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AN OVERVIEW OF THE PRESENT STATUS OF NANO TECHNOLOGY IN CANCER THERAPY

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ABSTRACT

Cancer is a highly complex disease to understand because it entails multiple cellular physiological systems such as cell signaling and apoptosis. Thus, the most common cancer treatments are limited to chemotherapy, radiation, and surgery. Recent developments in nanotechnology offer researchers opportunities to significantly transform cancer therapeutics. The nanotechnology is a multidisciplinary field, which recently has emerged as one of the most promising field in cancer treatment and is definitely a medical boon for diagnosis, treatment and prevention of cancer disease. Nanotechnology is the study and use of structures between 1 nm and 100 nm in size, which have properties of self-assembly, stability, specificity, drug encapsulation and biocompatibility as a result of their material composition. Clinical investigations suggest that therapeutic nanoparticles can enhance efficacy and reduced side effects compared with conventional cancer therapeutic drugs. The use of nanoparticles exhibits unique pharmacokinetics, high surface-to-volume ratios, may be constructed from a wide range of materials used to encapsulate/solubilize therapeutic agents for drug delivery or to provide unique optical, magnetic, and electrical properties for imaging and remote actuation. Nanomedicine application areas include drug delivery, therapy, diagnostic, imaging and antimicrobial techniques. This article aims at giving an overview of the present status of nanotechnology in cancer therapy.

KEY WORDS

Nanotechnology, Cancer Therapy, Drug Delivery, Therapy, Diagnostic and Imaging.

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INTRODUCTION¹⁻⁶

Cancer is a complex disease occurring as a result of a progressive accumulation of genetic and epigenetic changes that enable escape from normal cellular and environmental control. Other terms used are malignant tumors and neoplasm. One defining feature of cancer is the rapid creation of abnormal

cells which grow beyond their usual boundaries, and which can invade adjoining parts of the body and spreads to other organs, a process referred to as metastasis. Metastases are the major cause of death from cancer.

From a total of 58 million deaths worldwide in 2005, cancer accounts for 7.6 million (or 13%) of all deaths. More than 70% of all cancer deaths in 2005 occurred in low and middle-income countries. Deaths from cancer in the world are projected to continue rising, with an estimated 9 million people dying from cancer in 2015 and 11.4 million dying in 2030. The most frequent cancer types worldwide are (a) among men: lung, stomach, liver, colorectal, oesophagus and prostate; and (b) among women: breast, lung stomach, colorectal and cervical.

Conventional therapy

The conventional treatment options of cancer are surgery, radiation therapy and chemo therapy. However, all these methods have their own limitations (in surgery one loses the organ and the cancer may appear again, in radiation therapy even the healthy cells get burnt, cancerous cells burning is not uniform and the burnt part may become dead and non-functional, in chemotherapy treatment is harmful to healthy cells, approach is gross and rarely successful if the cancer is in advanced stage).

Conventional detection of the cancer is done by observing the physical growth/changes in the organ by X-rays and/or CT Scans and is confirmed by biopsy through cell culture. However, the limitation of these methods is that these are not very sensitive and the detection is possible only after substantial growth of the cancerous cells.

Conventional chemotherapeutic drugs are distributed nonspecifically in the body where they affect both cancerous and healthy cells, resulting in dose-related side effects and inadequate drug concentrations reaching the tumor. Non-specific drug delivery leads to significant complications that represent a serious obstacle to effective anticancer therapy. In addition, the occurrence of resistance phenomena reduces the efficacy of cancer treatment. Thus, the most common

cancer treatments are limited to chemotherapy, radiation, and surgery.

Recent developments in nanotechnology offer researchers opportunities to significantly transform cancer therapeutics.

Nanotechnology

One nanometer (nm) is one billionth, or 10^{-9} of a meter. For comparison, typical carbon-carbon bond lengths, or the spacing between these atoms in a molecule, are in the range 0.12 - 0.15 nm, and a DNA double helix has a diameter around 2 nm.

On the other hand, the smallest cellular life forms, the bacteria of the genus *Mycoplasma*, are around 200 nm in length. Many of the cells are of the dimensions of micro meter. These provide the possibility of nanoparticles entering the cells and detect/treat the molecular changes that occur due to cancerous causes, in small percentage of cells. Therefore, the necessary tools must be extremely sensitive.

Scientists and researchers hope that nanotechnology can be used to create therapeutic agents that target specific cells and deliver the toxin in a controlled, time-release manner. The basic aim is to create single agents that are able to both detect cancer and deliver treatment. The nanoparticles will circulate through the body, detect cancer-associated molecular changes, assist with imaging release a therapeutic agent and then monitor the effectiveness of the intervention.

The use of nanoparticles in cancer therapy is attractive for several reasons: they exhibit unique pharmacokinetics, including minimal renal filtration; they have high surface-to-volume ratios enabling modification with various surface functional groups that home, internalize, or stabilize; and they may be constructed from a wide range of materials used to encapsulate or solubilize therapeutic agents for drug delivery or to provide unique optical, magnetic, and electrical properties for imaging and remote actuation. The topology of a nanoparticle-core, coating, and surface functional groups-makes it particularly amenable to modular design, where by

features and functional moieties may be interchanged or combined.

Imaging and detection

Super paramagnetic nanoparticles are used for magnetic resonance imaging (MRI). They consist of an inorganic core of iron oxide coated or not with polymers like dextran. There are two main groups of nanoparticles:

1. Super paramagnetic iron oxides whose diameter size is greater than 50nm,
2. Ultra small super paramagnetic iron oxides whose nanoparticles are smaller than 50nm.

e.g. Dextran coated iron-oxide nanoparticles administered intravenously get phagocytosed by normal macrophages of the liver and lymph and the failure of these tissues to darken after iron oxide administration identifies invading cancer cells.

Gold nanoshells offer a promising alternative to MRI probes by providing contrast for optical imaging. These nanoparticles are constructed from a dielectric core (silicon) and a metallic conducting shell (gold). By varying the dimension of the core and shell, the plasmon resonance of these particles can be engineered to either absorb or scatter wavelengths of light, from UV to infrared. Particles that are tailored to scatter light in the near-infrared, where tissues have minimal absorbance, have been used to enhance imaging modalities such as reflectance confocal microscopy and optical coherence tomography (OCT).

Quantum dots, nanoscale crystals of a semiconductor material such as cadmium selenide, whose color properties depend on particle size. Quantum dots can be linked to antibodies and combined to create assays that are capable of detecting multiple substances simultaneously. They can be used to measure levels of cancer markers such as breast cancer marker Her-2, action, microfibril proteins and nuclear antigens. Quantum dots are robust and very stable light emitters. The photochemical stability and the ability to tune broad wavelengths make quantum dots extremely useful for biolabelling.

1. The core consists of the semiconductor material that emits lights.
2. The shell consists of an insulator material that protects the light emitting properties of the QD in the upcoming functionalization.
3. The shell is functionalized with a biocompatible material such as PEG or a lipid layer.
4. Additional functionalization can be done with several purposes (e.g. embed a drug for drug delivery, or assemble an antibody to become the QD target-specific).

Cancer Therapy

Currently, cancer fight drugs are toxic to both tumor and normal cells, thus the efficacy of chemotherapy is often limited by the side-effects of the drug. Some nanoscale delivery devices, such as dendrimers (spherical, branched polymers), silica-coated micelles, ceramic nanoparticles, and cross-linked liposomes can be targeted to cancer cells. This increase selectivity of drugs towards cancer cells and will reduce the toxicity to normal tissue⁴. This is done by attaching monoclonal antibodies or cell-surface receptor ligands that bind specifically to the cancer cells.

Nanoshells

Destruction of solid tumors using high heat has been in investigation for some time. Some thermal therapies include the use of laser light, focused ultrasound and microwaves. The benefits of using thermal therapeutics are that most procedures are non-invasive, relatively simple and have the potential to treat tumors where surgery is not possible. However, to reach underlying tumors, the energy sources have to penetrate healthy tissues, often destroying healthy tissue.

e.g. Nanoshell-assisted photo-thermal therapy (NAPT).

Nanoparticles and nanospheres⁵

Nanoparticles can be in the form of nanospheres (matrix systems in which drugs are dispersed throughout the particle) and nanocapsules (drug is confined in an aqueous or oily cavity surrounded by a single polymeric membrane).

Nanoparticles have the potential to overcome biological, biophysical and biomedical barriers currently faced by conventional administration of cancer drugs. If designed appropriately, nanoparticles may selectively target tumors, while protecting the drug from inactivation during transport.

Nanospheres loaded with anticancer drugs successfully increase drug concentration in cancer tissues.

Dendrimers

Dendrimers, 1 to 10 nanometer spherical polymers of uniform molecular weight made from branched monomers have been proven to provide a multifunctional cancer agent.

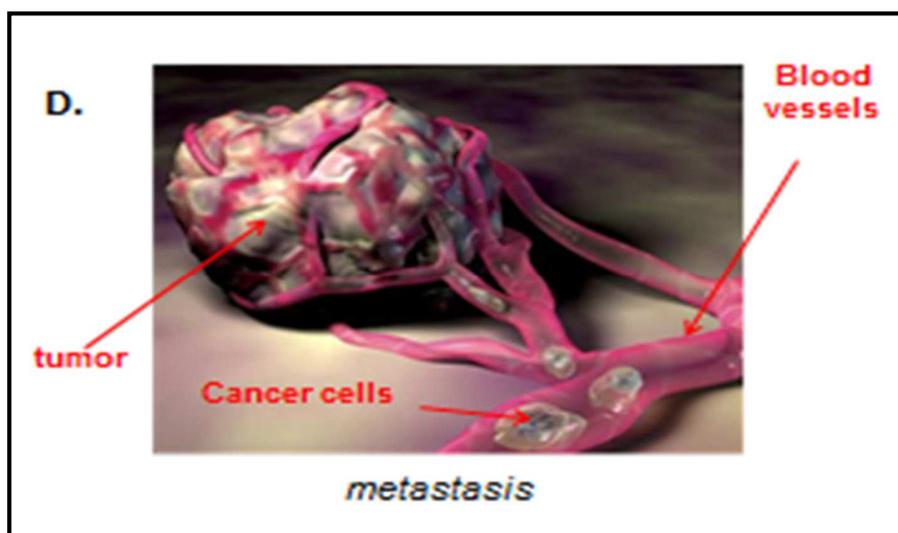


Figure No.1: Metastasis

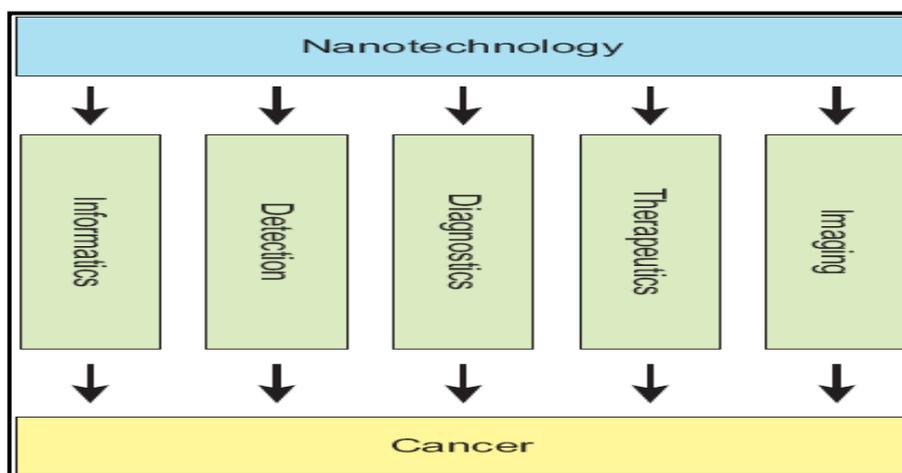


Figure No.2: Schematic diagram showing nanotechnology applications in cancer through molecular tumor imaging, early detection, molecular diagnosis, targeted therapy, and cancer bioinformatics

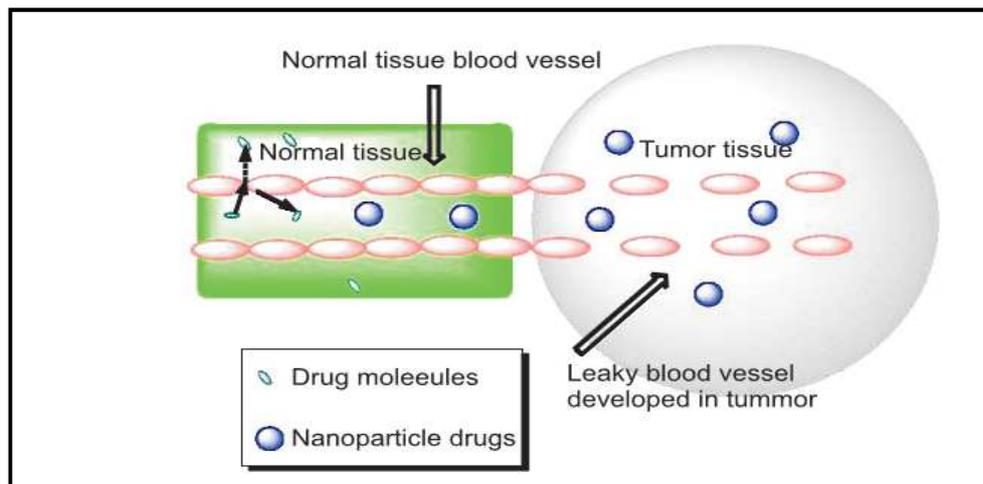


Figure No.3: Schematic diagram of nanoparticle accumulation in tumor tissue through EPR effect. Normal tissue vasculatures are lined by tight endothelial cells, thereby preventing nanoparticle drugs from escaping, whereas tumor tissue vasculatures are leaky and hyper permeable allowing preferential accumulation of nanoparticles in the tumor interstitial space (passive targeting)

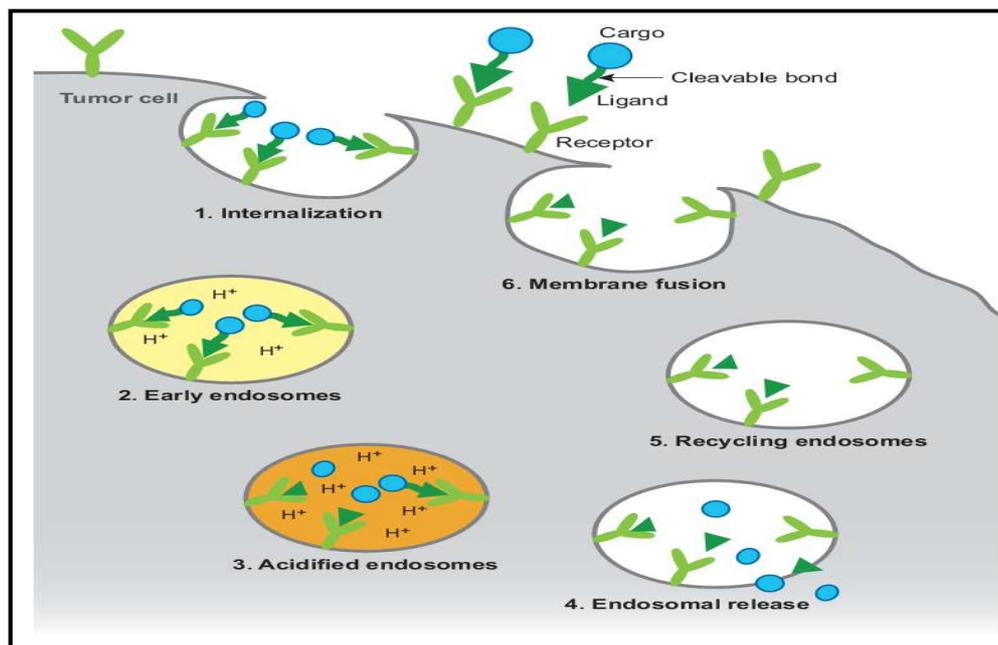


Figure No.4: Nanoparticle drug delivery and targeting using receptor-mediated endocytosis. The nanoparticle drug is internalized by tumor cells through ligand-receptor interaction. Depending on the design of the cleavable bond, the drug will be released intracellularly on exposure to lysosomal enzymes or lower pH

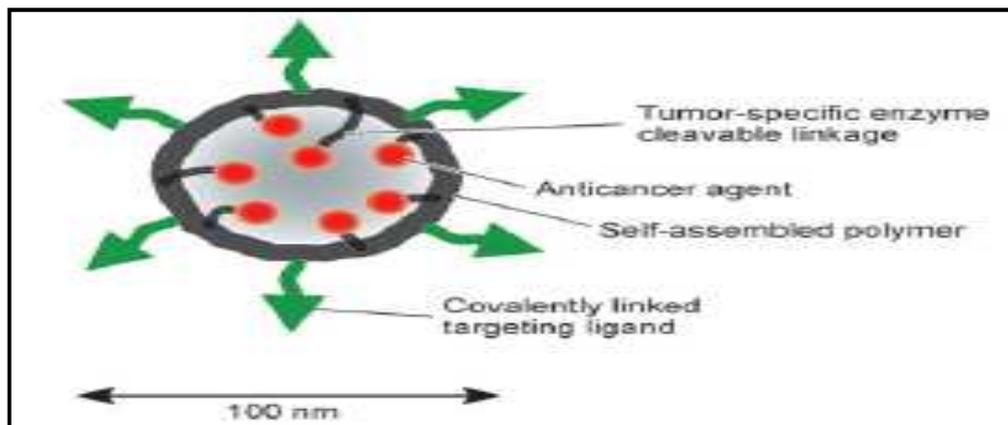


Figure No.5: A Targeted Polymer Nanoparticle (a)

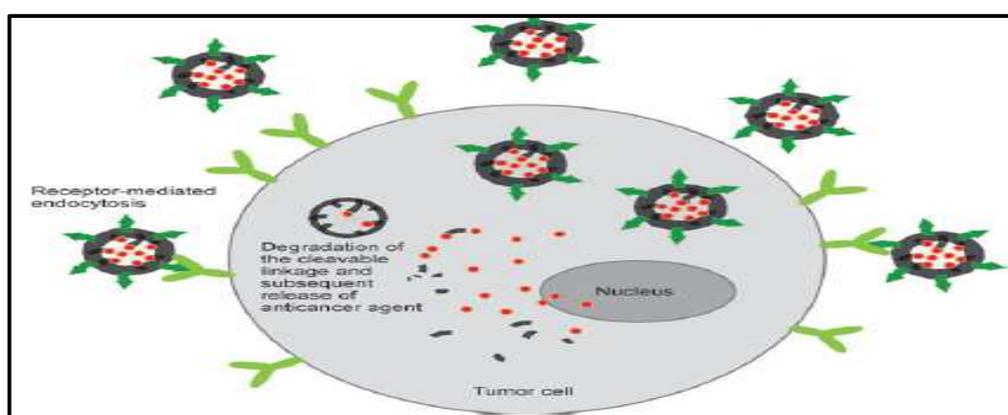


Figure No.6: A Targeted Polymer Nanoparticle (b)

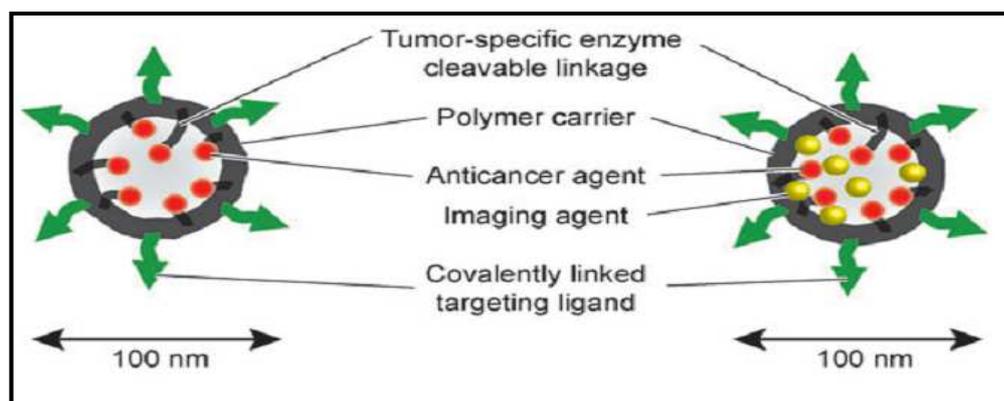


Figure No.7: A Targeted Polymer Nanoparticle (c)

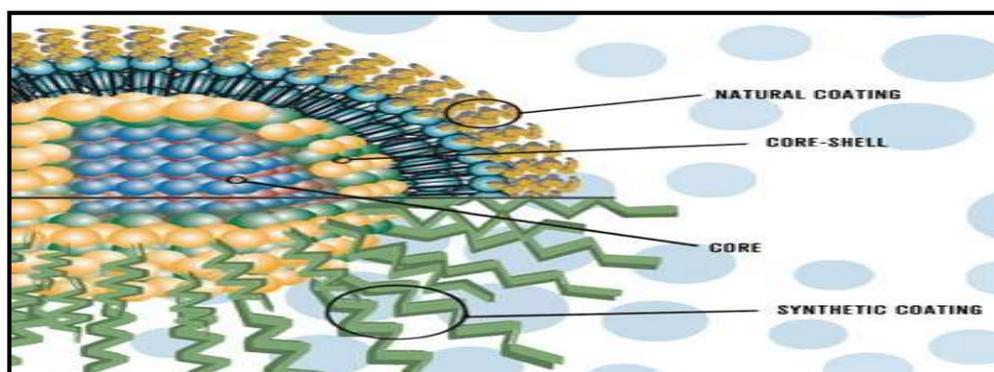


Figure No.8: Multifunctional Quantum dots

CONCLUSION

Nanotechnology is definitely a medical boon for diagnosis, treatment and prevention of cancer disease. The integration of nanotechnology into cancer diagnostics and therapeutics is a rapidly advancing field, and there is a need for wide understanding of these emerging concepts. The development of new nanoscale platforms offers great potential for improvements in the care of cancer patients in the near future.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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