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REVIEW ON NANOTECHNOLOGY FOR THE CANCER TREATMENT

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ABSTRACT

Nanoparticles are rapidly being developed and trialed to overcome several limitations of traditional drug delivery systems and are coming up as a distinct therapeutics for cancer treatment. It also discusses specific drug delivery by nanoparticles inside the cells illustrating many successful researches and how nanoparticles remove the side effects of conventional therapies with tailored cancer treatment. Recent scientific evidence shows the potential uses of nanomaterials as therapeutic agents, systems for selective and controlled drug release, and contrast agents for diagnosing and locating tumors. Finally, nanotechnology is still developing science can be defined as next generation techniques for cancer disease; at the same time it comes with many advantages to treat cancer patients.

KEYWORDS: Nanotechnology, Nanoparticles, Controlled drug release, Tumor.

1. INTRODUCTION

Cancer is one of the most serious fatal diseases in today's world that kills millions of people every year. It is one of the major health concerns of the 21st century which does not have any boundary and can affect any organ of people from any place.[1] Cancer is one of the main causes of human death and a major public health concern worldwide.[2,3] Cancer, the uncontrolled proliferation of cells where apoptosis is greatly disappeared, requires very complex process of treatment. Moreover, cancer, which is comprised of various cancer cell subtypes and variable components, can be induced by a variety of carcinogenesis.[4] To overcome these limitations and achieve better cancer therapeutic efficiency, it is necessary to design drug delivery system (DDS) to combine chemotherapy with other cancer treatments. Cancer treatment includes surgical removal, chemotherapy, radiation, and hormone therapy. Chemotherapy, a very common treatment, delivers anticancer drugs systemically to patients forquenching the uncontrolled proliferation of cancerous cells.[5]

Nanotechnology is the creation and utilization of materials, devices and systems through te control of matter on the nanometer scale.[6]

Nanocarrier systems can be designed to interact with target cells and tissues or respond to stimuli in well-controlled ways to induce desired physiological responses. They represent new directions for more effective diagnosis and therapy of cancer.[7] nanotechnology can be used for better cancer diagnosis.

2. Nanotechnology In Cancer Targeting

Nanotechnology has made a great revolution in selective cancer targeting. Nanoparticles can be designed through various modifications such as changing their size, shape, chemical and physical properties, and so forth, to program them for targeting the desired cells. They can target the neoplastic cells either through active or passive targeting.

2.1) Passive targeting

The most common route of administration of nanomaterial-based anticancer drugs is intravenous injection. This approach bypasses the absorption step across the intestinal epithelium required after oral administration.[8] At tumor sites, the vascular barrier is disrupted, and this enables nanocarriers to accumulate in the tumor tissue as depicted in Fig. 1.[9]
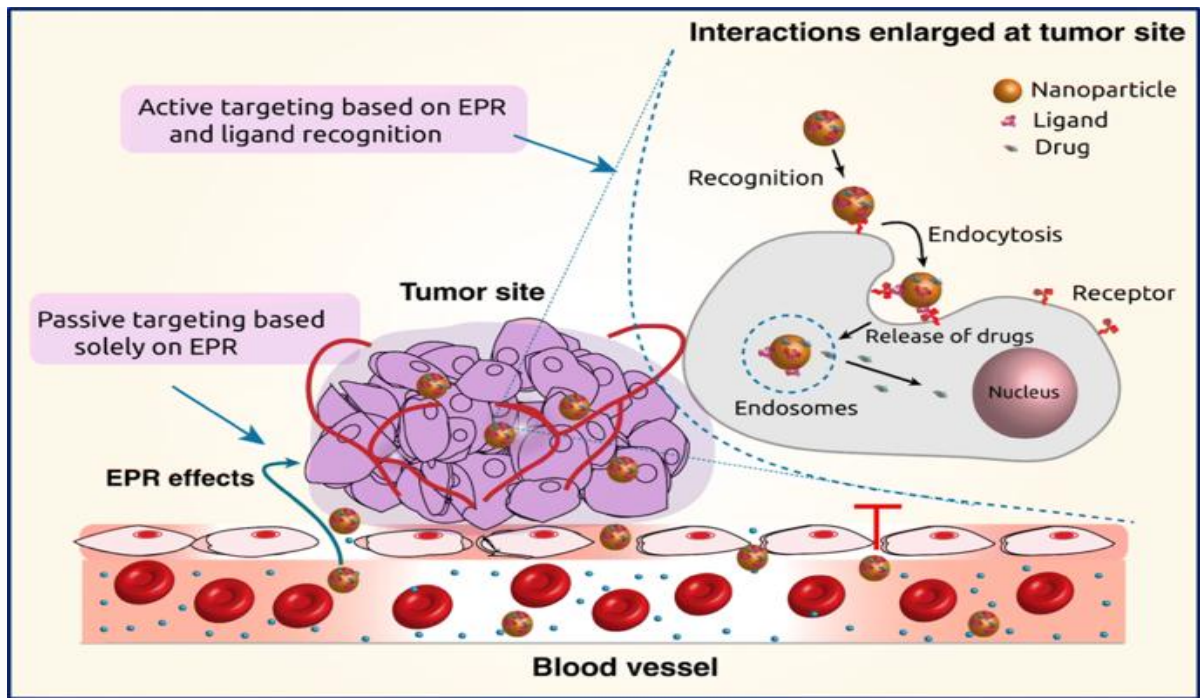
Fig. 1.

Graphical illustration of passive and active drug targeting strategies. In passive targeting, the nanocarriers pass through the leaky walls and accumulate at the tumor site by the enhanced permeability and retention (EPR) effect. Active targeting can be achieved using specific ligands that bind to the receptors on the tumor cells.

retention and facilitated uptake by the targeted cells (Fig. 2).[10] Chemical affinity for active targeting is based on different specific molecular interactions such as receptor–ligand-based interactions, charge-based interactions and facilitated motif-based interactions with substrate molecules.[11,12]

2.2) Active targeting
Active targeting, also known as the ligand-mediated targeted approach, involves affinity based recognition,
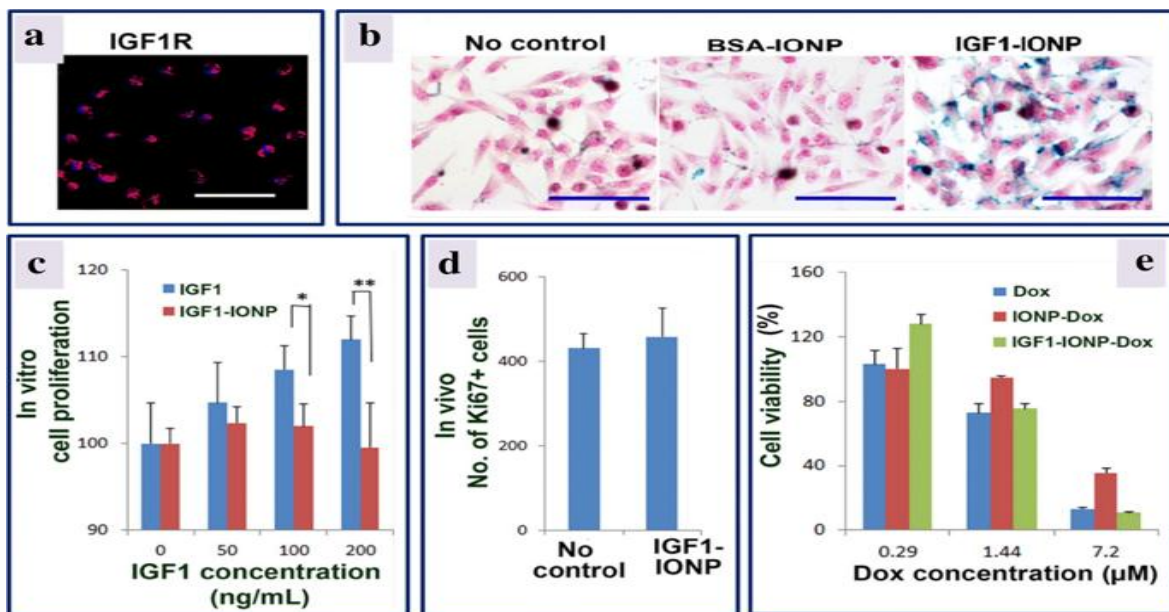

Fig. 2.

In vitro and in vivo effects of IGF1-IONPs (insulin-like growth factor 1-iron oxide nanoparticles) and IGF1-IONPs-doxorubicin on cell proliferation and viability. a The effect of IGF1R in MIAPaCa-2 cells was assessed by immunofluorescence labeling employing an anti-IGF1R antibody (shown in red color). b Prussian

blue staining of cells incubated for 4 h with different treatments at 20 μg/mL of iron equivalent dose. The cells are also counterstained with nuclear fast red. c The in vitro influence of IGF1 and IGF1-IONPs on cell proliferation. The % of viable cells after 96 h incubation with IGF1 or IGF1-IONPs, and for 4 h at equivalent IGF1 concentrations was estimated by cell proliferation assay, wherein *P < 0.05; **P < 0.001. d The in vivo effect on tumor cell proliferation of IGF1-IONPs in human pancreatic PDX-tumor xenografts. By using immunofluorescence labeling of an anti-Ki67 antibody, the Ki67-positive cells in tumor sections after two tail vein injections of 20 mg/kg iron dose of IGF1-IONPs are measured. e In vitro cytotoxicity of unconjugated and conjugated doxorubicin in MIA PaCa-2 cells. The scale bars are 100 μm.

3. Nanomaterials for Cancer Therapy

One of the main usage fields of optical nanoparticles is to allow better cancer detection. To start with, classical methods that are used in diagnosis have limitations. Classified methods such as X-rays, tomography or mammography require using mutagenic agents on cells that cause cancer, too. Sadoqi et al.[13] nanotechnology can be used for more efficient drug delivery system to tumors. Another of the significant missions of passive Nanoparticles used for anticancer drug delivery can be made from a variety of materials, including polymers, dendrimers, liposomes, viruses, carbon nanotubes, and metals such as iron oxide and gold.[14] So far, almost all the nanoparticle delivery systems which have been approved by the FDA or are currently in clinic trials are based on polymers or liposomes.[15]

a) Carbon Nanotubes

Carbon nanotubes are a new form of carbon molecule. Wound in a hexagonal network of carbon atoms, these hollow cylinders can have diameters as small as 0.7 nm and reach several millimeters in length.[16] Each end can be opened or closed by a fullerene half-molecule.

These nanotubes can have a single layer (like a straw) or several layers (like a poster rolled in a tube) of coaxial cylinders of increasing diameters in a common axis.[17]

b) Quantum Dots

It represents a special form of spherical nanocrystals from 1 to 10 nm in diameter. They have been developed in the form of semiconductors, insulators, metals, magnetic materials or metallic oxides. Quantum dots are used to track DNA molecules in cells, efficient alternatives to conventional lighting sources, biosensors used to detect agents of biological warfare.

c) Liposomes

Liposomes can be classified as unilamellar or multilamellar (MLV, 100 nm – 20 μm). Unilamellar liposomes are further divided into two categories: small size [small unilamellar vesicles (SUV), 25–100 nm] or large size [large unilamellar vesicles (LUV), 100–1000 nm]. SUV and LUV are both composed of a single lipid bilayer and a large aqueous core, and thus are suitable for loading hydrophilic drugs, while multilamellar liposomes (MLV) are composed of several lipid bilayers (up to 14 layers) and a limited aqueous space, thus being suitable for loading hydrophobic drugs.[18,19]

d) Dendrimers

Dendrimers are well defined, regularly branched macromolecules.[20] They are generally synthesized from either synthetic or natural elements such as amino acids, sugars, and nucleotides. These nanoparticles can be easily modified and conjugated to therapeutics. Alternatively, dendrimers can be loaded with drugs using the cavities in their cores through hydrophobic interactions, hydrogen bonds, or chemical linkages. The preclinical development of dendrimers has been focused largely on forming dendrimer-drug conjugates.

e) Polymeric micelles

Polymeric micelles range in size from 10–100 nm, each type having a narrow size distribution. This narrow size range is the most important property of polymeric micelles, ensuring high stability, sterility and long term circulation in the bloodstream. Polymeric micelles comprise of two structures: an inner core and an outer shell. The hydrophilic shell of the copolymer consists of hydrophilic non-biodegradable polymers (such as poly (ethylene oxide) (PEO), poly(*N*-isopropylacrylamide) (PNIPA), poly(alkylacrylic acid), and poly(ethylene glycol) (PEG)) and sustains stability in the aqueous medium enabling interactions with plasmatic proteins and cell membranes. The hydrophobic core of the micelles encapsulates various non-polar drugs (such as paclitaxel, doxorubicin, tamoxifen, camptothecin, porphyrins, *etc*.) and provides their controlled release.[21]

f) Nanoparticle Albumin-bound (nab) Technology

The nanoparticle albumin-bound (nab) platform utilizes albumin as a therapeutic carrier for the delivery of hydrophobic chemotherapeutics. Albumin is a natural carrier of hydrophobic molecules through reversible noncovalent binding.[22] In addition, albumin can bind to the glycoprotein (gp60) receptor and mediate the transcytosis of albumin-bound molecules.[23]

g) Solid lipid nanoparticles (SLNs)

SLNs which are in the size range of 10–1000 nm, are attracting major attention as a novel colloidal drug carrier with the potential to overcome limitations in drug delivery including poor drug loading capacity, size problems, unstable properties, uncontrolled drug release associated with polymeric nanoparticles, dendrimers and liposomes. SLNs offer unique properties such as small size, large surface area, high drug loading and entrapment efficiency, low toxicity, excellent physical stability, controlled drug release, protection of drugs from degradation, and avoidance of the use of organic solvents.

h) Nanowires

A nanometer-scale wire is made of metal atoms, silicon, or other materials that conduct electricity. Nanowires are built atom by atom on a solid surface. A nanowire is a very small wire that is composed of either metals or semiconductors. It is also known as a nanorod or quantum wire since the dimensions of the nanowire are in the order of a nanometer (10^{-9} meters). The nanowires have the potential to be used as components to create electrical circuits.

i)   Nanocrystals

Nanocrystals are grown from inorganic materials, including metals and semiconductors. Some researchers have made nanocrystals of silver, gold, platinum, palladium, ruthenium, rhodium, and iridium. Nanocrystals are approximately 10 nanometers in diameter.

j) Quantum Dots

A quantum dot is a semiconductor nanocrystal that is about 1 to 6 nanometers in diameter. It has a spherical or cubic-like shape consisting of thousands of atoms, A quantum dot ismade of cadmium selenide (CdSe), cadmium sulphide (CdS), or cadmium telluride (CdTe) and then coated with a polymer. The coating is used to prevent these toxic chemicals from leaking. The CdS is used for UV-blue, the CdSe for the bulk of the visible spectrum, and the CdTe for the far red and near infrared. The particle's size determines the exact color of a given quantum dot.

i)   Quantum Dots and Cancer

quantum dot nanoparticles in living animals to simultaneously target and image cancerous tumors. The quantum dots were first coated with a protective shell covering. Then special antibodies were attached to the surface of the quantum dots. After the quantum dots were injected into the body, they were guided to the prostate tumor of the living mice. Using a mercury lamp, the scientists were able to see the surface of the tumor illuminated by the accumulation of quantum dots on the cell. The scientists believe the ability to both target and image cells in vivo (in the body) represents a significant step in the quest to eventually use nanotechnology to target, image, and treat cancer, cardiovascular plaques, and neurodegenerative disease in humans.

k) Nanoshells

Nanoshells are a new type of nanoparticle composed of a substance such as a silica core that is coated with an ultrathin metallic such as a gold layer. Nanoshells are about 1/20th the size of a red blood cell and are about the size of a virus or about 100 nanometers wide. They are ball-shaped and consist of a core of nonconducting glass that is covered by a metallic shell, typically either gold or silver. Nanoshells are currently being investigated as a treatment for cancer similar to chemotherapy but without the toxic side effects. These nanoshells can be injected safely into the body as demonstrated in animal tests.

Once in the body, the nanoshells are illuminated with a laser beam that gives off intense heat that destroys the tumor cells. In preliminary testing, one research medical team is using nanoshells combined with lasers to kill oral cancer cells. Oral cancer is a cancerous tissue growth located in the mouth.

l) Metallic nanoparticles

Metallic nanoparticles are emerging as good delivery carrier for drug and **biosensor**. Although nanoparticles of various metals have been made yet silver and gold nanoparticles are of prime importance for biomedical use.

4. CONCLUSION

Nanotechnology provides opportunities to improve materials, medical devices and help to develop new technologies where existing and more conventional technologies may be reaching their limits. The applications of nanotechnology in drug delivery will be a potential priority research area for the pharmaceutical and biotechnology industries in the future due to its unique potential to overcome the limitations and drawbacks of conventional drugs. It may be possible to develop new strategies providing target-specific drug therapy through newly developed drug delivery systems in cancer treatment. It has made a great impact on selective recognizing of the cancerous cells, targeted drug delivery, and overcoming limitations of the conventional chemotherapies. As understanding of the importance of the nanotechnology, condition of life will be greater. Thus, nanotechnology has to be improved for the next generation.

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