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REVIEW ARTICLE

Nanoparticles in Cancer Treatment

Ahirrao SP*, Wagh MV, Yallatikar TP, Kshirsagar S

Mumbai Education Trust, Bhujbal Knowledge City, Aadgaon, Nasik, Maharashtra-422203, India.

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ABSTRACT

Nanotechnology is the rapidly developing subdivision of technology having significant benefits in clinical practices especially in cancer diagnosis, treatment and management. Nanotechnology can assist to have better diagnosis with less harmful effects. It has capacity to detect even a single cancerous cell in the toxic drugs to the cancerous cells. This article reviews current nanotechnology platform for anti-cancer drug delivery, including polymeric nanoparticles, liposomes, dendrimers, nanoshells, carbon nanotubes, superparamagnetic nanoparticles, nucleic acid based nanoparticles (DNA, RNAi, ASO), fullerenes, quantum dots, nanobubbles, paramagnetic nanoparticles, nanosomes, gold nanoparticles. This review article covers the advantages, challenges and potential of nanoparticles.

KEYWORDS

Nanotechnology, Neoplasm, Therapeutics, Combination, Quantum Dots Nano-Tubes

INTRODUCTION

Nanotechnology gifted many applications for scientific knowledge from multiple disciplines in science and engineering to design, modify and monitor the properties of matter at nanoscale dimensions[1]. Nanotechnology holds enormous potential for overcoming many of the problems associated with conventional methods, faces difficulties in the detection, treatment, and diagnosis of cancer[2]. In recent years, significant efforts have been devoted to develop nanotechnology to enhance the delivery of anticancer drug to tumour tissue while minimizing its distribution and toxicity in healthy tissue. Many nanotechnology platforms, such as polymeric nanoparticles, liposomes, dendrimers, nanoshells, carbonnanotubes, superparamagnetic nanoparticles, and nucleic acid-based nanoparticles [DNA, RNA interference (RNAi), and antisense oligonucleotide (ASO)], have been applied to the delivery of specific anticancer drugs, including small molecular weight drugs and macromolecules (protein, peptides or genes).

The physicochemical characteristics of nanotechnology platforms, such as composition, particle size, surface charge, surface fictionalization with hydrophilic polymers, and inclusion of tissue recognition ligands, will conduct their biodistribution and pharmacokinetics[3].

Hereby, the nanotechnology platforms could serve as customizable, targeted drug delivery vehicles capable of carrying large dose of therapeutic agents into malignant cells while avoiding healthy cells. This article overviewed current nanotechnologies for cancer therapy, focusing on the wide variety of nanotechnological platforms for anticancer drug delivery and nanotechnologies for combination therapeuticstrategies[4].

***Address for Correspondence:**
Ahirrao SP,
MET BKC, Institute Of Pharmacy,
Nasik-422203, Maharastra, India.
E-Mail Id: sapana.ahirrao@rediffmail.com

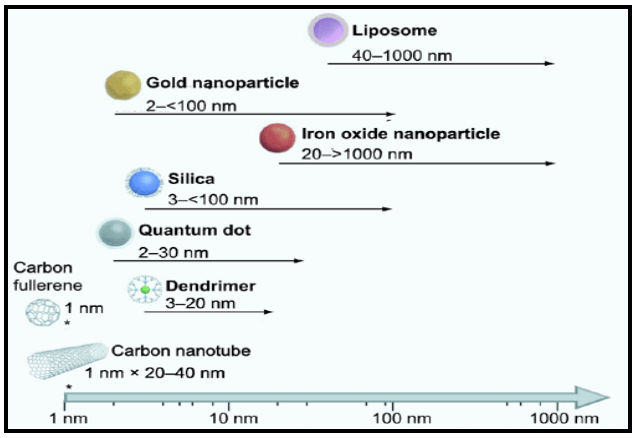

Figure 1: Different Sizes of Nanoparticles[5]

Cancer and Its Genetics

Before we delve fully into the main issue of this review which deals with applications of nanotechnology in cancer prevention, detection and treatment, we must address the underlying causes and the genetic mechanisms involved in cancer. The genetics of cancer is as follows.

In non-cancerous tissues growth is limited in the sense that cell reproduction is tightly controlled. After a certain number of cells have developed, feedback control (contact inhibition) limits cell division, allowing for tissue repair but not expansion. Cancer or neoplasm, on the other hand, involves tissues composed of cells that divide and/or grow abnormally. Cancer is a genetically rooted disease that involves the simultaneous occurrence of two general categories of cellular malfunctions. The precise number of genetic changes required for these malfunctions remains unresolved for any cancer.

The first category causes the replication of a cell to become permanently enabled due to a natural or carcinogen-induced genetic mutation, chromosome translocation or gene amplification. The second category is also due to genetic mutations, and causes the apoptosis complex, also known as the suicide complex, to become permanently disabled (Figure 1). As stated, both of these problems must occur in the same cell, at the same time, in order to cause cancer. Under normal circumstances, the cells carefully control their divisions using apoptosis complex activated by the p53tumour suppressor protein. There are other mechanisms triggering the apoptosis complex, including receptor mediated death, which is dependant to chemical messengers, especially tumour necrosis factors. But, when both of these mechanisms malfunction, the body has no other option. As the uncontrolled cell division continues, a cluster of fairly unspecialised cells committed to dividing develops and becomes larger and larger. In addition, the cluster of cells releases chemicals to promote abnormal capillary growth into the tumour. This kind of a cell cluster is known as a malignant tumour, and can severely damage the surrounding tissue as it sucks up essential nutrients and displaces healthy cells. Eventually, when the tumour grows large enough, some of the tumour cells can find their way into the bloodstream, forming tumours in other parts of the body. This latter phenomenon is known as metastasis. It effectively multiplies the cancer as well as its effects, and eventually will prove fatal to the patient[6].

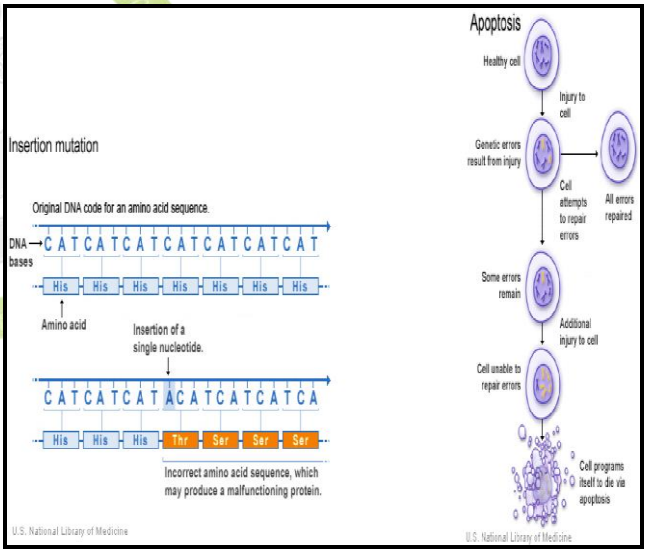

Figure 2: Mutation Causing Apoptosis[7]

Applications of Nanotechnology

Development of newer drug delivery systems with the help nanotechnology methods is being tried for conditions like cancer, diabetes, and viral-infections and in gene therapy. The main advantages of this modality of treatment are targeting of the drug and enhanced safety profile. Nanotechnology has also found its use in diagnostic medicine as contrast agents, fluorescent dyes and magnetic nanoparticles[8].

Table 1: Some Nanoparticles Use for Medical Application[8]

Study Phase	Product	Description	Use	Manufacturer
Preclinical	MRX952	Nanoparticle preparation-to encapsulate camptothecin analogues	Tumours	IMA Rx Therapeutics
Preclinical	Targeted nano therapeutics (TNT)™ system	TNT with polymer coated iron oxide magnetic particles	Solid tumours	Triton biosystem
Preclinical	AuroLase™	Gold nanoshell	Head and neck Cancer	Nanospectra Biosciences Inc
Preclinical	Dendrimer-Magnevist#	Dendrimer-Magnevist# PAMAM dendrimer	MRI imaging agent	Dendritic Nanotechnologies Inc
Phase 1	VivaGel®	Dendrimer based microbicide gel	HIV prevention	Starpharma Pty Ltd
Phase 1	INGN 401	Nanoparticle formulation of tumour suppression gene FUS1	Lung cancer	Introgen Therapeutics Inc
Phase 1&2	Cyclosert-Camptothecin – IT 101	β-Cyclodextrin polymer drug delivery system	Solid tumours	Calando Pharmaceuticals
Phase 2	VivaGel®	Dendrimer based microbicide gel	HSV prevention	Starpharma Pty Ltd
Phase 2	MRX 815	Nanobubble technology	Treatment of intravascular Clot	IMA Rx Therapeutics
Phase 3	Combidex® / Ferumoxtran 10	Iron oxide nanoparticle	MRI contrast agent	AMAG Pharmaceuticals
Marketed	Abraxane®	Albumin bound taxane Particles	Non-small cell lung cancer	Abraxis Oncology
Marketed	AmBisome®	Liposomal preparation of amphotericin B	Fungal infection	Astellas Pharma US
Marketed	Doxil®	Liposomal doxorubicin	Ovarian tumour	Ortho Biotech

Polymeric Nanoparticles

Polymeric nanoparticles are prepared from natural or synthesized polymers. Various biodegradable or unbiodegradable polymers can be used to prepare nanoparticles in order to achieve expected drug delivery performance and therapeutic effect. Among these, biodegradable polymeric nanoparticles for anticancer drug delivery have attracted great interest in recent years since they could provide controlled, sustained and targeted delivery. Polymeric nanoparticles, the most effective nanotechnology platforms, have emerged as a versatile carrier system for targeted delivery of anticancer drugs[4,9].

Bernardi investigated the effect of indomethacin loaded nanocapsules on a xenograft glioma model in rats. The rats presented a significant reduction in tumour size and half of them presented just residual tumour cells; Moreover, the animal survival rate was much larger in the drug loaded nanocapsules group than in the control (untreated), indomethacin and drug unloaded nanocapsules groups[10].

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 can neutralize the activity of excessive proteolysis in order to prevent the metastatic and invasive potential of breast tumour cells[11].

To stabilize the surface of nanoparticle 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 tumour site selectivity in vivo of ring-opening metathesis polymerization-based copolymers[12].

By covalent coupling of humanized monoclonal antibodies (anti-HER2) to paclitaxel-loaded poly (D, Llactic acid) nanoparticles, immunonano particles were prepared to actively target tumour cells which over express HER2 receptors[13]. Recently, Patil produced PLAPEG ligand conjugate nanoparticles by single step surface functionalizing technique, and found that simultaneous fictionalization with biotin and folic acid induced great efficacy of paclitaxel-loaded nanoparticles in a MCF7tumorxenograft model by enhancing drug accumulation in tumors[14].

Liposomes

As closed spherical vesicles, liposomes consist of a lipid bilayer which encapsulates an aqueous phase to store drugs[15]. With the size (90-150nm) which is slightly bigger than the conventional definition (≤100 nm), liposomes do not constitute novel nanotechnology, but a large portion of them are associated with nanotechnology research[16].

Forming lipid bilayers through hydrophobic interaction, liposomes are considered as excellent platforms for the delivery of hydrophobic and hydrophilic drugs. In particular, liposomes present considerable persistence in the blood. It facilitates efficient drug delivery to target tissues. Different lipids have different fatty acid chain lengths, different head groups, and different melting temperatures. Consequently, temperature[18] or pH sensitive[18,19,20] liposomes can be constructed by manipulating the formulation. The effectiveness of 1methylxanthine (1MTX) as a radio sensitizer and the in vivo efficacy of the temperature-sensitive liposomal 1methylxanthine (tslMTX) which combined with regional hyperthermia and ionizing radiation were evaluated [18]. Intraperitoneal injection of the tsl-MTX inhibited tumour growth in the mouse xenografttumor model; Moreover, the combination of ts-lMTX with regional hyperthermia and ionizing radiation obviously inhibited tumour growth[18]. Most recently, to target leukemic cells, pH sensitive immunoliposomes (ILs) including a terminally alkylated Nisopropylacrylamide (NIPAM) in the bilayer were coupled with the anti-CD33 monoclonal antibody[20].

Dendrimers

As highly branched artificial macromolecules with tree-like structures, dendrimers are monodisperse, three- dimensional molecules which have defined molecular weights and host-guest entrapment properties[21]. With the size ranging from 1 to 10 nm, dendrimers with different chemical structures and functional groups can be synthesized. Through a series of repeating chemical synthesis on the core, the size and shape of dendrimers are determined by the generation. The key useful character of dendrimers is the branches which can provide vast amounts of surface area for drugs and targeting molecules[16,22] .Meanwhile, the surface functionalities, interior branching, and chemical composition of the core play a significant role in reactivating the macromolecule[22].

Dendrimer is one of the most elegant nanotechnology platforms for targeted drug delivery. Conjugated with biotin as the targeting moiety, the in vitro targeting ability of partially acetylated generation 5 polyamidoamine (PAMAM) dendrimer (Ac-G5) in HeLa cells was assessed[23]. The multi-functional conjugate Ac-G5-biotin-FITC (fluoresceinisothiocyanate) showed much higher cellular uptake than the conjugate without biotin. The energy dependent uptake process can be blocked effectively by biotin-polymer conjugates, exhibiting an expected dose-response curve[22].

Nanoshells

As the layer-by-layer assembly of nanoparticles, polymeric nanoshells (20-60 nm) of diblock copolymers can be made by self-assembly of oppositely charged polymers forming a core/shell structure[24]. With a biodegradable polymer core and mixed lipid monolayer shell, a system of folic acid-conjugated nanoparticles was developed for targeted delivery of docetaxel[25].

Gold nanoshells (10 to 300nm) are optically tunable nanoparticles comprising a dielectric core with a thin gold shell surrounded .In order to achieving maximal penetration of light through tissue over the near-infrared, gold nanoshells can be designed by adjusting the core radius and the shell thickness[26]. Laser activated gold nanoshells thermal ablation is a selective and effective technique for the ablation of prostate cancer in an ectopic tumour model[27].

Carbon Nanotubes

As a distinct molecular form of carbon atoms which bond with each other via sp^2 bonds and present a hexagonal arrangement, carbon nanotubes were first discovered in the late 1980s[16,28]. Conceptually, carbon nanotubes are described as well ordered, hollow nanotubes formed when single or multiple graphene sheets are rolled into a cylinder[28,29]. The two forms of carbon nanotubes are single- and multi-walled carbon nanotubes. In the family of nanotechnology platforms, carbon nanotubes have been identified as a novel tool for anticancer drug delivery[30]. Apart from that, carbon nanotubes can immobilize molecules, such as antibodies, DNA and drugs[31,32,33] in order to penetrate cell membranes.

Heister[31] has used an oxidized single-walled carbon nanotube, consisting of a fluorescent marker and a monoclonal antibody at noncompeting binding sites, to delivery anticancer drug doxorubicin. However, because of the needle-like fiber shape, the safety of carbon nanotubes is concerned.

Recently, the biological impacts (cytotoxicity, DNA damage, and inflammation) induced by different sized multi walled and single walled carbon nanotubes, have been studied.

The results demonstrate that long and thick multi walled carbon nanotubes probably induce severe biological effects and may cause the augmentation of cancer risk [34].

Superparamagnetic Nanoparticles

Superparamagnetic nanoparticles, iron oxide magnetic nanoparticles with particle sizes of about 20 nm, are composed of Fe_2O_3 or Fe_3O_4 and do not keep any magnetism after removal of the magnetic field, hence, may be used *in vivo*[35]. Superparamagnetic nanoparticles can be used as contrast agents for magnetic resonance imaging (MRI), can be used for cancer thermal therapy,

and can concentrate in target sites through an external magnetic field.

Functionalized with recombinant single chain Fv antibody fragments (scFv), superparamagnetic iron oxide nanoparticles (SPIONs) could be used to target and image cancer cells[36]. Conjugated to luteinizing hormone releasing hormone (LHRH), SPIONs not only achieve breast cancer cell targeting but also play the role as contrast agents in the MRI of breast cancer xenografts[37]. The post-mortem neuropathologic studies of glioblastomamultiforme (GBM) patients treated with thermotherapy using magnetic nanoparticles were reported[38]. Magnetic nanoparticles were injected into the tumour and then heated in an alternating magnetic field. The instillation of magnetic nanoparticles in

GBM patients induced the uptake of nanoparticles in macrophages to a major extent, and the uptake was further promoted by magnetic fluid hyperthermia (MFH) therapy[38].

Nucleic Acid-based Nanoparticles (DNA, RNAi, and ASO)

Gene therapy refers to the direct transfer and expression of DNA into diseased cells for the therapeutic applications[39]. Veiseh et al.[40] have developed a ligand mediated nanovector by binding the chlorotoxin (CTX) peptide and pegylation of DNA complexing polyethylenimine (PEI) in nanoparticles which functionalized with an Alexa Fluor 647 near infrared fluorophore.

Mixed nanoparticles, prepared with generations 4 and 5 poly (amidoamine) (PAMAM) dendrimers and plasmid DNA, were confirmed to be effective for both in vitro and in vivo gene delivery to colon and liver cancer cells[41]. Based on oligonucleotides, RNAi and ASO therapies can shut down the expression of target genes to treat the disease[24]. Recently, siRNA nanoparticles were first designed with Poly (Propyleneimine) (PPI) dendrimers[42].

Fullerenes

Fullerenes, a carbon allotrope, also called as "buckyballs" were discovered in 1985[43]. The Buckminster fullerene is the most common form of fullerene measuring about 7 Å in diameter with 60 carbon atoms arranged in a shape known as truncated icosahedrons[44].

It resembles a soccer ball with 20 hexagons and 12 pentagons and is highly symmetrical[45].

Types of Fullerenes

Alkali doped fullerenes are structures with alkali metal atoms in between fullerenes contributing valence electrons to neighbouring fullerenes[46]. They occur because of the electronegative nature of the fullerenes.

Endohedral fullerenes have another atom enclosed inside the buckyball. If a metallic atom is enclosed, these are called as metallofullerenes[47,48]. Due to the small size of C60 fullerene, it is difficult to synthesize endohedral C60 fullerenes. However, larger fullerenes such as C82 or C84 fullerenes are used for synthesizing endohedral fullerenes. Endohedral metallofullerenes can be used for diagnostic purposes as radio contrast media in magnetic resonance imaging and other imaging procedures. Since the radioactive metal is enclosed within the buckyball, these are less toxic and safer. This method can also be employed for imaging organs as radioactive tracers[48].

Exohedral fullerenes also called as fullerene derivatives are synthesized by chemical reaction between the fullerene and other chemical groups. These are also called as functionalized fullerenes. Such fullerenes can be used as photosensitizes in photodynamic therapy for [malignancies. These generate reactive oxygen species when stimulated by light and kills the target cells. This method is now also being investigated for antimicrobial property as these cause cell membrane disruption especially in Gram positive bacteria and mycobacterium[49,50,51].

Heterofullerenes are fullerene compounds where one or more carbon atoms are replaced by other atoms like nitrogen or boron[43].

Fullerenes are being investigated for drug transport of antiviral drugs, antibiotics and anticancer agents [49,50,51,52]. Fullerenes can also be used as free radical scavengers due to presence of

high number of conjugated double bonds in the core structure. These are found to have a protective activity against mitochondrial injury induced by free radicals[53].

However, fullerenes can also generate reactive oxygen species during photosensitization.

This property can be used in cancer therapy[54].

Fullerenes have the potential to stimulate host immune response and production of fullerene specific antibodies. Animal studies with C60 fullerene conjugated with thyroglobulin have produced aC60 specific immunological response which can be detected by ELISA with IgG specific antibodies. This can be used to design methods of estimation of fullerene levels in the body when used for therapeutic or diagnostic purposes [55]. On intravenous injection, these get distributed to various parts of the body and get excreted unchanged through the kidney. Soluble derivates of fullerenes are more biocompatible compared to insoluble forms of fullerenes and have low toxic potential even at higher dose[55]. Further, the degree of purification of fullerene determines its cost and highly purified fullerenes are expensive, restricting its application in medical field[43].

Quantum Dots

Quantum dots are nanocrystals measuring around 2-10 nm which can be made to fluorescence when stimulated by light. Their structure consists of an inorganic core, the size of which determines the colour emitted an inorganic shell and an aqueous organic coating to which biomolecules are conjugated. The biomolecule conjugation of the quantum dots can be modulated to target various biomarkers[56].

Quantum dots can be used for biomedical purposes as a diagnostic as well as therapeutic tool. These can be tagged with biomolecules and used as highly sensitive probes. A study done on prostate cancer developed in nude mice has shown accumulation of quantum dots probe by enhanced permeability and retention as well as by antibody directed targeting. The quantum dots conjugated with polyethylene glycol (PEG) and antibody to prostate specific membrane antigen (PSMA) were accumulated and retained in the grafted tumour tissue in the mouse[57].

Quantum dots can also be used for imaging of sentinel node in cancer patients for tumour staging and planning of therapy. This method can be adopted for various malignancies like melanoma, breast, lung and gastrointestinal tumours[56]. Quantum dot probes provide real time imaging of the sentinel node with Near Infra-Red (NIR) fluorescence system. The NIR region of the electromagnetic spectrum produces reduced background noise and deeper penetration of rays, of up to 2 to 5 cm into the biological sample. However, the traditional fluorescence dyes yield low signal intensity when used in NIR region. This limitation is overcome, by using NIR fluorescence system with quantum dot probes. The fluorescence produced by quantum dots is much brighter than those produced by conventional dyes when used with NIR fluorescence system[58].

However, the application of quantum dots in a clinical setting has limitations owing to its elimination factors. Functionalization of the quantum dots which protects from the toxic core, leads to increase in size of the nanoparticle greater than the pore size of endothelium and renal capillaries, thus reducing its elimination and resulting in toxicity. Also, *in vivo* studies are lacking on the metabolism and excretion of quantum dots[56].

Nanobubbles

Cancer therapeutic drugs can be incorporated into nanoscaled bubble like structures called as nanobubbles. These nanobubbles remain stable at room temperature and when heated to physiological temperature within the body coalesce to form microbubbles. These have the advantages of targeting the tumour tissue and delivering the drug selectively under the influence of ultrasound exposure. This results in increased intracellular uptake of the drug by the tumour cells. It also provides an additional advantage of enabling visualisation of the tumour by means of ultrasound method[59,60]. Rapaport *et al*[61] have demonstrated the utility of nanobubbles in delivery of drugs like doxorubicin based on *in*

vitro and *in vivo* experiments using breast cancer cells MDA MB231 and mice with breast cancer xenograft respectively. On administration of nanobubble loaded doxorubicin, these reach the tumour tissue through leaky vasculature and get accumulated at the site of tumour. This is followed by formation of microbubbles by coalescing of nanobubbles which can be visualised by ultrasound techniques. When the site is focused with high intensity focused ultrasound (HIFU), it causes disruption of the microbubbles resulting in release of the drug. The microbubbles retained the drug in a stable state until stimulated by HIFU. This results in attainment of higher levels of drug in the target cells and hence reduced toxicity and increased efficacy. This method needs further exploration for its utility in treatment of various malignancies. Liposomal nanobubbles and microbubbles are also being investigated for their role as effective non-viral vectors for gene therapy.

Nanobubbles combined with ultrasound exposure has shown improved transfer of gene in both *in vitro* and *in vivo* studies[62,63]. Nanobubbles are also being tried as a therapeutic measure for removal of clot in vascular system in combination with ultrasound, a process called as sonothrombolysis. This method has advantages of being non-invasive and causing less damage to endothelium[64].

Paramagnetic Nanoparticles

Paramagnetic nanoparticles are being tried for both diagnostic and therapeutic purposes.

Diagnostically, paramagnetic iron oxide nanoparticles are used as contrast agents in magnetic resonance imaging. These have a greater magnetic susceptibility than conventional contrast agents. Targeting of these nanoparticles enables identification of specific organs and tissues[65]. The use of iron oxide in MRI imaging faces limitations like specificity and internalization by macrophages[66]. Paramagnetic nanoparticles conjugated with antibodies to HER-2/*neu* which are expressed on breast cancer cells have been used with MRI to detect breast cancer cells *in vitro*[67]. Study done by Leuschner *et al*[68] has demonstrated the *in vivo* detection of breast cancer cells using paramagnetic nanoparticles conjugated with luteinizing hormone releasing hormone as breast cancer cells express LHRH receptors. Thus, use of antibodies to direct the nanoparticle to the target site helped to overcome problems with specificity of action. Internalization of the nanoparticles by macrophages can be reduced by treatment with drugs like lovastatin which reduce macrophage receptor expression for the nanoparticle by reducing the recycling of receptor[66]. Further, injection of decoys of nanoparticle can be used to eliminate plasma opsonins and reduce uptake of the nanoparticles. Also, change of surface charge of the nanoparticle to neutral by covalent coupling to chemicals leads to an increase in circulation time[66].

Microcrystalline iron oxide nanonparticles (MIONs) have been studied by Knauth *et al*[69] in magnetic resonance imaging of brain. MIONs help in overcoming the disadvantage of surgically induced contrast enhancement with traditional contrast agents resulting in misinterpretation during intra-operative MR imaging of brain. Surgically induced contrast enhancement occurs in brain due to leak of contrast material from the cut end and oozing blood vessels in brain when MR imaging is done post-operatively. This is avoided when MIONs are used pre-operatively. These are rapidly taken up by the tumour cells[70], producing long lasting contrast enhancement of tumour and the remaining nanoparticles are removed from the circulation by reticuloendothelial system[71].

Magnetic microparticle probes with nanoparticle probes have been used for identification of proteins like prostate specific antigen. Here magnetic microparticles coated with antibodies together with nanoprobes with similar coating and a unique hybridized DNA barcode are used. The microparticle coated with antibody directed against prostate specific antigen combines with it to form a complex and can be separated by using magnetic separation. The presence of these separated complexes is determined by dehybridization of the complexed DNA barcode sequence and polymerase chain reaction for the

oligonucleotides. This allows prostate specific antigen detection at 30 attomolar concentration[72]. This sensitivity is much greater than conventional assays for prostate specific antigen.

Magnetic nanoprobes are used for cancer therapy:

Iron nanoparticles coated with monoclonal antibodies directed to tumour cells can be made to generate high levels of heat after these accumulate in their target site by means of an alternating magnetic field applied externally. This heat kills the cancer cells selectively. This method designed by Triton Biosystems, is about to enter clinical trials for solid tumours in 2009[73].

Nanosomes

Raoul Kopelman's group at the University of Michigan, USA, has been working on nanosomes also called as PEBBLEs (Probes Encapsulated by Biologically Localized Embedding) which integrate various aspects of medical applications such as targeting, diagnosis and therapy. These nanosomesare being developed for treatment of various tumours, in particular CNS tumours. Silica coated iron oxide nanoparticles coated with polyethylene glycol[74] and affixed with targeting antibody and contrast elements like gadolinium are used to access specific areas of brain involved with tumour.

Targeting aids in binding the nanoparticle specifically to the tumour cells and the contrast elements helps in better detection with magnetic resonance imaging. Subsequent treatment with laser can destroy the cells loaded with these nanoparticles by the heat generated by iron oxide particles by absorbing the infra-red light. Nanosomes can also be integrated with a photo catalyst which produces reactive oxygen species when stimulated by light and destroy the target tissue. This method has advantage over conventional drugs in being much safer without the adverse effects of cancer chemotherapy drugs and also the absence of development of drug resistance. Nanosomes are being developed to integrate more and more components in it for flexibility of its applications[75,76].

Gold Nanoparticles

These metallic gold nanoparticles exhibit a unique optical response to resonantly scatter light when excited at their surface plasmon resonance frequency[77]. The epidermal growth factor receptor is a cell surface receptor biomarker that is over expressed in epithelial cancer but not in normal cell. The ant epidermal growth factor receptor antibody conjugated nanoparticles specifically and homogeneously binds to the surface of cancer type cells with 600% greater affinity than to non-cancerous cell[78]. The successful conjugation of antibodies on gold nanoparticles can be ascertained by the addition of 10% common salt which also leads to aggregation of gold nanoparticles and result in visible color change from red to purple or gray[79]. Gold nanoparticles have been investigated in diverse areas such as in vitro assays,

In vitro and in vivo imaging, cancer therapy and drug delivery. Gold nanoshells are capable of enhancing the contrast of blood vessels in vivo suggested their potential use in magnetic resonance (MR) angiography as blood pool agents. SERS is an optical technique that offers many advantages over traditional technologies, such as fluorescence and chemiluminescence, including better sensitivity, high levels of multiplexing, robustness and superior performance in blood and other biological matrices[80].

Advantages of Nanoparticles

The use of nanoparticles has not only revolutionized the field of medicine but has helped in accurate, precise treatment of diseases, drug delivery. Various other uses of nanoparticles in various fields of medicine and cancer are fluorescent biological label[89], drug and gene delivery[90,] bio detection of pathogens[91] detection of proteins[92,] robing of DNA structure[93,] tissue engineering[94,] tumor destruction through heating (hyperthermia)[95], separation and purification of biological molecules and cells[96], MR imaging contrast enhancement[97].

Limitations

Cancer targeting is highly dependent on surface chemistry. Biocompatibility is a major issue in

use of nanoparticles. Ease of availability all over the world at basic levels (primary health care, government hospitals etc.,) and cost of nanotreatment are the main disadvantages of nanoparticles. Radiation therapy, a laser optic probe is used, which basically ensures that the infrared radiation is directed at the tumor and allows the treatment to be through the skin, from outside the body. Therefore, this new heat treatment is very similar to the current method of radiation therapy, but the nanoparticles alter the treatment in that they cause minimal damage to the healthy tissue[90].

CONCLUSION

Nanotechnology has become popular in the past few years due to minimal invasion and few side effects. Its use in the diagnosis and treatment of cancer has experienced exponential growth in past few years. Multifunctionality is the key advantage of nanoparticles over traditional approaches. Targeting ligands, imaging labels, therapeutic drugs and many other functional moieties can all be integrated into the nanoparticle conjugate to allow for targeted molecular imaging and molecular therapy of cancer. Nanoparticles hold new promises as means for earlier detection and better treatment of cancer. Despite the disadvantages faced with nanoparticles they offer new avenue to tackle this challenges.

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