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A COMPREHENSIVE REVIEW: NANOPARTICLES AND ITS TYPES

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ABSTRACT

Cancer is characterized by abnormalities in mechanisms that regulate cell cycle, leading to the survival and proliferation of malignant cancer cells. The advent of nanotechnology has revolutionized the arena of cancer diagnosis and its treatment.

Nanoparticles ranging (1-100nm) are used in the treatment of cancer owing to their specific advantages includes biocompatibility, reduced toxicity, excellent stability, enhanced permeability retention, and precise targeting. Due to these factors, they are being investigated more vigorously in multidrug resistance mechanisms. This review summarizes novel and emerging nanoparticles fabricated in research and clinical use, discusses current limitations and obstacles that hinder the translation from research to clinical use, and provides suggestions for more efficient adoption of nanomaterials in cancer therapy.

Keywords: Nanoparticles, multidrug resistance mechanisms, nanotechnology

INTRODUCTION

Cancer is the consequence of gene mutations leads to abnormalities in mechanisms that regulate cell cycle. In cancer, signalling pathways are thereby altered leading to proliferation of malignant cancer cells. Inhibition of physiological apoptosis contributes to cancer development as well as resistance to radiotherapy and chemotherapy. Cancer forms fatal disease with a complex pathophysiology. Conventional cancer therapies include chemotherapy, radiation therapy, targeted therapy, hormone therapy and immunotherapy. Owing to the limitations such as lack of specificity, cytotoxicity, and multi-drug resistance pose a substantial challenge for favourable cancer treatment. The advent of nanotechnology has revolutionized the arena of cancer diagnosis and treatment. [1, 2]

Nanotechnology is a science that deals with the formulation of nanosize particles employing diverse synthetic strategies, particle structure and size modification.[3] The use of nanoparticles materials provides incomparable liberty to customize the intrinsic properties of the drug in drug delivery systems such as drug release characteristics, dissolution, solubility, bioavailability, half-life period, and immunogenicity[4]Nanoparticles ranging from (1-100nm) can be used widely in the treatment of cancer due to their specific advantages such as biocompatibility, reduced toxicity, more excellent stability, enhanced permeability and retention effect, and precise targeting. The nanoparticle drug delivery system is specific that utilizes tumor and tumor environment characteristics. Nanoparticles not only solve the limitations of conventional cancer treatment but also overcome multidrug resistance. [5, 6] Nanotherapeutic drugs have made progress in the domain of drug delivery systems and in anti-tumor multidrug resistance (MDR) by providing a chance for drug combination therapy and inhibition of drug resistance mechanisms. [7]

Nanotechnology applied in cancer therapy

Properties of Nanoparticles

Medical nanotechnology uses materials with nano-range size, generally 1–100 nm. These materials are applied in therapeutic drugs and devices design [8]. They possess several characteristics: high surface-to-volume ratio enhanced electrical conductivity, super paramagnetic behaviour, spectral shift of optical absorption. They can be applied in drug transportation, controlled release. Due to this, increased permeability enables crossing through biological barriers and improved biocompatibility, nanomaterials provides several usages for cancer diagnosis and its treatment. [9] A common nanomaterial, super paramagnetic iron oxide Nanoparticles (SPION) has potential in cancer hyperthermia treatment due to its smaller size, higher targeting specificity, controllable releasing speed, and immune evasion capability [10]

The high surface to volume ratio of nanomaterials together with biomolecules increases specificity of chemical drug complex in targeted therapy [11].PDT (Photodynamic therapy) and PTT (Photothermal therapy) are emerging cancer phototherapeutic treatment methods with great potential intensive research. Owing to unique fluorescence properties some nanomaterials can be used in PDT and PTT [12].In PDT, a photosensitizer is accumulated in cancerous sites; when irradiated with certain wavelength light, singlet oxygen and other cytotoxic reactive oxygen materials are generated, causing apoptosis or necrosis PTT uses materials that possess high photothermal conversion efficiency to elevate the temperature of targeted cancerous areas, leading to cancer cell death [13].

Nanoparticles deeply penetrate in tissues thereby increasing permeability and retention effect. The surface characteristics impact bioavailability and half-life by effectively crossing epithelial casement [14]. They are coated with polyethylene glycol (PEG), a hydrophilic polymer, decrease opsonisation [15] Nanoparticles are particles with size of nanoscale. Polymeric nanoparticles (PNPs), mAb nanoparticles, extracellular vesicles (EVs), metallic nanoparticles are broadly researched nanoparticles (NPs)

Nanomaterials and its types used for cancer treatment

Polymeric Nanoparticles (PNPs)

PNPs are colloidal macromolecules with size ranging10–1000 nm. They are encapsulated or attached to nanoparticle exterior thus forming a nanocapsule to achieve regulated drug release in the target. The ingredients of nanoparticles including nonbiodegradable polymers such as polymethyl methacrylate (PMMA), polyacrylamide,polystyrene, and polyacrylates were used to fabricate nanoparticles [16, 17]. Biodegradable polymers such as polylactic acid, poly (amino acids), albumin, poly(lactic-coglycolicacid) (PLGA), poly(ε-caprolactone) (PCL) are known to reduce toxicity enhancing drug release [18]. PNPs loaded with cisplatin such as dexamethasone or α-tocopheryl succinate are used in treatment which prevents cisplatin-induced ototoxicity [19].

Polymeric nanoparticles loaded with anti-cancer drugs, small interfering RNAs (siRNA) radionuclide are designed polymeric nanoparticles possessing the ability to react to ultrasound effect.Fluorescent polymeric nanoparticles consists of fluorescent proteins, biocompatible biopolymers,inorganic quantum dots, and organic dyes proved to be diagnostic therapeutic tools [20]. Hydrophobic interactions in fluorescence studies enhance the anti-cancer efficacy [21]. Employing use of ultrasound in its manufacture helps enhance efficacy of drug delivery, therefore leads to reduction of side effects. As a result, improves traversing ability to overcome the barriers endothelial blood vessels, tissue endothelium, interstitium, nuclear membrane and BBB in cancer therapy. [22, 23]. But there are few limitations such as toxic degradation and toxic monomer aggregation hence, further studies has to be done for their improvement in fabrication [24].Few examples includes modified dextran-camptothecin (DE 310), HPMA copolymer-DACH-platinate (AP5346), HPMA copolymer-platinate (AP 5280), HPMA copolymerpaclitaxel(PNU166945), and HPMA copolymer-doxorubicin galactosamine (PK2) are under the clinical development [25].

mAb Nanoparticles

mAbs are used in designing novel anti-tumor nanoplatforms owing to their specific targeting ability and antitumor effect. They are conjugated with cytotoxic drugs to form antibody–drug conjugates (ADCs).With specific antigens expressed in cancerous cells and normal cells in different manner better specificity can be achieved [26]. An antibody-drug NP consisting of paclitaxel (PTX) core and a surface modified trastuzumab used to treat breast cancer with positive expression of human epidermal growth factor receptor 2(HER2) [27]. NP complex showed better antitumor efficacy than PTX or trastuzumab alone, and relatively lower cytotoxicity in human breast epithelial cell control was observed in NP complex group [28]

Extracellular vesicles

Extracellular vesicles (EVs) are double layered phosphor-lipid vesicles ranging from 50-1000nm in size [29]. Based on the origin, they are categorised into three groups: exosomes, microvesicles and apoptotic bodies [30, 31]. Exosomes are 40–200 nm nano-scale particles. They act as natural vehicles by delivering cytotoxic drugs and other anti-tumor drugs to the target sites. Exosomes loaded with doxorubicin (exoDOX) is used to treat breast cancer and has showed great results as compared to conservative treatment with doxorubicin by enhancing the cytotoxicity [32]. Exosome-mediated miRNA therapeutic is used in targeted cancer therapy [33]. They possess inherent biocompatibility, higher chemical stability and the ability to manage intercellular communications. Some obstacles of exosome NP application such as lack of exosomal isolation and purification unclears the mechanism of exosome in cancer treatment [34-36].

Nanoemulsions

Nanoemulsions (NE) are colloidal nanoparticles ranges from 10 to 1000 nm.They are widely used as drug nanocarriers have several advantages over most lipid-based nanomaterials and nanoparticles: optical clarity, thermodynamic stability, large surface area, convenience in manufacture, biodegradability, and ideal drug release profile [37].Three typical types of nanoemulsions can be formulated:(a) water in oil nanoemulsion system in which water is dispersed in an aqueous medium; (b) oil in water nanoemulsion system in which oil is dispersed in an aqueous medium; (c) bi-continuous nanoemulsion [38].

A nanoemulsion system consisting of temozolomide, rapamycin, and bevacizumab is used to treat advanced melanoma. Studies have shown enhanced cytotoxicity against melanoma cells and improved inhibition of tumor relapse, in vitro human and mouse cell models [39] nanoemulsions loaded with spirulina and paclitaxel showed an improved anti-tumor effect by regulating immunity through TLR4/NF- kB signaling pathways [40].

Dendrimers

The most peculiar characteristic of dendrimers is their highly branched and easily modifiable surfaces. They have defined molecular weight, versatile adjustable branches, narrow polydispersity index, superior solubility and bioavailability of hydrophobic drugs. The size of dendrimer polymers ranges mainly from 1 to 10 nm, while some are up to diameter of 14–15 nm [41, 42]. The synthesis of dendrimers is initiated by reacting an ammonia core with acrylic acid resulting into formation of “tri-acid “molecule, that further reacts with ethylenediamine to yield “tri-amine” This product further reacts with acrylic acid to give rise to hexa-acid, which further produces “hexa-amine”

Few dendrimers like polyamidoamine (PAMAM), PPI (polypropylenimine), PEG (poly(ethylene glycol)), Bis-MPA (2,2-bis(hydroxymethyl) propionic acid), 5-ALA(5-aminolevulinic acid), and TEA (triethanolamine)have been used in cancer treatment. A PAMAM dendrimer was designed to achieve MDR management, used for chemotherapy combined with photothermal treatment of liver cancer cells. [43].

Carbon nanomaterials

Carbon nanomaterials (CNMs) have been widely used because of their unique electronic, thermal, optical, and mechanical properties. CNMs can load chemical drugs through hydrophobic interactions due to inherent hydrophobic nature hence CNMs are considered as efficient drug delivery platforms [44, 45]. Several carbon nanomaterials like graphenes, fullerenes, carbon nanotubes (CNTs), carbon nanohorns (CNHs),carbon quantum dots (CQDs) and graphyne (GDY) are used in cancer treatment.

Graphene-based nanomaterials can be classified into several types depending on their composition, structure, and properties: single-layer graphene, multi-layer graphene, graphene oxide (GO) and reduced graphene oxide (rGO) [46]. GO and rGO are widely used due to their ability to target hypoxia and irregular angiogenesis. Graphene has unique properties like optical transmittance, chemical inertness, high density, molecular barrier abilities and high hydrophobicity[47].Fullerenes are large carbon-cage molecules composed of carbon allotrope with different conformation types such as sphere, ellipsoid, or tube. PEG modified fullerenes showed promising photodynamic effects on tumor cells [48]. Carbon nanotubes (CNTs) are cylindrical tubes, classified into two groups: single-walled CNTs and multi-walled CNTs. They can enhance immune response by interacting with immune cells and suppressing the tumor growth. They are used in thermal ablation therapy. A fluorescent single-walled CNT with mAb encapsulating doxorubicin is used to target colon cancer cells [49].

Quantum dots

Quantum dots are nanometer-scale semiconductor crystallites widely used as biomedical imaging probes. Due to their distinctive optical and electronic characteristics, they are known to improve the efficacy of fluorescent markers in biological imaging [50]. They also possess unique optical and electronic properties leading to fluorescence emission from visible to infrared wavelengths, large absorption coefficients, and high brightness levels photostability [51].

The most common use of carbon QDs is bioimaging , biosensing and cancer therapy because of the inherent grand surface suitable for molecular conjugation, superior biocompatibility, and rapid excretion. They are divided into three types as includes- graphene quantum dots, Nano-diamond quantum dots, and carbon quantum dots. The most commonly used quantum dots is graphene quantum dots. For example, quantum dots Aptamer – doxorubicin conjugate targets prostate cancer cells [52].

Metallic and magnetic nanomaterials

Metallic nanoparticles due to their because of their optical, magnetic, and photothermal features have been extensively studied in bio-imaging and drug delivery. Magnetic nanomaterials are mainly applied in MRI imaging. Magnetic NPs are loaded with chemical drugs targets cancerous

Cells [53]. Iron oxide nanoparticles (IONPs) consisting of Fe_3O_4/Ag were encapsulated with a gold are used in therapies [54]

Combidex®, an iron oxide NP formulation, is under clinical development can be employed in detection of nodal metastases [55].Also, Feraheme®, a ferumoxytol ontaining iron oxide NP formulation, can be employed in treatment of iron deficiency anemia and in prostate and testicular cancer[56,57]. Several magnetic NPs are used for thermal ablation of cancer cells [58,59]. For instance, Feridex®,and Resovist® are under clinical development can be employed for liver metastasis and colon cancer after further studies [60].

CONCLUSION

Cancer therapies based on the distinct features of NPs are widely used in treatment of several cancer types. NP-linked DDS are known to enhance pharmacokinetics, biocompatibility, tumour targeting and stability, thereby provides an apt platform for combination therapy. Research studies have shown that study size, intent, and timing of NP therapies during the therapy impact apparently during clinical studies. Certain limitations like deficiency of in vitro models that replicate in vivo stage, immunotoxicity and neurotoxicity still persists. The clinical efficacy, safety and tolerance of these new modalities should to be monitored.

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