enhance tumour and ice ball border imaging. Because of the improvement in picture quality, the ice balls may be coated more completely, improving the therapeutic effect. Furthermore, in imaging applications, metallic nanoparticles prevail. Different imaging processes may influence the metals utilised to create nanoparticles. Nanoparticles are constructed of various materials and are employed in diagnostic imaging methods [13].

MRI is widely acknowledged as the most effective noninvasive method for detecting tumors. However, challenges arise in clinical tumor detection when attempting to compare MRI signals between normal and malignant tissues for a better understanding of the former. Magnetic resonance imaging relies on measuring the magnetic characteristics of hydrogen nuclei within water molecules, offering a non-invasive approach to medical imaging. Changes in magnetization caused by protons in tissues result in unique properties for each anatomical structure. The use of contrast agents can enhance image clarity. In addition to cancer diagnosis, the increased permeability and retention effect associated with tumors significantly improve the contrast of magnetic nanoparticles [14-16].

Iron oxide magnetic nanoparticles are popular choices for MRI contrast agents due to their ability to selectively target individual cells. For example, studies indicate that MRI can identify liver cancer by observing the intracellular absorption of iron oxide nanoparticles by Kupffer cells in the liver. Although these nanoparticles exhibit low signal strength in healthy tissue and high signal strength in tumor tissue, they cannot enter cancer cells. Recent research suggests that modifying nanoparticle surfaces appropriately and incorporating tumor-specific bio-oligomers can enhance nanoparticle localization inside tumors, offering potential benefits in early detection of microscopic cancers. Targeting human transferrin with AuNanoparticles has been demonstrated to significantly improve the efficiency of brain tumor imaging. Researchers have effectively detected microscopic cancers using anti-epidermal growth factor receptor monoclonal antibodies in conjunction with paramagnetic nanoparticle probes [17, 18].

Drug delivery through nanoparticle targeting

The use of chemotherapeutic drugs has become standard practice when dealing with cancer. However, getting these drugs to concentrate where they will do the best in malignant tumors while avoiding accumulating in healthy tissue remains a major obstacle [19]. Sub-

stances taken orally can slow the proliferation of cells throughout the body, including in the bone marrow, hair follicles, intestine, and lymphocytes. Some potential side effects include a decrease in bone marrow function, the onset of mucositis, hair loss, and even death in extreme situations [20]. Compared to conventional therapeutic approaches, targeted drug delivery's higher efficacy and lower incidence of adverse effects have been shown. This procedure entails actively differentiating between normal and malignant cells for medicine administration. Using either active or passive targeting methods, several studies have shown that nanoparticles can selectively deliver chemotherapeutic medications to tumor cells. Nanoparticles have been demonstrated to have a critical function in facilitating the precise administration of immunotherapeutic agents in several experimental experiments [21].

Many pathophysiological features, such as temperature, the surface charge of tumor cells, pH, abnormal blood vessels, and influence passive targeting in tumor tissue [22]. Nanoparticles having a diameter of around 400 nm are easily passively transported to tumor tissue for tumor angiogenesis, which promotes blood vessel growth and retention [23]. However, due to the physicochemical features of the nanoparticles, the passive targeting strategy has several drawbacks. Surface charge, hydrophobicity, diameter, hydrophilicity, and molecule weight are all relevant characteristics of nanoparticles. In addition, it has been demonstrated that increased permeability and retention activity in tumor cells is insufficient when a passive targeting strategy is used [24]. Due largely to the constraints of passive targeting, there has been a shift in recent years toward active targeting in studying drug-delivery nanoparticles. This change has led to a greater focus on ligand targeting and other active targeting techniques.

Active targeting, also known as ligand targeting, involves the incorporation of ligands specific to tumor biomarkers into nanoparticles [25]. Nanoparticle internalization by tumor cells through receptor-mediated endocytosis after ligand-receptor interaction at the tumor surface. The intracellular milieu has an acidic pH, and certain enzymes break down the nanoparticles, releasing the drugs within. Current studies often use transferrin, glycoprotein epidermal growth factor receptor, and folic acid as targeted ligands [26]. To treat mice with breast cancer, researchers used gemcitabine-loaded EGFR-targeted stearyl nanoparticles [27]. They reported considerable drug enrichment and apparent efficacy. Researchers showed that gold nanoparticles coated with berberine hydrochloride may effectively deliver therapeutic drugs to folate receptor-expressing human cervical cancer cells by targeted delivery of folic acid [28].

In recent times, the use of short interfering RNA-mediated gene silencing therapy is one of the most promising emerging methods for combating cancer compared to traditional chemotherapy medications. While it is true that viruses may serve as carriers for siRNA delivery, it has been shown that viral vectors can lead to insertional mutagenesis and immunogenic responses [29]. In contrast, it has been claimed that selenium nanoparticles have significant promise as carriers for small interfering RNA due to the inherent properties of selenium, a trace element. Selenium has been found to possess the ability to diminish tumor incidence, mitigate medication toxicity, and modulate immunological function [30]. Furthermore, the surface of selenium nanoparticles may be modified with different tumor-targeting moieties, i.e., hyaluronic acid, RGD peptide, and folate, to augment their tumor-targeting capability [31]. In their study, researchers demonstrated the remarkable targeting efficacy of selenium nanoparticles functionalized with RGDfC peptide toward HeLa cervical cancer cells. In the context of targeted medication delivery for various cancers, RGDfC-Se@siRNA nanoparticles have the potential to be reused due to their unique binding ability with αvβ3 integrin, which is known to be substantially expressed by a diverse range of tumor cells [32]. The electrostatic interaction between positively charged RGDfC-SeNanoparticles and negatively charged siRNA enables a tight packaging of siRNA, as shown in their structural arrangement. The findings from animal investigations indicate that RGDfC-Se@siRNA Nanoparticles can effectively clathrin-associated endocytosis to enter tumor cells. Tumor cells can rapidly produce small interfering RNA, which effectively suppresses the expression of relevant genes and facilitates the production of reactive oxy-

gen species. This process hinders the proliferation of tumor cells and promotes their programmed cell death, also known as apoptosis [33]. Furthermore, certain types of Selenium nanoparticles have shown remarkable biological safety, as evidenced by their lack of discernible harmful effects on vital organs like the liver, kidney, lung, heart, spleen, and others in murine models [34, 35].

Although various nanoparticle systems have been developed for targeted drug delivery, most of these applications are currently limited to cell or animal testing with little support for clinical use. It's also important to remember that many nanoparticles are delivered within the tumor. The types of nanoparticles that may be employed efficiently for treating tumors are restricted by the mode of administration chosen. There is also a lack of alternate drug delivery techniques and specialized tools for nanoparticles.

This suggests that studying nanoparticles for targeted medication delivery may benefit from further investigation into various methods of nanoparticle administration. The available evidence indicates that a vascular interventional delivery method might be effective. The suggested approach relies first on medical imaging tools to pinpoint the location of the blood artery that nourishes the tumor. The nanoparticles are then delivered by guide wire to the selected tumor-feeding blood vessel. In addition, a magnetic field is utilized to confine the nanoparticles to a specific area. Since nanoparticles are not impacted by the presence of blood flow inside the vessel, they may be immobilized where they are needed. However, there are limitations on the types of nanoparticles that may be used for this purpose. The effectiveness of therapy for unbound tumor cells and micrometastasis will be reduced due to the intentional targeting of nanoparticles, which will modify the distribution of chemotherapeutic medicines throughout the body. However, the effect of targeting is typically enhanced, and future studies may give clearer proof of benefit when tailored drugs are utilized. It's also very unlikely that anti-cancer drugs could eliminate all tumor stem cells on their own. More success has been shown in targeting tumor stem cells using physical therapy adapted to nanoparticle formations' physical properties. The development of multifunctional nanoparticles that may act as drug carriers for cryosurgery, photothermal treatment, and photodynamic therapy is thus encouraged for future studies. Tumor therapy results may be improved by using these multifunctional nanoparticles.

Nanoparticles in the routine diagnosis and treatment of cancer

Nanodiagnostics utilize nanoparticles in clinical diagnostics, revolutionizing early cancer detection and increasing sensitivity [36]. Various nanomaterials, such as polymeric nanoparticles, dendrimers, carbon nanotubes, and quantum dots, are employed in cancer diagnosis. Enhancing the detection capabilities of nanoparticles involves combining them with targeted small molecules, such as aptamers, polysaccharides, antibodies, and peptides (**Table 1**) [37]. Gold nanoparticles have been extensively studied for their potential in cancer detection, with recent research showing a significant increase in fluorescence intensity for Au-doped nanoparticles. Detection of the cancer biomarker carcinoembryonic antigen using color imaging and fluorescence demonstrated a clear red color change, establishing a limit of detection (LOD) of 10.00 ng/mL. Further differentiation in fluorescence intensity improved the LOD to 0.10 ng/mL. Clinical samples confirmed the method's viability. An immunoassay approach was found effective in accurately measuring the liver cancer biomarker Hsp90, enhancing control over the location of immobilized antibodies. Additionally, miR-377-3p and miR-381-3p were identified as biomarkers for colorectal cancer diagnosis [38, 39].

Metallic nanoparticles

Metallic nanoparticles, ranging in size from 1 to 100 nm, are categorized as nanoparticles, nanowires, nanoplatelets, and nanostructures. Their propensity for aggregation and the formation of macroscopic structures is attributed to higher surface energy levels. To maintain stability in a liquid environment, two main strategies are employed. Static stabilization involves the creation of an electrical double layer by collecting negative ions, preventing nanoparticle aggregation through repulsion. Steric stabilization, an additional method, wraps metallic nanoparticles in polymers, surfactants, or ligands to prevent the formation of unwieldy

Table 1. Role of various Nanoparticles in cancer treatments

Cancer type	Results	Application	References
HeLa cervical and breast cancer lines	Initial in vitro cultivation of a compound with antimicrobial and antitumor properties.	Utilize as a potent microbiological and anti-carcinogenic agent.	[157]
Lung cancer biomarker	Biomarker hnRNPB1 for in vitro cancer diagnostics.	Thiol crosslinking of GNP with hnRNPB1.	[158]
Skin cancer	Spherical Au nanoparticles with Pt nanodots had higher absorbance and a wider absorption bandwidth.	The efficiency and photostability of nanoparticles in photothermal conversion are quite outstanding.	[159]
Breast cancer	Gold nanoparticles have shown potential as a diagnostic and therapeutic tool for breast cancer.	AuNanoparticles may have improved PTT-based early-stage breast cancer detection and therapy for advanced breast cancers.	[160]
Glioblastoma and melanoma cells	Minimal cytotoxicity was observed in normal cells during in vitro experiments.	The treatment of glioblastoma and melanoma.	[161]
microRNA biology	It has the potential to detect cancer under controlled laboratory and animal settings.	Identifying microRNA-155.	[9]
Neuroblastoma cancer	Apoptosis and oxidative DNA damage were both factors in the death of cancer cells caused by RA and Pt Nanoparticles (in vitro).	The initiation of programmed cell death (apoptosis) in malignant cells.	[162]
Tumor	Lowering protein absorption (in vitro) is one-way inert nanoparticle surfaces improve imaging.	Transportation of therapeutic substances to specified places inside the body to view malignant tissues constitutes the field of drug delivery for cancer imaging.	[163]
Cancer	Cancer treatment with gold nanoparticles and the detection of Nanoparticles in drug delivery systems.	AuNanoparticles can be easily modified with cancer cell surface receptor ligands and have a longer half-life and improved receptor-mediated endocytosis.	[164]
Colon cancer cells	The apoptotic death of cancer cells was induced in an in vitro experiment.	Proton therapy simulation for cancer treatment improved in effectiveness.	[165]
Cancer	Platinum-based nanoplatforms for multimodal imaging in biomedical diagnostics.	Malignant tumors treated with photodynamic treatment may also benefit from using Pt(II)-based compounds as photosensitizers.	[166]
Cervical and melanoma cancer cells	Gold Nanoparticles and a wide range of cancer cell lines inhibit cell proliferation and promote cell death.	The effects of gold nanoparticles on HeLa and A375 cells treated with tannic acid and green tea nanoparticles were due to apoptotic induction.	[167]
Lung cancer	Nano-enabled drug delivery devices can deliver sensitizer molecules to tumor cells to enhance radiation therapy.	As a result of many limitations of traditional therapies, nanotechnology has come to the rescue.	[168]
Detection of cancer biomarker CEA	The FRET method combined with fluorescence FITC enables more selective detection of cancer cells.	FITC fluorescence induced by FRET.	[38]
Breast Cancer	The biocompatibility of the radio enhancer is increased, and the nanoparticles are stabilized.	The nanosystem increased intracellular ROS in cancer cells and facilitated their demise when exposed to X-rays.	[169]
Cancer	Since AuNanoparticles can undergo surface modifications, they could be used to create biocompatible and functional nano-agents for cancer therapy.	Due to their malleability, AuNanoparticles could be exploited to develop cancer therapeutic nano-agents that are both safe and effective.	[170]

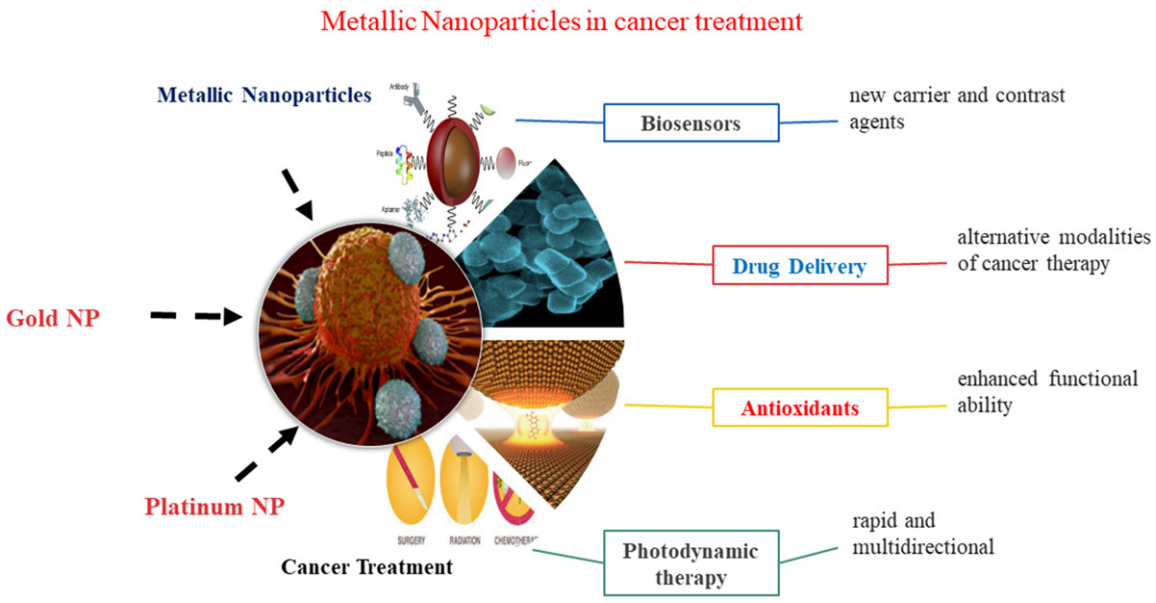

Figure 1. Metallic nanoparticles in cancer treatments.

chains. These stabilized metallic nanoparticles play crucial roles in the diagnosis and treatment of cancer cells (**Figure 1**).

Platinum nanoparticles: The medical application of nanoscale platinum has significantly expanded due to its intrinsic antioxidant capabilities with anticancer effects, preventing tumor formation. Functionalized platinum nanoparticles, when combined with specific ligands, enhance the effectiveness of tumor targeting. PtNanoparticles also enable optimized drug release mechanisms and improve drug delivery efficiency. However, recent studies indicate potential negative effects, with nanoparticle accumulation observed in critical organs and cells. Globally, platinum-based chemotherapeutic agents like cisplatin, carboplatin, and oxaliplatin remain widely used for cancer treatment [40].

Nevertheless, the absence of precision in cancer therapy results in detrimental consequences and a rise in drug resistance [41]. Biotechnology, nanomedicine, and pharmacology each employ platinum nanoparticles in their respective research endeavors. Human trials have not yet been conducted to evaluate the efficacy of inorganic platinum nanoparticle nanoformulations. According to Jeyaraj et al. (2019), it is hypothesized that enhancing the duration of circulation of platinum nanoparticles within the human body could yield greater advantages. To achieve this, it is suggested that coating the surfaces of these nanoparticles with a biocompatible substance such as polyvinylpyrrolidone (PVP) may be a viable approach [42]. In an experimental investigation, DOX (doxorubicin) was employed as a representative pharmaceutical compound to synthesize platinum nanoparticles functionalized with PVP (polyvinylpyrrolidone). The resulting nanoparticles exhibited an octopod morphology and uniform distribution throughout the sample. The system was employed to enhance the process of drug distribution and mitigate toxicity. The platinum-DOX conjugate system was observed to enhance both drug release and biocompatibility. The cytotoxic capacity of the system was evaluated using two distinct subtypes of intrinsic breast cancer cells, namely MCF-7 and MDA-MB-231. The study conducted revealed that the activation of the tumor suppressor gene PTEN is involved in the inhibition of the PI3K/AKT signaling pathway (**Figure 2**) [43].

Kankala et al. hypothesized that platinum nanoparticles can deeply infiltrate tumors and exhibit synergistic therapeutic impacts due to the catalytic assistance of free radical species in the platinum nanoparticles. The ultrasmall platinum nanoparticles were dispersed within chitosan and loaded onto zinc-doped mesopo-

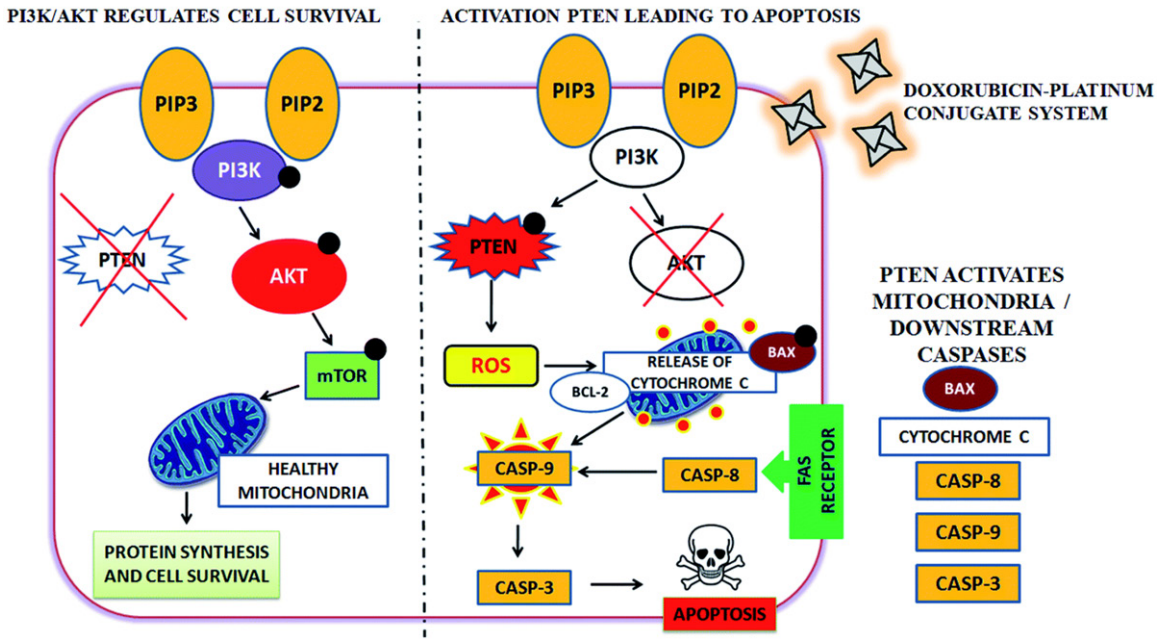

Figure 2. Using a doxorubicin-platinum conjugate system increases PTEN expression, inhibiting the PI3K/AKT pathway. Reproduced with permission from [43]. Copyrights (2021), RSC.

rous silica nanocarriers via self-assembly. The loading efficiency of doxorubicin molecules into the acidic microenvironment of the tumor was enhanced by the presence of zinc species incorporated into the siliceous frameworks, eliminating the requirement for supplementary functionalization [44]. The efficacy of anticancer treatment was improved through the disruption of established coordination interactions between the host and guest species, as Dhavale et al. (2021) demonstrated. The methodology greatly enhanced the elimination of tumors by enabling extensive infiltration into deep tumor regions while concurrently producing harmful free radicals to eliminate multidrug-resistant malignancies [45].

Gold nanoparticles: Gold nanoparticles, with their unique properties, find diverse biological applications, particularly in various imaging techniques. Their advantageous qualities, such as an extended half-life in the circulatory system, enhance tumor targeting for more precise cancer diagnoses. Gold nanoparticles demonstrate versatility in drug delivery, nucleic acid transport, radiation, and photothermal ablation. Their flexible synthesis, accommodating varied sizes and shapes, contributes to their clinical desirability, marked by reduced cytotoxicity and enhanced biocompatibility. Several diagnostic tools based on gold nanoparticles have received FDA clearance for commercial release, with ongoing testing of numerous formulations [46].

According to Umapathi et al. (2020), curcumin and isonicotinic acid hydrazide corona functionalized gold nanoparticles were developed to specifically target cancer. Both LK-2 lung cancer cells and TIG-120 fibrillary epithelial cells are very vulnerable to the toxicity of functional nanoparticles. Anticancer activity (ROS) was boosted by conjugating CUR and INH on Au-Nanoparticles [47]. Additional research revealed that the LK-2 and TIG-120 cells underwent apoptosis and morphological alterations. Furthermore, a comparison is made between these nanoparticles and standard cisplatin regarding their anticancer activity [48].

Palladium nanoparticles: Nanoparticles are composed of palladium. Palladium nanoparticles exhibit remarkable catalytic and optical properties, making them suitable for theragnostic purposes. According to scientific researchers, palladium nanomaterial has been employed as a prodrug activator, photothermal agent, and therapy for anticancer and antibacterial purposes. There have been assertions regarding the cost-effective biosynthesis

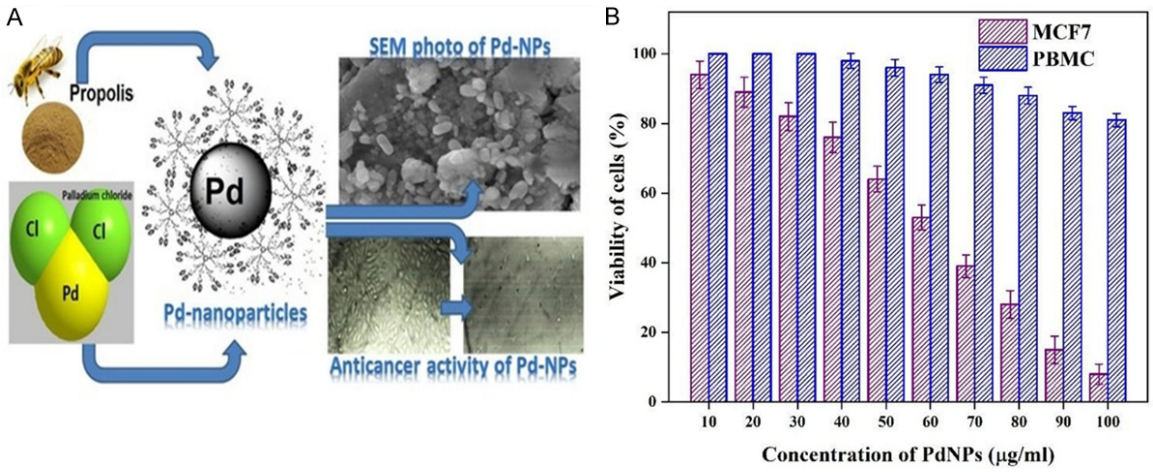

Figure 3. A. Mechanism of palladium nanoparticles activity against cancer. Reproduced with permission from [49]. Copyrights (2021), MDPI. B. The cytotoxicity of polyvinylpyrrolidone-coated palladium nanoparticles (PVP-Pd-Nanoparticles) against breast cancer cell lines was evaluated using the MTT assay. Reproduced with permission from [50]. Copyrights (2020), RSC.

of palladium nanoparticles through using Saudi propolis. According to Al-Fakeh et al. (2021), the palladium nanoparticles demonstrated a half-maximal inhibitory concentration (IC50) of 104.79 μg/mL, effectively achieving a therapeutic effect in the treatment of MCF-7 ductal cancer (**Figure 3A**) [49]. The palladium nanoparticles have undergone modifications to treat MCF7 breast cancer cells. This was achieved by utilizing PVP-functionalized palladium. As the dosage increased, PVP-coated palladium nanoparticles exhibited a significant decrease in the viability of MCF7 human breast cancer cells (**Figure 3B**). The hypothesized mechanism for the induction of death by the system involves the enzymatic activity of Caspase3/7, which is believed to cause damage to the mitochondrial membrane potential and nuclear DNA [50].

Silver nanoparticles: Antimicrobial wound dressings, topical lotions to prevent infection, and anticancer medicines are just a few of the many uses for silver nanoparticles, which are growing in popularity in biomedicine [51]. ROS, oxidative stress, and DNA damage are the key processes by which silver nanoparticles exert their effects. Reactive oxygen species (ROS) are crucial to cellular health because they maintain homeostasis. ROS, a consequence of cellular metabolism, plays an important role in intracellular signaling networks. However, silver nanoparticle-induced toxicity is mediated by an increase in intracellular reactive oxygen species (ROS) that destroys DNA, lipids, and proteins (**Figure 4**) [52].

After being taken in by the cell and broken down in the acidic cytosol, silver nanoparticles produce toxicity in the treated cells. Because of their propensity to disrupt fundamental cellular processes, including metabolism and cell division, silver nanoparticles have been associated with an increased risk of cancer and cell death [53]. According to Muhammad et al. (2021), adding silver nanoparticles to paclitaxel nanocrystals increases the drug's overall anti-cancer effectiveness against human cancer cells. The organic anti-cancer medicine paclitaxel was mixed with the inorganic tumor-targeting agents silver nanoparticles to create nanocrystals. The paclitaxel nanocrystals served as a mold for the polydopamine (PDA) coating. The PDA layer served as a connecting bridge for the in-situ synthesis and deposition of silver nanoparticles (RGDARF), and it was additionally grafted with the tumor-targeting peptide NR1. The cellular uptake efficiency, in vitro anticancer efficacy, and anti-migration impact of drug nanocrystals coated with NR1/AgNP were considerably enhanced. The studies showed that the effects of silver nanoparticles and paclitaxel on NR1-receptor interaction, pH-responsive drug release, and small size were additive or synergistic. These NR1-AgNP-decorated PTX nanocrystals struck an excellent balance between selectivity and biocompatibility. These nanocrystals have a significant degree of apop-

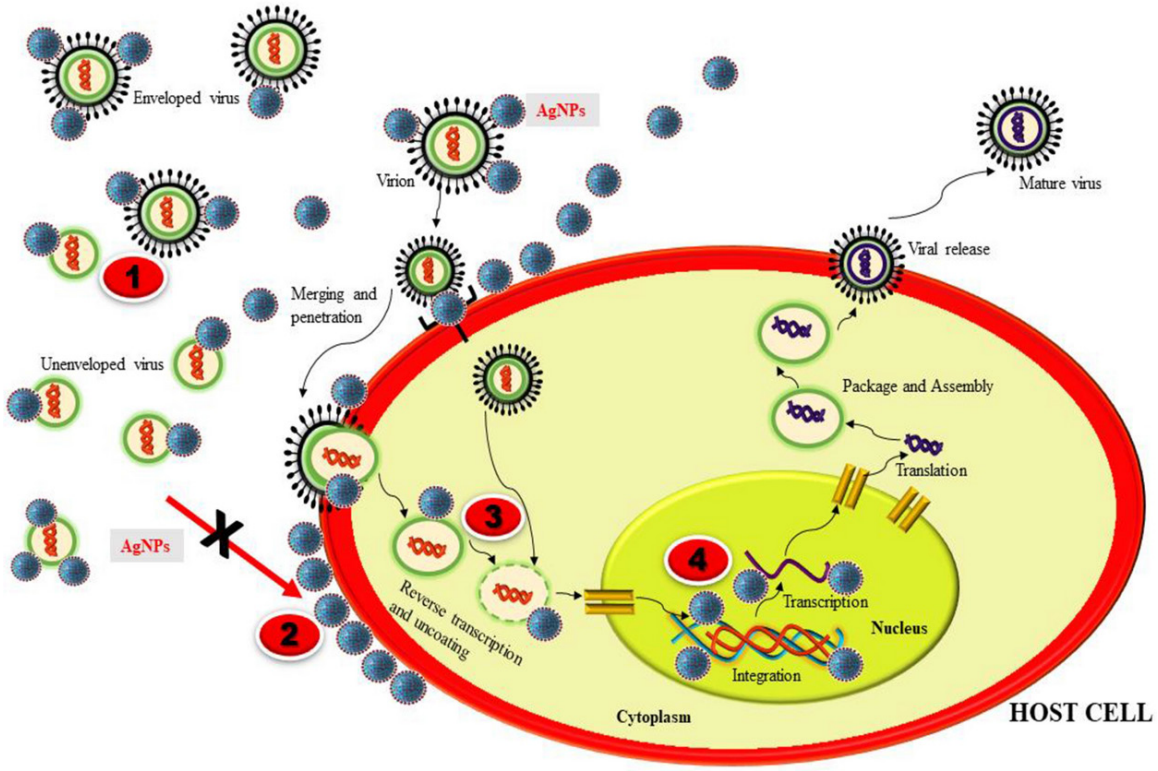

Figure 4. (1) The surface protein (gp120) of both enclosed and unenveloped viruses interacts with Ag nanoparticles. (2) Ag Nanoparticles prevent viruses from entering host cells. (3) Ag Nanoparticles impede the entrance of viruses into the nucleus of cells. (4) By interfering with the viral DNA, AgNanoparticles prevent viral reproduction. Reproduced with permission from [52]. Copyrights (2021), Springer.

totic efficiency, leading to membrane lysis, nuclear damage, mitochondrial malfunction, an increase in reactive oxygen species (ROS), and double-stranded DNA breakage [54]. Umapathi et al. (2020) and Muhammad et al. (2020) hypothesized that activation of p53 and caspase 3, as well as alteration of the Bax-to-Bcl-2 ratio, may be important to the potential acting mechanism and molecular foundation of these different pharmacological nanocrystals [47].

Magnetic nanoparticles

Magnetic nanoparticles, smaller than 50 nm, exhibit strong binding affinity, featuring protons, electrons, and ions with biocompatibility and no harmful effects. Their quick testing and low detection limit are advantageous, and their movement is governed by an external magnetic field, ensuring high saturation magnetization. Injected easily into the body, they maintain stability, allowing for tumor detection, localization, and intracellular drug delivery. The neutral pH in aqueous solutions further supports their stability, making them suitable for medicinal and environmental applications. Various synthetic routes, including chemical and physical methods, create nanoparticles with tailored properties, such as enhanced magnetic strength or improved medication delivery. Additionally, functionalized magnetic nanoparticles have been explored for cancer treatment using alternating magnetic fields or near-infrared light stimulation [55].

Due to their rapid degradation and unique cytotoxic mechanism when uncoated, iron oxide nanoparticles are useful for in vivo studies. The manipulation of magnetic spin is utilized to generate oxygen radicals for the goal of cancer diagnosis, and here is where iron oxide nanoparticles find their most common use. The capacity to control these nanoparticles with an external electromagnetic field should also be addressed. The introduction of locally hazardous reactive oxygen and reactive nitrogen species may result from such manipulation. Because of this property, nanoparticles may find

Table 2. Inorganic nanomaterials for cancer treatment

Sponsor	Indication	Clinical trials	Material description
Magnablate I	Prostate Cancer	NCT02033447 (Ph 0)	Magnetically sensitive iron nanoparticles for thermal ablation
NC100150/Clariscan/Feruglose/PEG-fero (Nycomed)	Microvascular imaging with MRI in tumors	NCT03455283 (Not Provided)	USPIO Nanoparticles with a polyethylene glycol carbohydrate coating
NanoTherm	Thermal ablation Local ablation in glioblastoma	Approved, 2010 (EMA)	Magnetite nanoparticles coated with aminosilane
Ferristene	Cancer gastrointestinal tract	Approved, 1993 (Sweden); Discontinued, 2002	Nanoparticles of iron oxide covered with polystyrene
Diafer	Deficiency in iron CKD-associated anemia	NCT02301026 (Not Provided) Approved, 2013	Colloid Iron Isomaltoside 5%
Radiogardase	Thallium: radioactive/non-radioactive	Approved, 2003 (FDA)	Prussian blue
Ferumoxtran-10/AMI-277	Breast Cancer Bladder cancer	NCT02751606 (Ph III) NCT00188695 (Ph I/II)	Dextran T-10-coated USPIO nanoparticles
CosmoFer	Iron deficiency in Anemia	NCT01428843 (Ph III), NCT01447628 (Ph II), NCT02086838 (Ph IV)	Low molecular weight iron dextran colloid
Monofer	Malignancies; Esophageal Cancer Recipients; Colorectal Cancer	NCT01895218 (Ph III), NCT02172001 (Ph III), NCT03888768 (Not Applicable), (Ph IV), NCT03957057 (Ph III)	1000 colloid units of iron isomaltoside, 10%
MagProbe	Leukemia detection	NCT01411904 (Not Applicable)	Nanoparticles of magnetic iron oxide

widespread use in the emerging area of tumor therapy. This kind of treatment makes healthy tissues less likely to have unwanted side effects. Compared to standard antitumor drugs, iron oxide nanoparticles loaded with anticancer drugs have several advantages. These benefits result from their remote controllability, as shown in a mouse model of breast cancer [56, 57]. Increasing evidence points to miRNA-155 overexpression as a biomarker for breast cancer. However, there are obstacles to mapping miRNA-155 since so few very sensitive technologies are currently available. To solve this problem, researchers have developed a fresh approach to producing miRNA-155-measuring magnetic nanoprobes in short order [58]. According to a different study, the longitudinal evaluation of LCDIO in malignant tumors revealed an increase in tumor cells in the bloodstream. This confirms that MRI is a useful tool for detecting tumors. Furthermore, there is evidence that LCDIO has a unique distribution pattern inside tumor cells. In areas of vigorous angiogenesis, however, LCDIO may be taken up by endothelial cells and macrophages as well. Additionally, in vitro cell culture investigations showed a significant correlation between LCDIO uptake and cancer cell growth [59]. The clinical trails of various mangnetic nanomaterials are given in **Table 2**.

Fe_3O_4 magnetic nanoparticles (MNanoparticles) were grafted with chitosan (**Figure 5A**), a naturally occurring hydrophilic and biodegradable polymer, to facilitate the delivery of the anticancer medication telmisartan (TEL). The increased amount of TEL concentration resulted in heightened loading capacity and efficiency (**Figure 5B**). The controlled release features of drug-loaded MNP-CS (MNP-CS-TEL) varied with pH (**Figure 5C**). Cytotoxicity investigations were conducted using the MTT method to assess the cell viability % of MNP-CS, MNP-CS-TEL, and Free TEL on PC-3 cancer cells (**Figure 5D**) [44].

Incorporating MNanoparticles into self-assembled hybrid nanoparticles provides benefits, including the ability to load vast quantities of medicines and regulate drug release. In this setting, nickel ferrite (NFO) nanoparticles have been employed to transport chemotherapeutic agents. To disperse zidovudine (AZT), a polyvinyl alcohol/stearic acid hybrid was employed with a polyethylene glycol (PEG) formulation containing NFO. Using NFO-reinforced hybrid nanoparticles, intracellular delivery of AZT was verified [60]. The use of environmentally friendly chemistry in MNP production is also highlighted. Using Arabic gum as a green reagent, nickel oxide nanoparticles were successfully synthesized. They employed the MTT assay on U87MG cancer cell lines to determine the cyto-

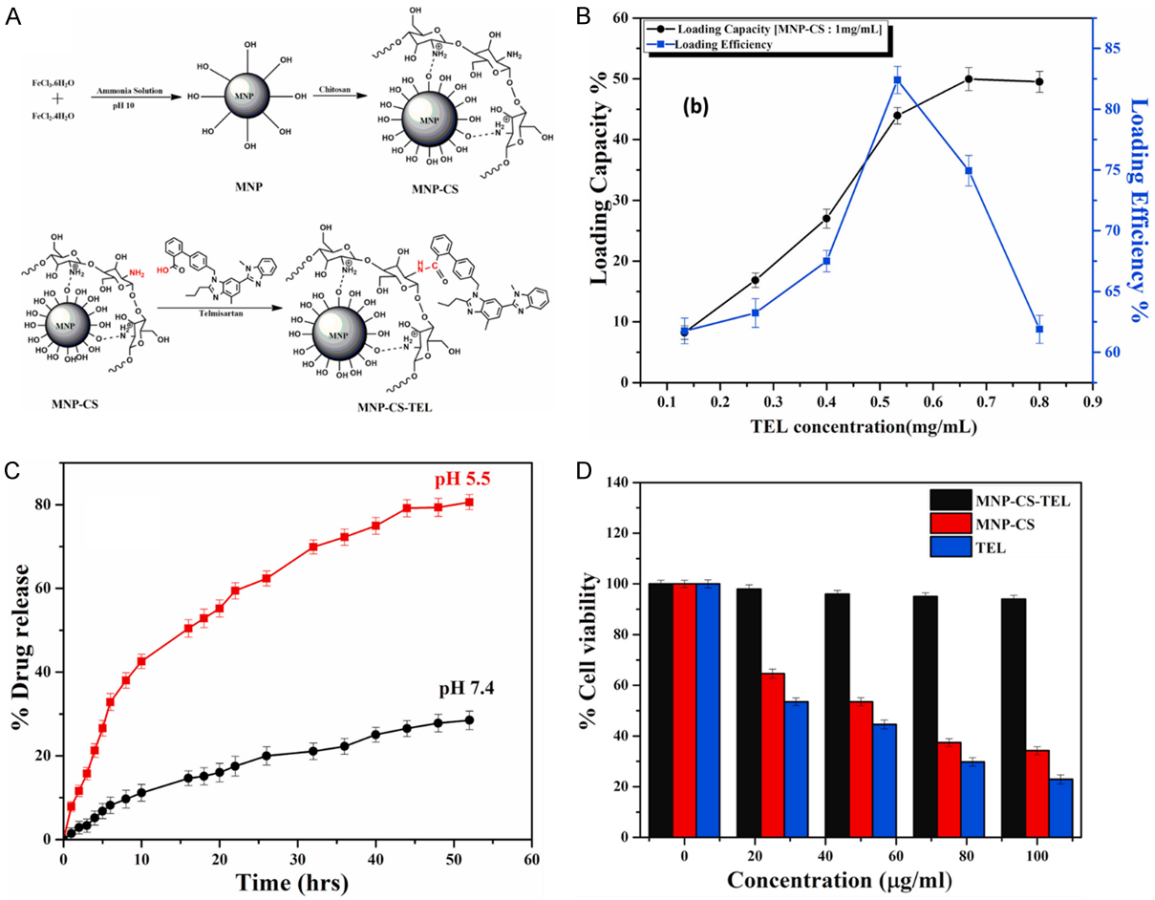

Figure 5. A. Fabrication of MNP-CS-TEL. B. Drug loading capacity variation with TEL concentration (MNP-CS: 1 mg/ml). C. Drug release profiles of MNP-CS-TEL at different pH and temperature conditions. D. In vitro cytotoxicity assay of MNP-CS, MNP-CS-TEL, and TEL on PC-3 human prostate cancer cell line using MTT assay. Reproduced with permission from [44]. Copyrights (2021), Elsevier.

toxicity of nickel oxide nanoparticles. The IC50 of this drug was determined to be 37.84 g mL when tested on U87MG cancer cells [61].

Polymeric-based nanoparticles for cancer diagnosis and treatment

Polymeric nanoparticles are a kind of nanoparticle whose size is generally between 1 and 1000 nm. Nanocapsules and nanospheres are two examples of the different structural configurations in polymer nanocomposites. These constructions are stronger mechanically, more electrically conductive, and more insulated thermally and optically. Advanced fluorophores with active pharmaceutical ingredients and drug delivery systems may increase luminosity while decreasing toxicity and bioaccumulation. Microencapsulation is the gold standard for drug delivery systems. Vaccines and tissue engineering are only two of the many areas where polymeric nanoparticles have been put to use. The nanoparticles protect the pharmaceutical molecules during drug delivery [62]. Antiviral drugs, antioxidants, vitamins, antisense oligonucleotides, anticancer drugs, and plasmid DNA are only some medications that have been delivered with the help of natural polymers. Synthetic polymers may be used to create polymeric nanoparticles. Based on whether or not they decompose, these PNanoparticles fall into one of two categories: biodegradable and non-biodegradable. In cutaneous and transdermal medication administration systems, non-biodegradable polyacrylates are employed to a lower degree than biodegradable polymers [63]. Transdermal medication delivery systems have used the biodegradable polymer poly-lactic-co-glycolic acid [64].

The quality of optical and magnetic resonance imaging to identify brain cancer has been improved with the help of PNanoparticles. Three-dimensional core-shell polymers called dendrimers may improve targeting and achieve a brain-blood-barrier crossing in this way. Dendrimers made of poly-amidoamine have become more popular for use in medication delivery. Dendrimers conjugated with tamoxifen are of special interest because of their function as drug carriers [65]. In order to lower the solution's surface tension for polymer-based nanoparticle synthesis, surfactants are often used. The monomer, the fundamental unit of a polymer, is next mixed with the surfactant. Subsequently, nanoparticles are formed as a consequence of polymerization of the monomer.

The disadvantages of polymeric nanoparticles are their decreased stability and their tendency to aggregate. The characteristics mentioned above might complicate some applications, including drug delivery. Further, the necessity for precise control of reaction conditions during the creation of polymeric nanoparticles may provide difficulties. Due to their susceptibility to oxidation, polymeric nanoparticles can only be used in certain situations. The necessity for precise monitoring of reaction conditions complicates scaling up polymeric nanoparticles for commercial usage. In cancer diagnosis and therapy, doxorubicin-loaded polymeric nanoparticles that glow in the near-infrared have been used [66]. In a different study, nanoparticles made of 99mTc-PLA/PVA/Atezolizumab were biodistributed to aid in the diagnosis of non-small cell lung cancer [67].

Methotrexate (MTX) was effectively encapsulated within chitosan nanoparticles (Meth-Cs-Nanoparticles) using the ionic gelation technique, aiming to enhance the anti-cancer potency of MTX. The created nanocarriers demonstrated the ability to encapsulate hydrophilic MTX to its fullest capacity effectively. In the study, nanoparticles loaded with MTX were synthesized to achieve optimal entrapment efficiency, which was determined to be 87%. These nanoparticles were subsequently assessed for their effectiveness in combating cancer. The in-vitro drug release study demonstrated a significant level of controlled release of MTX (methotrexate) in an acidic environment. In the context of in-vitro cytotoxicity studies conducted on MDA-MB-231 cell lines, it had been observed that Meth-Cs-Nanoparticles exhibit a significant inhibitory effect on cell viability. Specifically, at a concentration of 15 μg/mL and after 24 h of incubation, Meth-Cs-Nanoparticles inhibited 50% of cell viability. This inhibitory effect is notably higher than the impact observed with MTX alone. The body weight changes of rats in disease control (saline), free MTX, Cs-Nanoparticles, and Meth-Cs-Nanoparticles groups throughout the trial (**Figure 6A** and **6B**). The Meth-Cs-Nanoparticles group had a substantial drop in body weight compared to the sick control group, Cs-Nanoparticles group, and free MTX group ($P < 0.05$). Treatment group survival curves are shown in **Figure 6C**. **Figure 6D** shows tumor volume changes in rats treated with saline (diseased control), free MTX, Cs-Nanoparticles, and Meth-Cs-Nanoparticles nanoparticles. The diseased control group saw a significant rise in tumor volume from 370 to 1414 mm^3. In the free MTX group, tumor growth ranged from 270 to 885 mm^3, whereas Meth-Cs-Nanoparticles considerably inhibited growth (197-385 mm^3). Meth-Cs-Nanoparticles decrease tumor development more than free MTX. The tumor weight of the Meth-Cs-Nanoparticles group was broadly ($P < 0.05$) lower than the diseased control group (**Figure 6E**). The TIR values of the Meth-Cs-Nanoparticles and Cs-Nanoparticles groups were 78% and 58%, respectively, whereas the MTX group was 50%. These findings show that Meth-Cs-Nanoparticles had remarkable anti-tumor activity (**Figure 6F**). The findings suggested that cancer cells have demonstrated a high nanoparticle uptake capacity, leading to enhanced anti-cancer effects [68].

Advantages and disadvantages of polymeric nanoparticles

Polymeric nanoparticles possess several significant benefits. These include their diminutive dimensions, compatibility with biological systems, ability to degrade naturally, capacity to carry a substantial amount of medication, minimal or absent toxicity towards healthy cells, robust stability under physiological conditions, capability to transport imaging agents, controlled release of drugs, stability of the nanoparticles-drug complex at pH levels found in biological buffers, and the facilitation of interfaces

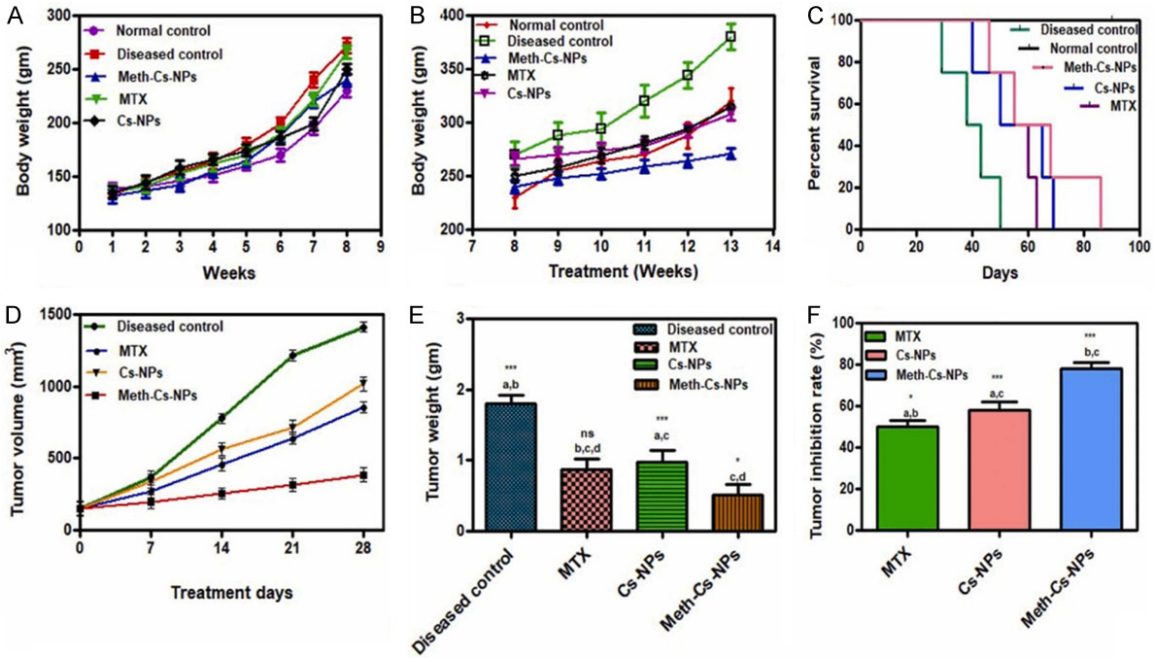

Figure 6. A. Before treatment: Body weight. B. After treatment: Body weight. C. Survival curve. D. Tumor volume curve: Slower tumor growth observed in the Meth-Cs-Nanoparticles group compared to the other three groups. E. Tumor weight comparison and tumor inhibition rate. F. Comparison of different samples.

between the nanoparticles-drug complex and receptors [63]. In addition to these benefits, further advantages include the simplicity of their preparation and the ability to effectively regulate both size and distribution. Polymeric nanoparticles have favorable protective properties against environmental conditions when used as carriers for encapsulated medicines. Polymeric nanoparticles provide advantageous characteristics such as effective medication retention and extended blood circulation durations [69]. Polymeric nanoparticles do not possess any significant drawbacks.

Nevertheless, the primary negatives that might be considered are the restricted targeting capabilities and the issue of therapeutic termination. Polymeric nanoparticles have the potential to induce autonomic imbalance disturbances. Polymeric nanoparticles have been shown to sometimes influence vascular and cardiac functioning [70].

Carbon-based nanomaterials

Particles measuring between 1 and 100 nm in size are considered nanoparticles [71]. The extraordinary qualities of nanomaterials have made them ideal for use in biomedical applications, ushering in medical research has entered a new era. Nanomaterials are distinguished from other substances by their superior thermal and mechanical stability, greater surface-to-volume ratio, and ease of derivatization. Carbon is a ubiquitous component of all living things, and it has piqued human curiosity for a long time due to its potential uses in medicine and environmental research (**Figure 7**). As a result of advancements in nanoscience, carbon compounds have shrunk from macroscopic to nanoscale dimensions. Since their development, carbon-based nanomaterials have received extensive study and are now an integral part of nanotechnology (**Table 3**). Multiple carbon allotropes have been reported to exist at present, each with its own unique set of hybridization patterns (sp3, sp2, and sp) and dimensional features (3D, 2D, 1D, 0D) [72]. Nanodiamonds, graphene, carbon nanocones, graphene oxide, carbon nanobuds, quantum dots, and carbon nanotubes are just some of the newly discovered forms of carbon that have been the subject of extensive study in recent years. Nano-electronics theragnostics, field emission display, energy storage, high-frequency electronics, and conversion are just some of the many places where these allotropes and

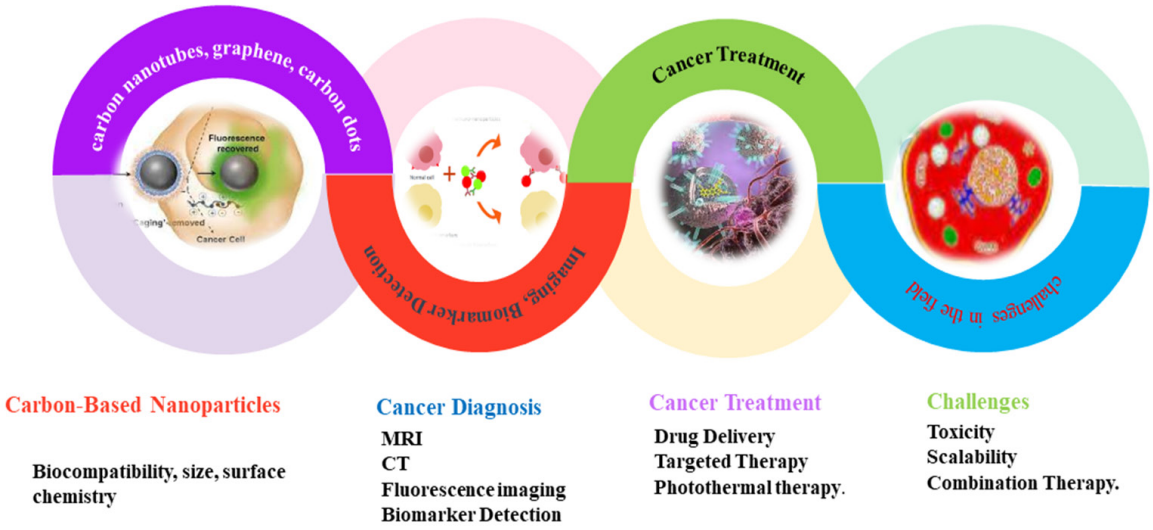

Figure 7. Role of Carbon-based nanoparticles and nanomaterials in cancer treatment and diagnosis.

Table 3. Various carbon materials (CNTs and Fullerenes) role in cancer treatment

Nanocomposites	Cancer type	Biomarkers	References
Carboxyfullerenes	Blood cancer	MMP-2, MMP-9	[171]
MWCNTs	Pancreatic cancer	Carbohydrate antigen 19-9	[102]
Red-fluorescent fullerene	Breast cancer	Protein and changes to the fullerene scaffold's structure lead to cytotoxic consequences.	[172]
DBCO-PEG5-NHS ester-modified CNTs	Hepatocellular carcinoma	Golgi protein 73 and Alpha-fetoprotein	[173]
Aminofullerenes	Lung cancer	Hsp90β, MYH9	[174]
Zein Nanoparticles/MWCNTs	HepG2 cell line	H_2O_2 monitoring HepG2 cells	[175]
Fullerene (C60)	The MTT experiment confirmed the cytotoxic potential of the nanocomplex in vitro	Higher cytotoxicity (in vitro) against cancer cells was observed in the C60 + LA nanocomplex	[176]
LyP-1 conjugated siRNA/MWCNTs	Pancreatic cancer	Delivery of siRNA	[177]
Fullerenes	Pancreatic cancer	Human serum albumin	[178]
Functionalized CNTs	HepG2 cell line	Sorafenib delivery	[179]

their functionalized versions have found a home [73]. Researchers in the area of biosensors have made extensive use of carbon-based materials in recent decades, intending to increase sensitivity and selectivity. Over time, these materials' use in biosensors has expanded beyond their primary functions to include their incorporation as electrode components.

Fullerene

Graphene, nanoclusters, nanowires, and carbon nanotubes are only some of the zero-, one-, and two-dimensional (2D) carbon compounds produced to improve their potential uses. Within the family of carbon nanostructures, fullerenes are among the most potent components. The carbon atoms in fullerenes are sp2 hybridized and organized in exceedingly symmetrical polyhedral clusters or cages by fusing five- and six-membered rings. These rings have either 70 or 60 atoms, thus the designations C70 and C60. The given numerical value is 45. Next, in line after C60 is its stable homolog C70, then C82, C80, C76, C74, and so on [74, 75]. Since their discovery, fullerenes have attracted a great deal of interest from scientists due to their unique electrochemical properties and stability. Geodesic and electrical bonding contribute to C60 molecular stability. In 1966, Daedalus proposed a theoretical framework for developing a thick, hollow carbonaceous structure on the inside. The C60 molecule, which has an Ih symmetric soccer ball shape, was initially introduced by Osawa in 1970. Kroto and Smalley's definitive discovery of fullerene C60 in 1985 was a major step for-

ward in the scientific community. This progress was made possible by vaporizing graphite with a Nd: YAG laser. The compound was named Buckminsterfullerene after the architect R. Buckminster Fuller, whose idea was to model a compound like a soccer ball [76, 77]. The sp2 hybridized carbon atom is an efficient electron acceptor because of its lengthy - conjugation. Several fields of study are now using fullerenes, including solar cells, medicine, nanoelectronics, and supercapacitors. The modest diameter range of fullerenes (7-10) and expanded options for surface chemical modification bode well for their potential biological action [78].

C60 has two different bond lengths, the 6:6 ring bonds, and the 6:5 linear bonds. The former are conceivably double bonds and seem shorter than the latter. Because C60's pentagonal rings are unlikely to form double bonds, its aromaticity is diminished, and not considered a superaromatic molecule. To conclude, C60 structures are typically characterized by electron-deficient alkenes possessing distinctive characteristics and a heightened reactivity towards entities that have an abundance of electrons. The ionization potential of this particular element is measured to be 7.8 electron volts (eV), while its electron affinity is determined to be 2.7 eV. C60 shows promise as a good option for various electrochemical applications due to its tendency to participate in electron transfer processes and its robust electrochemical characteristics [79-81].

The most common method for producing fullerenes is the low-pressure vaporization and inert gas of carbon-rich materials using an arc plasma. However, this method has a relatively small quantity of pure fullerenes [82]. Improved results and the ability to synthesize fullerenes on a wide scale are made possible using high-frequency arc plasma methods. Other synthesis methods have been established, including reactive precursors, vaporization, and chemical synthesis of a carbon source [83, 84].

Since fullerenes (C60) were discovered, biosensor research has dramatically shifted [85]. Researchers are interested in fullerenes because of their unique topological properties and electrochemical features, i.e., the ability to absorb light across a large spectrum (UV-visible), angular strain in the structure, a long triplet state lifetime, a photo-thermal effect, and reversible electrophilic and nucleophilic properties [86]. Consideration of the presence of functional groups and hydrophilicity is crucial for improving the performance of fullerene as a mediator in a biosensing device. These characteristics are essential for easing fullerene's incorporation into the targeted biomolecules. However, bioconjugation with physiologically active molecules is ineffective if these two characteristics are missing [87]. Functionalization strategies, including carboxy, amino, or hydroxyl groups, are required to overcome this difficulty. Functionalization strategies may vary from one area of application to another. Different biosensors (potentiometric, electrochemical, optical) and analytes (enzymes, proteins, antigens) result in other modifications of elemental fullerene [88]. The fullerene structure is modified by adding functional groups to facilitate efficient interaction with the target molecule. This will allow for a healthy flow of electrons between the electrodes and the analyte [89]. The fullerene molecule is immobile concerning the glucose oxidase enzyme within the setting of a glucose biosensor. The research claims that a positive association exists between the concentration of immobilized fullerenes and the sensitivity of the glucose biosensor [90, 91]. Both potentiometric and piezoelectric biosensors have been tested in experiments using fullerenes for urea detection. An acrylic-based hydrogen ion membrane was coated with a bioconjugate comprising fullerene and urease to create a potentiometric biosensor for urea detection. The results of the experiments showed that the bioconjugate was stable for a total of 140 days [92]. Fullerenes are crucial components in several biosensors for detecting biomolecules, including electrochemical, potentiometric, and piezoelectric biosensors, immunosensors, and DNA sensors [93]. Novel and notable characteristics in modifying or constructing biosensors include the capacity to quickly functionalize fullerenes, modify signals, and switch when exposed to light.

Carbon nanotubes

The prominence of carbon nanotubes during the 1990s has piqued the curiosity of scientists ever since. Nanostructures under consideration are made from a rolled-up sheet of graphene. Single-walled carbon nanotubes,

double-walled carbon nanotubes, and multi-walled carbon nanotubes have all been postulated as possible forms of these structures [94]. These materials exhibit various fascinating properties because of their small size and cylindrical shape. Carbon nanotubes, specifically individual single-walled carbon nanotubes, show promising attributes that could surpass conventional materials used in practical applications.

Carbon nanotubes may have far-reaching implications for the future of biology and medicine. Several studies have been undertaken to prove the usefulness of these materials in their respective fields of application [95]. Recent research has shown the efficacy of a matrix composed of various DNA and carbon nanotube combinations in identifying biomarkers linked to gynecologic cancers. Researchers have examined how biomarkers may change how carbon nanotubes behave optically. It was shown that this effect is sensitive to both the DNA sequence and the CNTs' chirality. Therefore, tracking the fluorescence spectra of many DNA-CNT hybrids may allow for the registration of a cancer fingerprint. This research reveals the feasibility of using nanostructures based on functional carbon nanotubes for detecting and treating several cancers, including pancreatic and liver [96].

CNTs for pancreatic cancer analysis and therapy: Pancreatic cancer, often known as PC in the medical literature, is an extremely common and deadly form of cancer that affects the pancreas. According to research, those diagnosed with this illness have a very low chance of surviving. It may also invade nearby tissues and spread to other organs [97]. When standard chemotherapy fails to control pancreatic cancer, surgery is typically necessary [98, 99]. However, most people with pancreatic cancer are often diagnosed at a later stage of the disease due to the lack of clinical symptoms in the early stages. In addition, the increased risk of metastasis in later stages reduces the effectiveness of surgical procedures [100]. Endoscopic ultrasonography and computed tomography have been routinely used to diagnose and stage pancreatic cancer [101], sometimes combined with fine needle biopsy. However, there are difficulties connected with using such approaches. The effectiveness of a complex endoscopic surgery relies significantly on the physicians' expertise and the accuracy with which they interpret CT scans. Thus, adopting a new strategy for early identification of pancreatic cancer is crucial. More and more people are interested in discovering and developing carbon nanotube-based new nanomaterials with different theranostic uses, especially in the field of cancer research. In addition, they have become more important in PC diagnosis and treatment. Several research has focused on the use of biomarkers for the diagnosis of cancer. Cancers of the pancreas, bile duct, liver, stomach, and colorectal tract may all be reliably diagnosed with the use of carbohydrate antigen 19-9 (CA19-9). To detect CA19-9, a biosensor based on MWCNTs was placed on microporous filter paper [102].

CNTs for liver cancer detection and therapy: According to most estimates, human liver cancer is the sixth most common cancer worldwide. Asia and Africa have a far greater incidence of this problem than Europe. About 75% of all cases of liver cancer are classified as either hepatocellular carcinoma or malignant hepatoma. Liver transplantation and surgical intervention are the standard treatments. However, these approaches only work in the early stages of hepatocellular carcinoma and fail miserably after the cancer has spread [103].

Chemotherapy is now the standard of care for this disease. The limited capacity to selectively target liver cancer cells, the widespread development of drug resistance, and the unpleasant side effects of this strategy all reduce its efficacy. Anti-angiogenesis drugs, such as tyrosine kinase inhibitors, are the mainstay of chemotherapeutic therapy for hepatocellular carcinoma. Although these drugs mainly target cancer cells, they can have side effects on healthy cells. These pharmaceuticals can potentially slow the growth of normal cells throughout the human body, including those in the bone marrow, the digestive system, and the hair follicles. These problems may find a solution in the revolutionary diagnostic and therapeutic strategies based on nanocarriers made possible by the development of nanotechnology. In order to identify liver cancer, cutting-edge diagnostic tools have been built using carbon nanotubes. CNTs' advantageous biochemistry and microstructure have been shown to facilitate the

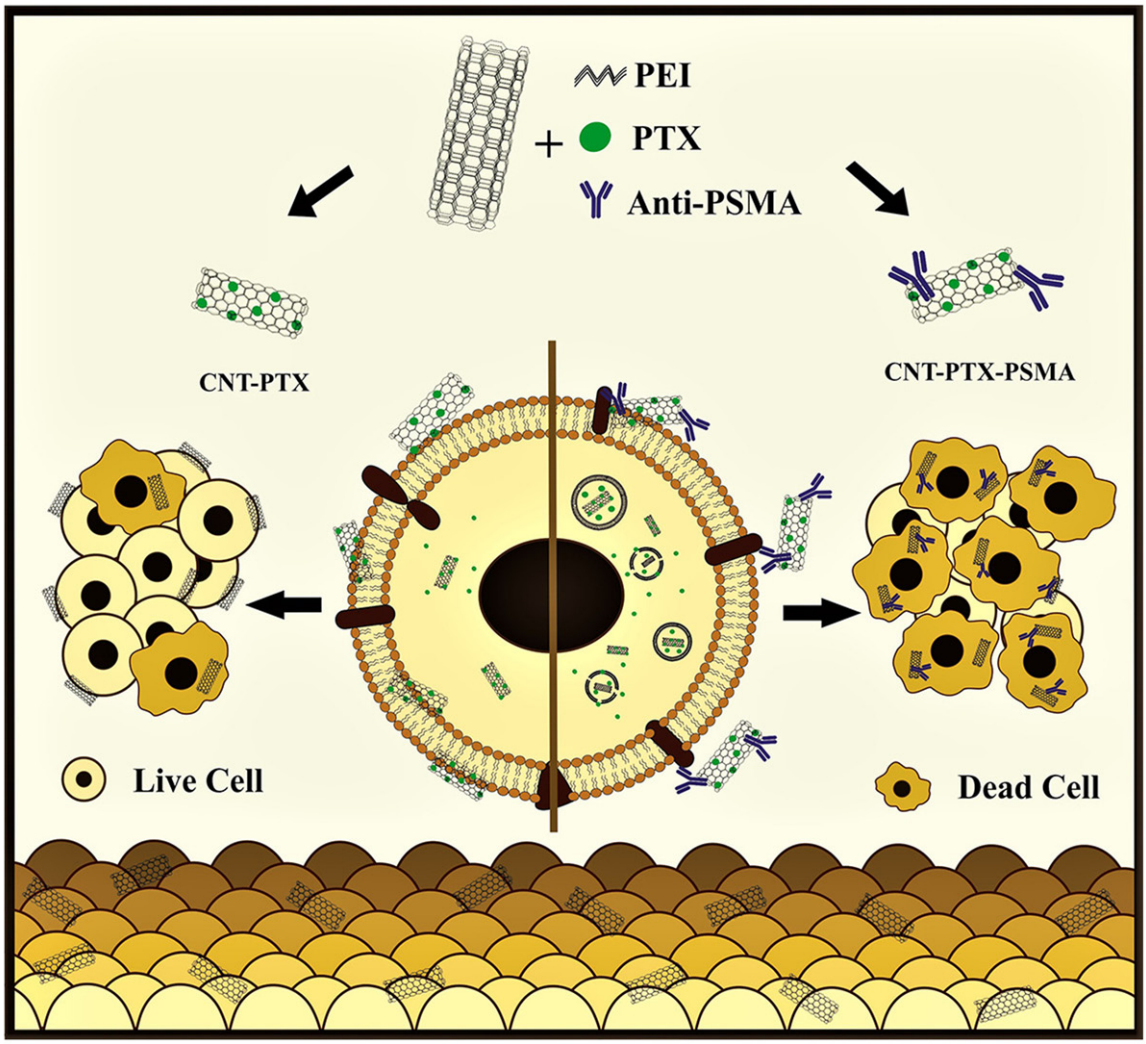

Figure 8. Mechanism of action of CNT-PTX on prostate cancer cell.

transport of anticancer medicines into the target cancer cells [104].

Paclitaxel (PTX), the first-line prostate cancer treatment, was added to polyethyleneimine-functionalized multiple-wall carbon nanotubes (CNTs) by Edson José Comparetti et al. These particles were then coated with PSMA antibodies to target prostate cancer cells. HCT-116 LNCaP prostate cancer cells (PSMA+), CaCo-2 colon cancer cells (PSMA-), and human peripheral monocytes and lymphocytes (PSMA-) were in vitro exposed to fluorescent CNT composites. Fluorescence microscopy and flow cytometry showed that CNT-PTX and CNTs interact diffusely with all cell types. Cytotoxicity analysis showed that PTX complexed with CNTs was more effective on the prostate (PSMA+) and colorectal cancer cells (PSMA-) than pure PTX or CNTs alone (**Figure 8**) [104].

Carbon dots

CDs' unique photoluminescence capabilities in the visible region have piqued the curiosity of the bio-imaging community [105]. This is because of their small size, passivated surface, and remarkable fluorescence properties, which include high photo-stability, a broad excitation spectrum, and tunable emission characteristics [106, 107]. Nanomaterials made of carbon have the potential to streamline both imaging and drug delivery [108]. It has been proposed that doxorubicin delivery and fluorescence imaging can be greatly improved by employing GQDs-MSNs (Graphene quantum dots-Meso-

porous silica nanoparticles) nanocomposite nanoparticles. Using this method, scientists can track the carrier's location within the cell and how the medicine is diffused from it [109]. The use of CDs could open up new paths of investigation for studying the detection of cancer cells. Specially functionalized cyclodextrins can penetrate many different kinds of cancer cells. Because of this, fluorescence imaging techniques can be used to probe the cancer cells with greater efficiency. An individual recognition procedure is required to interact with cancer cell surface groups and functional CDs [110]. Because of their capacity to selectively target the surface moiety of angiopep 2 found on glioma cells, PEGylated cyclodextrins like those stated cannot be rewritten from the user's description. Glioma imaging is more sensitive than imaging of normal brain tissue because of this specific recognition process [111]. The development of biocompatible CDs with a QY of over 20% has been the focus of several recent research and development efforts. These discs are designed for use in biosensing and bioimaging [112].

Carbon quantum dots may be improved for bioimaging applications through passivation and doping processes. CDs with a high QY could be useful in bioimaging because of the information they could store [113]. Carbon dots' potential application in fluorescent bio-imaging could be increased by incorporating heteroatoms, which can alter their intrinsic properties and boost the fluorescence quantum yield. Nitrogen doping is found to increase the quantum yield of CDs by 16% [114]. Carbon dots were studied for their luminous qualities as a potential bioimaging probe in confocal microscopy. Graphene quantum dots were produced from carbon black and used in this research [115]. Since the product displayed green fluorescence after being taken up by MCF-7 human breast cancer cells, we can infer that its biocompatibility is quite high [116, 117].

CDs may be used as a photosensitizer, allowing for the easier production of reactive oxygen species when exposed to light [118]. Short user-provided content precludes scholarly rewriting. Surface passivation, heteroatom doping, and the edge effect are the three ways carbon dots can be functionalized [119]. We used a one-pot microwave-assisted pyrolysis approach to create poly-dopamine passivated fluorescent carbon dots. The quantum yield of CDs was increased by a factor of three due to the insertion of N^{-} N-atoms, achieved without using PDA. Because of this occurrence, we now have a reliable photo-thermal conversion efficiency and unprecedented compatibility with living systems [120]. A novel drug delivery platform using hyaluronic acid-modified carbon dot-doxorubicin nanoparticles was synthesized easily. One-step hydrothermal treatment with citric acid and branch-PEI as core carbon source produced CD44-targeted HA-modified carbon dots (HA-CDs) as carriers in one hour. This method used HA as a carbon dot, hydrophilic group, and targeting ligand. The as-prepared HA-CDs were loaded with doxorubicin (HA-CD@p-CBA-DOX) through an acid-cleavable bond, which released the drug pH-responsively. In vitro tests, HA-CD@p-CBA-DOX showed excellent 4T1 cell cytotoxicity, hemocompatibility, and serum stability. Confocal laser scanning imaging and flow cytometry showed that 4T1 cells ingested DOX-loaded nanoparticles through HA-mediated CD44-targeting. Live imaging revealed that HA-CD@p-CBA-DOX increased tumor accumulation in vivo. In heterotopic and orthotopic 4T1 cell tumor models, HA-CD@p-CBA-DOX outperformed free DOX in vivo (**Figure 9A** and **9B**). HA-CD@p-CBA-DOX's biocompatibility was further validated by blood hematological and biochemistry tests showing no harm. HA-CD@p-CBA-DOX offers a targeted breast cancer treatment approach (**Figure 9C-E**) [121]. **Table 4** gives the summary of various carbon quantum dots nanocomposites in the treatment of cancers.

Graphene

To facilitate the advancement of a drug delivery system utilizing graphene oxide for the specific objective of anticancer therapy, it is feasible to integrate many anticancer agents, including Doxorubicin, Paclitaxel, and methotrexate, either onto the surface of GO or by immobilizing them via graphene [122]. The use of nanoparticles that are particular to certain cell types as carriers for medication has shown promise in effectively targeting cells at lower doses [123]. For example, a research investigation was carried out in which aptamer-coupled magnetic graphene oxide nanocarriers were synthesized

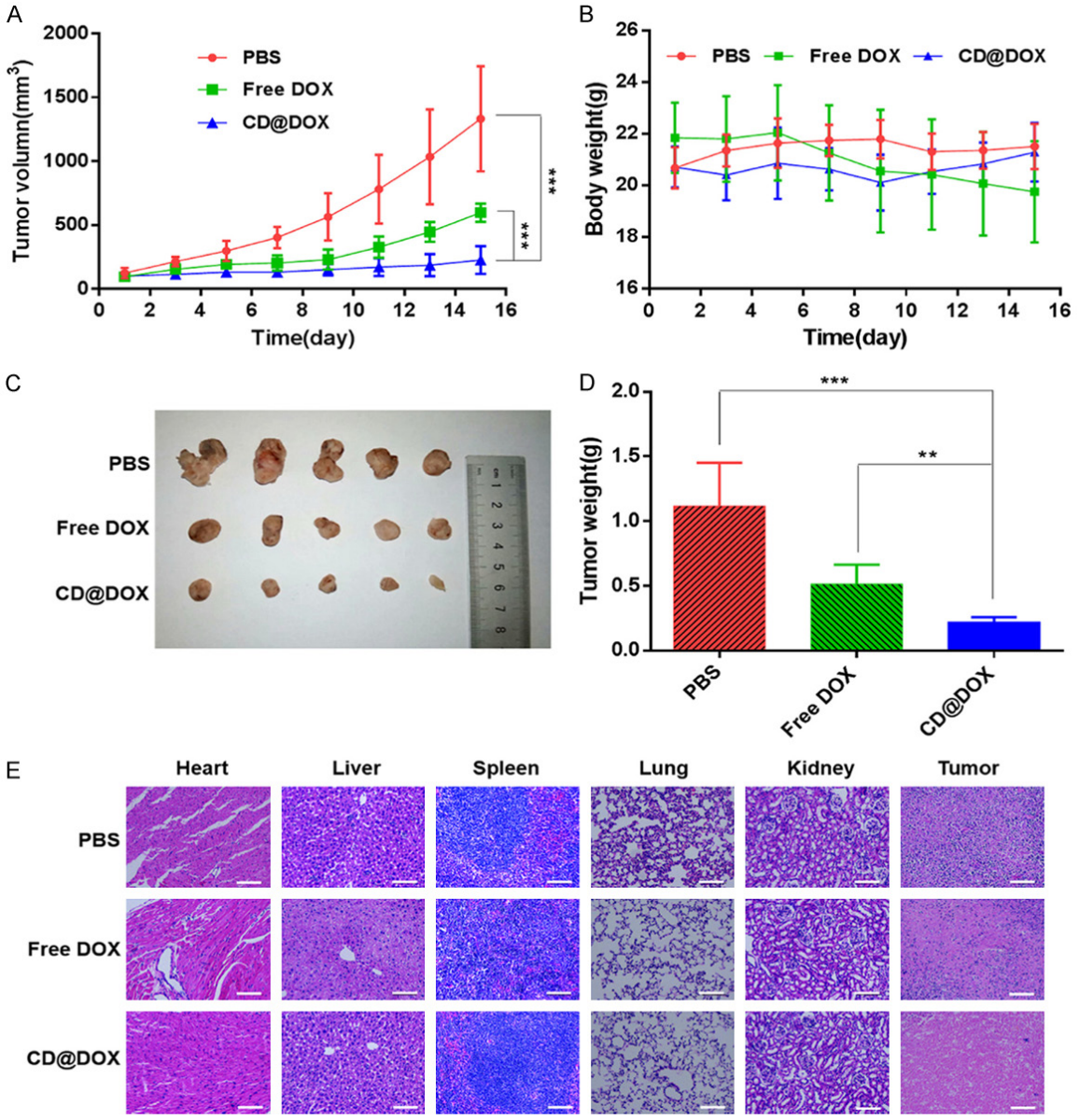

Figure 9. (A) The effects of injecting free doxorubicin and HA-CD@p-CBA-DOX into tumor-bearing heterotopic 4T1 mice on tumor volume. (B) The effects of free doxorubicin and HA-CD@p-CBA-DOX on the body weight of heterotopic 4T1 tumor-bearing mice. Picture (C) of the tumor. (D) Tumor masses at day 15 for all groups. (E) Tumor and major organ H&E staining after therapy. **p 0.01 and ***p 0.001 (n = 5, mean SD). The 100 m scale bar represents one hundred micrometers. Reproduced with permission from [121]. Copyrights (2020), Elsevier.

and successfully targeted the MCF-7 human breast cancer cell line.

The nanocarriers were determined to be extremely appropriate drug carriers for targeted drug delivery systems in the context of anticancer treatment [124]. The effective copolymerization of Graphene oxide with β-cyclodextrin was revealed in a study by researchers. The copolymerization procedure led to the incorporation of two medications, methotrexate and doxorubicin, which exhibit hydrophobic and hydrophilic characteristics, respectively. The copolymer demonstrated significant effectiveness in causing cytotoxicity in cancer cells [125]. A distinct inquiry was undertaken to produce superparamagnetic iron oxide-reduced graphene oxide, followed by the loading of the DOX medicine. The cancer cells demonstrate an acidic microenvironment with a pH value of

Table 4. Role of carbon/quantum dots against various cancers

Nanocomposite	Binding force	Synthesis	Highlights	References
HA-CD@p-CBA-DOX	Acid-cleavable bond	One-step hydrothermal	HA-CD@p-CBA-DOX showed better in vivo anti-tumor activity in heterotopic and orthotopic 4T1 cell tumors.	[121]
Carbon dots	Non-covalent electrostatic attraction, Covalently bonded and H-bonding	-	Their high quantum yield makes them an attractive bioimaging, sensing and targeted chemotherapeutic option.	[180]
UCNP-GQD/TRITC	GQD-UCNP and (TRITC-UCNP-GQD) covalent bonded	Hydrothermal method	Targeted mitochondrial photodynamic treatment with near-infrared light.	[181]
CQDs	-	Nucleic acid Targeting	Superior in vitro efficacy of PDT for cancer cell killing.	[182]
Se/N-CDs	Electrostatic interaction	Isothermal	PDT in the nucleus made Se/N-CDs more effective in inhibiting tumor growth in vitro and in vivo.	
Lu-TP&Gd-TP/GQD-RGD	Hydrophobic interactions, and π-π stacking	Hydrothermal method	PDT, BRT, and PTT are only some of the many possible combination therapies.	[183]
GrQDs	Controlling oxygen content using self-enriched O2	Immobilization of catalase Cell membrane coating	Tumor-specific accumulation, extended circulation times, and homotypic targeting mechanisms directed towards malignant cells.	[184]
GQD-SS-Ce6	Disulfide bond	Improved Hummers method	A redox-responsive photodynamic nanosystem that effectively inhibits tumor development.	[185]
GQDs	-	Peeling and exfoliating graphite flake	The ROS production from GQDs is much higher than that from regular photosensitizers.	[186]
GQDs@hMSN(DOX)-PEG	Covalent bond	Hydrothermally	PDT and an improved medication delivery system.	[187]
Cationic carbon dots	Nucleus targeting	Hydrothermal approach	Enhanced cytotoxicity toward malignant cells.	[188]
N-GQD-DOX-APTES	Covalent bond	Hydrothermal	Drug delivery to the nucleus with variable PTT.	[189]

4.3. The acidic situation facilitates the efficient release of drugs coated on graphene oxide, as graphene has been observed to exhibit sensitivity to acidic environments [126]. In a specific investigation, graphene oxide was successfully employed as a carrier for encapsulating doxorubicin and paclitaxel, combined with hyaluronic acid acting as the copolymer. This research's primary aim was to focus on breast cancer cell lines, specifically BT-474 and MDA-MB-231. The study's findings demonstrated that the drug-loaded combination successfully caused apoptosis while exhibiting no effect on BT-474 cells that lack CD44 receptor expression [127].

Avb3 integrin was also used as a ligand in this process to conjugate with PEG-PCL micelles loaded with DOX. The augmentation of endocytosis mediated by receptors allows the complex to be taken up by cancer endothelial cells, as was seen in prior work [128]. A research investigation was undertaken to examine the augmented anticancer efficacy of the GE11 peptide copolymer when combined with oridonin, a graphene oxide-loaded anticancer medication. This study aimed to enhance the internalization of graphene oxide in esophageal cells exhibiting overexpression of epidermal growth factor receptors.

To accurately characterize breast cancer cell lines, such as MCF-7 and MDA-MB-231, scientists employed a conjugation technique involving combining graphene oxide with polyethylene glycol and folic acid. The inclusion of substantial amounts of DOX and the subsequent development of characteristics like a near-infrared light-activated heater were observed through this conjugation process [129]. The potential enhancement of functionality and effectiveness can be achieved by integrating graphene oxide with superparamagnetic iron oxide. The composite material, GO-Fe_3O_4, exhibits favorable fluorescence-tracked transportation of doxorubicin, which is non-covalently bound to GO. The conjugation process yields a substantial loading of DOX onto GO, resulting in a considerable 2.5-fold increase in efficacy [130]. A detailed summary of various graphene-based materials is given in **Table 5**.

Other carbon materials

Many different types of carbon-based nanomaterials have been studied in recent decades for their potential in many fields of application, mostly owing to their desirable electrical properties. Carbon nanohorns, nanodiamonds with a nitrogen vacancy core, nanocarbon black, and nanofibers are only a few of the carbonaceous materials suggested for this purpose. Carbon-based materials are briefly described here.

Iijima discovered carbon nanohorns in 1998; nowadays, they are more often referred to by their other name, "single-walled nanohorns" [88, 131]. Conical shapes, made from sp2 carbon sheets, are typical of what scientists call single-walled carbon nanohorns. These structures' dimensions are 40-50 nm in length and 2-5 nm in width [132]. There are three unique morphological varieties of single-walled carbon nanohorns, and they are referred to as "bud-like", "dahlia-like", and "seed-like" [133]. Nanohorns' surface is a complicated mixture of hexagons, pentagons, and heptagons, resulting in a wide range of chemical characteristics. Carbon nanohorns of great purity may be produced in large quantities at room temperature. In addition, no toxic metal catalysts are used anywhere in the process. In addition, no further sanitation steps are required to evaluate their biocompatibility [134]. Significant improvements in conductivity and dispersibility, as well as remarkable field-emission characteristics, semiconducting properties, and thermal and chemical stability, are among the prominent aspects of these materials. Single-walled carbon nanohorns are very pure and lack metallic components, in contrast to carbon nanotubes. There may be uses for these nanoparticles in biosensor studies [135]. The first glucose biosensor ever made employed single-walled carbon nanohorns [136]. Nafion-SWCNH composite material encapsulated glucose oxidase, resulting in the biosensor. The Composite Nafion-SWCNH/glucose biosensor showed very good performance in terms of high sensitivity, high selectivity, and low detection limit. In order to create H_2O_2 biosensors, single-walled carbon nanohorns were employed as a novel and biocompatible substrate. Myoglobin, a heme protein, has been immobilized on the surface of non-covalently functionalized single-walled carbon nanohorns in the presence of poly (styrene sulfonate) to construct an electrochemical biosensor [137].

Table 5. Graphene-based materials for effective treatment of cancer cells

Nanocomposites	Size	Cancer cell line	Drug loading efficiency	Drug Used	Drug loading efficiency	Stability	Ref
Graphene oxide/gemcitabine/montmorillonite/chitosan	130 nm	MB-231-MDA cells	-	Gemcitabine	Within 24 hours, at a pH of 7.4, 23%.	Excellent physical, chemical, and thermal stability. The time frame is not specified.	[190]
Cyclodextrin dendritic-Graphene oxide	-	Human breast cancer cells	9.8%	Dox	Within 144 hours, 67% at pH 5.2 and 85% at pH 7.4.	-	[191]
Superparamagnetic graphene oxide	9.3 (± 2.7) nm	MCF-7, HeLa, and Caov-4 cancer cell lines	75%	Methotrexate	pH 7.4: 46% (3.1), pH 5.5: (3.3), 59% in 75 hours.	Functional at physiological pH. Lack of context about stability duration.	[192]
Mesoporous silica/nanoparticles/GO/topotecan	190 nm	MDA-MB-231 cells	36.6%	Topotecan	pH 5.5: 76.0%, pH 7.4: 45.0% within 24 hours.	-	[193]
Cyclodextrin/cystamine/pegylated functionalized graphene oxide	531 nm	Human liver cancer cell line	95.5%	Doxorubicin	72 hours later, 65.2% at pH 7.4 and 37.6% at pH 5.3.	Excellent resistance to the salt solution found in the human body. There is no set time limit.	[194]
Amino acids-functionalized GO foams	80 nm	HepG2 and MCF-7 cell lines	67.55%	Cisplatin	Within 7 hours, 68.1% at pH 7.4.	Excellent biocompatibility and storage stability.	[195]
Ferric oxide/Reduced graphene oxide/chitosan/doxorubicin	60 nm	MCF-7 and A549 cancer cells	98%	Dox	Within 10 hours, 96.6% at pH 5.5 and 10% at pH 7.4.	-	[196]
miRNA/-polyethylene glycol/nano-GO/folic acid - platinum	200-500 nm	SKOV 3 cells, and SKOV 3 DDP cells	6%	Platinum	Proportion: 90% at pH 5, -63% at pH 7.4. Under a day.	Excellent two-week stability in water, MES, PBS, and cell media.	[197]
Graphene oxide/magnetic iron oxide nanoparticles	< 100 nm	Human neuroblastoma/SH-SY5Y cells	-	Doxorubicin	Within 120 hours, the proportion is 28% at pH 7.4 and 45% at pH 5.5.	Increased solubility in water and stability for 24 hours.	[198]
Paclitaxel/graphene oxide/gold nanorods loaded into poly (tetramethylene ether) glycol/polyurethane	Average length and width of 34 ± 3 nm and 9.8.0 ± 1.2 nm	Human lung cancer cell lines/A549	-	Paclitaxel	80% after 96 h and 120 h under pH values of 5.5 and 7.4, respectively.	-	[199]

The term "nanodiamond" is used to describe carbon nanomaterials that have a diamond-like crystal structure. Nanomaterials with sp3-hybridized carbon atoms and sizes between 1 and 20 nm [138, 139]. Since the carbon atoms in these materials typically form bonds with hydrogen and other non-carbon elements, their properties are more like those of biological molecules than those of bulk diamonds. Many methods exist for synthesizing nanodiamonds, with the explosive detonation approach being the most common. This technique involves the controlled detonation of an explosive mixture of trinitrotoluene and hexogen in an oxygen-depleted, high-temperature, and high-pressure environment. Accordingly, "detonation NDs" is a frequent name for these types of NDs. Optical qualities include refractive index and excellent optical transparency, high thermal conductivity, high strength, and remarkable mechanical features, including hardness and high electrical resistivity. These are just a few of the unique physical attributes of nanodiamonds [140]. It's well known that nanodiamonds have the largest optical bandgap of any known material and are semiconducting [141]. Nanodiamonds are very useful for research in various areas, such as electronics, energy, optical computing, and environmental science, due to their unusual properties [142]. Nanodiamonds also show great promise in biosensing applications due to their high biocompatibility and low cytotoxicity. Nanodiamonds' functional groups on their surface and very flexible core make them a promising tool for the engineering of new enzymes, proteins, and composite materials [143, 144]. When it comes to bio-conjugation, which involves molecules like metalloproteins, DNA, antigens, and enzymes, nanodiamonds have put out a novel proposal. Recently, a team of scientists modified a diamond sensor using enzymes, allowing it to detect chemical changes. Urea has been detected in a number of solutions using this modified sensor with good results. In the process of creating an EDIS penicillin sensor, researchers have also looked at the pH-sensitive properties of O-terminated nanodiamonds [88, 145].

Nanodiamonds with an NV core have gained popularity in recent years as a highly sensitive material for application in many types of biosensors. The NV center is a kind of nanodiamond point defect. It is distinguished by the presence of a vacancy pair along the 111 crystallographic axes and the replacement of a carbon atom with a nitrogen atom [146, 147]. Carbon nano black is a powder with an extremely high surface area and a very tiny particle size distribution. Because of its high conductivity and large surface area, this nanomaterial is widely used in biosensing applications. Screen-printed electrodes improved with carbon black nanoparticles have been effectively manufactured by the research team led by Arduini et al. The electrode may now be utilized for the electrochemical detection of paraoxon thanks to the alterations made [148, 149].

One-dimensional carbon-based materials like carbon nanofibers have recently attracted a lot of interest from researchers and businesses for their potential in a wide range of fields. The size difference between carbon nanofibers and regular carbon fibers is one possible explanation for the differences between the two types of carbon fibers. Carbon nanofibers have diameters between 50 and 200 nm, whereas traditional carbon fibers often have dimensions on the micrometer scale. To make carbon nanofibers, an inexpensive electro-spinning method is used to first prepare polymer nanofibers as CNFs' precursors [150]. Another method for synthesizing CNFs is using catalytic thermal chemical vapor deposition growth. This is the standard approach for synthesizing cup-stacked CNFs and platelet CNFs [151, 152]. The addition of oxygenated groups, which alter the active surface, has the potential to improve CNF performance. Carbon nanofibers are porous, have a large surface area, and can absorb large volumes of liquid or gas. When it comes to electrical conductivity, carbon nanofibers are on par with carbon nanotubes. In contrast to CNTs, CNFs have a larger functionalized surface area that may be used to immobilize biomolecules, including proteins, enzymes, and DNA [153]. In addition, their oxygen-containing active spots on the surface provide for simple functionalization [154]. As a result, functionalization is crucial in maximizing the potential of biosensors by making use of their unique qualities. A glucose sensor made of cellulose nanofibers using amperometric detection. This research confirmed the extraordinary catalytic activity of soluble CNFs. The electro-catalytic activity of carbon nanofibers toward nicotinamide adenine dinucleotide was investigated

[155]. They studied the whole electrochemical behavior of NADH at a carbon electrode modified with CNFs and created an electrochemical biosensor employing CNFs as the catalyst [149]. The oxidation potential of NADH dropped by more than 300 mV after the change [156]. Carbon nanofibers have emerged as a frontrunner in the race to develop electrochemical biosensors and sensors, as shown by the studies as mentioned above.

Conclusion and future outlook

Nanoparticles exhibit strong potential as promising materials for the advancement of novel diagnostic and therapeutic platforms in the field of cancer research. In the field of diagnostics, the utilization of metal and carbon-based nanoparticles (AgNanoparticles) has been found to enhance the efficacy of biosensors. This enhancement is achieved by augmenting the electroactive surface area and facilitating the rate of electron transfer in electrochemical electrodes. Additionally, nanoparticles can also serve as redox mediators in this context. Nanoparticles have the potential to be investigated as colorimetric probes or utilized in surface plasmon resonance (SPR)--based biosensors. They have been found to exhibit antitumoral properties that can effectively target various cancer hallmarks, including oxidative stress, energy metabolism, and drug resistance, making them potentially valuable for therapeutic applications. Additionally, the utilization of nanoparticles in conjunction with various conventional chemotherapeutic drugs has been observed to potentially elicit cytotoxic effects in cancer cells. These characteristics have the potential to address the constraints commonly associated with traditional chemotherapy of combination, such as limited drug solubility, variations in drug pharmacokinetics, and challenges in achieving precise spatiotemporal drug delivery. This is particularly noteworthy as nanocarrier systems based on nanoparticles can be tailored for intelligent drug delivery. In addition to the administration of chemotherapy, the utilization of metal nanoparticles (MNanoparticles) has demonstrated encouraging outcomes in augmenting the efficacy of radiotherapy and photodynamic therapy for various forms of cancer.

In spite of the encouraging outcomes observed with nanoparticles as a novel therapeutic approach, their integration into clinical practice has not been realized thus far, primarily due to the insufficient understanding of their human-specific behavior and toxicity. Comprehensive nanoparticle characterization and the implementation of standardized experimental protocols are imperative in order to facilitate the comparison of findings across various research facilities and to establish a consensus on the toxicity and pharmacokinetics of these particles. Furthermore, it is imperative to investigate novel targeting and biomimetic approaches, such as employing nanoparticles that are coated with cancer cell membranes, in order to facilitate the progress of nanoparticles toward their clinical utilization.

Notwithstanding the advantages above, there exist numerous barriers that hinder the clinical implementation of therapies based on carbon-based materials (Graphene, CNTs, Carbon quantum dots, and carbon nanotubes). For example, the comprehensive investigation regarding the safety implications of carbon-based materials within the human body remains incomplete. While in vitro experiments conducted on various cell lines have provided evidence of the safety of carbon-based materials, in vivo tests using animal models are typically conducted over a relatively brief duration. Hence, further research is necessary to ascertain the potential clinical application of carbon nanotube-based nanomedicine in the human body, specifically with regard to its long-term safety. Moreover, numerous techniques for modifying carbon-based materials are considerably intricate when it comes to producing them on a large scale. Consequently, achieving controllable and reproducible industrial production of functionalized carbon-based materials poses an additional obstacle to their clinical application. On the contrary, carbon quantum dots (CQDs), which are a type of carbon nanomaterials, exhibit superior performance in terms of large-scale synthesis due to their relatively straightforward synthesis method, cost-effectiveness, and environmentally friendly nature. Regrettably, it has been observed that CQDs exhibit toxicity that is dependent on their concentration, thereby imposing restrictions on their potential applications. Hence, in order to mitigate toxicity, it is imperative to assess and enhance the precision of cancer cell targeting or targeting of tumor microenvironment

(TME) components in carbon-based therapies. In terms of diagnostic capabilities, graphene and its derivatives exhibit exceptional electronic properties, making them highly promising for cancer biosensing.

Disclosure of conflict of interest

None.

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