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NANOTECHNOLOGY AND ITS APPLICATION IN MEDICAL SCIENCES

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ABSTRACT

Nanotechnology is technology of controlling structure of material at reduced dimensional scale at individual molecule level. Its application in life sciences research, at cell level sets exciting role in healthcare and diagnosis. Some unique nano materials are carbon nanotubes and inorganic nanowires. Quantum dots nanocrystals possess remarkable electronic properties by changing their size, due to this it is used in biomedical imaging applications. Dendrimers have improved physical, chemical and biological properties compared to traditional polymers, because of its shape and presence of internal cavities it can be used as nanovehicles.

KEYWORDS: Nano Technology,

Nano technological approach presents revolutionary opportunity to fight many diseases like Diabetes mellitus, neurodegenerative diseases as well as detecting virus or microorganisms causing infections. Nano particle mediated transport across blood brain barrier can provide treatment to brain tumour and even to Alzheimer's and Parkinson's disease.

Another important field of application of nanotechnology are biomaterials used in orthopaedic or dental implants. Nanopores are finding use as new nanoscale technology for cancer detection. Over next 10-15 years nanotechnology may transform science technology and society offering significant opportunity to enhance human health. The safety of nanomedicine is not yet fully defined. However, it is possible that nanomedicine in future would play a crucial role in treatment of many human diseases and enhancement of natural human physiology.

Nanotechnology is an emerging technology which has an impact on every aspect of life. All natural materials and systems establish their basic units in nanoscale. All the natural materials have their basic entities in nanoscale while the non natural material faces many challenges. However, nanotechnology is more than miniaturization.

Many revolutionary applications such as novel sensing technologies, implant technologies are currently being developed. Most significant impact of nanotechnology will be at biomaterials. It will fundamentally restructure the technologies currently used for manufacturing medicine, communication, transportation and many other application areas .The aim of nanomedicine may be broadly defined as the comprehensive monitoring, control, construction, repair, defence and improvement of all biological systems working from molecular level using engineered devices.

The term nanotechnology was first defined by Tokyo Science University, Norio, Taniguchi in a 1974 paper [Taniguchi, 1974]. As per Rice University, there are three types of nanotechnologies-

a) Wet nanotechnology is study of biological system that primarily exists in water environment.
b) Dry nanotechnology focuses on carbon, silicon and inorganic materials.
c) Computational nanotechnology permits modelling and stimulation of complex nanometer scale structures.

HISTORY

The first results related to development of nano medicine could be identified in late 60's at ETH Zurich [Kreuter, 2007]. During early 2000's European science Foundation showed that nanotechnology if applied to medicine bring revolution in diagnosis and disease treatment. In June 2003, some commissioned academies to investigate about certain issues ethical, health or safety in relation to nanotechnology. The final report was published in July 2004 with 21 recommendations for a sure, safe and responsible development of nanotechnology [UKRS and RAE, 2004].

In 2004, The Commission of the European Communities released its communication on European strategy for nanotechnology [CECC, 2004]. On other side the Atlantic Ocean, the National Institutes of Health (NIH) released their first roadmap on nanomedicine in 2004. [NIH, 2004] NIH later in 2005 and 2006 established eight nanomedicine Development Centres, which served the purpose of centrepiece of NIH Nanomedicine Roadmap Initiative.

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In 2004 The National Cancer Institute (NCI) as a part of NIH, launched the cancer nanotechnology plan, a strategic initiative to transform clinical oncology and basic research through directed application of nanotechnology. NCI Alliance for cancer is a comprehensive, systematised initiative encompassing both public and private sector to increase use of nanotechnology in cancer diagnosis and treatment.

NANOMATERIALS

Nanomaterials can be categorised as organic and inorganic types. Organic head is as follows-

1) C_{60}- In 1985 the discovery of existence of a perfectly symmetrically arranged carbon atoms was a major breakthrough and open a novel field of carbon chemistry (Kroto et. Al, 1985). This molecule was formally called buckminster fullerene after American architect Buckminster Fuller. It is produced by vapourisation of graphite into helium using laser beam. C_{60} is easiest to produce and cheapest.
2) Carbon nanotubes- It is considered as fourth allotrope of carbon. They are considered as elongated fullerenes carbon nanotubes rolled up, highly ordered hexagonal carbon honeycomb sheets, which on its end may be open or closed. Technologies like electric arc discharge (Ebbessen and Ajayan, 1992), Laser ablation (Thess et al 1998) and chemical vapour deposition (Kong et al 1998).
3) Other carbon nanotube based material- Carbon atom in all types of nanotubes can be substituted with another element such as boron and nitrogen. Synthesis of Boron or Nitrogen doped carbon nanotubes was first reported in 1994.

INORGANIC MATERIAL

1) fullerene like molecule-synthesis and structural characterisation of soluble and entirely inorganic spherical fullerene like molecule have been reported incorporating copper, chlorine, iron, carbon, phosphorus and nitrogen (Bai et.al.2004).
2) Inorganic nanowires- Nanowires have no inner cavity. It can be synthesised using large variety of material as metal like silver, bismuth, cadmium and large variety of semiconductors viz. zinc.
3) Quantum dots-These are spherical nanosized crystals, can be almost with all semiconductor metal (cds, cdTe, ZnS), alloys can also be used. Quantum dots varies in size from 2 to 10 nm in diameter. Quantum dots have core made up of semiconductor, coated by ZnS.
4) Dendrimers- Derived from word Dendron: tree, so these are synthetic, complex, spherical molecules with very well defined chemical structures first synthesised in early 1980's. The first dendritic structure thoroughly investigated were polyamidoamine (PAMAM) dendrimers also known as Starbust dendrimer.

NANOMEDICAL APPLICATIONS

a) In vitro diagnostics- Traditionally to study blood, body fluids or tissue samples in vitro is intensively laborious work, sometimes the sample deteriorates and sometime procedure prove to be time consuming (for even urgent cases), may harvest inaccurate results. On the contrary nanotechnology requires smaller samples and harvest POC (point of care) diagnostics.

- In vitro tool of diagnosis can be single biosensor or many integrated biosensors. This biosensor contains biological liquid which signals specific biological molecule in solution and a transducer convert these signals to quantifiable signal.
- Some devices for diagnostics have been developed to measure parts of genome using DNA fragments as reusing elements called gene chip.

b) In vivo diagnostics- Traditionally imaging technique could detect only appearance of tissue (diseased) later contrast agents were introduced to identify locus of disease. On the contrary application of nanotechnology refines imaging tools and contrast agents towards end goals of detecting disease even at single cell level.

- This technique helps in identification of location of locus of inflammation, developing tumour and visualisation of vascular structure.

Present imaging methods detects cancer and metastasis, but for confirming whether tumour is malignant or benign, or it requires biopsy. If nanotechnology is applied following would be achieved-

- Specifically identification of cancerous cells.
- Enable to be seen.

IMPLANTS

Monitoring of swallowable imaging 'pill' shows circulating nanomolecules in diseases like Diabetes/ AIDS. Nanobiopsies allow to determine type of tumour specially brain tumour which is difficult to diagnose. To map brain tumour, nano patterned pen collect protein from brain fluid. These floating cells get

removed from target area in brain, without removing brain tissue.

NANOPHARMACEUTICALS

Now - a - days third generation vectors (still underdeveloped) combining bio-degradable core and a polymer envelope (PEG) with membrane recognition legend has been used. Nanoparticles can be used as drug carriers for chemotherapeutics to deliver medications directly to tumour while sparing healthy tissues. [Christine, 2008]

Nanocarriers presents following advantages-

- Drug reaches target cell without being degraded.
- Enhance drug absorption in cancer cells.
- Avoid side effects and its interaction with normal cells.

A. Passive targeting- It works on "Enhanced permeability and retention". Certain tumours tend leads to leaky blood vessels causing nanoparticles to seep to site of damage and accumulate, thereby reducing accumulation of cytotoxic drug and reducing its side effects.

B. Active targeting- Molecules that bind particular cellular receptor can be attached to a nanoparticle so that it particularly targets receptors. It can also be used to bring drugs into cancerous cells.

C. Destruction within- In this technique nanoshells are used to destroy tumours thermally. Infra-red light selectively kills tumour cells without disturbing surrounding healthy cells.

D. Drug delivery device- Nanopumps are tested for insulin delivery. The precision of nanofabrication of ultra small devices with reservoirs and release pharmaceutical ingredients

REGENERATIVE MEDICINE-

It is process of regenerating tissues or organs which have lost their fractions due to age, disease, damage or some genetic defects. Regenerative medicine could also empowers physicians to grow tissues and organs in laboratory and safely implant them when body can not heal by itself.[NIH, 2006] Under this category stem cells exhibit enormous self repair potential and claim to be regenerative medicine in future. Another regenerative medicine is biomaterial. Nanotechnology covers the fabrication of materials, such as nanoparticles and scaffolds for tissue engineering, and surface nano patterning to elicit specific biological responses from host tissues [Elisabeth, 2008].

NANOTECHNOLOGY IN GENE THERAPY

Gene therapy is a newer modality of approach for treatment of many genetic disorders including Diabetes mellitus [Niu et.al., 2008] cystic fibrosis [Davis and Cooper, 2007] and alpha 1 antitrypsin deficiency Viral vectors used for gene transfer have the limitations of safety concerns and stimulation of immune system with production of antibodies against viral vectors. Further, naked DNA cannot cross negatively charged cell membrane as these are also negatively charged [Pathak et.al., 2008, Arruda et.al., 2004]. Hence there is a need of some mode to transfer genetic material like nanoparticle based gene therapy.

Nieu et. al. used human insulin in chitosan nanopartices to transfer STZ Diabetic rat through gastrointestinal tract. A" hybrid nanomedicine" designed by workers of North western University and Argonne National Laboratory consist of TiO_2 Semiconductor nanoparticle of dimension 4.5 nm linked covalently to oligonucleotide DNA[Freitas, 2005]

ETHICAL CHALLENGES WITH NANOMEDICINES

In future, nanotechnology may add a new possibility of linking human and machine as brain implants may raise new ethical issues. A nanoformulation of drug which is based on a previously approved drug in microformulation can undergo a shorter approval pathway by means of abbreviated new drug application if bioequivalence can be demonstrated to its microformulation drug. However, if bioequivalence cannot be demonstrated it would necessitate approval of all stages of new drugs application. Further non drug is designed as a new chemical entity the evaluation procedure becomes more stringent [Nijhara and Balakrishnan 2006].

HAZARDS OF NANOMEDICINES-

C_{60} fullerene can cause oxidative stress and depletion of GSH in brain in fishes by entering through olfactory bulb [Elder et.al., 2006]. Studies done on monkeys and rats have been accumulation of carbon and manganese nanoparticles in olfactory bulb through olfactory pathway [Elder et.al., 2006, Oberdorster, 2004]. This shows that the medicine may intervene blood brain barrier, may result inflammatory reactions in brain. Toxicity of nanoparticles can cause inflammatory bowel disease and may cause organ damage. Their application in humans needs further researches and more precautions.

CONCLUSION

Nanotechnology provides opportunities to develop smart devices and technologies for various diseases treatment. It is expected to accelerate scientific as well as economic activities in medical research and development. This science has potential to detect, diagnose, treat and prevent diseases.

I t can diagnose difference between normal and abnormal cells. Use of nanotechnology in medicine needs adequate evaluation of its risks and safety factors.

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