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Nanotechnology- A Potent Pharmacological Tool

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Abstract- Nanotechnology is a growing field & it encompasses almost all disciplines of Science & Engineering. The application of Nanotechnology has tremendous potential in healthcare, particularly for the development of better pharmaceuticals, nano enabled drug delivery to specific tissues, promises capability to enhance drug penetration into cells and other means to improve drug activity. The efficacy of a drug can be increased if it is delivered to its target selectively and its release profile is controlled. Nano-structures have shown capabilities like detecting cancer at earliest stages, pin pointing its location in the body and delivering anti-cancer drugs specifically to malignant cells. Nano-scale materials can readily interact with bio-molecules on both the cell surfaces and within the cells. Hence a Nano-scale material may contribute to cancer therapy by being a drug carrier. Nano-scale structures attached with antibodies and loaded with drugs can serve as a targeted drug delivery vehicle that can transport chemo-therapeutics or therapeutic genes into diseased cells while sparing the loading of healthy cells with drugs. Targeted drug delivery would improve the therapeutic efficacy and enable a reduction in dose, thus minimizing side effects of the drugs. Dendrimer, silica-coated micelles, ceramic Nano-particles and cross-linked liposome have already shown potential for being a drug carrier. Some challenges are associated with the Nanotechnology as it relates to drug effectiveness, toxicity, stability and pharmacokinetics and drug regulatory control. This review aims at integrating various applications of the most recently developed nanomaterials that have tremendous potential for the pharmacological screening.

Key words - Nanotechnology, Drug delivery, Nanostructures, Health care, Pharmaceuticals.

1. INTRODUCTION

Nanotechnology can simply be defined as the technology at the scale of one-billionth of a metre. It is the design, characterization, synthesis and application of materials, structures, devices and systems by controlling shape and size at nanometer scale (Stylios et al, 2005[1]; The Royal Society and the Royal Academy of Engineering, 2004,)[2]. It is the ability to work at the atomic, molecular and supramolecular levels to create and employ materials, structures, devices and systems with basically new properties (Weller, 1993[3];Roco, 2003[4]). Scientifically, nanotechnology is employed to describe materials, devices and systems with structures and components exhibiting new and significantly improved physical, chemical and biological properties as well as the phenomena and processes enabled by the ability to control properties at nanoscale (Miyazaki and Islam, 2007[5]). Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macro molecular scales, where property differs significantly from those at a larger scale. Nano materials cross the boundary between nanoscience and nano technology and bridges these two areas (The Royal Society and the Royal Academy of Engineering, 2004[2]; Michael and Pitkethly, 2004[6]; Rittner, 2001[7]).

Materials exhibit unique properties at nanoscale of 1 to 100 nm. Materials at nano scale lie between the quantum effects of atoms and molecules and the bulk properties of materials. It is in this 'no-man's-land' where many physical properties of them are controlled by phenomena that have their critical dimensions at the nanoscale (Michael and Pitkethly, 2004[6]; Holister and Harper, 2002[8]; Jones and Mitchell, 2001[9]). The changes in properties are due to increase in surface area and dominance of quantum effects which is associated with very small sizes and large surface area to volume ratio (Williams, 2008[10]). For instance, copper is opaque at macro scale but becomes transparent at nanoscale (Zong et al, 2005[11];Gao et al, 2003[12]), platinum is inert which becomes a catalyst at nanoscale (Luo et al, 2005[13]; Tian et al., 2007[14]). A well known insulator, silicon, becomes a conductor at nanoscale (Patel, 2008[15]; Hu et al, 2003[16];Heron, 2007[17]). The properties of gold at nanoscale is quite significant, depending on the size of the nanoparticles, melting point ranging from 200 to 1068^0C and colour from yellow to blue, violet, pink, red; and have the ability to act as catalyst (Cortie, 2004[18]; Cortie, 2002[19]; Overbury, 2005[20]; Jain et al, 2008[21]).

Nano particles for pharmaceutical purposes are defined in the Encyclopedia of pharmaceutical technology as 'solid colloidal particles ranging in the

size from 1-1000nm.Theyconsist of macromolecular materials and can be used therapeutically as drug carriers, in which the active principle is dissolved, entrapped or encapsulated or to which active principle is adsorbed or attached'(Kreuter, 1994)[22].

2. NANOTECHNOLOGY IN NATURE

Nature has enough evidence of nanotechnology, based on its ability to work at the atomic, molecular and supramolecular levels. The mechanisms of the biological and physical world operate mainly at the range of 1 to100 nm. The diameter of a hydrogen atom is about 0.1nm which is too small to be seen with human eyes. A molecule may be made up of 20 to 30 atoms and has a diameter of about 1nm. The width of a DNA molecule is about 2.5nm, a typical protein is between 1 to 20nm and ATP biochemical motor is 10 nm in diameter (Roco, 1999[23]). The human hair is about 10, 000nm thick while human cells range from 5,000 to 200,000 nm in size. Although this is larger than nanoscale, the viruses that attack human cells fall within 10 to 200nm, which is within the nanometre region (Yin, 2007[24]). Nature is the ultimate in nanotechnology, producing nanostructures that offer functional proteins and many other compounds at cellular level of great significance to life on earth.

Photosynthesis is carried out in green plants by cells of nanosize, which employ energy to synthesize organic compounds by using cheap raw materials they pick up. Moths' eyes are antiglare and antireflective due to nanotechnology which helps to reduce easy predation on them while the colours on butterfly wings are due to light being bounced off nanoscale layers in the structure of the wings (Smith, 2006)[25]. Nature depicts how soluble molecules that are able to recognize and bind to specific materials can be used to shape and control the growth of crystals and other nanostructures. Sufficient knowledge and insight into the principles of natural systems would enhance the design and fabrication of man-made nanostructures that may mimic the functions of natural systems. For instance, biomolecules such as proteins, peptides, DNA, lipids and carbohydrates can act as templates - their shapes and chemical properties can be employed - to arrange inorganic substances such as metals on nanoscale (Bittner, 2005)[26].

Research presently seeks systematic approaches to fabricate man-made objects at nanoscale and to incorporate nanostructures into macrostructures as nature does (Roco 2003[4]; Roco,1999[23]; Smith, 2006)[25]. Such approaches and concept - which may differ from the living systems in aqueous medium - as self-assembly, templating of atomic and molecular structures on other nanostructures, interaction on surfaces of various shapes, self repair and integration on multiple length scales may be utilized as models (Roco 2003[4]; Roco, 1999[23]).

3. HISTORY OF NANOTECHNOLOGY

The platform for nanotechnology is believed to have been laid by Richard Feynman, a physicist at California Institute of Technology, in an after-dinner speech in 1959, 29th December, titled, "There is plenty of room at the bottom", at the American Physical Society's Winter Meeting of the West (The Royal Society and the Royal Academy of Engineering, 2004[2], Miyazaki and Islam, 2007)[5]. Feynman is known to have explored the possibility of manipulating materials at the scale of individual atoms and molecules, imagining the whole of the Encyclopedia Britannica written on the head of a pin and foreseeing the increasing ability to examine and control matter at the nanoscale (Sahoo, 2007)[27]. He is stated to have noted that the capabilities of atom-by atom assembly and nano engineering could lead to new materials and pathways similar to the biological system (Matija, 2004)[28]. He presented a technological vision of miniaturization of materials, manipulating and controlling things on a small scale called 'Nanotechnology'.

Although nanotechnology is widely considered to be an invention of modern science, they actually have a very long history. Nanoparticles were empirically used by artisans as far back as the 9th century in Mesopotamia to generate a glittering effect on the surfaces of pots. The colour effect of butterfly wings was copied by the Romans about 1600 years ago. The glass cup known as Lycurgus cup in the British Museum, due to nanoparticles of gold and silver, looks jade green in natural light and an impressive red colour when a bright light shines through it (Smith, 2006)[25] In the manufacture of car tyres, carbon nanoparticles are included while the red and yellow colours seen at sunsets are due to nanoparticles in the atmosphere (Smith, 2006)[25]. Indian craftsmen and artisans used nanotechnology to make weapons and long lasting cave paintings about 2000 years ago while studies found existence of carbon nanoparticles on the famous sword of Tipu Sultan (ancient ruler of the Kingdom of Mysore, India) and Ajanta paintings (one of Indians' cave paintings)(Visakhapatnam PTI, 2008)[29].The first scientific description of nanometer-scale metals was provided by Michael Faraday in his classic paper (Faraday 1847)[30], but the development of nanomaterials depended mainly on their visualization and the characterization of their physical and chemical properties. The first observation and size measurements of nanoparticles were carried out using an ultramicroscope by Zsigmondy in 1902 (Wikipedia, 2008[31], Zsigmondy, 1926)[32]. The term nanotechnology was first used in 1974 by Norio Taniguchi, who used it to refer to the ability to engineer materials at nanoscale (Miyazaki and Islam 2007[5]; Sahoo, 2007) [27].

Modern instrumental techniques have drastically increased our ability to precisely measure particle size distributions and many other parameters that are correlated with nanoscale objects. For example, techniques such as transmission and scanning electron microscopy have facilitated the direct visualization of individual nanoparticles with atomic accuracy (Horber and Miles, 2003[33]; Karoutsos, 2009[34]). As a result of these advances, scientists have developed exquisite and highly sophisticated methods to generate nanoscale materials with different sizes, compositions, and geometries. In the 1980s, two more inventions such as scanning tunneling microscopy (STM) by Gerd Binnig and atomic force microscopy(AFM) by Henrich Rohrer which enabled the imaging of individual atoms or molecules as well as their manipulation led to significant progress in the field nanotechnology (Miyazaki and Islam 2007[5]; Cortie, 2004[18]; Matija, 2004)[28]. In 1985, Fullerene C60 was discovered by Kroto's and Smalley's research groups. Afterwards, in 1986, Eric Drexler began to promote and popularize nanotechnology through speeches and books - "Engines of creation, pp. the coming era of nanotechnology" (Miyazaki and Islam, 2007)[5]. In 1991, Iijima discovered carbon nanotubes and these paved way for the progress in research and development in the field of nanotechnology (Miyazaki and Islam, 2007[5]; Matija, 2004[28]; Roco, 2004)[35].

3.1. *Nanotechnology for Pharmacological Purpose*

The application of nanotechnology has tremendous potential in health care, particularly for the development of better pharmaceuticals. Nano enabled drug delivery has already been successful in delivering drugs to the specific tissues within the body and promises capability that will enhance drug penetration into cells as well as other means to improve drug activity. It is known that the efficacy of a drug can be increased if it is delivered to its target selectively and its release profile is controlled.

Nano materials has shown the capability of performing clinical functions like detecting cancer at earliest stages, pin pointing its location in the body and delivering anticancer drugs specifically to malignant cells. The nano scale materials can control the spatial and temporal release of therapeutic agents or drugs. These are much smaller than cells or many cell organelles. Most animal cells are 10,000 to 20,000nm in diameter. This means that nano scale materials smaller than 50 nm can easily enter most cells while those smaller than 20nm can transit out of blood vessels. As a result nano scale devices can readily interact with biomolecules on both the cell surfaces and within the cells. Hence a nano scale materials may contribute to cancer therapy by being a drug carrier (Sharon and Sharon, 2007[36]).

Nano scale materials attached with anti bodies and loaded with drug can serve as targeted drug delivery vehicle that can transport chemo-therapeutics into diseased cells while sparing the loading of healthy cells with drugs. Targeting a drug to its site of action would not only improve the therapeutic efficacy but also enable a reduction in total dose of drug, which must be administered to achieve therapeutic response, thus minimizing unwanted toxic effects of the drugs. The Pharmacological applications of some of the well-known nanomaterials are listed below.

3.2. *Magic bullets*

The magic bullets are the compounds with specific structures designed to combat specific diseases and leave all else alone. These were envisioned by Paul Ehrlich, the Medicine Nobel Laureate in 1908 (Winau et al, 2004)[37]. Many nanostructures have been developed that fit the magic bullets definition. These nanostructures could include all of the nanosized drug carrier systems such as polymeric nanoparticles, liposomes, micelles, and polymer drug conjugates. Some newer nanostructures being developed include nanocages, nanogels, nanofibers, nanoshells, nanorods, and nanocontainers (Vasir et al, 2005)[38]. For example, surface functionalized carbon nanotubes are used for gene delivery vectors (Singh et al, 2005)[39] and gold nanoshells are able to attach to tumors and selectively destroy them under near-infrared light irradiation (Hirsch et al, 2003)[40]. Development of magnetic nanocargoes is of keen interest because they provide potential benefit for the use of localized magnetic field gradients to attract the drug-loaded particles to a chosen site, as well as the ability to hold them there until the therapy is complete and then to remove them (Vasir et al, 2005)[38].

Recently hollow magnetic silica nanocomposites, nanospheres, and nanotubes were synthesized (Zhou et al, 2005)[41]. These hollow nanostructures can load drug like ibuprofen, making the hollow nanocomposites promising for drug delivery (Zhou et al, 2005)[41]. These integrate magnetic properties into hollow nanostructures, thus advancing toward Ehrlich Ts dream. Future study in evaluating the drug release from the drug-loaded nanocomposite is surely an immediate task for realizing these magic nanobullets.

3.3. *Quantum Dot (Q-dot) nanocrystals*

Quantum Dots are nanocrystals composed of a core of a semiconductor material, enclosed within a shell of another semiconductor that has a larger spectral band gap.

The use of quantum dots for cancer imaging is one of the most promising applications for the future. Suitably functionalised quantum dots can target

specific subcellular targets, which is the need of hour in oncological studies. Q-dots can start their action from sub-cellular (genetic) level, therefore may be a possible 'cure' of cancer is also possible in near future. Advantages of using Q-dots are that cancer detection in early stages is possible, it can be used to localisetumours near skin and similar analogues are being considered for deep tissue optical imaging (Zheng et al, 2007)[42]. They are highly angiographic contrast agents in vessels supplying murine sqamous cell carcinoma. Also they show no significant photobleaching or degradation even after an hour of continuous excitation (Smith et al, 2004)[43]. Stability together with temoral resolution of optical detection makes them particularly attractive candidates for pharmakokinetic imaging studies. Moreover these technologies are associated with equipment costs much lower than competing technologies such as MRI (Alivisatos et al, 2008)[44].

Q-dots are generally composed of atoms from groups II and VI elements (e.g., CdSe and CdTe) or groups III and V elements [e.g., indium phosphide (InP) and indium arsenide (InAs) of the periodic table. In general, quantum dots consist of a semiconductor core, overcoated by a shell to improve optical properties, and a cap allowing improved solubility in aqueous buffers (Ying et al, 2008)[45]. Among the range of available Q-dots, the ones composed of CdSe cores overcoated with a layer of zinc sulfide (ZnS) are produced by a range of well-developed synthetic routes (Medintz et al, 2005)[46]. These Q- dots become highly fluorescent and feature such attractive optical properties as high quantum yield, large absorption cross section, and high photostability (Michalet et al, 2005[47], Somers et al, 2007)[48]. Q-dots have been systematically tried in virtually all fluorescence-based assays and in vivo imaging procedures (Smith et al, 2004[43]; Michalet et al, 2005[47]; Alivisatos et al, 2005[49]).

These have the potential to function as multimodal imaging platforms in vivo and the ability to detect an optical nano particle preoperatively with clinical imaging modality offered a distinct advantage to clinicians engaged in image-guided surgical applications (Daneshvaret al, 2008[50]; Charles and Cao,2008)[51]. In addition to being excellent fluorescent probes, these can be used as photoacoustic and photothermal contrast agents and sensitizers, thereby providing an opportunity for multimodal high-resolution (300 nm) photoacousticphotothermal fluorescent imaging as well as photothermal therapy (Shashkov et al, 2008)[52]. Q- dots have potential for the study of intracellular processes at the single-molecule level, high-resolution cellular imaging, long term in vivo observation of cell trafficking, tumour targeting, and diagnostics(Michalet et al, 2005[47]; Kaji et al, 2007)[53]. Human metaphase chromosomes from transformed lymphocyte cultures and breast cancer cell line SK-BR-3 were analyzed by fluorescence in situ hybridization based on streptavidin-linked CdSe Q-dots (Xiao and Barker, 2004[54]; Xiao et al, 2005)[55]. The use of streptavidincoupled Q-dots for live-cell imaging has also been reported (Lidke et al, 2007)[56]. Q-dots can be covalently linked with biorecognition molecules such as peptides, antibodies, nucleic acids, or small-molecule ligands for use as biological labels in molecular and cellular imaging (Bailey et al, 2004[57]; Smith et al, 2008)[58]. Biological applications of Q-dots include fluorescence resonance energy transfer analysis, gene technology, fluorescence labeling of cellular proteins, cell tracking, pathogen and toxin detection, and in vivo animal imaging (Patel et al , 2007[15]; Jamieson et al, 2007[59]; Walling et al, 2009[60]; Smith et al, 2006[25]; Michalet et al, 2008[61]; Medintz et al, 2008)[62].

3.4. *Ceramic nanoparticles*

Ceramic nanoparticles are particles fabricated from inorganic compounds with porous characteristics such as silica, alumina and titania (Orive et al, 2005[63]; Medina et al, 2007[64]; Rawat et al, 2006)[65]. They can be prepared with the desired size, shape and porosity. Their sizes are less than 100nm and are able to avoid uptake by the reticulo-endothelial system as foreign bodies. Entrapped molecules such as drugs, proteins and enzymes are protected from denaturation at physiological pH and temperature as neither swelling nor change in porosity occurs (Rawat et al, 2006)[65]. Hence, they are effective in delivering proteins and genes. However, these particles are not biodegradable and so there is concern that they may accumulate in the body and cause harmful effects(Medina et al, 2007)[64].Biodegradable biosilicon , being highly porous can release medicine slowly over a period of time (Fahmy et al, 2005) [66]; Kim and Nie, 2005[67]; Biondi et al, 2008)[68].

3.5. *Gold nanoparticles*

Gold exhibits favourable optical and chemical properties at nanoscale for biomedical imaging and therapeutic applications (Medina et al, 2007)[64]. It can be manipulated to obtain the desired size in the range of 0.8 to 200nm. The surface can be modified with different functional groups for gene transfection, modified into gene delivery vector by conjugation and also modified to target proteins and peptides to the cell nucleus (Xu et al, 2006,Liu et al, 2010)[69-70].

The strong plasmon absorption and photothermal conversion of gold nanoparticles has been exploited in cancer therapy through the selective localized photothermal heating of cancer cells, and in the case of gold nanorods or gold nanoshells, the localized surface plasmon resonance can be tuned to the near-

infrared region, making it possible to perform in vivo imaging and therapy (Jain at el, 2008[21]; Giersig and Khomutov, 2008[71]; De et al, 2008)[72]. When irradiated with focused laser pulses of suitable wavelength, targeted nanoshells, nanorods, and nanocages can kill bacteria and cancer cells (Cortie, 2004[18]; Cheon et al, 2014[73]; Cao, 2004[74]). The nanopartcles-antibody bioconjugates exhibited long-term resistance to agglomeration, and scientists described optical detection of antibody-conjugated nanoparticles bound to surgically resected human pancreatic cancer tissue (Nagarajan and Hatton, 2008)[75]. Gold nanoparticles having two kinds of functional molecules (cysteamine and thioglucose) significantly enhanced cancer killing (Woo and Moon, 2009)[76]. The nano shell-enhanced optical coherence tomography has the potential for molecular imaging and improved detection of diseases (Krumov et al, 2009)[77]. Au_3Cu_1nanoshells were reported to be capable of enhancing the contrast of blood vessels in vivo, which suggested their potential use in magnetic resonance angiography as blood pool agents (Li et al, 2008)[78]. Combination of local heating and polyethylene glycol (PEG)-coated gold nanoparticles loaded with tumor necrosis factor-α resulted in enhanced therapeutic efficacy over either treatment alone (Byrappa et al, 2008)[79]. Covalent coupling of gold nanoparticles to retargeted adenoviral vectors allowed selective delivery of the nanoparticles to tumour cells, thereby, showing promise for hyperthermia and gene therapy as a combinatorial therapeutic approach (Juillerat and Jeanneret, 2008)[80]. 20 nm gold nanoparticles coated with thioctic acid-terminated PEG (5000) showed promise as potential drug delivery vehicles and diagnostic imaging agents (Koper, 2002)[81].Utilization of gold nanocages for cancer detection and treatment results showed improved optical coherence tomography image contrast when these were added to tissue phantoms, as well as the selective photothermal destruction of breast cancer cells in vitro when immunotargeted gold nanocages were used (Geurts and Wagner, 2005)[82].

3.6. *Silver nanoparticles*

The nano-silver based wound dressing acticoat has been on the market since 1998 (Becker, et al, 2007)[83]. Silver(I) carbene complexes encapsulated in nanofibers are promising materials for sustained and effective delivery of silver ions with maximum bactericidal activity over a longer period of time primarily as part of wound- or burn-dressing materials (Kobayashi et al, 2009)[84]. Various synthetic routes currently used for developing stable silver nanoparticles and their diagnostic biomedical optical imaging and other biomedical applications have been reported (Willems and Wildenberg, 2005)[85]. The photophysical characteristics and electrochemiluminescence of the silver nanoparticle clusters give them remarkable advantages over larger nano particles in applications such as molecular sensing (Xu et al, 2006)[69]. Silver nanoparticles fabricated in HEPES buffer exhibit potent cytoprotective and postinfection anti-HIV-1 activities toward Hut/CCR5 cells (Müller, 2009)[86]. Nano-Ag sepiolite (low-melting-point soda-lime glass powder containing monodispersedsilver nanoparticles) powder exhibited a high antibacterial (against gram-positive and gram-negative bacteria) as well as antifungal activity (Hoshino et al, 2007)[87].

3.7. *Magnetic nanoparticles (MNPs)*

Magnetic nanoparticles (MNPs) are a major class of nanoscale materials with the potential to revolutionize current clinical diagnostic and therapeutic techniques. Magnetic nanoparticles include nanowires, nanospheres, nanotubes and magnetic thin films. Since the size, shape, orientation, distribution, etc. of the magnetic nanoparticles can be controlled by controlling the processing conditions it will be possible to tailor the particles for specific applications. Due to their unique physical properties and ability to function at the cellular and molecular level of biological interactions, these are being actively investigated as the next generation of magnetic resonance imaging (MRI) contrast agents (Corot et al, 2006)[88] and as carriers for targeted drug delivery (Pankhurst et al, 2003[89]; Dobson, 2006)[90]. With a wide range of applications in the detection, diagnosis, and treatment of illnesses, such as cancer (Lal et al, 2008[91];Ferrari , 2005)[92], cardiovascular disease (Wickline, 2007)[93], and neurological disease (Corot et al, 2004)[94], MNPs may play a significant role in meeting the healthcare needs (Vlerken and Amiji, 2006[95]; Kohler et al, 2005[96]; Wan et al, 2007[97]; Xu and Sun, 2007[98]; Pankhurst et al, 2003[89]; Arruebo et al, 2007[99]; Varadan et al, 2009[100]; Sun et al, 2008)[101].

The ability of MNPs to enhance proton relaxation of specific tissues and serve as MR imaging contrast agents is one of the most promising applications of nanomedicine. MNPs in the form of superparamagnetic iron oxides (SPIO) have been actively investigated as MR imaging contrast agents for over two decades (Weissleder et al, 1995)[102]. With applications, such as bowel contrast agents and liver/spleen imaging already on the market (Wang et al, 2001[103]; Bonnemain et al, 1998)[104], SPIOs have led the way for MNPs into the clinic.

Super paramagnetic iron oxides (SPIO) nanoparticles (15-60 nm) can be coated with dextran, phospholipids, or other compounds to inhibit aggregation and passive or active targeting agents (Gupta and Gupta, 2005)[105]. Upon controlled

surface functionalization and coupling with fragments of DNA strands, proteins, peptides, or antibodies, SPIO nanoparticles can be used for drug delivery, magnetic separation, MRI contrast enhancement, and MFH (Shubayev et al, 2009[106]; Xu and Sun, 2009[107]; Shankar et al, 2011[108]).As therapeutic tools, MNPs have been evaluated extensively for targeted delivery of pharmaceuticals through magnetic drug targeting (MDT) (Senyei et al, 1978[109]; Neuberger ,2005)[110] and by active targeting through the attachment of high affinity ligands (Torchilin, 2006[111]; Zhang et al, 2002[112]; Veiseh et al, 2005)[113].

MNPs have the potential to overcome limitations associated with systemic distribution of conventional chemotherapies. With the ability to utilize magnetic attraction and/or specific targeting of disease biomarkers, MNPs offer an attractive means of remotely directing therapeutic agents specifically to a disease site, while simultaneously reducing dosage and the deleterious side-effects associated with non-specific uptake of cytotoxic drugs by healthy tissue.

3.8. *Magnetic nanowires*

Most magnetic nanowires are compatible with living cells and can be functionalized with biologically active molecules. Their applications include biosensing and construction of nucleic acids sensors. Many efforts have been made to explore the applications of single segment and multiple-segment magnetic nanowires in biomedicine (Son et al, 2005)[114]. Compared to nanospheres, multifunctionality can be more easily realized on multi segment nanowires (Reich et al, 2003)[115]. Magnetic nanowires used in biomedicine are metal cylindrical electrode(s) positioned in nanoporoustemplates(Varadan et al, 2009)[100] and have shown potential for use in biosensing applications and construction of nucleic acids sensors(Lord et al, 2009)[116]. Functionalization with biomolecules involving two-segment nickel-gold nanowires served as synthetic gene delivery systems (Salem et al, 2003)[117]. The binding of pcDNA3 to the nickel segment of the nanorod provided a strong immune stimulatory adjuvant effect to the antigen bound on the gold segment (Salem *et al*, 2005)[118]. Separation of heterogeneous cell mixtures based on the differences in physical size of the cells has been achieved with magnetic nanowires (Hultgren et al, 2005)[118].

4. RISK OF NANOTECHNOLOGY

Despite the great potentials of nanotechnology, its safety in humans, animal and plants, and effects on the environment are of concern. Also, military application is of concern as chemical weapons fabricated from nanoparticles will be more deadly than present chemical weapons. This is due to the fact that the smaller a particle, the greater its impact either positively or negatively. Some nanoparticles show increased toxicity due to their increased surface area(Dunphy Guzman et al, 2006,52)[120]. Studies have shown carbon nanotubes to be cytotoxic and to induce granulomas in lungs of laboratory animals. Also, metals and metallic oxide nanoparticles such as copper, cobalt, titanium oxide and silicon oxide have inflammatory and toxic effects on cells (Dunphy Guzman et al, 2006,52)[120]. However, studies and debates are going on about the benefits and risks of nanotechnology (Cobb and Macoubrice , 2004[121], Roco, 2003[4], Oberdörster et al, 2005, 53-55.)[122] Optimistically, the benefits of nanotechnology are enormous and so studies which include the health, environmental, ethical and safety issues should indicate how to maximize the benefits and reduce the risks. Macro- and microtechnologies had their risks, yet the benefits were accepted.

5. CONCLUSION

This review has summarized the major types of nano materials that have potential applications in various ailments and targeted drug delivery. The application of nanotechnology to medicine is a rapidly developing area of investigation. In the near future, it appears highly likely that nanotechnology will play an important role in assessment and treatment of various diseases. Indeed, some of the nanomaterial-based therapies and diagnostics presented here outperform conventional materials in terms of efficacy, reliability, and practicality. Continued optimization of nanomaterial properties will be necessary to determine the applicability of these methods in modern healthcare practice. Nano particles of various formulations have been developed to diagnose and treat diseases for which conventional therapy has shown limited efficacy. In particular, the use of nano particles as MRI contrast agents and drug carriers have drawn enormous attention, as it holds great potential of providing new opportunities for early cancer detection and targeted therapies. Keeping in view the diversity of engineered nano particles, their several possible side effects should not be overlooked. Further research is required on the interaction of nanomaterials with biological systems from the perspective of safe use of nanomaterials. Experts are of the opinion that nanomaterials have the potential to provide revolutionary methods for the prevention, diagnosis, and treatment of some fatal diseases.

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REFERENCES

[1] Stylios, G. K,; Giannoudis P.V., Wan, T. (2005): Applications of nanotechnologies in medical practice. Injury, **36** (4), pp. 6-13.

[2] The Royal Soc. & The Royal Acad. of Engineering (2004). Nanoscience and nanotechnologies: opportunities and uncertainties, The Royal Soc. &The Royal Acad. of Engg. Report, pp. 1-116. http, //www.nanotec.org.uk/finalReport.html

[3] Weller, H. (1993). Colloidal semiconductor Q-particles: Chemistry in the transition region between solid state and molecules.Angew. Chem., **32**, pp. 41-53.

[4] Roco, M. C. (2003). Nanotechnology, pp. Convergence with modern biology and medicine. Curr. Opinion Biotech., **14**, pp. 337-346

[5] Miyazaki, K.; Islam, N. (2007). Nanotechnology systems of innovation - An analysis of industry and academia research activities. Technovation., **27**, pp. 661-671.

[6] Pitkethly, M. J. (2004). Nanomaterials- the driving force. Nanotoday, **7**, pp. 20-29

[7] Rittner, M. N. (2001). Opportunities in nanostructured materials, GB-201, Part A: Electronic, Optoelectronic, and Magnetic Applications; Part B: Biomedical, Pharmaceutical, and Cosmetic Applications; and Part C: Energy, Catalytic and Structural Applications. Business communications Co. Inc., Norwalk, CT, USA.

[8] Holister, P.; Harper, T. E. (2002). The Nanotechnology Opportunity Report, CMP Cientifica, Madrid.

[9] Jones, A,; Mitchell, M. (2001). Nanotechnology: Commercial opportunity, Evolution Capital Ltd., London.

[10] Williams, D. (2008). The relationship between biomaterials and nanotechnology. Biomaterials, **29**(12), pp. 1737-1738

[11] Zong, R. L.; Zhou, J.; Li, B.; Fu, M.; Shi, S. K.; Li, L. T. (2005). Optical properties of transparent copper nanorod and nanowire arrays embedded in anodic alumina oxide. J. Chem. Phys., **123**, pp. 094710-094715.

[12] Gao, S.; Zhao, Y.; Gou, P.; Chen, N.; Xie, Y. (2003). Preparation of $CuAlO_2$nanocrystalline transparent thin films with high conductivity. Nanotechnology, **14**, pp. 538-541.

[13] Luo, J.; Maye, M. M.; Kariuki, N. N.; Wang, L.; Njoki, P.; Lin, Y.; Schadt, M.; Naslund, H. R.; Zhong, C. J. (2005). Electrocatalytic oxidation of methanol: carbon supported gold-platinum nanoparticles catalysts prepared by two-phase protocol. Catalysis Today, **99** (3-4), pp. 291-297.

[14] Tian, N.; Zhou, Z. Y.; Sun, S. G.; Ding, Y.; Wang, Z. L. (2007). Synthesis of tetrahexahedral platinunanocrystals with high-index facets and high electro-oxidation activity. Science, **316**, pp. 732-735.

[15] Patel HR, Patel M, Patel G, Patel GN, Patel NJ (2007). Quantum dots: A novel technique for drug delivery and therapy. Pharmainfo. net., **5** (6).

[16] Hu, X.; Guo, T.; Fu, X.; Hu, X. (2003). Nanoscale oxide structures induced by dynamic electric field on Si with AFM. Applied Surface Science, **217**(1-4), pp. 34-38.

[17] Heron, J. S.; Fournier, T.; Bourgeois, O. (2007). Surface effect on the phonon transport of silicon nanowire. J. Physics, pp. Conferences Series, **92**, pp. 1-4.

[18] Cortie, M, B. (2004). The weird world of nanoscale gold. Gold Bull., **37**, pp. 12-19

[19] Cortie, M. B. van der Lingen E (2002). Catalytic gold nanoparticles. Materials Forum, **26**, pp. 1-14

[20] Overbury, S. (2005). Catalysis at the nanoscale. Oakridge National Laboratory Review, **38** (3).

[21] Jain, P. K.; Huang, X.; El-Sayed, I. H.; El-Sayed, M. A. (2008). Noble metals on the nanoscale: optical and photothermal properties and some applications in imaging, sensing, biology and medicine. Accounts of Chemical Research, **30** (20).

[22] Kreuter, J. (1994). Encyclopedia of Pharmaceutical technology, **10**, pp. 165, Dekker, New York

[23] Roco, M. C. (1999). Towards a US National Nanotechnology Initiative. J Nanoparticle Res, **1**, pp. 435-438.

[24] Yin, J. (2007). Chemical engineering and virology, pp. challenges and opportunities at the interface. Am. Inst. Chem. Eng J, **53** (9), pp. 2202-2209.

[25] Smith, A. (2006). Nanotechnology, pp. lessons from Mother Nature. Chemistry International, **28**(6), pp. 10-11.

[26] Bittner, A. M. (2005). Biomolecular rods and tubes in nanotechnology. Natyrwissenschaften, **92**, pp. 51-64.

[27] Sahoo, S. K.; Parveen, S.; Panda, J. J. (2007). The present and future of nanotechnology in human health care. Nanomedicine, pp. NBM, **3**, pp. 20-31.

[28] Matija, L. (2004). Reviewing paper, pp. Nanotechnology, pp. Artificial versus natural self-assembly. Fac Mech Eng (FME) Trans, **32**, pp. 1-14.

[29] Visakhapatnam PTI (2008). Indian craftsmen, artisans used nanotech 2000 years ago.

http://www.deccanherald.com/Content/Jan62008/national2008010645193.asp?section=updatenews.

[30] Faraday, M. (1847). The Bakerian lecture: Experimental relations of gold (andother metals) to light. Phil. Trans. R. Soc.Lond.**147**, pp. 145-181.

[31] Wikipedia, History of Nanotechnology. Wikipedia:Free encyclopaedia. http, pp. //en.wikipedia.org/wiki/History of bnanotechnology.

[32] Zsigmondy, R. A. (1926). Properties of Colloids. Nobel Lecture, December 11. 1926. http://nobelprize.org/nobel prizes/chemistry/laureates/1925/zsigmondy-lecture.pdf.

[33] Horber, J. K.; Miles, M. J. (2003). Scanning probe evolution in biology. Science, **302**, pp. 1002-1005.

[34] Karoutsos, V. (2009).Scanning probe microscopy: Instrumentation and applications on thin films and magnetic multilayers. J. Nanosci. Nanotechnol., **9**, pp. 6783-6798.

[35] Roco, M. C. (2004). The US national nanotechnology initiative after 3 years (2000-2003). J. Nanoparticle Res., **6**, pp. 1-10.

[36] Sharon, Sharon. (2007). Nano forms of Carbon, 1st Ed., Monad Nanotech Pvt. Ltd, India.

[37] Winau, F.; Westphal, O.; Winau, R. (2004). Paul Ehrlich - in search of the magic bullet. Microbes Infect., **6**, pp. 786-789.

[38] Vasir, J. K.; Reddy, M. K.; Labhasetwar, V. D. (2005). Nanosystems in drug targeting: Opportunities and challenges. Curr. Nanosci., **1**, pp. 47 – 64

[39] Singh, R.; Pantarotto, D.; McCarthy, D.; Chaloin, O.; Hoebeke, J.; Partidos, C. D. (2005). Binding and condensation of plasmid DNA onto functionalized carbon nanotubes: toward the construction of nanotube- based gene delivery vectors. J. Am. Chem. Soc., **127**, pp. 4388 -4396

[40] Hirsch, West J. L. (2003). Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance. Proc Natl. Acad. Sci. U S A, **100**, pp. 13549 - 13554.

[41] Zhou, W. L.; Gao, P.; Shao, L.; Caruntu, D.; Yu, M.; Chen, J. F.; O'Connor, C. J. (2005). Drug loaded magnetic, hollow silica nanocomposites for nanomedicine. Nanomedicine, **1**(3), pp. 233-237

[42] Zheng, Y.; Gao, S.; Ying, J. Y. (2007). Synthesis and cell-imaging Applications of glutathione-capped CdTe quantum dots. Adv. Mater. **19**, pp. 376-380.

[43] Smith, A. M.; Gao, X.; Nie, S. (2004). Quantum dot nanocrystals for in vivo molecular and cellular imaging. Photochem. Photobiol. **80**, pp. 377-385.

[44] Alivisatos, A. P.; Gu, W.; Larabell, C. (2008)**.** Quantum dots as cellular probes. Annu. Rev. Biomed. Eng., **7**, pp. 55-76.

[45] Ying, J. Y.; Zheng, Y.; Selvan, S. T. (2008). Synthesis and applications of quantum dots and magnetic quantum dots. Proc. SPIE, 6866, pp. 02.

[46] Medintz, I. L.; Uyeda, H. T.; Goldman, E. R.; Mattoussi, H. (2005). Quantum dot bioconjugates for imaging, labelling and sensing. Nat. Mater., **4**, pp. 435-446.

[47] Michalet, X.; Pinaud, F. F.; Bentolila, L. A.; Tsay, J. M.; Doose, S.; Li, J. J. (2005). Quantum dots for live cells, *in vivo* imaging, and diagnostics. Science, **307**, pp. 538-544.

[48] Somers, R. C.; Bawendi, M. G.; Nocera, D. G. (2007). CdSe nanocrystal based chem-bio-sensors. Chem. Soc. Rev., **36**; 579-591.

[49] Alivisatos, A. P.; Gu, W.; Larabell, C. (2005). Quantum dots as cellular probes. Annu Rev Biomed Eng.**7**, pp. 55-76.

[50] Daneshvar, H.; Nelms, J.; Muhammad, O.; Jackson, H.; Tkach, J.; Davros, W.; Peterson, T.; Vogelbaum, M. A.; Bruchez, M. P.; Toms, S. A. (2008). Imaging characteristics of zinc sulfide shell, cadmium telluride core quantum dots. Nanomed., 3, pp. 21-29.

[51] Charles, Y.; Cao, Y. C. (2008). Nanomaterials for biomedical applications. Nanomed., **3**, pp. 467-469.

[52] Shashkov, E. V.; Everts, M.; Galanzha, E. I.; Zharov, V. P. (2008). Quantum dots as multimodal photoacoustic and photothermal contrast agents. Nano Lett. **8**, pp. 3953-3958

[53] Kaji, N.; Tokeshi, M.; Baba, Y. (2007). Quantum dots for single bio-molecule imaging. Anal. Sci., **23**, pp. 212-214.

[54] Xiao, Y.; Barker, P. E. (2004). Semiconductor nanocrystal probes for human metaphase chromosomes. Nucleic Acids Res., **32**, pp. 1-5.

[55] Xiao, Y.; Telford, W. G.; Ball, J. C.; Locascio, L. E.; Barker, P. E. (2005). Semiconductor nanocrystal conjugates, FISH and pH. Nat Methods, **2**(10), pp. 723.

[56] Lidke, D. S.; Nagy, P.; Arndt-Jovin, D. J. (2007). In vivo imaging using quantum dot-conjugated probes. Curr. Protoc. Cell Biol., **36**, pp. 25.1.1-25.1.18.

[57] Bailey, R. E.; Smith, A. M.; Nie, S. (2004). Quantum dots in biology and medicine. Physica E., **25**, pp. 1-12.

[58] Smith, A. M.; Duan, H.; Mohs, A. M.; Nie, S. (2008). Bioconjugated quantum dots for in vivo molecular and cellular imaging. Adv. Drug Deliv. Rev., **60**, pp. 1226-1240

[59] Jamieson, T.; Bakhshi, R.; Petrova, D.; Pocock, R.; Imani, M.; Seifalian, A. M. (2007). Biological applications of quantum dots. Biomater., **28**, pp. 4717-4732.

[60] Walling, M A.; Novak, J. A.; Shepard, J. R. E. (2009). Quantum dots for live cell and in vivo imaging. Int. J. Mol. Sci., **10**, pp. 441-491

[61] Michalet, X.; Bentolila, L. A.; Weiss, S. (2008). Molecular imaging: Physics and bio applications of quantum dots, Chapter 8.

[62] Medintz, I. L.; Mattoussi, H.; Clapp, A. R. (2008). Potential clinical applications of quantum dots. Int. J. Nanomed., **3**, pp. 151-167.

[63] Orive, G.; Hernandez, R. M.; Gascon, A. R.; Pedraz, J. L. (2005). Micro and nano drug delivery systems in cancer therapy. Cancer Therapy, **3**, pp. 131- 138.

[64] Medina, C.; Santos-Martinez, M. J.; Radomski, A.; Corrigan, O. I.; Radomski, M. W. (2007). Nanoparticles: Pharmacological and toxicological significance. Br. J. Pharmacol., **150**, pp. 552-558.

[65] Rawat, M.; Singh, D.; Saraf, S.; Saraf, S. (2006). Nanocarriers, pp. promising vehicle for bioactive drugs. Biol. Pharm. Bull., **29**(9), pp. 1790-1798

[66] Tarek, M. Fahmy.; Peter, M. Fong.; Amit, Goyal.; Saltzman, W. Mark. (2005), Materials today: Targeted for drug delivery. **8**, pp. 18-16

[67] Kim, G. J.; Nie, S. (2005). Targeted cancer nanotherapy, Materials today, 8, 28-33.

[68] Biondi, M.; Ungaro, F.; Quagil,a F.; Netti, P. A. (2008). Controlled drug delivery in tissue engineering, Adv. Drug Deliv. Rev., **60**, pp. 229-242.

[69] Xu, Z. P.; Zeng, Q. H.; Lu, G. Q.; Yu, A. B. (2006). Inorganic nanoparticles as carriers for efficient cellular delivery. Chem.Eng. Sci., **61**, pp. 1027-1040

[70] Gang, Liu.; Magdalena, Swierczewska.; Seulki, Lee.; Xiaoyuan, Chena. (2010) Nano Today, pp. functional nanoparticles for molecular imaging guided gene delivery, **5**(6), pp. 524–539.

[71] Giersig, M.; Khomutov, G. B. (2008). Nanomaterials for application in medicine and biology (NATO Science for Peace and Security Series B: Physics and Biophysics), 1st ed. Springer.

[72] De, M.; Ghosh, P. S.; Rotello, V. M. (2008). Applications of nanoparticles in biology. Adv. Mater., **20**, pp. 4225-4241.

[73] Jongpil, Cheon.; Sungwon, Chung.; Steven, M. Crooks.; Jaeki, Song.; Jeakyeong, Kim. (2014). Educational Technology & Society: An Investigation of the Effects of Different Types of Activities during Pauses in a Segmented Instructional Animation, pp. **17** (2), 296–306.

[74] Cao, G. (2004). Nanostructures & nanomaterials, Synthesis, properties & applications, Imperial College Press, 1st edn.

[75] Nagarajan, R.; Hatton, T. A. (2008). Nanoparticles: Synthesis, stabilization, passivation and functionalization. ACS Symposium Series 996, Oxford University Press Inc, USA.

[76] Woo, K.; Moon, J. (2009)**.** Method for the production of bio-imaging nanoparticles with high yield by early introduction of irregular structure.

[77] Krumov, N.; Perner-Nochta, I.; Oder, S.; Gotcheva, V.; Angelov, A.; Posten, C. (2009). Production of inorganic nanoparticles by microorganisms. Chem. Eng. Technol., **32**, pp. 1026-1036.

[78] Li, Z.; Jia, Z.; Luan, Y.; Mu, T. (2008). Ionic liquids for synthesis of inorganic nanomaterials. Curr.Opin.SolidState Mater. Sci., **12**, pp. 1-8.

[79] Byrappa, K.; Ohara, S.; Adschiri, T. (2008). Nanoparticles synthesis using supercritical fluid technology - towards biomedical applications. Adv. Drug Deliv. Rev., **60**; pp. 299-327.

[80] Juillerat-Jeanneret, L. (2008). The targeted delivery of cancer drugs across the blood-brain barrier, pp. chemical modifications of drugs or drug-nanoparticles? Drug Discov. Today, **13**, pp. 1099-1106.

[81] Koper, O. B.; Klabunde, J. S.; Marchin, G. L.; Klabunde, K. J.; Stoimenov, P.; Bohra, L. (2002). Nanoscale powders and formulations with biocidal activity toward spores and vegetative cells of bacillus species, viruses, and toxins. Curr. Microbiol., **44**, pp. 49-55.

[82] Geurts, J.; Wagner, V. (2005). Raman analysis of embedded monolayers and quantum dots. Phys. Status Solidi B., **242**, pp. 2644-2649.

[83] Becker, C.; Hodenius, M.; Blendinger, G.; Sechi, A.; Hieronymus, T.; Muller- Schulte, D.; Schmitz-Rode, T.; Zenke, M. (2007). Uptake of magnetic nanoparticles into cells for cell tracking. J. Magn. Magn. Mater., **311**, pp. 234-237.

[84] Kobayashi, T.; Hirai, H.; Iino, M.; Fuse, I.; Mitsumura, K.; Washiyama, K.; Kasai, S.; Ikeda, K. (2009) Neuropharmacology, pp. nhibitory effects of the antiepileptic drug ethosuximide on G protein-activated inwardly rectifying K+ channels. **56** (2), pp. 499-506.

[85] Willems; van den, Wildenberg. (W&W) (2005). Roadmaps at 2015 on nanotechnology application in the sectors of materials, health & medical systems, energy.

[86] Muller, J.; Huaux, F.; Lison, D. (2006). Respiratory toxicity of carbon nanotubes, pp. how worried should we be? Carbon, **44**(6), pp. 1048-1056.

[87] Hoshino, K.; Ly, H. Q.; Frangioni, J. V.; Hajjar, R. J. (2007). In vivo tracking in cardiac stem cell-based therapy. Prog. Cardiovasc. Dis., **49**, pp. 414-420.

[88] Corot C, Robert P, Idee JM, Port M(2006). Recent advances in iron oxide nanocrystal

technology for medical imaging. Adv. Drug Deliv. Rev., **58**, pp. 1471-1504.

[89] Pankhurst QA, Connolly J, Jones SK, Dobson J (2003). Applications of magnetic nanoparticles in biomedicine. J. Phys. D, pp. Appl. Phys., **36**, pp. 167-181.

[90] Dobson, J. (2006). Magnetic nanoparticles for drug delivery.Drug Dev. Res., **67**, pp. 55-60.

[91] Lal, S.; Clare, S. E.; Halas, N. J. (2008). Nanoshell-enabled photothermal cancer therapy, pp. impending clinical impact. Acc. Chem. Res., **41**, pp. 1842-1851

[92] Ferrari, M. (2005). Cancer nanotechnology, pp. Opportunities and challenges. Nature Reviews Cancer, **5**, pp. 161-171.

[93] Wickline, S. A.; Neubauer, A. M.; Winter, P. M.; Caruthers, S. D.; Lanza, G. M. (2007). Molecular imaging and therapy of atherosclerosis with targeted nanoparticles. J Magn. Reson. Imaging, **25**, pp. 667- 680

[94] Corot, C.; Petry, K. G.; Trivedi, R.; Saleh, A.; Jonkmanns, C.; Le, J. F.; Blezer, E.; Rausch, M.; Brochet, B.; Foster-Gareau, P.; Baleriaux, D.; Gaillard, S.; Dousset, V. (2004). Macrophage imaging in central nervous system and in carotid atherosclerotic plaque using ultra small superparamagnetic iron oxide in magnetic resonance imaging. Invest. Radiol., **39**, pp. 619-625

[95] vanVlerken, L. E.; Amiji, M. M. (2006). Multi-functional polymeric nanoparticles for tumour-targeted drug delivery. Expert Opin. Drug Delivery, **3**, pp. 205-216.

[96] Kohler, N.; Sun, C.; Wang, J.; Zhang, M. (2005). Methotrexate-modified super paramagnetic nanoparticles and their intracellular uptake into human cancer cells. Langmuir, **21**, pp. 8858-8864.

[97] Wan, J.; Cai, W.; Meng, X.; Liu, E. (2007). Monodisperse water-soluble magnetite nanoparticles prepared by polyol process for high-performance magnetic resonance imaging. Chem.Commun., 5004 -5006.

[98] Xu, C.; Sun, S. (2007). Monodisperse magnetic nanoparticles for biomedical applications. Polym. Int., **56**, pp. 821-826

[99] Arruebo, M.; Fernandez-Pacheco, R.; Ricardo-Ibarra, M.; Santamarıa, J. (2007). Magnetic nanoparticles for drug delivery. Nanotoday, **2**, pp. 22-32.

[100] Varadan, V. K.; Chen, L.; Xie, J.; Abraham, J. (2009). Magnetic nanowires and their biomedical applications in Nanomedicine: Design and applications of magnetic nanomaterials, nanosensors and nanosystems, John Wiley and Sons Ltd, Chapter **6**, pp. 215-272.

[101] Sun, C.; Lee, J. S. H.; Zhang, M. (2008). Magnetic nanoparticles in MR imaging and drug delivery. Adv. Drug Deliv. Rev. **60**, pp. 1252-1265

[102] Weissleder, R.; Bogdanov, A.; Neuwelt, E. A.; Papisov, M. (1995). Long-Circulating Iron-Oxides for Mr-Imaging. Adv. Drug Deliv. Rev.,**16**, pp. 321-334.

[103] Wang, Y. X.; Hussain, S. M.; Krestin, G. P. (2001). Super paramagnetic iron oxide contrast agents, pp. physicochemical characteristics and applications in MR imaging. Eur. Radiol., **11**, pp. 2319-2331.

[104] Bonnemain, B. (1998). Super paramagnetic agents in magnetic resonance imaging, pp. Physicochemical characteristics and clinical applications - A review. J. Drug Target.,**6**, pp. 167-174.

[105] Gupta, A. K.; Gupta, M. (2005). Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. Biomater., **26**, pp. 3995-4021.

[106] Shubayev, V. I.; Pisanic, T. R.; Jin, S. (2009). Magnetic nanoparticles for theragnostics. Adv. Drug Deliv. Rev., **61**, pp. 467-477.

[107] Xu, C.; Sun, S. (2009). Super paramagnetic nanoparticles as targeted probes for diagnostic and therapeutic applications. Dalton Trans., pp. 5583-5591.

[108] Swetha, Shankar.; Dino, P. Massoglia.; Dantong, Zhu.; Gabriela, C. M.; Terrence, R. Stanford, and Emilio Salinas (2011). Tracking the Temporal Evolution of a Perceptual Judgment Using a Compelled-Response Task, The Journal of Neuroscience., **31**(23) , pp. 8406 – 8421

[109] Senyei, A.; Widder, K.; Czerlinski, G.; Magnetic guidance of drug-carrying microspheres (1978). J. Appl. Physiol., **49**, pp. 3578-3583.

[110] Neuberger, T.; Schopf, B.; Hofmann, H.; Hofmann, M.; von Rechenberg, B. (2005). Superparamagnetic nanoparticles for biomedical applications, pp. Possibilities and limitations of a new drug delivery system. J. Magn. Magn. Mater., **293**, pp. 483-496.

[111] Torchilin, V. P. (2006). Multifunctional nanocarriers. Adv. Drug Deliv. Rev. **58**, pp. 1532-1555.

[112] Zhang, Y.; Kohler, N.; Zhang, M. Q. (2002). Surface modification of super paramagnetic magnetite nanoparticles and their intracellular uptake. Biomaterials, **23**, pp. 1553-1561

[113] Veiseh, O.; Sun, C.; Gunn, J.; Kohler, N.; Gabikian, P.; Lee, D.; Bhattarai, N.; Ellenbogen, R.; Sze, R.; Hallahan, A.; Olson, J.; Zhang, M. Q. (2005). Optical and MRI multifunctional nanoprobe for targeting gliomas. Nano Lett., **5**, pp. 1003-1008.

[114] Son, S. J.; Reichel, J.; He, B.; Schuchman, M.; Lee, S. B. (2005). Magnetic nanotubes for magnetic-field assisted bioseparation, bio-

interaction, and drug delivery. J. Am. Chem. Soc., **127**, pp. 7316-7317.

[115] Reich, D. H.; Tanase, M.; Hultgren, A.; Bauer, L. A.; Chen, C. S.; Meyer, G. J. (2003). Biological applications of multifunctional magnetic nanowires. J. Appl. Phys., **93**, pp. 7275-7280

[116] Lord, H.; Kelley, S. O. (2009). Nanomaterials for ultrasensitive electrochemical nucleic acidsbiosensing. J. Mater. Chem., **19**, pp. 3127-3134.

[117] Ben, Salem, H.; Ben, Salem, I.; Nefzaoui, A.; Ben, Said. M. S. (2003). Effect of PEG and olive cake feed blocks supply on feed intake, digestion, and health of goats given kermes oak (Quercus coccifera L.) foliage. Anim. Feed Sci. Technol., **110** (1), pp. 45-59

[118] Salem, A. K.; Hung, C. F.; Kim, T. W.; Wu, T. C.; Searson, P. C.; Leong, K. W. (2005). Multi-component nanorods for vaccination applications. Nanotechnology, **16**, pp. 484-487.

[119] Hultgren, A.; Tanase, M.; Felton, E. J.; Bhadriraju, K.; Salem, A. K.; Chen, C. S.; Reich, D. (2005). Optimization of yield in magnetic cell separations using nickel nanowires of different lengths. Biotech. Prog., **21**, pp. 509-515

[120] Dunphy, Guzman, K. A.; Taylor, M. R.; Banfield, J. F. (2006). Environmental risks of nanotechnology, pp. National nanotechnology initiative funding, 2000-2004. Environ. Sci. Technol., **40**, pp. 1401-1407.

[121] Cobb, M. D.; Macoubrice, J. (2004). Public perceptions about nanotechnology, pp. risks, benefits and trust. J. Nanoparticle Res., **6**, pp. 395-405.

[122] Oberdorster, G.; Oberdorster, E.; Oberdorster, J. (2005). Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Env. Health Perspectives, **111**(7) , pp. 823-839