International e-Conference on New Horizons And Multidisciplinary Applications In Science And Technology
In Association withInternational Journal of Scientific Research in Science and Technology
Volume 9 | Issue 6 | Print ISSN: 2395-6011 | Online ISSN: 2395-602X (www.ijsrst.com)

Current Trends of Nanotechnology in Cancer Therapy : A Review

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ABSTRACT

Nanotechnology is one of the fastest developing areas in the 21st century. In diagnostics and therapeutics of various diseases, several different types of nanosystems are being used. Significant attention has also been given to nanotechnology to overcome the shortcomings of conventional anticancer therapy. Cancer nanotechnology is a comparatively recent interdisciplinary field of extensive research that links the fundamental sciences, like chemistry, biology, medicine, and engineering. In recent decades, several organic and inorganic nanomaterials have developed as pioneering tools for tumor diagnostics and therapeutics due to their novel features, including drug protection, solubilization effect, active/passive tumor targeting, controlled release of drugs, which lead to improved anticancer efficacy while minimizing the side effects. This review is an overview of nanomaterials' key characteristics, for example, size, surface characteristics, and tumor targeting. It also compiles the advances and prospects in applications of nanotechnology for anticancer therapy along with a brief overview of the preparation of different kinds of nanoparticles.

Keywords: Nanotechnology, Cancer, Drugs, Nanosystems, Nanomaterials, Nanoparticals

I. INTRODUCTION

Cancer is one of the primary diseases that threaten human lives. It is a number one cause of death worldwide, especially in developing nations, and is accountable for an estimated 9.6 million deaths in 2018, according to WHO (World Health Organisation). The modern therapeutic methods, including surgery, chemotherapy, and radiotherapy, are linked to high systemic toxicity, restricting their tolerability and clinical applicability. Lower specificity and sensitivity in recognizing precancerous conditions and initial malignancy with a low false-positive rate, failure to identify the tumor stage, and high costs also entail limited traditional cancer screening technology. Through various studies, it is becoming apparent that the low survival rate is due to the lack of adequate drug delivery systems. Recently, nanomaterials have gained considerable interest from researchers inquisitive about cancer therapeutics because of their versatile physical and chemical properties to facilitate the transport of the antitumor medication to oncogenic tissue while minimizing its concentration and toxicity in healthy tissue. Properties of nanoparticles (NPs) have rendered many nanoparticle-based therapeutic

applications into clinical trials within the last decade. Various inorganic and organic nanomaterials have appeared as innovative methods for tumor detection and treatment.

This review deals with the recent development and novel solution that made possible by the advent of nanotechnology with stress on therapeutic agent delivery, and tumor imaging, including inorganic nanomaterials, like carbon-based nanoparticles, magnetic NPs, gold NPs, and emerging organic nanomaterials, such as liposomes, polymeric micelles, polymeric nanoparticles, and dendrimers.

II. PROPERTIES OF NANOMATERIALS USED IN DRUG DELIVERY SYSTEM

- **Size**

Nanomaterials are small in size and are comparable to biological macromolecules like peptides, proteins, and nucleic acids. They usually have a diameter of tens of nanometers and are about a hundred times smaller than the size of one cancer cell. Nanomaterials show a more extensive intracellular absorption than micron-sized particles because of their small size and dimensional similarities to biomolecules and thus are ideal candidates for the delivery of cancer-targeted drugs[1,2]. Although conventional nanotechnology investigates particles between 1 and 100 nm in size, the development of nanoparticles with sizes from 100 to 200 nm has been identified as ideal for intravenous administration in the human body[3]. This size range prevents the active renal elimination (NP size <5 nm), the aggregation in the liver (NP size <50 nm) and spleen (NP size >200 nm) while retaining the ability to extravasate through the tumor fenestrae (NP size <200 nm)[4]. One of the advantages of nanomaterials is that their size can be tailored. The dimensions of NPs also influence circulation half-life and tumor aggregation[5].

- **Surface Properties**

Surface features can enhance NPs stability and increase their circulation in the blood, which then increases passive accumulation in oncogenic cells through the EPR (enhanced permeability and retention) effect5. Furthermore, surface properties can efficaciously affect the hydrophobic and electrostatic interactions between NPs and clearance by opsonization (enhanced attachment)[6].The hydrophilic surface of nanomaterials can preferably avoid the capture of macrophages. PEGylation, which refers to the process of covalent and non-covalent attachment or amalgamation of polyethylene glycol (PEG) or its derivatives to NPs, is one of the most favored approaches to effectively limit plasma proteins binding, interaction with opsonins, and clearance by the RES system[7,8].

- **TumourTargeting by Nanoparticles**

One of the benefits of nanotechnology for chemotherapeutics is selective tumor targeting, i.e., the potential to distinguish carcinogenic cells from healthy cells and selectively destroy the malignant cells. Generally, NPs can target the tumor cells either by two mechanisms-active and passive[9].

a) Passive Targeting.

This approach can efficiently improve drug bioavailability and efficacy: it uses the anatomical and functional discrepancies between healthy and tumor vasculature to transport the drug to a targeted site or might involve a localized transfer[10]. As apoptosis is suspended in malignant cells, they continue absorbing nutrients abnormally through the blood vessels and causing them wide and leaky around the cells incited by angiogenesis.Due to deformities in the basement membrane and reduced numbers of pericytes, leaky blood vessels are formed, which quickly proliferate endothelial cells[11]. Hence, molecules' permeability to pass through the vessel wall

into the interstitium surrounding tumor cells is increased.The pore sizes of leaky endothelial cells vary from 100 to 780 nm[12,13]. Thus,nanoparticles below this scale can easily move through pores. As a result, it helps to efflux the nanoparticles to cluster around the cancer cells[5,14]. Nanoparticles are often targeted to a distinct region of capillary endothelium to accumulate the drug within a particular organ and perforate the neoplastic cells by passive diffusion or convection.Lymphatic drainage imbalance facilitates the diffusion process. The tumor interstitium contains a collagen network and a gel-like fluid. The latter has strong interstitial pressures that oppose the molecules' internal flux. Consequently, drugs that enter the interstitial area in the tumor interstitium may have prolonged retention time. This characteristic is known as the enhanced permeability and retention (EPR) effect and aids tumor interstitial drug aggregation[15,16]. Nanoparticles can selectively accumulate by improved permeability and retention effect and then diffuse into cells[17]. The distinctive microenvironment of tumor cells varies from that of normal cells also contributes to passive targeting. Hyperproliferative, fast-growing melanoma cells have a high metabolic rate, but the limited supply of oxygen and nutrients is typically not sufficient for them to maintain this. Tumor cells, therefore, utilize glycolysis to gain additional energy and induce an acidic environment. The pH-sensitive liposomes are engineered to be physiologically stable at a pH of 7.4, but they degrade to release the active drug in target tissues where the pH is less than physiologic values, such as in the acidic environment of tumor cells. Also, tumor cells express and release unique enzymes that are involved in their movement and survival mechanisms[10].

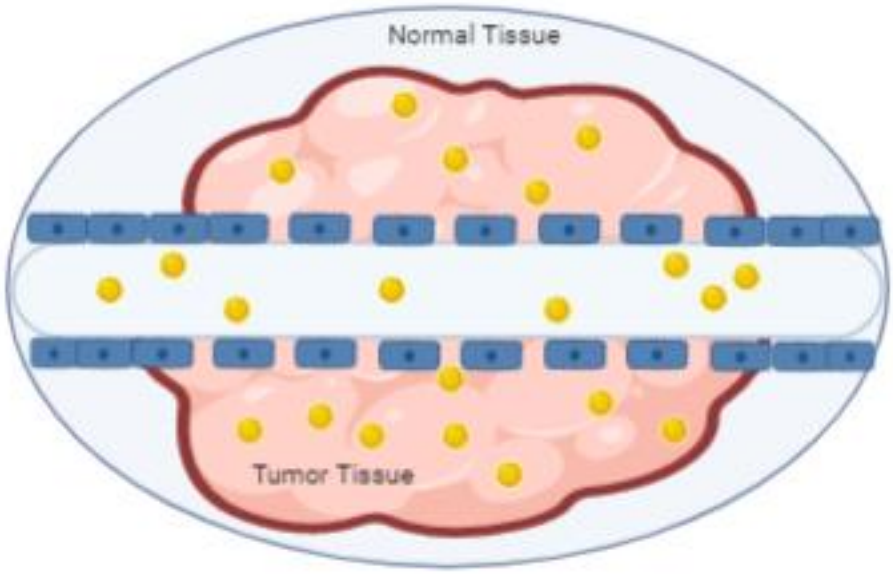

Fig.1: Passive targeting by Enhanced Permeability and Retention (EPR).

b) Active Targeting.

The passive drug delivery systems employing a binary structure conjugate inevitably have intrinsic limitations to the degree of targeting specificity they will achieve. To overcome these limitations active targeting is encouraged[10]. In the case of active targeting, nanoparticles containing the chemotherapeutic agents are designed in such a way as they directly interact with the defective cells. Active targeting is predicated on molecular recognition[14,18]. Hence, the surface of the nanoparticles is modified to target the malignant cells. Usually, targeting agents are attached to the surface of nanoparticles for molecular recognition. Designed nanoparticles target the cancerous cells either by ligand-receptor interaction or antibody-antigen recognition[19,20]. The active targeting delivery system has three main components: (i) an apoptosis-inducing

agent (an anticancer drug), (ii) a targeting moiety-penetration enhancer, and (iii) a carrier. Particles containing chemotherapeutic agents are engulfed by phagocytes and rapidly removed by the reticuloendothelial system (RES). A range of strategies was developed to sustain the nanoparticles in the bloodstream one of which is the modification of the polymeric composition of the carrier. Nanoparticles are coated with hydrophilic polymers to avoid washout and remain in the bloodstream for a longer period that can sufficiently target cancerous cells[14]. Hydrophilic polymer coating on the nanoparticle surface repels plasma proteins and escapes from being opsonized and cleared. This is defined as a "cloud" effect[21,22]. Commonly employed hydrophilic polymers are polyethylene glycol (PEG), poloxamines, poloxamers, polysaccharides, and so forth[23,24]. Cancerous cells have some receptors that are overexpressed on their surface that make them distinguishing. Attachment of the complementary ligands on the surface of nanoparticles makes them able to target only the cancerous cells. Once the nanoparticles bind with the receptors, they rapidly undergo receptor-mediated endocytosis or phagocytosis by cells, resulting in cell internalization of the encapsulated drug[14]. A variety of chemical and biological molecules have been used to direct NPs to malignant cells expressing the molecular target receptor including monoclonal antibodies, small molecules, and nucleic acid aptamers[25–27].

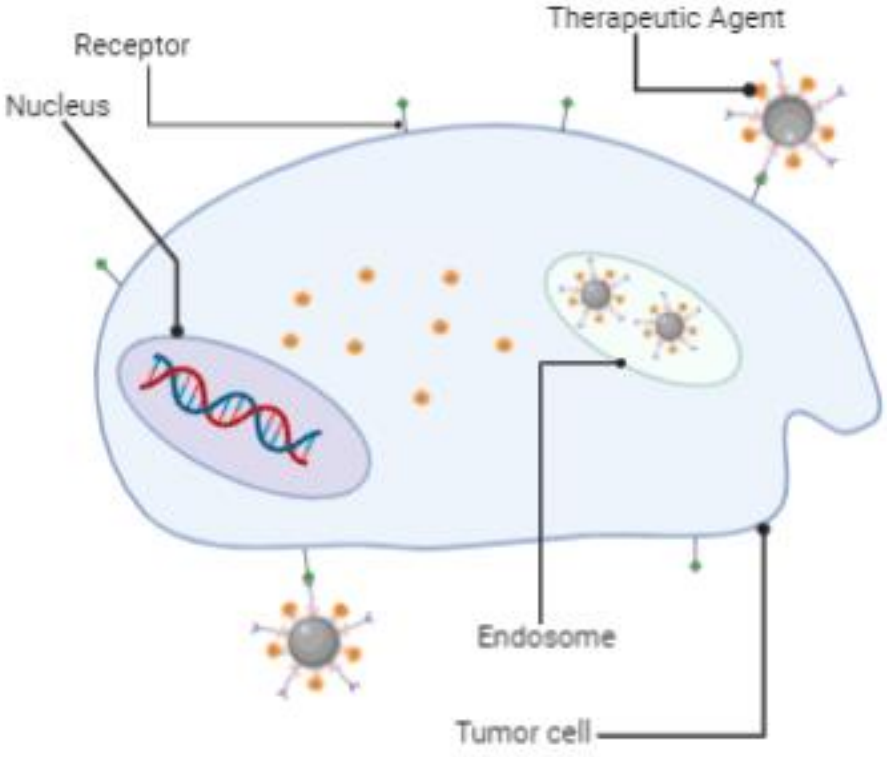

Fig.2: Active targeting.

III. ORGANIC NANOMATERIALS FOR CANCER THERAPY

a) Polymeric Miscelles

Polymeric micelles (PMs), are spherical, nano-sized colloidal particles with amphiphilic block copolymers i.e., hydrophobic core for water-insoluble and hydrophilic shell meant to hydrophilic drug molecules. The hydrophobic shell is equipped with PEG, which helps to stabilize the carriers and protect them from degradation by reducing unspecific interactions in vivo[28,29]. The hydrophobic core is made up of several natural or synthetic polymers, including polysaccharides, poly(ε-caprolactone) (PCL), poly(lactide) (PLA), and

poly(lactic-co-glycolic acid) (PLGA). The hydrophobicity gives an ideal medium to capture hydrophobic drugs, helping to solve their poor water solubility. The small size with narrow distribution likewise makes polymeric micelles perfect nano-drug delivery systems as it could avoid rapid renal excretion, helping to obtain a long circulation time[30,31]. As they could load and deliver drugs to the desired function site, improving the pharmacokinetics of the loaded drug and decrease non-specific toxicity, polymeric micelles have been broadly investigated as drug carriers in recent decades. The special properties of micelles are critical micelle concentration (CMC), cumulative number, size, and shape of the final structure. These properties are dependent on the polymer chains in copolymer blocks. Polymer micelles with lower CMC has a higher solubility for the loaded drug and higher micelle stability[32].

Since the natural pH gradient exists in the tumor microenvironment and intracellular endo/lysosome, pH-sensitive degradable micelles are recently emerging as a promising platform for antitumor drug delivery[33,34]. Recently, intracellularly acid-switchable micelles were prepared for accomplishing combinational therapy against drug-resistant tumors[35]. Furthermore, while modified with the nucleosome-specific monoclonal antibody, the micelles showed greatly enhanced endocytosis efficiency and antitumor efficacy.

Micelles are extremely efficient in DDS due to their high capability, drug loading variable, high stability in physiologic conditions, lower dissolution rate, more drug accumulation in the targeted place, and surface modifications. Two polymer micelles, called NK911 and NK105, have been acquainted with the medication showcase and contain doxorubicin and paclitaxel, individually[36,37].

b) Liposomes

Liposomes were first discovered by Alec D. Bangham in 1961. These are self-assembling NPs with closed membrane structures. They are concentric lipid bilayer vesicles in which aqueous phase is encapsulated by a membranous lipid bilayer mainly comprising of natural and/or synthetic phospholipids which constitutes both hydrophobic tail and hydrophilic polar head. The liposomes encapsulate the solvents freely floating in the inside[38].

Liposomes can be created from cholesterol and natural nontoxic phospholipids and can be synthesized by the sonication or extrusion method[39]. The polymer cores are then mixed with the lipids at adequate molar ratios to synthesize lipid-polymer hybrid nanoparticles by high-pressure homogenization, needle extrusion, or simply vortexing[38]. After vortexing, unilamellar liposomes are extruded under high pressure, which can be further purified by column chromatography or ultracentrifugation[5]. Many liposome-based nanoformulations of natural drugs likenux vomica, quercetin, and diospyrin have been manufactured and analyzed for their antitumor, anticancer, and antioxidant activities.

These structures are suitable for drug delivery as they have an amphiphilic and viable nature with easy surface modifications. For example, PEG (polyethylene glycol) modified liposome to deliver H_2O_2 and catalase (CAT) to relieve tumor hypoxia[40].Liposome/protamine/hyaluronic acid (LPH) is designed to carry nucleic acids via positive and negative charge interaction between protamine and nucleic acid[41].Besides, liposomes can effectively load various bioactive molecules, including enzymes and nucleic acids[42,43]. They have been proven to be beneficial for therapeutic compound stabilization, cellular and tissue uptake of therapeutic compounds, and bio-distribution of compounds to target sites in vivo[44,45]. For instance, Doxil, a PEGylated liposomal DOX, has been approved by the US Food and Drug Administration (FDA) for cancer therapy, as it could improve the plasma pharmacokinetics and tissue distribution[5].

Liposomes can also be functionalized with imaging contrast agents, providing combined diagnostic and therapeutic functions. Recently, a theranostic liposomal drug delivery system was prepared to realize a real-time image of bio-distribution by MRI and accomplish chemotherapy through the carried anticancer drug. Compared to commercial MRI contrast agent Omniscan®, this liposome showed a 36-fold higher T1 relaxation rate; moreover, its circulation time could reach 300 min in vivo[46].

c) Polymeric Nanoparticles

The most well-known NP drug carriers are polymers. Polymeric NPs are composed of either natural polymers like chitosan, gelatin, agarose, etc or synthetic polymers such as poly(ε-caprolactone) (PCL), poly (lactic-co-glycolic) acid (PLGA), polyvinyl alcohol (PVA), polyethylene glycol (PEG), etc[47]. Several methods are used for the synthesis of polymeric NPs, including emulsification and solvent evaporation/extraction[48], nanoprecipitation (solvent displacement)[49,50], supercritical antisolvent method[51], and salting-out[52,53].

Polymeric NPs display excellent pharmacokinetic properties, including drug load and drug stability, compared to polymeric micelles. They can improve the therapeutic effect of anticancer treatment through passive targeting via the EPR effect[5]. In these polymeric structures, drugs can be adsorbed on the surface or entrapped in the core of the polymeric matrix. The advantages of polymer NPs are their high stability and mass production. Polymer NPs contain vesicular (nanocapsules) and matrix systems (nanospheres)[18]. In nanocapsules, the drug is stored in a polymer cistern. However, in nanospheres, the drug disperses on the polymer matrix[54–56].

Abraxane is the first polymer nanodrug to be introduced into the pharmmaceuticalmarket in 2005. It contains NPs of paclitaxel drug, which is related to albumin. This formulation contains no chromophore electroluminescent (EL) compound. Chromophore-EL increases the solubility of paclitaxel[18]. It has been demonstrated that nanotechnology can overcome the limitations of the science of formulation.

Polymeric NPs loaded with imaging agents, namely, gadolinium complexes and magnetic NPs have been extensively explored to image cancer by magnetic resonance imaging (MRI). Typically, imaging agents were encapsulated into the core of the polymeric NPs[5].

d) Dendrimers

Dendrimers are monodisperse macromolecules with extremely branched tree-like structure and specific form and size. Their surface is often altered with chemical reactions and physical interventions[18]. They could load drugs and gene molecules through simple electrostatic interactions, encapsulations, and covalent conjugations. Dendrimers possess empty internal cavities and a remarkably higher density of surface functional group (-NH_2 or -COOH), which makes them suitable vectors for anticancer therapeutics. Furthermore, due to their exceptionally small size, dendritic carriers (1–15 nm), can be cleared from the blood through the kidneys, which can decrease their toxicity in vivo.

Drug molecules are attached to dendrimers in complex or capsule forms[37,57]. In the 70s, Fritz Vögtle and Donald Tomalia were the primary ones who attempted dendrimers synthesis and invented tree-like structures by conjugating the monomers to each other[58]. Vivagel® is the first dendrimer NP system that was introduced to the pharmaceutical market[18]. Due to its dendrimer structure, Vivagel® prevents the attachment of the virus to the host body[59,60].

Polyamidoamine(PAMAM) is the most extensively studied dendrimer as its surface contains a great number of amine groups, which could be used to conjugate various functional moieties. Moreover, the anticancer effect could be improved by the combined function of PTX and the dendrimer[5].

Dendrimers can be synthesised by the divergent and convergent synthesis approaches. In the former approach, the synthesis begins with the preparation of the core of the dendrimer, then the arms are attached to the core by adding building blocks in a step-by-step manner[61].While, the latter involves preassembly of the complete wedge-shaped branching units, which are coupled to the central core moiety in the final step[62].

The novel morphology of dendrimers makes them a promising candidate for diagnostic applications. For example, to accomplish in vitro and in vivo computed tomography (CT) imaging of cancer cells, an acetylated dendrimer to entrap gold NPs was introduced. Li et al. (2013) prepared multifunctional dendrimer-based gold NPs (AuNPs), as a dual-modality contrast agent, were prepared for in vitro and in vivo CT/MRI of breast cancer cells[63].

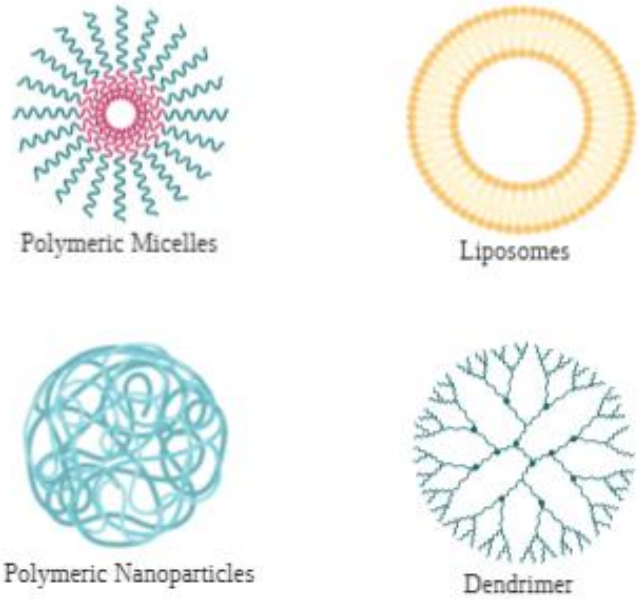

Fig.3: Few organic nanoparticles for drug delivery

IV. INORGANIC NANOMATERIALS FOR CANCER THERAPY

a) Gold Nanoparticles

AuNPs are one of the most exploited metal nanoparticles exhibiting intriguing features, such as size-related electronic, magnetic, and optical properties. Gold nanoparticles can be made using different chemical methods such as the Brust method, Martin method, and Turkevich method[64–66].

Au NPs are promising in cancer theranostics due to their superior synthesis, modification, and biocompatibility. Au NPs are often used for Photothermal therapy (PTT) due to their superior biocompatibility, simple Au-thiolbioconjugation chemistry for the attachment of desire molecules, a small diameter that enables tumor penetration, efficient light to heat conversion, and the ability to be tuned to absorb near infrared light, which penetrates tissue more deeply than other light wavelengths[67]. The localized surface plasmon resonance and multivalent coordination effects on the surface of the NP are ideal for photothermal imaging, therapy-controlled drug release, and targeted drug delivery[68]. However, Au NPs can convert NIR light into heat, which

can then be applied to a specific site for hyperthermia. Hence, utilizing the Au NPs as a photothermal agent can release heat which can ablate tumor cells directly[69].

It is observed that the cellular uptake of gold nanoparticles depends on surface functionalization, nature of the ligand, molecular weight, and grafting density[70]. It is also found that the cellular uptake rate depends on the aspect ratio of the gold nanoparticle. For instance, the cellular uptake rate of the rod-shaped gold nanoparticle was lower than that of the spherical-shaped[71]. Due to the high surface-to-volume ratio of gold nanoparticle, they are covered with a protective layer to lower down the very high reactivity of the nanoparticle. The protective layer is made up of a polymer such as anionic poly(acrylic acid), neutral poly(2,3-hydroxy-propylacrylamide), and thermoresponsive poly(N-isopropylacrylamide)[72]. He & C.L. Chow(2016) found that the presence of the layer did not affect the secondary electron yield from the nanoparticle[73].

Cytotoxicity of most Au NPs depends on various parameters such as size, cell type, tissue distribution, tissue absorption, and penetration capacity. It was reported that small Au NPs (4–5 nm) have higher toxicity potential than large particles (18–20 nm)[74]. Research showed that Polyethylene Glycol-coated Au NPs had a transfection efficiency and cell uptake greater than 45% with low cellular toxicity, and can be used as a DNA and drug delivery system[75]. Thus, PEG is used as a common coating material on Au NPs to reduce NP interaction with biological specimens. PEGylation also extends their blood circulation time by lowering their removal by the reticuloendothelial system (RES)[76,77]. Moreover, PEG represented an ideal linker for different targeting ligands, i.e., tumor necrosis factor α and galactose[78,79]. Moreover, AuNPsare an alternative for the delivery of nucleic acids to improve gene therapy ensuring both low environmental degradation and protection against nucleases as well as facilitating cell entry[80].Au NPs are effective radiosensitizers in medical applications such as drug delivery and cancer therapy. In biomedical and cancer therapy applications, Au NPs can act as a contrast agent and dose enhancer in image-guided nanoparticle-enhanced radiotherapy using kilovoltage cone-beam computed tomography[81,82].

b) Carbon based Nanomaterials

i). Carbon Nanotubes

The carbon nanotubes were formerly described by Iijima in 1991[83]and are the most examined carbon-based nanomaterials. The carbon nanotubes are cylindrical tubes of sp^2 graphite sheets with diameters within the nanoscale, which can be organized in single-walled or multi-walled carbon nanotubes[84,85]. These materials are usually synthesized using methodologies based on arc discharge or chemical vapor deposition of graphite[86]. The electronic and optical properties of these nanomaterials depend on the diameter and the relative orientation of the graphene basic hexagons with respect to the axis tube[87–89]. They are used as nanomedicine for cellular imaging and are also promising drug carriers for targeted drug delivery in cancer therapies[90]. They emit heat on absorbing photons from the near-infrared (NIR) light, suggesting their potential use in the thermal ablation of tumors within the range of NIR[90–92]. Marangon and colleagues (2016) observed that the multi-walled carbon nanotubes could induce the photothermal ablation of SKOV3 cancer cells, only 10% of SKOV3 cells remained viable after NIR laserirradiation[93]. The cytotoxic effect of nanotubes was further enhanced by combining them with themtetrahydroxyphenylchlorin. The novel properties of CNTs allow them to be used as multifunctional therapeutic agents for cancer treatment. Harrison and Resasco in 2013 provided a method using modified CNTs for detecting and destroying cancer tumors[94].

However, their potential toxicity can be a major hurdle for any further application. Therefore, extensive efforts are needed to investigate the nanotoxicology of CNT to assess the potential risk they may hold[90,92].

ii). Graphene

The graphene is the building block of other graphite materials, such as 3D graphite, carbon nanotubes, and fullerenes[95]. This material exhibits a honeycomb lattice formed by a single-atom-thick layer of sp^2 hybridized carbon atoms and can be classified according to the oxygen content, number of layers in the sheet, or their chemical composition[96]. Graphene possesses brilliant optical and chemical properties[97]. The graphene oxide (GO) and reduced graphene oxide have been one of the most explored for biomedical applications among different graphene materials.

GO, an oxygenated derivative of graphene can be formed using the Brodie,Staudenmaier, Hummers, and improved Hummers' methods[98,99]. It can be used as a photothermal agent for efficient PTT owing to its intrinsically high NIR absorbance with satisfactory therapeutic outcomes. The reduction of GO can lead to dramatically enhanced NIR absorbance since chemical reduction can reestablish a portion of π conjugation[100]. Dai and co-workers proved that reduced nano-GO (nRGO) with significantly increased NIR optical absorption could be used as a highly efficient PTT agent against cancer[101].

Graphene and GO with extremely large specific surface areas could interact with different biomolecules and have substantial potential in biosensing, gene transfection, drug delivery, and cancer treatment. Delocalized p-electrons on the graphene plane allow the binding of aromatic drug molecules via π-π stacking. By conjugating targeting ligands to functionalized GO, targeted drug delivery to specific types of cancer cells can be achieved. Utilizing the photothermal effect, GO and its derivatives have also been used as nanocarriers for combined PTT chemotherapy[100]. For example, PEGylatednano-GO with DOX loaded on the surface has been shown to achieve combined cancer therapy[102]. Compared with chemotherapy alone or PTT alone, the synergetic treatment showed much higher therapeutic efficacy towards cancer. Recently,Toomeh et al., have studied the selective enhanced cytotoxicity effect of radiotherapy in combination with graphene oxide nanoflakes in cancer stem cells that lowers the risk of cancer recurrence[103]. GO and its derivatives can also be used for biomedical imaging. Dai and co-workers found that GO exhibited fluorescence from the visible to NIR range and used GO for cellular imaging[102].

However, autofluorescent interference of biological tissues affects the visible fluorescence of GO, resulting in limited applications in biomedical imaging. To overcome this problem external NIR fluorescent dyes have been used to label GO for efficient in vitro and in vivo imaging. Radiolabeling based nuclear imaging has prominent advantages, including superior sensitivity and anability to quantitatively analyze whole-body images compared with fluorescent labeling and imaging[100].

Although the current research progress isdistinguished, yet only a few nanocomposites have been assessed at the animal level, and nanocomposites have not been used in the clinic. Therefore, more efforts are still needed to address issues related to the biodegradation, excretion, andpotential long-term toxicity of graphene.

c) Magnetic Nanoparticles

Magnetic nanoparticles have been developed by employing nickel, cobalt, Prussian blue, and gadolinium, but magnetic iron oxide (usually maghemiteγ-Fe_2O_3 or magnetite Fe_3O_4) NPs remain the most widely researched MNP-based cancer theranostics due to their low systemic toxicity and strong MRI contrast properties.

These nanomaterials can be synthesized by various methods such as co-precipitation of salts with stabilizing polymer, thermal decomposition, hydrothermal and solvo-thermal synthesis, sonochemistry, and reverse microemulsion.MNPs generally consist of a magnetic core-shell and a polymer coating[104].Ficai et al showed that

the properties of the magnetite are changed completely by the presence of the shell, making it suitable for a wide range of medical and non-medical applications[105].

MNPs act as capable (MRI) agents due to their increased magnetization upon application of an outer magnetic field along with excellent T_2/T_2^* relaxation abilities[106–108]. Consequently, MNPs are widely utilized in several cancer theranostics applications including MRI imaging, biosensors, bioseparations, theranostics, delivery, magnetic hyperthermia, photodynamic therapy, and photothermal ablation therapy.

Superparamagnetic nanoparticles, iron oxide magnetic nanoparticles with particle sizes of about 20 nm do not keep any magnetism after removal of the magnetic field, hence, may be used in vivo[109]. Superparamagnetic nanoparticles can be used as contrast agents for magnetic resonance imaging (MRI), in cancer thermal therapy, and can concentrate on target sites through an external magnetic field. Vigor and his colleagues demonstrated that superparamagnetic iron oxide nanoparticles (SPIONs) could be used to target and image cancer cells when functionalized with recombinant single-chain Fv antibody fragments (scFv)[110].

Although they have been exploited in many fields such as imaging techniques, biosensors and bioseparations, drug transport, drug and gene delivery, etc. yet, no single MNPs formulation has been approved for cancer therapeutic use until today due to their toxicity because of the excessive release of iron ions[90].

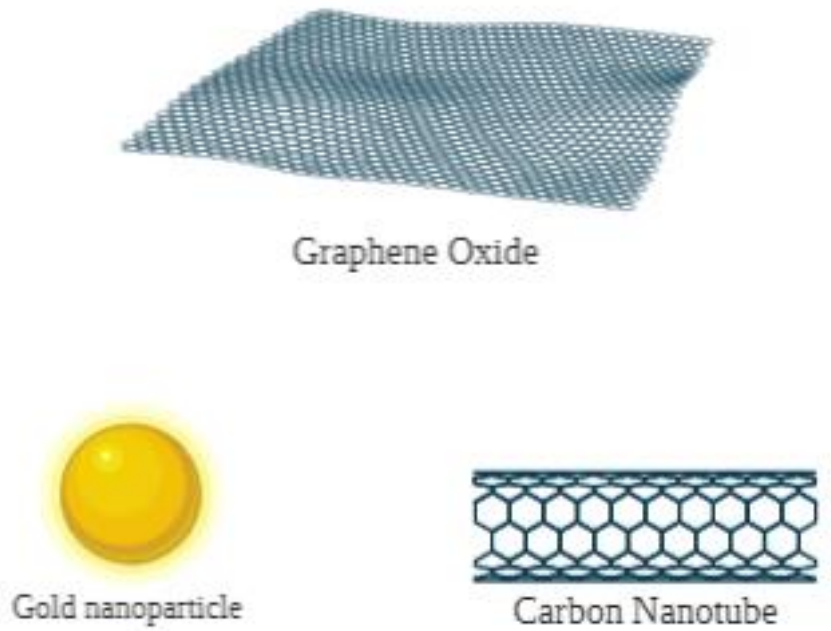

Fig.4: Few inorganic nanoparticles for drug delivery

V. CONCLUSION

Various kinds of NPs with diverse configurations have been developed with the advancement of nanotechnology. They are acknowledged to be a significant step toward enhancing the function of particles. Nanoparticles with a small size can penetrate tumor vasculature through EPR. Besides, functionalization with hydrophilic polymers offers a long circulation half-life and prolonged tumor tissue exposure to chemotherapeutic agents. Nanoparticles may be used as vectors for cytotoxic drugs to enhance pharmacokinetics and biodistribution, reducing undesirable side effects dramatically. They are used as polymer, lipid, metal, ceramic, and so forth carriers in drug deliveries.

These nanoparticles can also be transformed with biochemical and chemical moieties, which bind precisely to the targeted tissues for better confinement of the tumor tissues' treatment. NPs can also be used in the diagnosis and treatment of diseases and biomedical imaging. Exploiting nanotechnology will offer more ways to target several tumor molecules concurrently and develop efficient therapeutic strategies.

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