AMERICAN JOURNAL OF PHARMTECH RESEARCH

Journal home page: http://www.ajptr.com/

Approaches of Nanomedicine in Cancer Therapy

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ABSTRACT

Cancer is the leading cause of mortality worldwide. Treating the cancer is one of the major challenges in modern science as the drug delivery to solid tumors is a seminal challenge to develop more effective cancer therapies. A well-designed drug delivery system can potentially enhance the efficacy of a treatment by improving drug accumulation in the tumor. Application of nanotechnology to prevent and treat the cancer disease is known as nanomedicine. Cancer diagnosis and treatment can be achieved to a greater extent by the application of nanotechnology principles to biomedicine. Over these years targeted treatment for cancer has been greatly improved by the approaches based on nanotechnology. Nanoparticles have the potential to increase the specificity in treating cancer cells while leaving the healthy cells. The goal of this review is to discuss the current state of nanomedicine in the field of cancer detection and the subsequent application of nanotechnology to treat cancer by using nanoparticles such as dendrimers, quantum dots, nanocells, nanocrystals, and nanoshells for the detection and treatment of cancer.

Keywords: Cancer, Drug delivery, Quantum dots, Nanomedicine, Nanotechnology, Drug Therapy.

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Received 18 July 2016, Accepted 30 July 2016

Please cite this article as: Yadav KP *et al*., Approaches of Nanomedicine in Cancer Therapy. American Journal of PharmTech Research 2016.

INTRODUCTION

Now a day, cancer plays a major role in mortality. Scientist have done great research to know the causes of cancer, and for the diagnosis and the treatment, great progress has been made for the treatment of cancer, but still mortality rate is high because exact cure was not found. In 1600 BC cancer was found in Egyptian papyrus and it is an incurable disease in 19th century. Improved techniques and histological control has been made for the surgical removal of tumors by giving anesthesia. In 1940s nitrogen mustards are considered as a starting point of antineoplastic chemotherapy targeting all tumor cells [1]. Before 1950, tumors were removed by surgery. After 1960, radiation therapy is used to control local disease. Cancer remains one of the most life-threatening diseases. To fight against the cancer US government passed the National Cancer Act in 1971 and President Nixon declared a "war on cancer" [2].

The recent treatment of cancer reveals that drugs shows limited action on tumor cells when they are given in chronic stage of cancer, in this treatment drugs target mainly tumor cells but not on cancer stem cells [3, 4]. Indeed, conventional cancer therapies target neoplastic cells that are largely fast-growing, suggesting that cancer stem cells may survive due to their high resistance to drugs and slower proliferation rate [5].

Nanotechnology has dimensions of 1 to 100 nanometers but as per scientific community they can be up to 1000nm. The physical and chemical properties of the nano sized particles enable them as drug delivery carriers and as diagnosis probes. Surface functionalization and incorporation of a therapeutics load can be achieved as the size range of nanoparticles have maximum surface to volume ratio. When compared to conventional drug delivery carriers these particles have better access to tumor sites. Due to this unique technique the hope of treating diseases like cancer this is second leading disorder. This accounts for 12.5% of deaths [7].

Two key objectives for effective cancer treatment are:

a) Its early detection; and

b) Treating cancer cells without effecting normal functioning cells.

Quantum dots, Nano shells, Nano crystals, Nano cells and dendrimes are nanoparticles which play a prominent role in cancer detection.

Nano medicine has increased activity in both patent and publications [9, 10]. This has also raise in research encompassing many facets of medicine including biomaterials, active implants, in vivo imaging, in vitro diagnostics, therapeutic materials, and gene and drug delivery. The progress of nanotechnology worldwide is expected to exceed $1 trillion by 2015 and market revenues are close

to $3 trillion worldwide [11, 12]. Nano medicine also have growing amount of $1 billion in the United States, $600 million in Japan, and $400 million in Germany.

Nobel Prize winner Richard Feynman invented robots and introduced another series of robots at a smaller scale until near atomic scale is reached [13, 14]. This concept was later seized due to submarine-like Nano machines as they independently protect and prolong life by rebuilding damaged tissues, repairing virus-damaged cells, supporting or reconstructing damaged limbs and organs, and even reversing aging [15].

Nano medicine has better outcomes in the following conditions to:

- Diabetes research for glucose sensors and Nano-pancreases [16];
- Tuberculosis and other respiratory diseases [17, 18];
- Neurological diseases such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis [19];
- Hemophilia [20];
- Bone healing and osteoporosis [21];
- Hair growth [22].

Nano medicine has greater importance in cancer therapy compared to normal chemotherapeutic treatments, as they have improved activity in tumor specificity, fewer side effects, improved efficacy and treat various cancer types [23– 26]. These Nano medicines are designed in such a way that the drug must be delivered to solid tumors in such a way that initial blood contact until drug action within the tumors. The drug must address the drug delivery so that only sufficient drug reaches the tumor so that toxicity is reduced in the patient.

Doxil ® and Abraxane ® are the successful drug carriers in the field of cancer therapy. These both exhibited simple in concept in design but they didn't show any improved efficacy compared to traditional chemotherapy [27, 28]. In the US, the cancer patients might increase four times as fast as population growth through 2030 [29]. Because of this growing up of population the cancer researches the burden of drug therapy and new improved methods of testing these solutions must be developed.

OBSTACLES IN CANCER DIAGNOSIS AND TREATMENT

Late stage diagnosis

Mortality is usually increased due to this late detection [30, 31]. To prevent this mortality the test to identify the symptoms is an important goal [30]. Diagnosing cancer through the biomedical imaging tools like magnetic resonance imaging, ultrasound and positron emission tomography have several

limitations that they can't detect the tumor cells > 1 cm and also has the risk of renal toxicity [32]. Routinely used techniques for diagnosis of cancer are PET, CT and MRI, with the use of small molecule imaging agents like iodinated small molecules, 2-deoxy-2-(18F) fluoro-D-glucose FDG and chelated gadolinium. Poor stability, rapid clearance and low signal intensity the major limitations of these techniques which led the researchers to use nanoparticles. [33].

Challenges in Targeting, Transport and Treatment

Chemotherapys problem in treating, transport and delivery of drug has always been that a pharmacologically active concentration of drug at tumor cells is only achieved at the expense of the rest of the body [34]. The sub optional and intermittent dosing and use of chemotherapy altogether results in toxicity of the body which results in massive contamination [35]. Due to poor stability and solubility of traditional chemotherapeutics the activity was disregarded on at drug screening in the laboratory. When the drug is administered, the monocytes and reticulo endothelial system clear the drug so adequate amounts of drug is needed to travel in viable state to reach the targeted site [37].

Accurate delivery of drug is more difficult due to the unpredictable blood flow and often abnormal vasculature in tumors, particularly in necrotic and seminecrotic regions [38, 39]. Treating cancer with the use of Antibiotics, small interfering RNA and nucleic acids drugs such as aptamers, anti-sense DNA/RNA have shown great effect but they are imitated by serum nucleases, opsonization and clearance by Macrophages and renal system. Some of the stable nucleic-acid-lipid particle (SNALP) have used Nano carriers have effectively overcome these barriers [40].

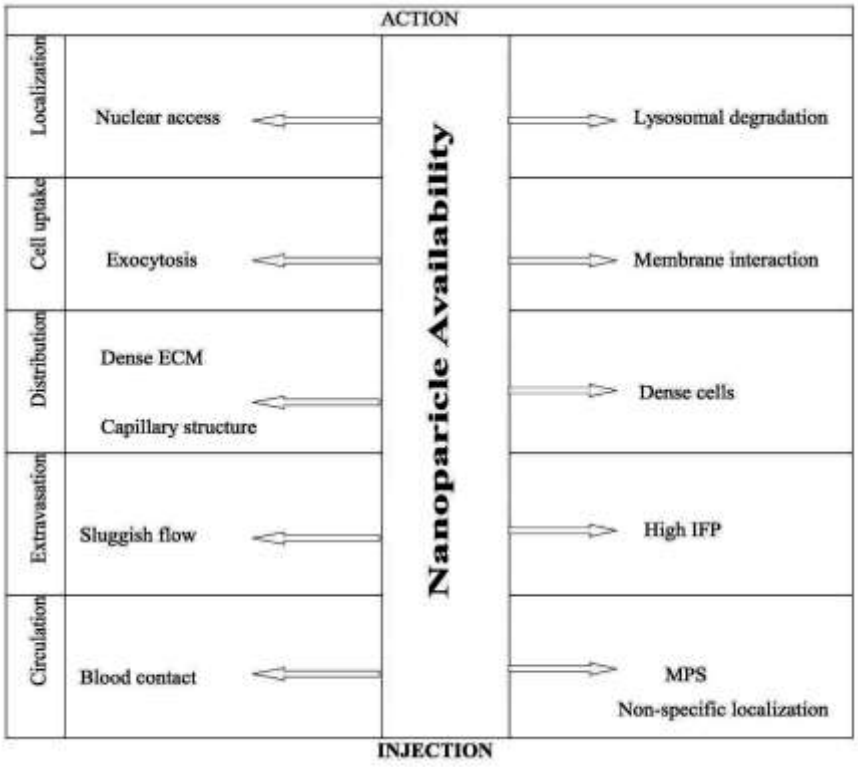

Figure 1: Barriers to drug Access.

Chemo resistance

Mesenchymal morphology increased DNA repair ability, overexpression of ant apoptotic proteins, drug efflux transporters, detoxifying enzymes and Quiescence, are the unique properties of Cancer stem cells (CSC). So chemoresistence is a major cause of failure in cancer therapy [41]. Because of these efficient properties they escape during current radio and chemotherapies. So these survive the chemotherapy and result in rise to metastasis and increase in malignancy and resistance.

Chemo resistance can be divided into two types: intrinsic and acquired. **Intrinsic chemo resistance** these withstand to chemotherapeutic agents due to their genetic and phenotypic characters**. Acquired chemo resistance** can occur after prolonged exposure to chemotherapeutic agents [42, 43]. Multidrug resistance may occur due to cross resistance to different structurally-related drugs by mutation and to other drugs they undergo multidrug transporters [42]. This results in reduced drug retention and the alteration in response of tumor [44].

Systemic Barriers

The purpose is to solubilize and protect the drug from clearance and degradation to target site. In nanoparticles they directly contact blood stream after administration these have high ratio of surface to bulk atoms which result in high surface energies and unusual behaviors [45]. The behaviors include aggregation which can impact the polydispersity and bio distribution of the

particles. Due to these high surface energies they bind to blood proteins [46]. These binding helps in signaling to **MPS** macrophages so it aids in engulfing the circulating nanoparticles to accumulate outside the tumor [45, 47]. MPS, also known as the reticular endothelial system (RES), the tissue embedded with macrophages that clear foreign substances. Due to both MPS activity and unique porous sinusoid structures in the liver it collect large quantities of nanoparticles which helps in filter and cleaning of blood [48]. Nanoparticles are generally large enough to avoid renal clearance [49]. Currently, **PEGYLATION** is process of applying poly ethylene glycol to surface of nanoparticles which helps in preventing the protein absorption and **MPS** uptake. This grafted polymer forms a brush-like barrier that slows rate of binding thus helps in increased circulation of nanoparticles. Usually long circulating drug carriers are expected to show more bio distribution and increased intratumoral accumulation to conventional treatments.

The **EPR** (enhanced permeability and retention) effect is said to be done when efficacy of treatment is increased. Both permeability and retention are related to physiological abnormalities resulting from rapid growth of the tumor and it modifies the local microenvironment. Rapid and uncontrolled growth is major hallmark of cancer [52]. This growth of cells within a confined space causes cells and stress arises resulting in crushing of blood and lymph vessels [53]. Due to this lack of intact the tumor performs simple diffusion process to deliver oxygen and nutrients and also to remove their wastes. When the tumor cell reaches one millimeter diameter the hypoxic conditions become dominant in the core causing hypoxic cells to release factors to promote angiogenesis [54]. Angiogenesis proceeds rapidly to supply the tumor resulting in tortuous, chaotic, and disorganized vasculature. These vessels are disorganized resulting in large gaps so large particles like proteins and nanoparticles diffuse [55-57]. Due to enhanced permeability of EPR these nanoparticles diffuse faster into tumor cell compared to normal tissues.

The diffused nanoparticles destroy lymph vessels due to solid compressive stress so without functioning lymph vessels the fluid flows out to periphery before it can be cleared [53]. Hydraulic pressure maintains rate of flow in tumor from tightly packed cells and dense collagen matrix. Due to this retention the tumor ability to clear drug carriers from the tissue is limited [58.] This is the advantage that EPR provides cancer Nano therapies over traditional chemotherapy. The EPR was discovered in the mid-1980s which has great attention to nanotechnology is a next major breakthrough in cancer treatment [59].EPR is said to be a form of micro environmental targeting, they attack the pathogenic tumor lymph and blood vessels to achieve tumor specificity [61].

Most tumors are only a few centimeters in diameter, a small fraction of the total size of the patient [62]. This micro environmental targeting is problematic to treat metastatic cancers because they are

too small and cannot be effected by Nano therapies so adjuvant therapy with chemotherapeutic drugs are used to prevent cancer spreading and relapse.

The EPR effect predicts that higher concentration must in tumor rather than surrounding tissues which improves efficacy of treatment. This effect is proven in preclinical studies in animal models but the clinical benefit has yet to be seen [63, 64]. The models are necessary for designing and testing drug carriers. Tumors models that are developed in mice are grown faster than normally occurring tumors which a condition which thins the rapid angiogenesis resulting in disorganized vasculature [65, 66].

The patient — Compliance and individuality

Tolerance to the discomfort and effects of chemotherapy differs within the individuals as the Drug pharmacokinetics and pharmacodynamics differ from individual to individuals. In case of pre-existing condition or illness these will affect the cancer treatment or may lead to refuse it and the morbid illness and elderly patients may end up with discontinuing chemotherapy. Genetic variation across individuals affects a drug's pharmacokinetics and pharmacodynamics [67, 35].

CURRENT NANOTHERAPEUTICS: OVERCOMING THE OBSTACLES

Polymeric nanoparticles, liposomes, dendrimers, Nano shells, carbon nanotubes, and super paramagnetic nanoparticles are some of Nano therapies. Due to their small size and various structural and physicochemical features these enter the tumor vasculature through enhanced permeability and retention effect (EPR). The use of cancer specific targeting residues (e.g. antibodies, ligands, and lectins) can also achieve tumor cell targeting.

Polymeric nanoparticles

Polymeric nanoparticles are prepared from natural or synthesized polymers. Biodegradable or unbiodegradable polymers can be used for the therapeutic effect. Due to controlled, sustained and targeted delivery the biodegradable polymeric nanoparticles are attracted greatly. The effect of indomethacin loaded Nano capsules on a xenograft glioma model in rats was observed by Bernardi [70]. Then significant reduction in tumor size and the animal survival was much higher compared in the drug loaded Nano capsule group than in the control (untreated) [70].

Polymeric nanoparticles can deliver not only small molecular weight drugs but also macromolecules such as genes and proteins. A system made up of poly (D, Llactidecoglycolide) nanoparticles, a potent protease inhibitor (cystatin) and cytokeratin specific monoclonal antibody, has been reported. It neutralizes the activity of excessive proteolysis which prevents metastatic and invasive potential of breast tumor cells [71]. To stabilize the surface of nanoparticles or achieve active targeting, conjugating, grafting and adsorbing hydrophilic polymers, such as polyethylene

glycol (PEG), are usually used. Copolymer pegylation and folate conjugation can improve the stability of self-assemblies in aqueous medium and the tumor site selectivity in vivo of ring opening metathesis polymerization based copolymers [72]. By covalent coupling of humanized monoclonal antibodies (antiHER2) to paclitaxel loaded poly (D, Lactic acid) nanoparticles, immune Nano particles were prepared to actively target tumor cells which over express HER2 receptors [73] .

Recently Patil [74] Produced PLAPEG ligand conjugate nanoparticles by a single step surface functionalizing technique, and found that simultaneous functionalization with biotin and folic acid induced great efficacy of paclitaxel loaded nanoparticles in a MCF7 tumor xenograft model by enhancing drug accumulation in tumors. Mitoxantrone loaded polybutyl cyanacrylate nanoparticles (DHADPBCANPs) have presented a good effect on orthotopically transplanted hepatocellular carcinoma (HCC) in nude mice. Therefore, the activity and toxicity of DHADPBCANPs in individuals with unresected HCC were evaluated in a phase II clinical trial [75]. The median survival was much longer in the DHADPBCANPs group than in the DHAD injection group (5.46 months vs. 3.23 months) [75].

Polymeric nanoparticles are currently the most widely investigated nanotechnology platform for cancer therapy, despite many challenging defects or drawbacks need to be resolved before clinical application. It is also considered as the most promising vehicle for site targeting anticancer drug delivery and disease diagnosis because of its good variability of chemical structures through chemical modification and the resulting flexibility of physicochemical characteristics enabling its diverse drug delivery applications.

Liposomes

These are generally spherical vesicles consists of a lipid bilayer which encloses an aqueous phase to store drug [76]. With the size (90150 nm) which is slightly bigger than the conventional definition (100 nm), liposomes do not constitute novel nanotechnology, but they are associated with nanotechnology research [77]. Liposomes are the excellent platforms for the delivery of hydrophobic and hydrophilic drugs as they form lipid bilayers through hydrophobic interaction. Liposomes have persistency in blood so they greatly target tissues. Chain lengths, head groups and melting temperatures differ within fatty acids consequently temperature or pH sensitive liposomes can be constructed by manipulating the formulation. In in vivo the effectiveness of 1methylxanthine (1MTX) as a radio sensitizer and temperature sensitive liposomal 1methylxanthine (tslMTX) which combined with regional hyperthermia and ionizing radiation were evaluated [78]. In the mouse xenograft tumor model the intraperitonial injection of the tslMTX has better inhibition of tumor

growth and when combination with regional hyperthermia and ionizing radiation obviously inhibited tumor growth [78].

Most recently pH sensitive immunoliposomes (ILs) with terminal alkylated including Nisopropylacrylamide (NIPAM) in the bilayer were coupled with the antiCD33 monoclonal antibody [81]. The pH sensitive immunoliposomes could be more effective in acute myeloid leukemia therapy as The pH sensitive ILsCD33 Immunoliposomes reported high cytotoxicity against HL60 cells. US Food and Drug Administration (FDA) approved commercial liposomes. Doxorubicin encapsulated liposomes (Doxil), has strong antitumor activity against a wide range of cancers which is said to be best example.

Dendrimers

These dendrimers are highly branched macromolecules which are 1 to 10 nm in size, monodisperse, three dimensional molecules with tree like structures. Different chemical structures and functional groups can be synthesized [82]. Due to their branches they can provide area for drugs and targeting molecules [77, 83]. The composition of core, interior branching and surface functionalities aid in reactivating the macromolecule [83]. Conjugated with biotin as the targeting moiety, the in vitro targeting ability of partially acetylated generation 5 polyamidoamine (PAMAM) dendrimer (AcG5) in HeLa cells was assessed [84]. The multifunctional conjugate AcG5biotinFITC (fluorescein isothiocyanate) showed much higher cellular uptake than the conjugate without biotin. Biotin polymer blocks the energy dependent uptake process exhibiting an expected dose response curve.

Nano shells

Nanoparticles usually present layer by layer in polymeric Nano shells (2060 nm) of diblock copolymers they self-assemble of oppositely charged polymers forming a core/shell structure [85]. Targeted delivery to docetaxel can be done with a biodegradable polymer core and mixed lipid monolayer shell; this is a system of folic acid that conjugated with nanoparticles [86]. Gold Nano shells (10 to 300 nm) consists of dielectric core with a thin gold shell is surrounded around it these are optically tunable [87]. Gold Nano shells are designed by adjusting core radius and shell thickness in order to achieve maximal penetration of light through the tissue over the near infrared [87]. Ectopic tumor model of prostate cancer is effectively treated by laser activated gold Nano shells [88].

Carbon Nanotubes

These are first discovered in the late 1980's they have distinct molecular form which bond with each other sp 2 bonds and present a hexagonal arrangement [89] . Carbon nanotubes are described as well ordered, hollow nanotubes formed when single or multiple graphene sheets are rolled into a

cylinder [90]. They are present in two forms such as single and multiwall carbon nanotubes. These are considered as novel tool for anticancer drug delivery in the family of nanotechnology platform [91]. Antibodies, DNA and drugs can be immobilized by carbon nanotubes in order to penetrate cell membranes [92-94]. Heister performed a work where the anticancer drug doxorubicin delivered directly to noncompeting binding sites by using an oxidized single walled carbon nanotubes, consisting of a fluorescent marker. Because of the needlelike fiber shape, the safety of carbon nanotubes is concerned. The augmentation of cancer risk and severe biological effects are seen recently when long and thick multiwall carbon nanotubes are used [95].

Super paramagnetic nanoparticles

Super paramagnetic nanoparticles, iron oxide magnetic nanoparticles with particle sizes of about 20 nm, are composed of Fe2 O 3 or Fe3 O 4 and when removal of magnetic field they do not keep any magnetism hence, may be used in vivo [96]. Super paramagnetic nanoparticles can be used as contrast agents for magnetic resonance imaging (MRI), cancer thermal therapy, and can concentrate in target sites through an external magnetic field. Cancer cells can be imaged when F recombinant single chain Fv antibody fragments (scFv); super paramagnetic iron oxide nanoparticles (SPIONs) are used [97]. Conjugated to luteinizing hormone releasing hormone (LHRH), SPIONs along with breast cancer cell targeting but also act as contrast agents in the MRI of breast cancer xenografts [98]. The studies are performed in the postmortem neuropathologic studies of glioblastoma multiforme (GBM) patients they are treated with thermotherapy using magnetic nanoparticles [33]. In this Magnetic nanoparticles were injected into the tumor and then heated in an alternating magnetic field. This resulted in uptake of nanoparticles in macrophages to a major extent, and the uptake was further promoted by magnetic fluid hyperthermia (MFH) therapy [99].

Iron Oxide Nano crystals

Diagnosing and monitoring of various diseases including cancer can be done using Magnetic resonance imaging (MRI).the major problem associated with MRI is that its low insensitivity. Sensitivity and efficacy of MRI for detection and imaging cancer can be improved by Nanotechnology [100-102]. An Inorganic nanoparticles cores is coated by a suitable coating material and are used as magnetic nanoparticles in biomedical applications [103-105]. The stability and solubility of the Nano formulation can be increased by these suitable coatings. They also target the moiety to increase the imaging sensitivity and to do real-time monitoring. Enhanced proton relaxation is one of the most added-value properties that make magnetic nanoparticles one of the best contrast agents for biomedical applications of MRI [106].

Among nanoparticles Super-magnetic iron oxide is most widely used. As a bowel contrast agent SPION (Lumerin, Gastromark) and (Endorem, Feridex) for spleen/liver imaging has been used [101, 107]. One of the major successfully in this class of nanoparticles is Combidex®, an ultra-small super-magnetic iron oxide (USPIO). It is used for identifying the late-stage clinical trials for the detection of lymph node metastases [108]. SPIO nanoparticles are used for Imaging of liver tumors [109]. Ferumoxides are the first SPIO nanoparticles that were used for the detection of focal lesions in liver. Size range of 120-180 nm nanoparticles consisting of SPIO were incorporated into T10-dextran. Since then, varieties of iron oxide-based nanoparticles of different sizes and different coatings have been applied and are available in the market [110]. Preliminary toxicity studies of these magnetic nanoparticles have reported that these are relatively safe for clinical use [111-113].

Quantum dots

Properties of quantum dots like Photo stability, fluorescence intensity, small size (2-10 nm) and tunable surfaces make them very ideal for optical imaging and helps in detecting hundreds of cancer biomarkers in blood assays or tissue biopsies at pg/mL concentrations [114]. most commonly used as quantum dots are Selenides or sulfides of cadmium and zinc. Based upon their size the wavelength of light is emitted by the quantum, The light emitted is much more intense and stable than their other fluorescent counterparts and hence very useful in optical imaging [115]. the most common quantum dot formulations used in biological applications are Cadmium selenide (CdSe), cadmium telluride (CdTe), indium phosphide (InP), and indium arsenide (InAs) [114]. As the inorganic core is covered by an inorganic shell, Photo stability and fluorescence properties of the core are increased. Solubility and stability of quantum dots in the blood are enhanced by coating the surface of the shell with another layer. Blinking is the major limitation of quantum dots in imaging. This is caused due to fluctuation of the quantum dots between the light emitting and non-emitting states. This limits the amount of signal obtained at a specific time [116].

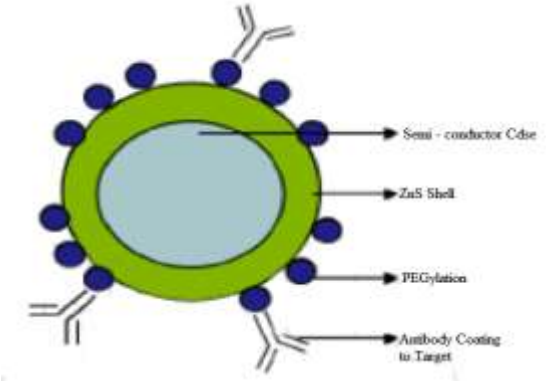

Figure 2: Quantum Dots.

NANOPARTICLES AS THERAPEUTIC AGENTS

Nanoparticles can also be used as therapeutic agents and help to treat cancer cells in the photodynamic therapy. Upon excitation by light they have the ability to alter the substrate molecule by intercrossing. The property of small inorganic molecules to generate heat upon excitation in the photo thermal therapy is taken advantage of inducing apoptosis or necrosis of cells.

Photo thermal therapy

Inorganic molecules such as gold or carbon nanoparticles are used as sensitizers. These sensitizers absorb light in the near-infrared region and convert it to thermal energy, causing heat in the vicinity. Treatment of cancer though the Thermal ablation therapy has been used for many decades, but the damage to nearby tissues has limited the use of this technique [117]. However, targeted destruction of the tumor cell has been possible with the advent of photodynamic therapy (PDT). PEGylation and active targeting of nanotubes are used in the treatment cancer [118].

Photodynamic therapy

They act by altering vicinity, resulting release of singlet oxygen species (reactive oxygen species). Apoptosis or necrosis is caused by the oxidative stress to the surrounding cells [115]. Lasers are used over wide range of visible wavelengths for exciting Photosensitizers. Because of the limited penetrability of visible light only superficial tumors such as skin, lung, esophagus, prostate, head and neck, colon and rectum are treated.

Photosensitizers cause target cell death where photosensitizer has accumulated because the half-life of the reactive oxygen species is only a few milliseconds. Circulation time of photosensitizers in blood can be enhanced and renal clearance can be prevented by precoating them using Polyethylene glycol. Photosensitizers can be targeted to the cancer cells by antibody conjugation to the surface that over express the antigen on the surface

IMPROVING TARGETING, TRANSPORT AND DELIVERY

Nano delivery systems successfully help the chemotherapy drugs by improving pharmacokinetic profiles, help targeting the required site, and improve drug delivery, cell uptake, targeting [119]. Two main factors for improving targeting, transport and delivery are:

1 The EPR - enhanced permeation retention

2 The potential ability of Nano drug delivery systems to overcome the limitations of anticancer drugs.

1. The **EPR** effect is because of two properties of tumors. Firstly, increased vasculature is seen in tumors that allow macromolecules and colloidal particles up to 600. Secondly, the interstitial fluid

from tumor tissues is not effectively cleared by the lymphatic system. Nanoparticles selectively target tumor tissues in normal tissues other than the spleen, liver and kidney which are impermeable to molecules that are larger than 2nm and reduce side effects. The nanoparticles have prolonged contact with tumor cells due to their enhanced permeation and retention properties. And also in addition the nanocarriers release the drug slowly ultimately resulting in reduced drug distribution and toxicity to normal tissues.

2. The ligand coated nanoparticles interact with cell surface receptors leading to uptake by cytosis. Size, shape and charge of uncoated nanoparticles governs their Cellular uptake. Positively charged nanoparticles are taken up more readily Due to differences in electrostatic attraction [120]. Corona forms leading to cell entry by interacting with specific serum proteins the. Recent studies indicated that rod-shaped are internalized better than spherical structures [121]. The cell death is induced by up taking larger nanoparticles [122].

3. Nano sized drug delivery systems can potentially overcome the Low aqueous solubility and stability and high nonspecific toxicity of anticancer drugs

IMPROVING COMPLIANCE

Life expectancy, quality and reduced cost are the main advantage of Nano therapy. The recovery time is very short and risk of effect of other infections is also reduced, the costs of diagnosis is less in Nano therapy treatment. Because of these advantages and improved effect the compliance is quiet good [123].

CONCLUSION

Nanomedicine is a remarkable tool to approach the difficult task of treating various diseases. Nanotechnology has made a profound impact on cancer detection and therapy. The technology has been grown exponentially in the recent years, and it had the most impact on contemporary science. Cancer detection and treatment by technologies involving nanoparticles are mainly in preclinical stages. There is tremendous potential for nanotechnology in cancer detection in its early stages. Cancer can be eradicated more effectively by loading chemotherapeutic agents targeted to the tumor site by using nano carriers and also eliminate adverse side effects. Conventional invasive therapies for cancer detection and treatment, which includes biopsies, irradiation and painful therapies, can be replaced by the applications of Nanotechnology. To reach the promise of Nanomedicine, it is necessary to take a step back and look at the problems facing drug delivery as a whole rather than designing around only one or two obstacles. Incremental designs may not be sufficient to accomplish the task of treating cancer effectively. Instead, a revolution in concept is

needed; one that incorporates a healthy respect for the complexity of both body and tumor and the ability of each to protect itself from harm. Ultimately if the researchers can develop methods to detect tumors at early stages before the tumors begin to vascularize and metastasize, cancer will become easily controllable via surgical resection.

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