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Nanoparticles in cancer treatment: a review

Abstract

Nanotechnology has revolutionized cancer treatment by introducing novel chemotherapy methods One promising approach involves using nanoparticles to deliver medication, reducing systemic toxicity and targeting specific areas for treatment. Nanoparticles can be an effective drug delivery technique, therefore, nanotechnology has been intensively researched and used to treat cancer. The use of nanotechnology in the treatment of cancer has drawn more and more attention during the past ten years. For the treatment of primary and advanced metastatic tumors, the creation of smart targeted nanoparticles (NPs) that can deliver medications directly to cancer cells at a sustained rate may result in greater efficacy and less hazardous side effects. These nanomaterials have been modified for a variety of cancer therapies to overcome toxicity and lack of selectivity, boost drug capacity as well as bioavailability, and target cancer cells, tumor microenvironment, and immune system. In addition to their therapeutic advantages, nanoparticles have also become essential in cancer diagnosis.

Keywords: nanomaterials, nano carriers, cell targets, nanoparticles, tumors, targeted metabolism

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Abbreviations: FDA, food and drug Administration; NPs, nanoparticles; EpCAM, epithelial cellular adhesion molecule; SPIONs, superparamagnetic iron oxide ; NPs, Gd Gadolinium

Introduction

The greatest cause of mortality and disability worldwide is cancer, which poses a serious danger to public health. Every year, more people are receiving cancer diagnoses; this year, that figure is expected to rise by 1.9 million. The number of cancer fatalities is increasing, especially in emerging and middle-income countries. Cancer prevention is a long-term objective, but sadly, not all cancers can be stopped.[1] As a result, various treatment modalities are required to lower the cancer fatality rate. The majority of individuals believe that traditional medicine consists of procedures like surgery, chemotherapy, and radiation. Current cancer treatment options include chemotherapy, immunotherapy, radiation therapy, hormone therapy, and surgery. These approaches have significantly enhanced patients' survival rates and treatment outcomes. However, there are still uncertainties and limitations associated with their use today. Yet, every cancer treatment plan has drawbacks that frequently result in recurrence and metastasis. Also, there's a chance that the therapy's designated target tissues, such organs, could endure unforeseen damage.[2]

One of the most significant limitations in cancer treatment is the challenge of drug targeting and delivery. This is due to the issue of non-selective tissue toxicity, as well as the presence of various barriers (such as physiological, physical, and enzymatic barriers) that hinder the effective partitioning and distribution of drugs to their intended target site. In recent years, there have been notable advancements in the field of drug targeting and delivery, which have become a focal point of research discussions.[3]

Years of research have consistently shown how dynamic the disease is, and despite better treatment options, there are still serious side effects from strong chemotherapies.[4] Patients suffer when more severe therapy are required, especially when aggressive tumors lie dormant and subsequently reappear.[5] The omnipresent establishment of resistance mechanisms is one of the biggest obstacles to developing an effective cancer treatment. As the primary oncogenic pathways are shut down, resistance mechanisms are triggered in parallel signaling pathways and reroute, enabling the growth of the tumor.[6] The heterogeneity of tumor cells, patient tumors, genetic mutations, and epigenetic patterns can all restrict the effectiveness of therapeutic interventions and contribute to the development of drug resistance.[7]

Clonal heterogeneity influences the biology of the entire tumor and is known to promote cancer growth and metastasis.[8] Although new medications and targets can improve cancer treatments, cancer's adaptive nature finds a way to survive. The main therapeutic modalities utilized to treat malignant cells are chemotherapy, phototherapy, radiation therapy, and surgery. These techniques harm healthy cells in addition to malignant ones. Increasing the safety and effectiveness of cancer therapy is scientists' and doctors' primary goal. The greatest method for treating cancer is drug targeting, which combines the destruction of both malignant and healthy tissues with immune system dysfunction and highly reproducing cells. These days, researchers are adopting a fresh form of biotechnology called nanotechnology to address these negative effects.

The pharmacokinetics of chemotherapy has improved, and the systemic toxicities have decreased, thanks to recently developed nano-technological techniques such vigorous targeting transporter, selective targeting, and drug delivery in tumour tissues. It aids in directing chemotherapeutics to malignant cells and neoplasms both specifically and directly. In order to protect the drug from rapid deprivation and allow it to reach the tumour site at the proper therapeutic concentrations, without distribution to normal sites to prevent unwanted effects, the expansion of drug transfer in cancer has accelerated the emergence of innovative nanomaterials and nanocarriers.

Nanomaterials and nanocarriers for targeted distribution have also increased the therapeutic effectiveness of radiation therapy and the direction of surgical removal of malignancies. Hence, it lowers mortality and raises the likelihood that cancer patients will survive. Cancer nanomedicine has been clinically translated for many years, and the number of nano-based treatments and parts for imaging, diagnosis, and radiation therapy has constantly expanded.[9] For instance, the CellSearch® system is the first diagnostic blood test approved by the FDA that uses cell labelling and magnetic nanoparticles (NPs) targeting EpCAM to detect circulating tumor cells. When used with

traditional scanning technologies like magnetic resonance imaging, positron emission tomography and computed tomography, nano-based imaging contrast agents like superparamagnetic iron oxide NPs (SPIONs) and gadolinium (Gd)-based contrast agents improve tumor detection and imaging *in vivo*.[10]

Targeted NPs improve solubility, half-life, and drug loading capacity while reducing toxicity in healthy cells and stopping drug breakdown. NPs-based cancer treatment maintains superior specificity, biocompatibility, less cytotoxicity, prolonged half-life, regulated drug release, and high loading capacity of pharmaceuticals in comparison to conventional chemical cancer treatment approaches.[11] When anticancer medications are encapsulated with NPs, the target cells are less likely to develop resistance to them; for instance, the anticancer drug Metformin conjugated with NPs is more efficient than using Met alone to treat cancer.[12] Moreover, target-specific NPs can be employed to regulate as well as inhibit the genes involved in the regulation of metastasis. Lysine Demethylase 6 A (KDM6A-mRNA) may be used in conjunction with mucoadhesive NPs to prevent bladder cancer metastases.

Cancer cell metabolism and targets

Cancer cells acquire specific modifications in a variety of metabolic pathways to satisfy the demands of unregulated proliferation. In general, the key nutritional metabolic pathways (glucose, amino acids, and lipids) are abnormally affected by cancer cells' metabolic reprogramming. Energy is produced from glucose in both healthy and malignant cells through oxidative phosphorylation in the mitochondrion and glycolysis in the cytoplasm. A crucial component of glycolysis known as the pentose phosphate pathway, helps malignant cells achieve their anabolic and anti-oxidative stress requirements.

Pyruvic acid, produced by the breakdown of glucose, provides acetyl-CoA for the tricarboxylic acid cycle, a key site for the creation of bioenergy and a precursor to biosynthesis.[13] Also abnormally elevated in cancers are the absorption and upregulated de novo synthesis of amino acids, which play a variety of significant roles. The primary factor promoting tumor growth is an increase in glutamine metabolism. The tricarboxylic acid cycle, reduced glutathione production, and one-carbon metabolism are additional processes involved in amino acid metabolism.

Moreover, cancer cells exhibit increased absorption of exogenous lipids and hyperactivation of the lipogenesis pathway, which results in the production of important lipid cell structures like cell membranes. The cytoplasmic acetyl-CoA that is produced from glucose is used to make fatty acids and cholesterol. In order to fuel the tricarboxylic acid cycle and create adenosine triphosphate, long-chain fatty acids break into acetyl-CoA via fatty acid oxidation. This process is crucial for cancer cell proliferation, treatment resistance, and metastatic spread.[14] Endometrial carcinoma is one of the most prevalent gynecological cancers. Key contributors to its development are metabolic disorders and estrogen imbalance.

In recent years, metabolic problems have become more prevalent, which has coincided with a rise in the prevalence of endometrial carcinoma patients worldwide and their mortality.[15] It has been discovered that diabetes increases the risk of endometrial carcinoma. Those with diabetes have a twofold increased risk of developing endometrial carcinoma compared to those without diabetes. Hyperglycemia is one of the primary clinical signs of diabetes and a significant contributor to the link between diabetes and cancer. As a result, a novel approach to the clinical care of diabetic endometrial carcinoma patients may entail controlling blood glucose levels or causing disruptions to the molecular signaling network involved in glucose metabolism.[16]

To mimic hyperglycemia in endometrial carcinoma people with diabetes, Ishikawa was grown with a high concentration of glucose (IshikawaHG). IshikawaHG was found to rewire its metabolism in response to glucose, with enhanced glycolysis and decreased oxidative phosphorylation. Pyruvate dehydrogenase kinase 1 is shown by proteomics to facilitate glycolysis in IshikawaHG. Moreover, JX06, a brand-new Pyruvate dehydrogenase kinase 1 inhibitor, and metformin work together to significantly lower the proliferation of IshikawaHG, despite the fact that it is resistant to metformin. JX06 is included within NPs (JX06-NPs) constructed of a reduction-sensitive biodegradable polymer for drug delivery. JX06-NPs suppress the growth of IshikawaHG and patient-derived endometrial carcinoma cells in vitro more potently than JX06 alone does. JX06-NPs concentrated in the tumor of an endometrial carcinoma-bearing mouse with diabetes after intravenous injection, and JX06-NPs and Met together significantly slowed the growth of tumors in endometrial carcinoma mice with diabetes. According to the study, combining JX06-NPs and metformin could be a promising novel adjuvant therapy for endometrial carcinoma patients who have diabetes. This is so that it stops the endometrial carcinoma from growing significantly and targets the metabolism of the malignancy.

Divergent and convergent metabolic phenotypes make up cancer metabolism. These traits help to explain the biological underpinnings of metabolic reprogramming and its potential therapeutic uses. Tumors of many different sorts react to various stimuli in a consistent manner. Oncogenic mechanisms that boost redox homeostasis, macromolecule synthesis, and energy production are among these characteristics. Many converging characteristics define malignancy. Glycolysis, which can be started by a range of different oncogenic stimuli and even hypoxia, is one of the convergence features.[17]

Subtype-selective or idiosyncratic phenotypes occur from the activation of heterogeneous pathways by particular inputs, which give birth to diverse features. Examples of divergent pathways include metabolic preferences that separate tumors with distinct oncogenotypes and the rise of (R)-2HG in tumors with IDH1 or IDH2 mutations. It is essential to comprehend metabolic heterogeneity because it influences how we think about using metabolic reprogramming to treat cancer. Targeting these traits may provide more tolerable toxicity profiles, but efficacy would be constrained to particular subsets because diverse features are only present in certain subgroups of malignancies.

Metabolic nanomedicine superiority

The conventional approach of using medications that target metabolism has some drawbacks, including poor drug distribution selectivity and systemic toxicity.[18] Due to its precise targeting, enhanced drug payload and regulated release, and strong biocompatibility, nanotechnology has significantly overcome these constraints. Nanocarriers can help cargo medications accumulate in the local tumor microenvironment, increase the tolerated dose, and support the curative efficacy of a metabolic therapeutic plan. Many metabolic-targeted medications and compounds enclosed in nanoparticles have amazing targeting and anti-cancer properties thanks to sophisticated nanotechnology. The well-known increased permeability and retention and the intricate design of the nanoparticles to achieve better-targeting tropism are two factors contributing to this advantage. (Table 1)

Table 1 Nanoparticles: targeting cancer metabolism

Nanoparticle	Nanocarrier Material	Targets	Mechanism
Nanoenabled Energy Interrupter	ZIF8; hydrophilic shell	GLUT1 mRNA	GLUT1 specific depletion
GNR/HA-DC	plasmonic gold nanorods	GLUT1	inhibiting glucose uptake and glycolysis
l-Arg-HMON-GOx	hollow mesoporous organosilica nanoparticle	endogenous glucose	cutting off the energy supply and generating toxic H2O2
Lip-(2DG + Dox)	liposomes	hexokinase	inhibit glycolysis; promote mitochondrial depolarization and apoptosis
2DG-PLGA-NPs	poly (lactic-co-glycolic acid) nanoparticles	hexokinase	induce antitumor immunity
GSH-responsive nanoprodrug	pluronic F126	HK II and IDO-1	restrained glycolysis and reduce the kynurenine
RBCm@Ag-MOFs/PFK15 (A-RAMP)	metal–organic frameworks; red blood cell membrane shell	PFK-2/FBPase-2/PFKFB	inhibit glycolysis
Copper-depleting nanoparticle (CDN)	semiconducting polymer nanoparticle	mitochondrial ETC	shifts metabolism pattern
polymersome nanoparticle	amphiphilic grafted-polyphosphazene nanovesicle	mitochondrial ETC	inducing mitochondrial malfunction and apoptosis
IR780@Pt NPs	β-CD and adamantyl group	mitochondrial	mitochondrial dysfunction
UCNPs- MSN- MnO2 (UNMM)	the mesoporous silicon middle layer; MnO2 gatekeeper layer	mitochondrial ETC	inhibit respiration metabolism and generate O2
VSeM-N=CH-PEG	acidity-cleavable PEG	mitochondrial ETC	interfere ETC
ACSN	carrier-free	mitochondrial ETC	interrupt ETC, relieve the hypoxia microenvironment
LMGC	liquid metal nanoparticles	endogenous glucose	inhibit glycolysis; increased H2O2 level
Pt-Pd@DON	porous Pt–Pd nanoflowers	binds covalently to multiple enzymes that use glutamine	glutamine analog
ABFP NPs	BSA-based NPs	GDH1	inhibiting the decomposition of mitochondrial Gln
AM-L@NBS	DSPE-PEG2k-Maleimide; CD44-specific polypeptide (A6) modified liposome	GSH	exhaust intracellular GSH; upregulate ROS levels
CuO2@mPDA/DOX-HA (CPPDH)	copper peroxide	GSH	Cu + catalyzed H2O2 to produce •OH

HA, hyaluronic acid; DC, diclofenac; GOx, glucose oxidase; 2DG, 2-Deoxy-d-glucose; PLGA, poly (lactic-co-glycolic acid); HK II, hexokinase II; IDO-1, 2,3-dioxygenase 1; A-RAMP, RBCm@Ag-MOFs/PFK15; PFK15, 1-(4-pyridyl)-3-(2-quinoline)-2-propyl-1-one; PFKFB3, 6-phosphofructo-2-kinase/fructose-2, 6-bisphosphatase 3; CDN, Copper-depleting nanoparticle; ETC, electron transport chain; VES, vitamin E succinate; DON, 6-diazo-5-oxo-l-norleucine; GDH1, Glutamate dehydrogenase 1; CPPDH, CuO2@mPDA/DOX-HA; DOX, doxorubicin.

Nanomaterials in Cancer treatment

Nanoparticles: Polymeric in nature: Extracellular vesicles, polymeric nanoparticles, metal nanoparticles, and mAb nanoparticles are all commonly explored nanoparticles. Colloidal macromolecules with a submicron size of 10–1000 nm are referred to as polymeric nanoparticles.[19] A nano capsule or nanosphere is created when drugs are enclosed within or affixed to the surface of nanoparticles. Biodegradable polymers have been created to optimise medication release kinetics, lessen toxicity, and boost biocompatibility.

Active targeting and passive targeting are the two basic ways to distribute drugs. Drug penetration through a dense extracellular matrix is challenging, whereas excessive angiogenesis has an objective benefit known as EPR. While a tumour requires a lot of nutrients and oxygen to grow, tumour-induced angiogenesis also creates a lot of immature blood vessels, which inhibits lymphatic drainage.[20] Chemical medications can enter malignant locations because of these permeable blood vessels. Drug particle size is important, though, because malignant cells cannot be penetrated by ordinary particles. On the other hand, due to weakened lymphatic drainages, nanoparticles and similar chemical drug delivery systems can readily enter and accumulate in targeted areas.

The bioavailability of polymers can be increased by coating them with polysorbates, using the polysorbates' surfactant effect to solubilize and fluidize endothelial cell membranes. PNPs interact with blood-brain barrier endothelial cell membranes and enhance endocytosis thanks to surface coating.[21] Polymeric nanoparticles can deliver a variety of chemicals to target sites, including anti-cancer medications, small interfering RNAs (siRNA), radionuclides, and specially designed polymeric nanoparticles with the ability to react to ultrasound, thanks to novel nanocarriers that work differently from conventional chemical therapy. As diagnostic instruments, fluorescent polymeric nanoparticles are employed. A theragnostic approach combines diagnosis and therapy simultaneously. In recent years, fluorescent polymeric nanoparticles have been recognised as innovative theragnostic materials. Nanomaterials with intricate structures are created to perform therapeutic and diagnostic tasks. Fluorescent proteins, biocompatible biopolymers, inorganic quantum dots, and organic dyes are the typical components of a fluorescent polymeric nanoparticles.[22]

Cyclodextrin polymer-based nanoparticles for siRNA administration increase delivery efficacy *in vivo*. According to investigations, adamantane-Polyethylene glycol and adamantane-PEG-transferrin modified with transferrin are suitable for delivering nucleic acids *in vivo*. With high radiochemical yields, electrophilic aromatic substitution can be employed to encapsulate radionuclides like I125 in nanoparticles. This simple method can be used to store radionuclides in the stable core.[23]

a. mAb nanoparticles: In the last few months, mAb nanoparticle research has advanced. Monoclonal antibodies (mAbs) are widely employed in targeted therapeutics due to their precise targeting capacity and anti-tumor activity. Moreover, mAbs have taken the lead in the development of innovative anti-tumor nanoplatforms in recent years.

Antibody-drug conjugates are mAbs that have been combined with cytotoxic drugs to further boost the therapeutic effectiveness of anticancer medications. By using distinct antigens that are expressed differently in cancerous and healthy cells to direct the drug complex, better specificity and reduced toxicity can be attained.[24] A mAb called trastuzumab (Herceptin) is used to treat breast cancer that expresses the human epidermal growth factor receptor 2 in a positive manner (HER2). The results of studies using trastuzumab (Tmab) with the Antibody-drug conjugates system demonstrate better.

b. Phospholipid vesicles: Extracellular Vesicles are bilayer phospholipid vesicles that are usually between 50 and 1000 nm in size. Several cell types continuously secrete extracellular vesicles that vary in size, origin, and composition. Exosomes, micro vesicles, and apoptotic bodies are the three main categories of extracellular vesicles based on their origin.[25] The size of exosomes ranges from 40 to 200 nanometres. Extracellular Vesicles are used in long-distance communication and contain DNA, RNA, and protein. Exosome NPs can evade immune surveillance and incorporate easily into target cells since the exosome membrane shares lipids and chemicals with the origin cells, making exosome NPs the ideal carriers for combining with already effective anti-tumour compositions and techniques.

DNAs and RNAs are used in gene therapy to cure cancer. Gene therapy is being investigated utilising a variety of methods, such as restoring mutant proto-oncogenes like p53, inhibitor of growth 4 (ING4), phosphatase and tensin homolog (PTEN), and CRISPR-associated proteins (Cas) system gene editing.[26] Small RNAs like siRNAs and microRNAs have the ability to cause RNA interference (RNAi) (miRNAs). RNAi influences pathological and physiological processes.

c. Nanomaterials made of Lipid: Current research and clinical trials are focusing a lot of emphasis on three primary kinds of lipid-based nanomaterials: liposomes, solid lipid nanoparticles, and nanostructured lipid carriers. The first enclosed microscopic phospholipid bilayer nano system, or liposome, was certified in 1965. Liposomes are spherical vesicles that are typically 20 nm to more than 1 um in size and made up of unilamellar or multilamellar phospholipids. A liposome typically consists of a hydrophilic core and a bilayer of hydrophobic phospholipids. Depending on the pharmacokinetic characteristics of the drug, this type of structure allows for the trapping of both hydrophilic and hydrophobic medicines. Hydrophilic medications are contained in the aqueous core of liposomes with the standard structure, and hydrophobic medications are contained in the lipid bilayer.

Medicines enclosed within the liposome's core cavity are guarded against environmental deterioration while travelling through the human bloodstream. Liposomes can be divided into two categories based on these two criteria: unilamellar vesicles and multilamellar vesicles. The size and number of bilayers are two crucial factors that impact the loading amount and half-life of medications. Small unilamellar vesicles and large unilamellar vesicles are additional classifications of unilamellar vesicles. Multilamellar liposomes have the form of an onion-like structure, but unilamellar vesicles can be generated inside of other vesicles to create multilamellar concentric phospholipid spheres that are spaced apart by water molecules.[27]

d. Mini emulsions: Colloidal nanoparticles known as nano emulsions are formed of oil, emulsifying agents, and aqueous phase. Nano emulsions can range in size from 10 to 1000 nm. Drug nanocarriers called nano emulsions are frequently employed; they are typically solid spheres with an amorphous, lipophilic surface and a negative charge. The three common types of nano emulsions are (a) water in oil nano emulsions systems, in which water is dispersed in an aqueous medium; (b) oil in water nano emulsions systems, in which oil is dispersed in an aqueous medium; and (c) bi-continuous nano emulsions. Nano emulsions are heterogeneous mixtures containing oil droplets in aqueous solutions. Nanodroplets are distributed with small size.[28]

In comparison to the majority of lipid-based nanomaterials and nanoparticles, nano emulsions have a number of advantages, including optical clarity, thermodynamic stability, large surface area, ease of fabrication, biodegradability, and the perfect drug release profile. The study of membrane-modified nano emulsions is broad. Co-delivery using nano emulsions is one way to increase drug effectiveness and bioavailability. Test results of a NE drug carrier system including PTX and spirulina polysaccharides demonstrated that this combination could enhance PTX's anti-tumour effects by modulating immunity via TLR4/NF-B signalling pathways. To treat metastatic melanoma, a nano emulsions system containing temozolomide, rapamycin, and bevacizumab was developed. In vitro studies on human and mice found that parenteral administration of some drugs increased cytotoxicity against melanoma cells and improved suppression of tumour recurrence, migration, and angiogenesis.[29]

e. Dendrimers: Unique macromolecules known as dendrimers have a hyperbranched, well-defined design. Dendrimers' highly branching and adaptable surfaces are their most noticeable feature. These dendrimer polymers typically range in size from 1 to 10 nm, while some big dendrimers that have been specially constructed can have diameters as large as 14 to 15 nm. The dendrimer molecules are composed of three main structural components: a central core that encapsulates therapeutic substances in a noncovalent manner, branches that comprise the internal dendritic structure, and an outside surface conjugated with functional surface groups. A number of dendrimers, including polyamidoamine, polypropylenimine, poly(ethylene glycol), 2,2-bis(hydroxymethyl) propionic acid, 5-aminolevulinic acid, and triethanolamine, have been created for the treatment of cancer.[30]

Dendrimers differ from conventional nanomaterials in that they have a specialised structure that gives them special properties such as a defined molecular weight, flexible modifiable branching, a low polydispersity index, and higher solubility and bioavailability of hydrophobic medicines. Dendrimers are effective nucleic acid nanocarriers because they can form compounds with nucleic acids due to their cationic nature and positively charged surfaces. Two well investigated dendrimers with various application methods are polyamidoamine and polypropylenimine. Using fluorescence imaging, a polyamidoamine dendrimer/carbon dot nanohybrid was created to regulate Multi Drug Resistance and monitor cancer cells at the same time.

f. Nanomaterials of Carbon: The term "carbon nanomaterials" refers to a class of materials with various subcategories based on the element of carbon. Because to their distinctive electrical, thermal, optical, and mechanical qualities, carbon nanomaterials have found extensive utility in a variety of industrial and medical domains. Carbon nanomaterials are thought to be more biocompatible and secure than metal-based nanomaterials in cancer diagnostic applications. Due to their inherent hydrophobicity, carbon nanomaterials can load chemical medicines through "- stacking" or hydrophobic interactions, making them effective drug delivery platforms. Graphene, fullerenes, carbon nanotubes, carbon nano-horns, carbon quantum dots, and graphene are among the carbon nanomaterials that have undergone extensive research for use in the treatment of cancer. Although all of these materials are composed of carbon components, there are significant differences in the morphological structure, characteristics, and uses of these nanomaterials.[31]

A two-dimensional crystal made of a sp2-hybridized carbon sheet, graphene exhibits exceptional mechanical and electrical properties. Moreover, it has been extensively studied for biomedical uses, such as the treatment of cancer. Graphene is an excellent substrate for drug administration, because it has a high surface-to-volume ratio and a lot of branches that contain oxygen. With the physically irreversible adsorption of the Ac-(GHHPH)4-NH2 peptide sequence, which is known to resemble the anti-angiogenic domain of histidine-proline-rich glycoprotein, a GO-peptide hybrid was created.

Allotropes of carbon make up the molecules known as fullerenes. Fullerenes can be shaped as a hollow sphere, ellipsoid, or tube. Fullerenes that are typical include C60, C70, C82, etc. A metallofullerene can be created by incorporating metal atoms. The majority of the metal atoms included within fullerenes are either lanthanides or Group III transition elements. Metallo-cullerenes can be employed as a magnetic resonance imaging material because the intra-fullerene electrons can go from the metal atom to the fullerene cage. Fullerenes have the potential to scavenge free radicals as one of their properties, making them antioxidants.[32]

Carbon Nanotubes are rolls of graphene that have had their carbon atoms sp2 hybridised, forming cylindrical tubes. Carbon Nanotubes range in size from one nanometre to several micrometres. Carbon Nanotubes can be separated into single-walled carbon nanotubes and multiwalled carbon nanotubes depending on how many layers have developed inside of them. Two disadvantages of Carbon Nanotubes are their poor water solubility and toxicity. To address the aforementioned issues and increase the bioavailability of Carbon Nanotubes, numerous investigations on surface functionalization and material alterations have been conducted. Carbon Nanotubes, which are carbon-based nanomaterials, can interact with immune cells to trigger an immunological response, which in turn strengthens immunity and slows the growth of tumours.

g. Quantum dots: Due to their unique optical and electrical properties, quantum dots are the subject of extensive research as biomedical imaging probes. They are frequently utilised to increase the efficacy of fluorescent markers in biological imaging and are typically nanometre-scale semiconductor crystallites. In contrast to organic fluorophores, quantum dots have special optical and electrical characteristics, such as size and composition-driven tunable fluorescence emission from visible to infrared wavelengths, large absorption coefficients, and high brightness levels photostability.

Graphene quantum dots, nanodiamonds, and Carbon Dots are the three types of typical quantum dots based on carbon. Bioimaging, which can be used for cancer sensing and imaging, is the most popular application of carbon quantum dots. Graphene quantum dots are regarded as novel nanomaterials in biosensing and cancer therapy due to their better biocompatibility, quick excretion, and inherent large surface suited for molecular conjugation. For biocompatibility and pH sensitivity, a photoluminescent glycodendrimer with terminal -cyclodextrin molecules system was developed and used. Graphene quantum dots were utilised to create a surface on which PAMAM could grow. Following UV light stimulation at 365 nm, the emission spectra from Graphene quantum dots and GQDs-PAMAM-CD were captured. As a result, it demonstrated greater effectiveness in eliminating cancer cells than DOX alone could, and the presence of Graphene quantum dots made it a possible imaging agent with photoluminescent activity.[33]

h. Metallic and magnetic nanomaterials: Because of their unique optical, magnetic, and photothermal properties, metallic nanoparticles have been intensively researched in bio-imaging and drug delivery. Metallic substances can be combined in a variety of ways with flexible carriers including NPs, liposomes, dendrimers, or CNMs. MRI imaging is the major use of magnetic nanoparticles. The negative effects of traditional chemotherapy are decreased because magnetic nanoparticles (NPs) laden with chemical medicines can target cancer cells while being guided by an external magnetic field.

When metal particles are conjugated, the nano system is capable of PTT and bioimaging. Fe3O4/Ag-based iron oxide nanoparticles (IONPs) were enclosed in a gold shell. Due to the gold shell in the NIR region, IONPs and PTT demonstrated MRI contrast capabilities. Metallic materials are frequently utilized in PTT, PDT, CDT, and immunotherapy for the treatment of cancer. Using nano catalyst, CDT is a Fenton- or Fenton-like reaction-based medicinal approach.[34]

Conclusion

Nanotechnology has made remarkable advancements in cancer diagnosis, detection, therapy and overcoming multidrug resistance. It offers a wide range of opportunities to improve therapeutic outcomes and has revolutionized the field of research with its contemporary dynamics. Nano-medicine a key component of nanotechnology, has emerged as a prominent research area, with extensive research conducted over the past two decades, including numerous completed patents and clinical trials. Developing nanoparticles poses challenges due to the lack of suitable in vitro models that accurately mimic the *in vivo* state. Current therapeutic applications of nano-formulations rely on in vitro evaluations using cell lines, which fail to capture the complexity and specificity of nanoparticle-cell interactions *in vivo*. Nevertheless, it is evident that nanotechnology is an emerging field and has proven to be highly beneficial in cancer treatment. To establish a solid framework for nanotechnology, a comprehensive understanding of the cellular, pharmaceutical, and physiological components governing nanotechnology-based drug delivery is crucial.

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Conflicts of interest

The authors declare no competing interests.

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