Review Article

Nanoparticles: A Novel Avenue in Cancer Therapy

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ABSTRACT

Cancer is a major health concern in the world. Chemotherapy is widely used to treat cancer either alone or in combination with other therapy. Chemotherapy is associated with several problems such as lack of specificity, poor aqueous solubility and multidrug resistance. Nanotechnology has emerged as promising approach to treat cancer effectively. Nanotechnology based nanoparticles have shown great potential in overcoming limitations of conventional chemotherapy. Nanoparticles have several properties such as tunable size and required surface characteristics which make them ideal candidate for drug targeting. Several types of nanoparticles are engineered to target tumor sites without causing any harm to normal cells. Major advantage of drug loaded nanoparticles is, they reach to tumor sites with minimal loss and affect only defected cell without any harm to normal cells. Nanoparticles accumulate specifically to desired cell either by passive or ligand based target mechanism. Some nanoformulations have approved and some are under clinical trials. This review discusses different types of nanoparticles along with targeting strategies. It also discusses the potential of nanoparticles in cancer diagnosis and treatment.

Keywords: Nanoparticles, nanotechnology, tumor imaging, photodynamic therapy, photothermal therapy, theranostic agent.

INTRODUCTION

Cancer is a disease characterized by uncontrolled proliferation of cells. Cancer is one of the major health concerns which affect millions of people. There are over 100 types of cancer and each is classified by the organs or tissues where the cancers form[1]. According to World Cancer Report 14 million new cases of cancer with 8.2 million cancer related deaths (in 2012) are reported[2]. Treatment of cancer includes surgical removal, radiation, chemotherapy and hormone therapy[3]. Chemotherapy is a first line treatment in almost all types of cancer. However, it accompanies with a major problem lack of selective toxicity, results in the damage of normal healthy cells which will narrow down therapeutic index, and thereby results in side effects and poor outcome[1]. Treatment of cancer lacks selective delivery of systemically administered chemotherapeutic agents, poor solubility and distribution, unfavorable pharmacokinetics and high-tissue damage or toxicity[4]. It reported that amount of drug accumulated in normal viscera is 10-20 fold higher than that in the same weight of tumor site and many anticancer drugs are not able to penetrate more than 40-50 mm (equitable to combined diameter of 3-5 cells) from the vasculature[1]. To circumvent such obstacles, it has become important to develop novel and effective ways to remove cancer cells[5].

Nanotechnology has emerged as a promising approach in cancer treatment. Nanotechnology is a technology performed on nano-scale (size range from 1nm to 1000 nm)[6].

Nanomedicines are utilized to overcome the several limitations of conventional drug delivery system[3]. Nanoparticles have unique physical and chemical properties which provide them better access to tumor sites. Nano size and tunable surface properties make Nanoparticles suitable for cancer treatment[7].

In this review we will briefly discuss the local drug delivery systems by means of various nanoparticles which serve as an appropriate platform in the treatment of cancer.

Nanoparticle Properties

Nanoparticles have shown potential in overcoming various challenges of conventional cancer therapy. Major disadvantages of conventional chemotherapy are non-specificity and toxicity.

Size

Nanoparticles have tunable size. Nano-carriers are large enough to prevent their rapid leakage into blood capillaries but small enough to escape by macrophages capture that are lodged in reticuloendothelial cell. The size of the sinusoid in the spleen and fenestra of the Kuffer cells in the liver varies from 150 to 200 nm[8] and the size of gap junction between endothelial cells of the leaky tumor vasculature may vary from 100 to 600 nm[9]. The maximum size of nanoparticles allowing penetration through cell membranes is known to be 500 nm[10]. Long term circulation is important for targeted delivery and sustained release. Particle size is known to be intrinsically related to the rate of clearance from the blood circulation[10].

Surface Characteristics

Surface characteristics also determine the life span of nanoparticles during circulation in blood. Nanoparticles should have hydrophilic surface to avoid macrophage

capture[11]. This can be achieved either by coating of nanoparticles with hydrophilic polymers or by forming block copolymers with hydrophilic and hydrophobic domain[10]. Additionally, tumor cells bear relatively high negative surface charge than normal cells. Cationic nanoparticles bind with negatively charged phospholipids head groups preferentially expressed on tumor endothelial cells. Cytotoxicity potential of polymeric nanoparticles largely depends on cell internalization and sub-cellular localization of the nanoparticles which is governed by nature of polymeric surface charge. Cationic nanoparticles have been found to sensitize the cancer cells to effects of paclitaxel for improved anticancer activity[12].

Challenges overcome by Targeted Nanoparticles in Cancer Treatment

Various problems such as poor aqueous solubility, high systemic toxicity, lack of specificity to target site associated with conventional chemotherapy can be overcome by targeted nanoparticles. Additionally, some cancer cells develop drug resistance over drug treatment course. Targeted nanoparticles have shown potential to overcome these limitations[6,13,14].

Majority of chemotherapeutics are hydrophobic in nature and unable to cross the aqueous environment (e.g., the body and tissue fluids *in vivo*) surrounding a cell and then penetrate the cell membrane to eventually reach intracellular targets. Additionally, on intravenous administration these drugs aggregate and cause local toxicity. Encapsulation is an efficient approach to overcome this limitation. Park and co-workers found that nano-sized micelles based on amphiphilic block copolymers could serve as a carrier for the delivery of drugs poorly soluble in water (such as paclitaxel), significantly increasing the drug concentration in an aqueous medium by a factor of more than 1000[13].

Anti-cancer drugs distribute indiscriminately to normal organs and tissues because of lack of tumor specificity. Thus, cancer cells are exposed to a lower concentration of the drug than normal cells, resulting in not only decreased effectiveness but also increased toxicity[15]. The functionalization of the nanoparticles helps to achieve extended blood residence time, reduce nonspecific distribution, and target tissues or specific cell surface antigens with a targeting ligand (peptide, aptamer, antibody/antibody fragment, small molecule)[12]. It is also achieved by encapsulating drugs in nanoparticles such as liposomes. PEGylated liposomal doxorubicin (with brand names of Doxil in the US and Caelyx in Europe)[16] has been shown to significantly improve the therapeutic index of doxorubicin both in preclinical and clinical studies[17].

Drug resistance has emerged as a major obstacle limiting the therapeutic efficacy of chemotherapeutic agents. Among several mechanisms of drug resistance, P-glycoprotein is the best known and most extensively investigated. It has been suggested that nanoparticles may be able to circumvent P-glycoprotein– mediated resistance. One possible mechanism is that nanoparticles may avoid recognition by the P-glycoprotein efflux pump by means of being enveloped in an endosome when entering the cell, leading to high intracellular drug concentrations. Ligand-targeted strategies, especially those using receptor-targeting ligands, may have particular potential for overcoming drug resistance because these ligands are usually internalized via receptor-mediated endocytosis. Indeed, a folate receptor–targeted, pH-sensitive polymeric micelle containing doxorubicin and transferrin-conjugated paclitaxel-loaded nanoparticles exhibited greater inhibitory activity against drug-resistant MCF-7 cells and/or xenografts than their nontargeted free drug counterparts[11].

Types of Nanoparticles used in Cancer Therapy

Polymer based Nanoparticles

Biodegradable polymers such as chitosan, gelatin and collagen poly caprolactone or non biodegradable polymers such as poly lactic acid (PLA) and poly Lactico Glycolic acid (PLGA) are used to prepare colloidal solid particles[1]. It is reported that polymeric nanoparticles have more efficacy for targeted delivery of anticancer agent such as paclitaxel[18]. Polymeric nanoparticles (figure 1) possess unique physicochemical characteristics which provide them higher stability, sharper size distribution, sustained and more controllable drug-release profile and higher loading capacity for poor water soluble drugs[19]. For instance, Danhier prepared paclitaxel loaded PEG-PLGA based nanoparticles grafted with RGD peptide and found that these nanoparticles delayed tumor growth more efficiently and prolonged survival time of mice compared with non-targeted nanoparticles[20].

Polymer Derived Nanoparticles

Micelles (figure 1) assembled with hydrophobic reservoir as drug carrier and hydrophilic shell makes the particle an ideal candidate for i.v. administration[11]. Paclitaxel loaded micellar formulation consisting PEG and modified polyaspartate NK105 was prepared. Preclinical studies in mice had shown that reduced dose of NK105 had same antitumor activity with high dose of free paclitaxel. Additionally, NK105 have shown less hypersensitivity reactions in patients suffering from pancreatic, bile duct, gastric, and colonic cancers compared to systemic paclitaxel treatment during the phase I trial[21].

Lipid based Nanoparticles

Liposomes (figure 1) in the range of 30-100 nm are formed with various phospholipids such as phosphatidylcholine, phosphatidylethanolamine, phosphatidylglycerol and phosphatidylserine, and other molecules such as cholesterol. Polyethylene glycol coated liposomes have increased circulation time of liposome from few hours to approximately 45 hours[19]. O. Brien studied and found that PEGylated liposomal doxorubicin

has prolonged circulation time which facilitate greater uptake PLD liposomes in tumor tissues. Additionally, PLD liposomes reduced drug delivery to normal tissues[22].

In the study Chang found that survival rate of mice and bioavailability of doxorubicin was higher when treated with novel peptide ligand coupled with liposomes carrying doxorubicin[15].

Dendrimers

Dendrimers (figure 1) are synthetic polymers, uni-molecular, mono-dispersible, multi-branched and three dimensional structures with well defined molecular weights with a size of 1-10 nm made up of macromolecules such as poly (*N*-isopropylacrylamide)-polystyrene and poly(ethylene oxide)-poly(-benzyl-L-aspartate)[18,1].

The structure of dendrimers involve initiator core, layers of branched repeating units and functional end groups on outer shell. Both water soluble and insoluble drug can be given concurrently with the help of dendrimers[19].

Lai prepared by conjugating doxorubicin to polyamidoamine dendrimers with the help of pH sensitive and insensitive linkers to improve efficacy and reduce side effects of these drugs[23].

Carbon Nanotubes

Carbon nanotubes (figure 1) are formed by rolling single or multiple grapheme sheets to form cylinder[18].

Carbon nanotubes are completely insoluble in all solvents but chemical modification can render them to water soluble and functionalized so that they can be linked to wide variety of active molecules such as peptide, protein, nucleic acid and therapeutic agents.

Methotrexate, an anticancer agent covalently linked to carbon nanotubes with fluorescent agent[11]. There is lack of toxicity results because no clinical trials are performed using carbon nanotubes.

Gold Nanoparticles

Gold nanoparticles (GNPs) are used to detect tumors and metastasis in many solid tumors[6]. Easy conjugation with bio-molecules and high absorption efficiencies are the two unique characteristics of gold nano-materials which make them ideal candidate for therapeutic applications[24].

GNPs (figure 1) are conjugated with tumor necrosis factor (TNF) alpha which mainly accumulate in tumor sites and therefore prevents the toxic effects of TNF on healthy tissues.

Additionally, gold nanoparticles have been used to deliver anticancer therapeutic agents. For instance, Methotrexate is highly water soluble drug which results in poor tumor retention but after conjugating with GNPs tumor retention and therapeutic efficacy of drug increases[25]. GNPs can be used targeted delivery of chemotherapeutics. Patra demonstrated high intratumoral concentration of gold using GNP-cetuximab-gemcitabine nano-complex compared with untargeted GNPs with minimal retention in liver or kidney[26].

Radioactive properties of gold can be utilized for cancer treatment. Chanda N. proposed that ^{198}AuNPs will serve as new generation of therapeutic agents with potential to eliminate serious clinical impediments associated with existing heterogeneous (seed-based) brachytherapy agents for treatment of various types of human cancers.

Gum Arabic glycoprotein- ^{198}AuNPs complex was prepared. Intratumoral administration of this complex in mice resulted in significant tumor regression and effective control in tumor growth of prostrate over 30 days without any harm to nontargeted organs[28].

Magnetic Nanoparticles

Magnetic nanoparticles (figure 1) have been investigated and studied in past few years. It was studied that oleic acid coated iron oxide nanoparticles when embedded with chemotherapeutics such as doxorubicin and paclitaxel loading efficiency was increased up to 95%[18].

Jurgons R. studied effects of magnetic nanoparticles and chemotherapeutic agent complex in rabbits[29].

Moreover, Kohler fabricated Methotrexate-magnetic nanoparticles complex or Methotrexate- PEG-magnetic nanoparticles complex to target folate receptor over expressing cancer cells. This complex induces apoptosis in cancer cells and minimizes toxicity of methotrexate to normal cells[24].

Quantum Dots

Due to unique physical properties quantum dots have become area of intense research that can be utilized for cancer. Quantum Dots(QD) (figure 1) are usually made up of inorganic transition metal such as cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs) as a core elements inside a shell of zinc sulfide (ZnS). Small size and ability to conjugate with targeting molecule give them easy access to systemic circulation and specific retention in tumor sites[7]. Bagalcote fabricated QD-Aptamer complex that could deliver chemotherapeutic agent and sense drug delivery simultaneously based on mechanism of Fluorescence Resonance Energy Transfer[24].

Nanodiamonds

Nanodiamonds (NDs) are used for targeted delivery. Nanodiamonds were bound to doxorubicin and this complex was encapsulated with polymer microfilm in order to achieve sustained release of drug for period of 1 month[18]. NDs (figure 1) have emerged as unique nano-carrier due to their biocompatibility, scalable synthetic methods and carbon surface which facilitate bio agent attachment. ND attachment has shown to increase imaging efficacy, sustain drug release, boost therapeutic efficiency and improve drug safety profile in both cell based and animal model[18].

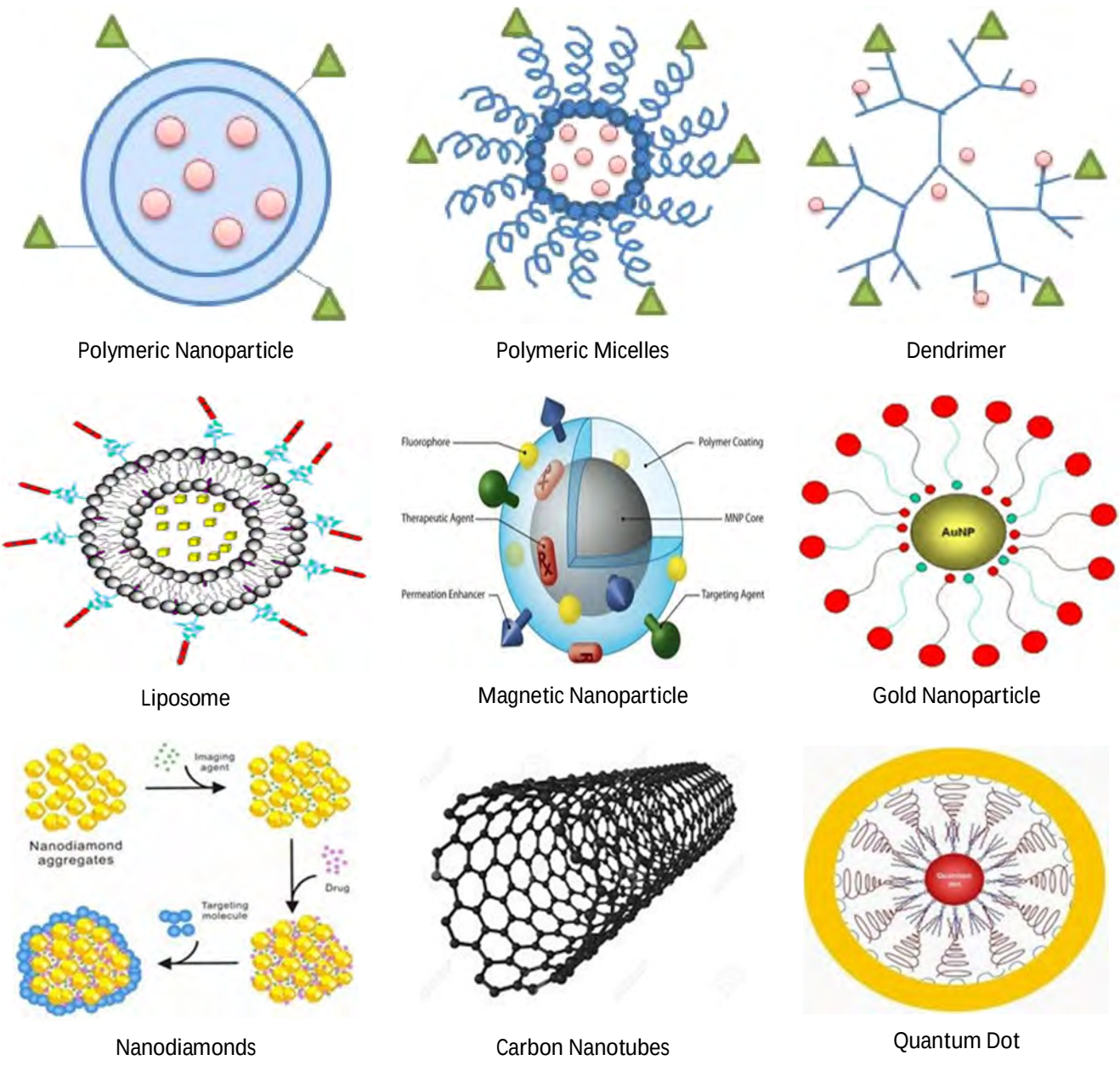

Figure 1: Types of Nanoparticles Used in Cancer Therapy

Examples of Nanomedicines for Cancer approved by FDA and those undergoing Clinical Trials

Following table represents some examples of nanoformulations which are either approved or under clinical investigations.

Table-1 Examples of nanomedicines for cancer approved by FDA and those undergoing clinical trials[30]

Drug Product	Active Ingredient	Manufacturer	Indications	FDA Approved Date/Clinical Trial State
Doxil(Caelyx)	PEGylated Doxorubicin	Orthobiotech, Schering-Plough	Ovarian/Breast Cancer	November 1995
Abraxane	Albumin-bound paclitaxel Nano-spheres	Abraxis Biosciences, Astragenecea	Various Cancers	Jan 05
	Nab paclitaxel in combination with gemcitabine	Celegene	Metastatic Pancreatic Cancer	September 2013

Myocet	Liposome encapsulated Doxorubicin	Elan Pharmaceuticals/Sopherion Therapeutics	Breast Cancer	2000 Approved in Europe and Canada
DaunoXome	Liposome encapsulated Daunorubicin	Gilead Science	HIV related Kaposi sarcoma	Apr-96
DepoCyt	Liposomal Cytarabine	Skye Pharma, Enzon	Lymphomatous meningitis	Apr 99
Oncaspar	PEGasparginase	Enzon	Acute Lymphocytic leukemia	Feb 94
Onco- TCS	Liposomal Vincristine	Inex	Non-Hodgkin Lymphoma	In clinical phase I/II
LEP-ETU	Liposomal Paclitaxel	Neopharma	Ovarian/Breast/lung Cancers	In clinical phase I/II
Aroplatin	Liposomal Cisplatin Analog	Antigenics Inc.	Colorectal Cancer	In clinical phase I/II
OSI-211	Liposomal Lurtotecan	OSI	Lung Cancer/Recurrent Ovarian	In clinical phase II
SPI-77	Stealth Liposomal Cisplatin	Alza	Head& Neck Cancer/Lung Cancer	In clinical phase III
EndoTAG-I	Paclitaxel	Medigene, SynCore Biotechnology	Breast Cancer, Pancreatic Cancer	In clinical phase II
Marqibo	Vincristine	Talon Therapeutics	Philadelphia Chromosome negative Lymphoblastic Leukemia	Aug 12
ThermoDox	Doxorubicin	Celsion Corporation	Hepatocellular Carcinoma	In clinical phase III

Targeting Strategies of Nanoparticles in Cancer Therapy

Nanoparticles are designed to target desired cell by various modifications such as changing in chemical and physical properties[3] and for a desired therapeutic effect anticancer drug should be able to reach tumor sites through the penetration of barriers in the body with minimal loss of volume and activity during circulation. In addition to this, after reaching tumor sites the drugs should have ability to selectively kill tumor cells without affecting normal cells[11]. Drug loaded nanoparticles reach to tumor sites either by passive targeting or active targeting. Drug loaded nanoparticle is represented in figure 3.

Passive Targeting

Passive targeting is based on the accumulation of dug around regions of tumor with leaky vasculature known as enhanced permeation and retention (EPR) effect[31]. Defective vascular architecture induces an EPR and permits accumulation of nanoparticles in the tumor interstitial space (figure 2)[6]. Due to lack of apoptosis cancerous cells proliferate abnormally and suck nutritious agents through blood vessels forming leaky blood vessels and these leaky blood vessels are also formed due to basement membrane abnormalities and decreased number of pericytes lining rapidly proliferating endothelial cells. The pore size of leaky endothelial cells ranges from 100 to 780nm. Nanoparticles of below this size range easily pass through cells. Drug loaded nanoparticles can be targeted to specific organ by passive diffusion or convection and lack of lymphatic drainage facilitates diffusion process. Loose lymphatic network and leaky vasculature of tumor sites resist inward flow of molecule which provides high retention time in tumor interstitium[3]. Liu had shown passive targeting of quantum dot probe in leaky vasculature (figure 3)[34].

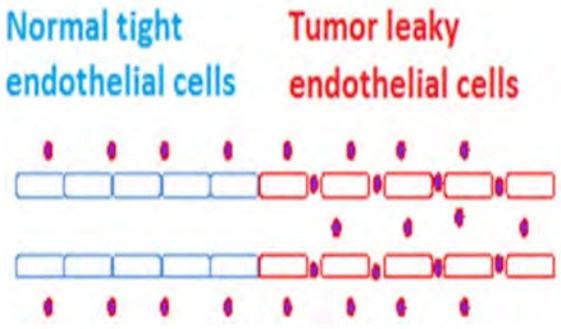

Figure 2: Nanoparticles accumulation in tumor tissue through EPR effect.

Active Targeting

Active targeting agents having selective affinity to interact with specific cell are attached to drug carrier nanosytems by various modifications for active targeting[18].

Nanoparticles target tumor sites either by ligand receptor interaction or antigen antibody recognition[3]. Cell surface antigen and receptor should have several properties that make them ideal tumor specific targets. First, they should express on tumor cell and not expressed on normal cells. Second, the expression on targeted tumor cells should be uniform. Last, cell surface antigen and receptor should not be shed into blood circulation[11]. Various ligands are used to for tumor specific targeting. Here we represent some examples of ligands and their functions (Table-2).

Table 2: Ligands employed for tumor-specific targeting and its function[32]

Types of Ligands	Functions
Folate	Nonimmunogenic
Folate Nanoparticles	Involved in human growth, development, cell division and DNA synthesis
Folate Conjugated Nanoparticles	Used on human cervical carcinoma cell
Transferrin	Essential role in iron homeostasis and cell growth
Transferrin Receptor	Initiates receptor mediated endocytosis and internalization of transferring
Transferrin Mediated Targeting	Enhancement of anticancer activity
Transferrin Conjugated Nanoparticles	Enhance antitumor activity and also contributes to the photo stability & sustain release of drug
Vasoactive Intestinal Peptide receptor	Angiogenesis
Polymer- Conjugated Angiogenesis Inhibitor TNP-470 (Caplostatin)	Inhibits hyper-permeability of tumor blood vessels
Integrin avb3	Used targeting moiety on nanovectors
PLGA Nanoparticles	Delivering natural products like curcumin
Chitosan Nanoparticles	Inhibition of tumor Growth Induction of Tumor Necrosis

Conjugation of complimentary ligands on the surface of nanoparticles renders them to target on cancer cells. Nanoparticles bind with receptor; they undergo receptor-mediated endocytosis or phagocytosis by cells resulting in internalization of the encapsulated drugs[3]. For instance, Folate targeted conjugate binds with folate receptor on the cell surface. This complex of receptor and ligand form endosome that is internalized by plasma membrane. These endosomes are transferred to target cells. When pH of endosome become acidic, lysozyme activates and release drug from conjugate and reaches to target cells with the help of targeting agent. Folate receptor releases from the conjugate returns to the cell membrane[11]. Liu presented high affinity binding of quantum dot-antibody conjugate to tumor antigens via active targeting (figure 3)[34].

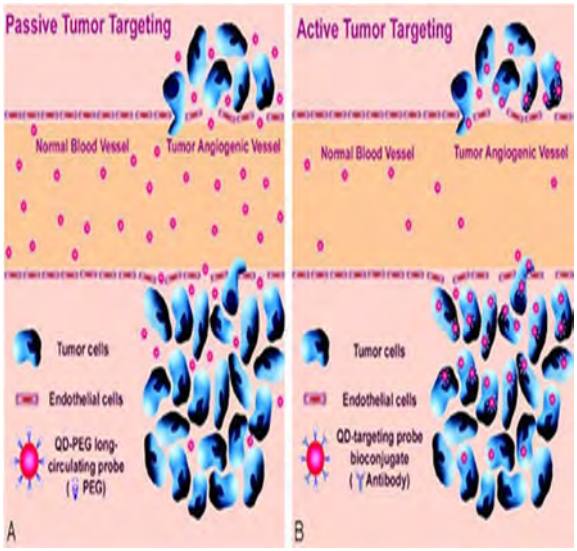

Figure 3: Targeting strategies of nanoparticles in cancer therapy[34]

Applications of Nanoparticles

Nanoparticles as Drug Carrier

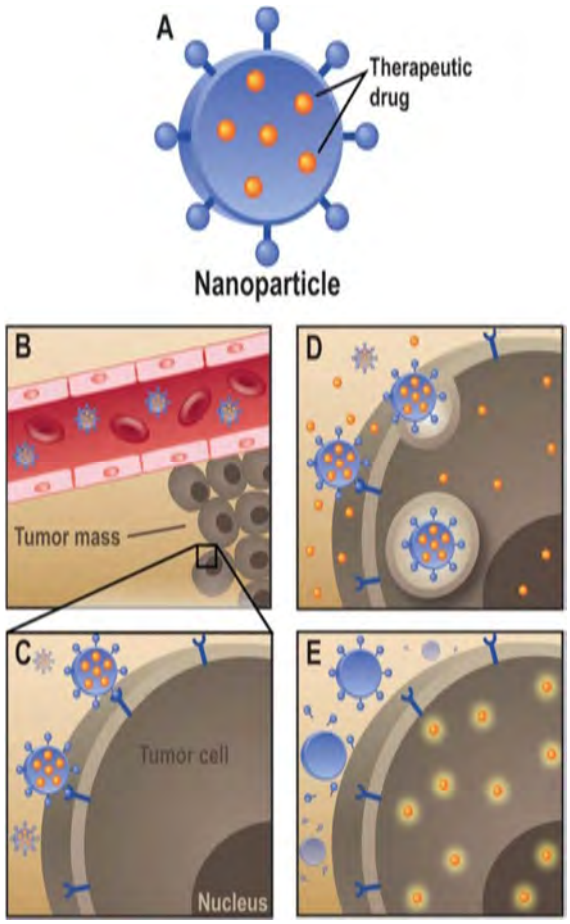

Figure 4: The criteria nanoparticles need to fulfill to be effective carriers for chemotherapeutic drugs. (a) The nanoparticle carrier must bind or contain the desired chemotherapeutic drug(s). (b) The nanoparticle-drug complex must remain stable in the serum to allow for the

systemic delivery of the drug. (c) The nanoparticle-drug complex must be delivered only to tumor cells. (d) The nanoparticle must be able to release the drug once at the site of the tumor. (e) After drug delivery, the residual nanoparticle carrier must be safely degraded.

Nanoparticles that serve as carriers either bind drug on their surface or encapsulate the dug to prevent it from degradation[33]. Nanoparticles have ability to penetrate through small capillaries which allow efficient drug accumulation at tumor sites. A sustained and controlled release of drugs at tumor sites can be possible over a period of days or even weeks[34].

PEGylation gives stealth like characteristics to nanoparticles, resulting in increased stability due to inhibition of recognition by mononuclear phagocytic cell. Nanoparticle-drug complex is targeted to tumor site either passively or actively (figure 4)[33]. Cegnar have studied that by using PLGA nanoparticles as carrier containing cystatin, a potential anticancer drug inhibit the tumor-associated activity of intracellular cysteine proteases cathepsins, to limit tumor growth, and showed that PLGA nanoparticles are useful for a rapid delivery of protein inhibitors into tumor cells, enabling an effective inhibition of the intracellular proteolysis[34].

Additionally, conjugated polymer-drug nanotherapeutics, such as NC-6004 [a cisplatin-incorporated PEG-poly (glutamic acid) block copolymer micellar formulation] and ProLindac™ (a diaminocyclohexane-platinum hydroxypropylmethacrylamide prodrug), are in late-stage clinical trials[35].

Nanoparticles as therapeutic agent

Photodynamic Therapy

Photodynamic therapy utilizes photosenstizers which absorb light of certain wavelength and engender cytotoxic oxygen based molecular species which cause cellular damage and death by oxidative stress resulting in apoptosis, necrosis or autophagy (Figure 5).

Currently, photodynamic therapy is being explored in the treatment of several cancers including skin, bladder, prostate, lung, esophageal, pancreatic, stomach and head and neck cancer to name a few.

Photo sensitizers transfer energy which they absorb from light either oxygen molecule to produce singlet oxygen or surrounding molecules to form free radicals which subsequently generates superoxide, hydrogen peroxide and hydroxyl radicals. Nanoparticles used in photodynamic therapy either act passively or actively[33].

Samia prepared a conjugate of CdSe quantum dots and a photo sensitizer, silicon phthalocyanine. In the study, it was observed that quantum dots can sensitize photodynamic agent either through a fluorescence resonance energy transfer (FRET) mechanism or interact directly with molecular oxygen through triplet energy transfer process. Both mechanisms subsequently generate reactive singlet oxygen species that can be used for cancer treatment[36].

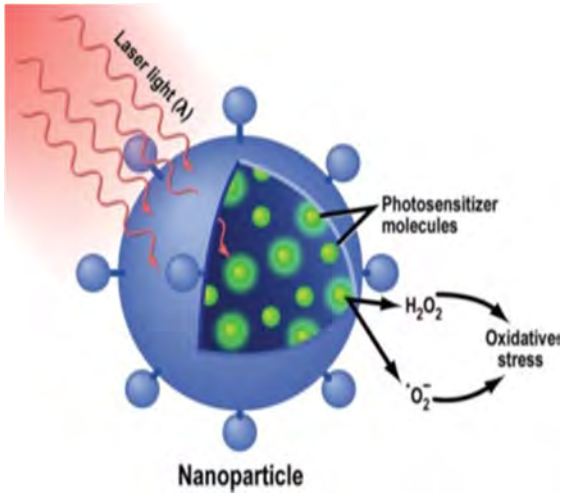

Figure 5: Nanoparticles in Photodynamic Therapy

Photothermal Therapy

Nanoparticles can be used in photothermal therapy to cause localized destruction of tumors after absorption of light due to their efficient light-to-heat conversion. The controlled and selective heating of nanoparticles allows thermal damage to be confined to the tumor while minimizing any damage to surrounding normal tissue (figure 6). 36 Nobel metal nanoparticles (such as gold nano-spheres, nanorods and nanocages) and carbon nanotubes show strong absorption in NIR region of electromagnetic spectrum especially at 650 to 900 nm due to surface Plasmon resonance. Most biological tissues exhibit minimal light absorption in this range, thereby allowing for increased depth penetration of light[33]. Halas and coworker prepared a conjugate of HER2 antibody and gold nano-shell to target over expressing HER2 breast carcinoma cell. In this study, it was demonstrated that NIR irradiation causes a rise in the temperature of the target regions of between 40 to 50° C, which selectively destructed the carcinomas. In addition, the survival rate of mice treated with HER-gold nano-shells and NIR irradiation was excellent compared with the controls (non-specific antibody or NIR light alone)[37,24].

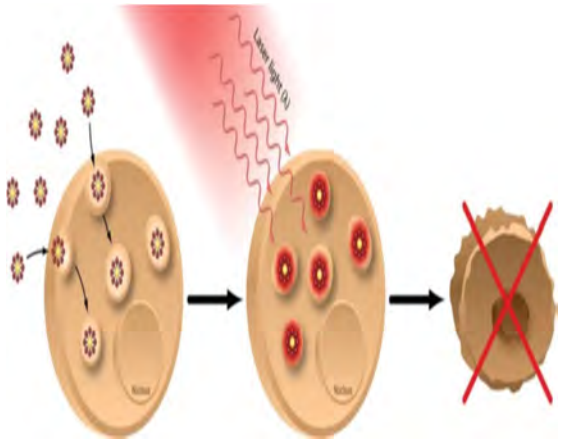

Figure 6: Nanoparticles in Photothermal Therapy.

Nanoparticles in Tumor Imaging

Various types of nanoparticles such as liposomes, dye-molecule-doped silica nanoparticles, quantum dots, dendrimers, gold nanoparticles, immunotargeted nano-shells, per fluorocarbon nanoparticles, nano-shells, and magnetic nano-crystals are used in molecular imaging. Additionally, Antibody-conjugated paramagnetic liposomes (diameter 300–350 nm) are used to visualize tumor angiogenesis *in vivo* by magnetic resonance imaging (MRI)[34]. Kobayashi and Brachbiel found that by conjugating gadolinium to dendrimers targeting to desired site and imaging of kidney, vascular, liver and tumor have been successfully achieved[39].

Nanoparticles as Theranostic Agent

Theranostic agents are agents used simultaneously in diagnosis and treatment. Designing of such multipurpose nanoparticle will accelerate drug development[33]. Guthi described a multifunctional methoxy-terminated PEG-b-PDLLA micelle system that is encoded with a lung cancer-targeting peptide (LCP) and loaded with SPIONs together with doxorubicin for MR imaging and therapeutic delivery, respectively. Carbon nanotubes (CNTs) have been studied for photo acoustic and optical imaging since they have a strong optical absorbance in the high-near infrared region of the electromagnetic spectrum (i.e. 700-1100 nm), where biological systems have a transparent window. This therefore makes them ideal for near-infrared photothermal ablation therapy, with the temperature within tumors shown to increase in a light-dependent and CNT dose-dependent manner[38,21].

Future Prospective

Emergence of nanotechnology has brought change in vascular imaging and drug delivery. On the website ClinicalTrials.gov, a registry of federally and privately supported clinical trials conducted in the US and around the world, it is revealed that over 70 nanomedicines approaches are currently in clinical trials for cancer treatment and imaging[40]. Drug loaded nanoparticles targeting neoplastic sites have shown potential in minimizing adverse effects and specific targeting. Nanoparticles have shown to overcome the limitations of conventional cancer therapy. The future of nanoparticles will depend on rational design of nanotechnology material and tools based around detailed and thorough understanding of biological processes rather than the forcing application of some material currently in business. It is hoped that, in the end nanoparticles based therapeutics will become an integral part of mainstream medicine and a standard in a drug industry[41].

Based on the full spectrum of cancer nanomedicines in clinical trials and on the market, it is highly expected that the forthcoming generations of nanoformulations will have targeting moiety, may carry multiple drugs that could potentially be released in a controlled manner, and will be equipped with an imaging capacity[42].

CONCLUSION

Nanotechnology has emerged as a promising technology in the field of medicine. Nanoformulations have shown great potential in cancer therapy not only by limiting challenges proposed by conventional chemotherapy but also by improving the survival rate.

Some nanoformulations for cancer are already in market and some are under preclinical and clinical investigation. Nanoparticles have already shown exciting results in cancer therapy and holds even greater promise for cancer patients in future.

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