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REVIEW ARTICLE

NANO MEDICINE: AN EMERGING TREND IN MOLECULAR DELIVERY

Panda Priyabrata.*[1], Mishra Sangeet Sarita[1], Pati Kanhu Charan[2]

[1] Roland Institute of Pharmaceutical Sciences, Berhampur-10, Odisha, India

[2] Abbott Healthcare Pvt. Ltd., Baddi-173205, Himachal Pradesh, India

*Author for Correspondence- priyabrata.panda.rockstar@gmail.com

ABSTRACT

Nanobiopharmaceuticals has involved, understanding issues related to target specific drug delivery. Previously the traditional dosage forms showed a greater difficulty in achieving bioavailability and therapeutic index. So addition of various functionalities to nano size materials interfacing them into various biological molecules has improved the drug delivery. Integration of nanomedicinals with biotechnology has brought a radical change in the research field both in vivo and invitro. It has paved the way to new therapies, surgical interventions and advanced drug delivery systems. Nanoparticles as nanomedicines opens the potential for crossing various biological barriers within the body especially the potential to cross the blood brain barrier may open new ways for drug delivery into the brain. Nanoparticles as drug delivery systems can be designed to improve the pharmacological and therapeutic properties of the drug. This manuscript has emphasized various nanobiopharmaceuticals in the field of cancer therapy, regenerative medicine, drug delivery, diagnostic devices, gene therapy and tissue engineering.

Keywords: Nanobiopharmaceuticals, target specific drug delivery, regenerative medicines, tissue engineering, cancer therapy.

INTRODUCTION:

Nanomedicine is the engineering application of nanotechnology to medicine. It is the engineering of molecularly precise structures typically 0.1 mm or smaller and ultimately, molecular machines. It is the preservation and improvement of human health, using molecular tools and molecular knowledge of the human body.[1]Nanomedicine this generation exploits various nanoparticle devices such as dendrimers, carbon fullerenes (buckyballs) and nanoshells to target specific tissues and organs. These nanoparticles may serve as diagnostic and therapeutic antiviral, antitumor or anticancer agents. Nanomedicine uses organic polymer or lipid-based systems such as polymeric micelles, liposomes and solid lipid nanoparticles, and various nanocrystal based systems which are now leading nanodevice market products. Drug delivery and related pharmaceutical development in the context of nanomedicine consists of at least two components, one of which is a pharmaceutically active ingredient, although nanoparticle formulations of the drug itself are also possible. The whole system leads to a special function related to treating, preventing or diagnosing diseases sometimes called smart-drugs. In the medical world, nanotechnology is also seen as a boon since these can help with creating smart drugs. These help to cure people faster and without the side effects that other traditional drugs have. We will also find that the research of nanotechnology in medicine is now focusing on areas like tissue regeneration, bone repair, immunity and even cures for such ailments like cancer, diabetes, and other life threatening diseases. The primary goals for research of nano-bio-technologies in drug delivery include:[2]

- More specific drug targeting and delivery,
- Reduction in toxicity while maintaining therapeutic effects,
- Greater safety and biocompatibility, and
- Faster development of new safe medicines.

Nanomedicine:

Nanomedicine refers to highly specific medical intervention at the molecular scale used for curing disease or repairing damaged tissues such as bone, muscle, or nerve. Nanometer is defined as one-billionth of a meter. Biological molecules and structures inside living cells operate at the size scale of about 100 nanometers or less.[3] Nanomedicine, enabled the development of nanoparticle therapeutic carriers which as systems are selectively and passively target to tumors through the enhanced permeability and retention effect, so they are perfectly ready for the deliverance.

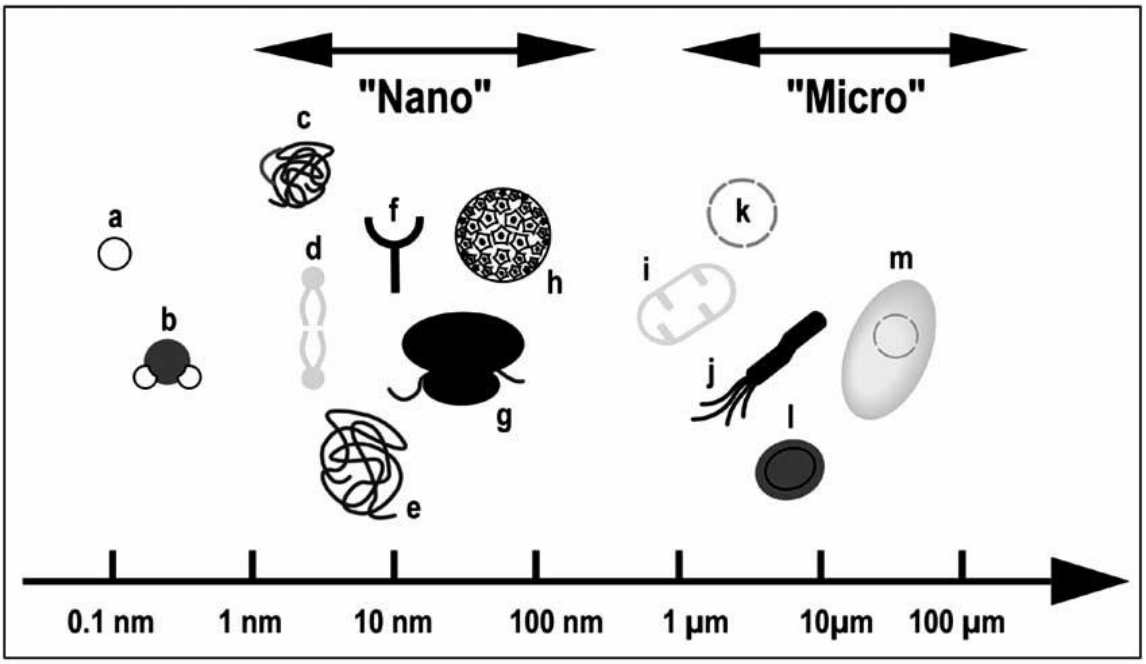

Figure 1: Typical size of nano- and micro-objects (horizontal axis: log-scale) from left- to right: (a) Hydrogen atom (~0.1nm) , (b) water molecule (diameter: ~0.4nm), (c) peptide aptamer (size ~3nm), (d) lipid bilayer (thickness ~5nm), (e) protein (size ~10nm), (f) antibody (size ~10nm), (g) ribosome (diameter ~30nm), (h) human papillomavirus (diameter ~60nm), (i) mitochondrion (length ~1 um), (j) *Helicobacter pylori* (length ~3um), (k) nucleus (diameter ~3um), (l) erythrocyte (diameter ~8um), (m) mammalian cell (diameter ~20um).[4]

Mechanism of drug delivery via nanoparticle:

Nanoparticles help in providing site specific drug delivery by enhancing permeability and retention effect without passing into the reticuloendothelial system. There are two main methods which are generally used or applied with drug using nanoparticle as carrier for enhanced permeability and retention effect.

1) Surface bound method: In this method, the drug particles are adhered to the surface of the nanoparticles.

2) Core bound method: In such methodology, the drug particles are concentrated to the matrix of the nanoparticle and are carried to the targeted site into the body.

Drugs are delivered by the help of nanoparticles by adding them to a reaction mixture during polymerization process. The main aim of delivering drugs via nanoparticle is not only to provide better therapeutic results but also to reduce cost and tumor suffering by reducing the cost of drugs to the public health system.[5]The potential of eliminating a tumorous outgrowth without any collateral damage through nanomaterial based drug delivery have laid to design drug delivery systems on functionalized nanoparticles. Nanoparticles were earlier used as a carrier for vaccine and anticancer drugs. The successful result of nanotechnology in the field of nanomedical sciences is the delivery of drugs through the blood brain barrier for targeting brain tumors. Doxorubicin is an anticancer drug but it cannot cross the blood brain barrier. Thus integration of Doxorubicin with polysorbate 80 leading to the formation of polybutylcyanoacrylate nanoparticles can increase its delivery to the brain to a large extent. Nanoparticles have the ability to penetrate deep into tissues and get absorbed by the cells efficiently. They play a vital role in the creation of DNA delivery vectors. Submicron colloidal particles have been used as nanoparticles for the purpose of drug delivery and they act as major carriers for several classes of drugs like anticancer, antihypertensive and hormones.[6]

The procedure generally involved for targeted drug delivery by the help of nanoparticle include:-

Step1

The drug of interest is dissolved, entrapped, adsorbed, attached or encapsulated into or onto a matrix.

Step2

Thus depending on the method of preparation Nanoparticles, nanospheres or nanocapsules can be constructed to possess different properties and release characteristics for the best delivery or encapsulation of therapeutic agents.

Deliveries of drug by the help of nanoparticle have the following advantages:

1) High surface to volume ratios

2) Modifiable platforms

3) Tunable size

The size and shape of nanoparticle is highly important for application in drug delivery processes as they control the perfusion of materials through the endothelium and diffusion through tissues.[7]

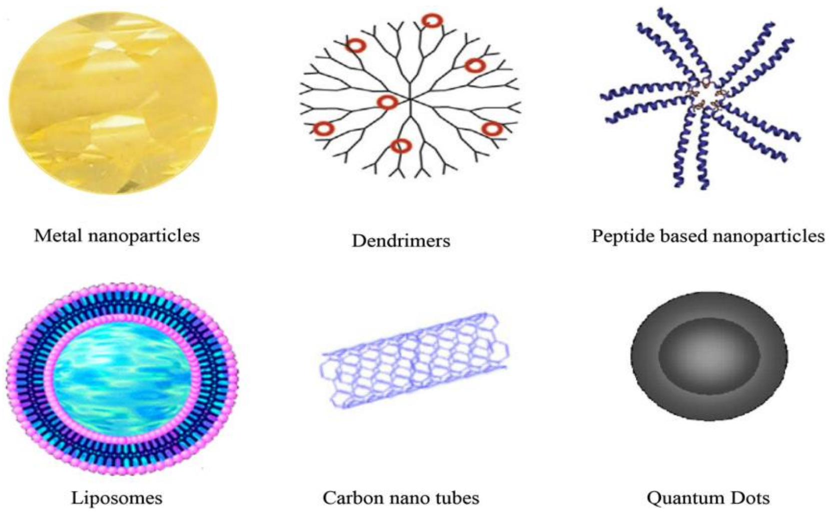

Figure 2: Example of metal nanoparticles, dendrimers, peptide-based nanoparticles, liposomes, carbon nanotubes and quantum dots that help in drug delivery system[6]

Nanotechnology in cancer treatment:

Cancer is the most dreadful disease of the century. Many drugs are being researched everyday for treating this dreadful disease. Cancer is also known as malignant neoplasia. In cancer, cells divides and grow uncontrollably leading to the formation of a primary tumor mass followed by vascularisation and then finally subsequent spread of cancer cells to other parts of the body where secondary tumor formation takes place. They may travel to various parts of the body through lymphatic system or blood streams. Today cancers are of many types mainly lungs, stomach, liver, blood, colon and breast cancer. Exposure to radiations, lack of physical activity, obesity and effects of carcinogens such as tobacco, smoke, chemicals and infectious agents causes cancer. The two general classes of genes that are affected by the unrestricted growth of cell leading to genetic abnormalities are

1. Proto-oncogenes
2. Tumor suppressor genes

Proto-oncogenes stimulates cell division and their mutated forms are called as oncogenes, in the contrast Tumor suppressor genes, codes for proteins that inhibit cell division whose adverse effects include loss of normal DNA replication, control over the cell, orientation and adhesion with tissues and interaction with the protective cell of the immune system. The present trend of treatment options for cancer includes surgical resection, radiation and chemotherapy. Dose limiting toxicity and patient morbidity are the speed breakers that affect the efficacy of chemotherapeutic drugs. At these stage nanomedicines, an advancement of nanotechnological science has emerged as novel therapeutic modalities for cancer treatment.[8]

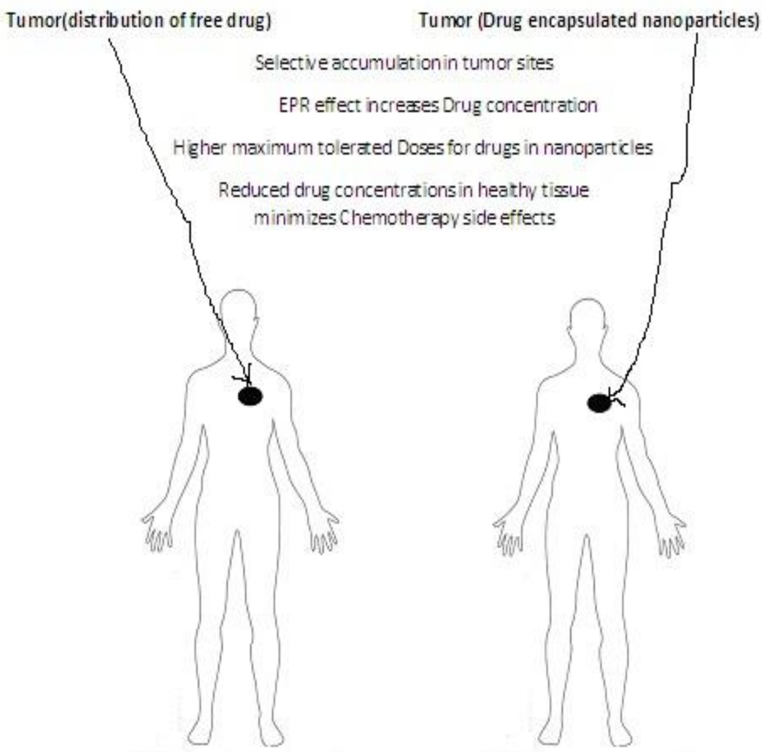

Figure 3: Advantages of drug encapsulated in a nanopoarticle over free drug[9]

Monitorpost-treatment relapse technique:-This is another nanoscale device that is used for the treatment of cancer.Nanoscale sensor is planted into the body and is capable of detecting the growth of cancerous cells in patients. This technique is very helpful in detecting cancer cells at an early stage which would reduce mortality rates dramatically.[10]

Nanoparticles generate supersonic shock waves to target charge:- A nanosized bomb is used for target drug delivery to cancer tumors without damage to any other cells. The nanothermites produce shock waves in the Mach3 range. The drugs are administered via needle by the help of a device which would send a pulse into the tumor.

Nanoscale therapeutic systems include polymeric micelles, polymers-drug-conjugates, dendrimers and inorganic particulates and these play a vital role in treatment of cancer.

Liposome Nanoparticles for cancer:-

Lipids help in the formation of nanoparticle vesicles through the self assembly of amphiphillic liquids and excipients.The liposomal formulation is a bilayer based on hydrophobic interactions with the hydrophilic head groups positioned towards the aqueous environment. The physical and chemical properties of liposomes can be precisely changed to control surface change, size and functionality.These can be achieved by simple mixing commercially available lipid molecules.

A pegylated liposome DOXIL which is used to treat multiple types of cancer is a better example to understand liposome liposomal drug delivery systems. Doxin is loaded with doxorubicin by diffusion process based on an ammonium salt gradient. The nanocarriers containing the drug or therapeutic load is released into the cytoplasm by changing the zeta potential with changes in solution pH.[9]

Polymer drug conjugate nanoparticles for cancer:-

The side chain grafting of drugs to polymer chains helps in the delivery of high doses of chemotherapeutic drugs and thus leads to the formation of polymer drug conjugates. The size of polymer drug conjugates is generally below 20nm.HPMA-doxorobucin, Xyotax are some of the nano drugs that are presently under trials for multiple cancer therapeutics including prostate, breast, neck, colorectal cancer and recurrent NSCL. Xyotax is commonly called as polyglutamate paclitaxel, Paclitaxel is grafted to polyglutamic acid to reach a drug load of 80-40% by weight.[9]

Biological nanoparticles for cancer:-

Bacteria are biological nanoparticles that are unicellular microorganism which encapsulate essential components of the cytoplasm as well as hydrophobic and hydrophilic molecules."Nanocell" is an example of biological nanoparticles which is being used for cancer therapy which mainly consists of anucleate globular bacteria having size nearly about 400nm.It has no signs of toxicity when experimented with large animals such as pigs and monkeys with repeated dosages at high titers. The main advantage of Nanocells is that it can be loaded with molecules of different solubility and charge such as doxorobucin, paclitaxel through drug diffusion into bacteria within a few hours.[9]

The novel prospects in nanomedicine for enhanced tumor treatment include

1. Active Targeting Strategies
2. Controlled Release strategies
3. Multistage drug Delivery

Nanotechnology for CNS drug delivery:

The part of the nervous system consisting of the brain and spinal cord is called Central nervous system. The brain is a challenging organ for drug delivery. First, the incidence of degenerative diseases in the brain will increase with the aging population. Secondly, the blood brain barrier (BBB) is well-known as the best gatekeeper in the body toward exogenous substances .All the current therapeutic strategies are not efficient in treating disorders related to the CNS.The disease alleration symptoms are partial as opposed to disease modifying effects. With increasing rise in demographics, there is also dramatically increase in neurodegenerative disease. The current therapeutic treatment procedures are associated with severe side effects.CNS disorders are one of the essential and largest areas in pharmaceutical world and hence require adequate treatment. Thus biotherapeutic agents like proteins, peptides, monoclonal antibodies, growth factors and nucleic acids are performed under trials to have a profound effect on halting the progression of neurodegenerative disorders and also helps in providing unique function of restoring damaged cells.[11]Drug delivery to the cns for therapeutic advancement of nanodegenerative disorders such as Alzheimer’s is complicated by restrictive mechanism imposed at the blood brain barrier. Hence opsonisation by plasmaprotiens in the systemic circulation is additional impedance to cerebral drug delivery for treatment of Alzheimer’s disease.[12]

Major barriers to CNS delivery include:[11]

1. The blood-brain barrier (BBB): The selective permeability barrier that separates the circulating blood from the brain extracellular fluid in CNS is the blood brain barrier. It maintains the constancy of the internal environment of the brain. It protects the brain from foreign substances in the blood that may injure the brain. It also protects the brain from hormones and neurotransmitters. In the blood brain barrier, macromolecules are unable to cross the capillary brain endothelial cells as they form tight junctions preventing most of the potential drugs from reaching their CNS targets. The table1. Drawn below shows different transport pathways across blood brain barrier. Transcellular lipophillic pathway and adsorptive transcytosis are prominent transport pathways in drug delivery across the BBB. Most drugs enter the brain via transcellular lipophillic pathway.

2. The blood-cerebrospinal fluid barrier: The choroid plexus epithelial cells and the arachnoid membrane form the blood cerebrospinal fluid barrier. Ependymal epithelium is the functional unit of choroid plexus. It has less surface area and hence pose les obstacle in drug delivery to CNS. The BBB possesses tight junctions between the endothelial cells whereas the blood-CSF barrier posses tight junctions between the epithelial cells of the choroid plexus thus preventing the drug from entering the CSF.

Table 1: Different transport pathways across blood brain barrier [11]

Name of the transport pathway	Agents involved	Description
Paracellular aqueous pathway	Water soluble agents	Tight junctions present in blood brain restrict penetration of water soluble agents.
Transcellular lipophillic pathway	Lipid-soluble agents	Lipid bilayer membrane of the endothelium provides diffusive route for lipid-soluble agents
Transport proteins	Glucose,aminoacids,nucleoside,vinca alkaloids,cyclosporinA,AZT	The endothelium contains transport carriers for glucose,aminoacids and other substances
Receptor Mediated Transcytosis	Insulin,Transferin	Protein such as insulin and transferrin are taken up by specific receptor mediated endocytosis and transcytosis.
Adsorptive Transcytosis	Albumin, other plasma proteins	It uptakes native plasma proteins such as albumin.

Nanosuspensions and Liposomal Nanomedicines:

Nanosuspension:[10 13 14 15]

Nanosuspension is a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle in which the diameter of the suspended particle is less than 1µm in size and stabilized by surfactants. Nanosuspensions can be used to enhance the solubility of drugs that are poorly soluble in aqueous as well as lipid media. As a result, the rate of flooding of the active compound increases and the maximum plasma level is reached faster. More than 40 percent of the drugs are poorly soluble in water. Obviously poorly water soluble drugs show many problems in formulating them in conventional dosage forms. Critical problems associated with poorly soluble drugs are:

1. Low bioavailability

2. Erratic absorption.

Drugs having such properties are Itraconazole and Carbamazepine. Nanosuspensions formulation approach is used for drugs with high log P value, high melting point and high dose. The major advantages of nanosuspensions are

1. Increase in the dissolution velocity and saturation solubility of the drug.
2. Improved biological performance.
3. Ease of manufacture and scale-up.
4. Long-term physical stability.
5. Versatility.

Table 2: Potential benefits of Nanosuspension technology over other Conventional formulation technologies over poorly soluble drug[15]

Drug Formulations	Benefits of Nanosuspensions
Oral	*Rapid onset *Improved bioavailability
Intravenous	*Rapid Dissolution *Tissue Targeting
Ocular	*Higher bioavailability *More consistent dosing
Inhalation	*Higher bioavailability *More consistent dosing
Subcutaneous Intracellular	*Rapid onset *Reduced tissue irritation

Application of nanosuspensions in drug delivery:

1. Oral drug delivery:

Antibiotic indicated for non-complicated P. falciparum malaria and leishmanial infections shows poor bioavailability (10–15%) because of its dissolution-rate and limited absorption and has to be administered in high doses (750 mg twice daily).Administration of atovaquone as a nanosuspension resulted in a 2.5-fold increase in oral bioavailability as compared to the commercial product.

2. Parenteral drug delivery:

Clofazimine, a poorly water-soluble anti-leprotic drug, has been successfully formulated as a nanosuspension. Absence of any harsh solvents/co-solvents and/or any potentially toxic ingredient in nanosuspensions enables them to bypass the limitations of parentral administration attributed to conventional formulations strategies. Hence, nanosuspensions enable significant improvement in the parentrally tolerable dose of the drug, leading to a reduction in the cost of the therapy and also improved therapeutic performance.

3. Ocular drug delivery:

Nanosuspensions can prove to be a boon for drugs that exhibit poor solubility in lachrymal fluids. For delivery of such drugs, approaches such as suspensions and ointments have been recommended. Although suspensions offer advantages such as prolonged residence time in and avoidance of the high tonicity created by water-soluble drugs.

4. Pulmonary drug delivery:

Budesonide, a poorly water-soluble corticosteroid, has been successfully formulated as a nanosuspension for pulmonary delivery. Currently such drugs are delivered as suspension aerosols or as dry powders by means of dry powder inhalers.

5. Targeted drug delivery:

Nanoparticulate systems have shown tremendous potential in targeted drug delivery, especially to the brain. Successful targeting of the peptide dalargin to the brain by employing surface modified polyisobutyl cyanoacrylate nanoparticles has been a major achievement in targeted delivery.

Liposomes and biopolymer fields have led to recent advancements in the field of nanomedicines with the help of carrier systems that are capable of encapsulating therapeutic agents which ranges from conventional drugs to the new genetic drugs like antisense oligonucleotides or small interfering RNA(siRNA). Liposomes have advantages over polymer based nanoparticles for formation of therapeutics. The main motive in developing a liposomal nanomedicine is to design a liposomal nanoparticle allowing the drug particle to accumulate at the site of interest associated with either an appropriate rate of drug retention or the ability to taken up by target cell. Liposomes represent a highly flexible platform. The range from multi laminar vesicles with diameters of several microns to small, unilaminar vesicles with the diameter of 20 nm.

Liposomal nanoparticles for delivery of genetic drugs:[16]

Genetic drugs help in generating gene expressions and presents DNA vectors for ribozymes, gene therapy and antisense oligonucleotides. Antisense oligonucleotides possess immunostimulatory applications. Genetic drugs exhibit inherent sensitivity to rapid inactivation by nucleases and rapid elimination from circulation for the formulation of liposomal nanoparticles. The nanoparticles should be of well defined sizes for effective biodistribution and perfect accumulation at disease sites.

Nanomedical Devices:

1. **Nanobiosensor:** A device that responds to chemical species in biological samples or using biological components is called as biosensor. It integrates a biological element with a physiochemical transducer. The transducer produces an electronic signal proportional to a single analyte. The major component of biosensor include:[17]

1) Biological element	5) nucleic acid	9) receptor
2) Microorganism	6) organelle	10) antibody
3) Tissue	7) enzyme	
4) Cell	8) enzyme component	

All these components help in binding the targeted molecule. The physiochemical transducer measures the physical change by acting as an interface occurring during the reaction at the bioreceptor and then transforming that energy into measurable electrical output. The transducer passes signals to a microprocessor where they are amplified and analyzed. The potential applications of nanobiosensor include:

1) Clinical diagnostics

2) Food and agricultural processes

3) Detection of warfare agents

Nanobiosensors are effectively used for sensing a wide variety of fertilizers, pesticides, herbicide, pathogens, and moisture and soil pH. The various types of biosensor include:[18]

1) Optical biosensors

2) Nanotube based biosensor

3) Electrical biosensor

4) Viral nanosensors

5) Electrochemical biosensors

6) Nanoshell biosensors

7) Nanowire biosensors

Medical application of nanobiosensor includes:[19 35]

1)Identification of particular cells or places in the body in need by measuring changes in volume,concentration,displacement,velocity,gravitational ,electrical and magnetic forces.

2) It helps in recognizing tumor cells, most notably those off cancer, at the molecular level in order to deliver medicines.

2. Nanorobots: Medical nanorobots helps in performing in vivo cytosurgery.An in vivo cytosurgery known as chromosome replacement therapy, a nanorobot extracts existing chromosomes from a particular diseased cell and replaces them with new ones in the same cell. Synthetic microbes called biobots which are engineered bacterial microbes that helps in the production of useful vitamins, hormones, enzymes and cytokines to nourish the deficiency in the patient body.[5]Vascular system helps in the introduction of surgical nanorobots into the body. Another engineered nanorobot is “FEMTOLASER” which is used for performing anatomy of roundworm neurons after which the axons functionally regenerate. A femtolaser acts like a pair of “nano-scissors” by vaporizing tissue locally while leaving the adjacent tissues unharmed. Femtolaser surgery has performed the following operations successively which includes:

1) Localized nanosurgical ablation of focal adhersions adjoining living mammalian epithelial cells.

2) Microtube dissection inside yeast cells

3) Non invasive intratissue nanodissection of plant cell walls and selective destruction of intracellular single plastids.

Another most advancing feature of nanorobts in nanomedicine is “microbives” that could patrol the blood stream, seeking out and digesting unwanted pathogens including bacteria, viruses or fungi.It helps in complete clearance of severe septicemic infection in hrs or less. Nanorobots do not increase the risk of septics because the pathogens are completely converted into harmless sugars, amino acids.[20]

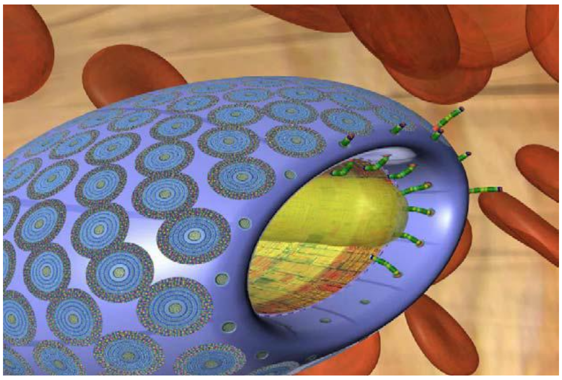

Figure 4: Nanorobotic artificial phagocytes called ‘‘microbivores’’that could patrol the bloodstream, seeking out and digesting unwanted pathogens.[20]

3.Nanopores: Fabrication of tiny cell containing chambers within single crystalline silicon wafers can be achieved by the help of nanopores.These chambers interface with the biological environment present in the surrounding through polycrystalline silicon filter membranes having high density and nanopores of uniform size of 20nm allowing passage of small molecules such as oxygen, glucose and insulin but restrict the passage of large immune system molecules such as immunoglobulin and graft borne-virus particles.[19]Nanopore materials are used in the treatment of several chronic medical conditions including diabetes mellitus. Nanopores can be used as devices to protect transplanted tissues from the host immune system utilizing the benefit of transplantation. Beta cells of pancreas can be enclosed within the nanopore device and implanted in the recipients body. This provides the tissue sample nutrients from the surrounding tissues and at the same time remain undetected by the immune system. This hence serves as a new modality for treatment for insulin dependent diabetes mellitus. Nanopores play major role in DNA sequencing. Recent researches are being made on modified nanopores that have the ability to differentiate DNA strands based on difference in base pair sequence. Researches are also being done on nanopores that have the ability to differentiate purines from pyridines.[21] On a recent research inorganic nanoporous materials with well ordered phases such as imodic alumina and nanoporous silica have gained considerable attention for use in biomedical application.[22]

4. Quantum dots: Quantum dots are those nanomedical devices having tiny crystal particles that grow when stimulated by ultraviolet radiation. They are mainly used to detect cancer and identify their location in the body. They bind to the sequence of DNA that is associated with disease. They work on a specific mechanism that is the quantum dots get stimulated with light and hence emit unique bar codes making the cancer associated DNA visible. These structures offer new capabilities for multicolor optical coding in gene expression studies, high throughput screening, and in vivo imaging.[23]

5. Dendrimer: A dendrimer is a molecule having the potential to link treatment with detection and diagnosis. They have the size as that of an average protein molecule and are branched. Thus their surface area increases allowing scientists to attach therapeutic agents or biologically active molecule. Dendrimers are used to distribute genes to cells without triggering a negative immune retort.[24] They are mainly used in the treatment of cancer. The major components of a dendrimer includes:-

1) A molecule that recognizes a cancer cell

2) A therapeutic agent to kill those cells

3) A molecule that recognizes the signals of cell death

6. Nanotubes: Advancement in the field of nanotechnology has led to the discovery of a growing number of new materials including the “CARBON NANOTUBES”. Nanotubes are generally carbon rods which are about half the diameter of a molecule of DNA. They help to identify DNA changes associated with cancer. Nanotubes have the ability to detect the presence of altered genes and can find the exact location of their changes. They can also detect the specific mutations in the DNA and hence bind to them. They are also used for providing structure for broken bones allowing new bone material to grow.[25 34]

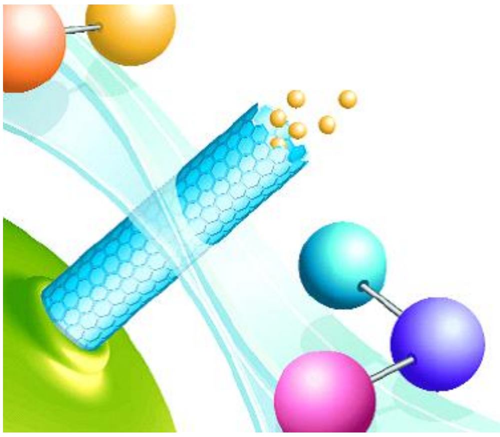

Fig 5: A nanotube crosses a biological barrier to deliver drugs, antibodies, diagnostic devices, or possibly all three.[26]

7. Nanopore sequencing: This is an ultra-rapid method of sequencing based on pore nanoengineering and assembly. A small electric potential draws a charged strand of DNA through a pore of 1–2 nm in diameter in a haemolysin protein complex, which is inserted into a lipid bilayer separating two conductive compartments. The current and time profile is recorded and these are translated into electronic signatures to identify each base. This method can sequence more than 1000 bases per second. This technology has much potential for the detection of single nucleotide polymorphisms, and for gene diagnosis of pathogens. [27]

8. Super paramagnetic iron oxide crystals: These entities are usually prepared by the alkaline co-precipitation of appropriate ratios of $Fe2^{+}$ and $Fe3^{+}$ salts in water in the presence of a suitable hydrophilic polymer such as dextran or poly(ethylene glycol). This yields an iron core of 4 –5 nm in diameter, which is hexagonally shaped and surrounded by dextran or poly(ethylene glycol) molecules. These crystals possess

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large magnetic moments when brought into a magnetic field, thus producing a localized disturbance in magnetic field homogeneity, but the magnetic memory is lost when the field is removed. Due to such induced magnetic disturbances, there exist a large susceptibility difference between super paramagnetic iron oxide crystals and the nearby protons, causing rapid dephasing of spins and resultant decrease in T2 relaxation times with a loss of local signal intensity. But the effects of these crystals on T1 relaxation times are relatively minor, compared with the T2 effects. These crystals are therefore "negative enhancers".

Iron oxide crystals are also amenable to surface functionalization with small surface functional groups or multivalent small molecules as well as by conjugating proteins, antibodies, and oligonucleotides for active-targeting in vivo or for in vitro diagnostic procedures. Recently a number of small libraries of surface-functionalized iron oxide nanoparticles were synthesized from the parent aminated dextran caged iron oxide nanoparticles. These parent particles were first labeled with fluoresceins, thus generating particles that are both magnetic and fluorescent, then activated with N-succinimidyl 3-(2-pyridyldithio) propionate, and reacted with thiol-containing surface modifiers. Fluorochrome attachment allows the screening by a wide range of high-throughput fluorescence-based screening methods as well as FACS.[28 29 30]

Nanotechnology in Tissue engineering:

Human tissue engineering and regenerative medicine in general brings out excellent results in improving patient treatment, faster recovery, improved prognosis and a proper biologically favorable situation where the body can be stimulated to heal itself. According to EDUCOME (European Medical Technology Industry Association) Regenerative medicine/tissue engineering is a rapidly growing multidisciplinary field involving the life, physical and engineering sciences that seeks to develop functional cell, tissue, and organ substitutes to repair, replace or enhance biological function that has been lost due to congenital abnormalities, injury, disease, or ageing.[31]Number of researches carried out in the field of nanotechnology has led to the creation of implantable tissues, some of which are already used in humans like skin and cartilage and have also entered clinical trials like bladder and blood vessels. Cells seeded into three dimensional biocompatible scaffolds under suitable bioreactor conditions results into functional structures resembling native tissues. To recapitulate proper tissue functionality, scaffolds should also establish a tissue specific microenvironment to maintain and regulate all behavior and function. The development of scaffolds which mimic the architecture of tissue at the nanoscale level is one of the major challenges in the field of tissue engineering. To meet this challenge the development of "nanofibres" has enhanced the scope of nanomedicine in tissue engineering. Electro spinning, self assembly and phase separation are the three techniques which are currently available for the synthesis of nanofibres. Nanofibres acts as an efficient carrier for the controlled delivery of protein, drugs and DNA.[33] The hierarchically arranged nanofibres within the extracellular matrix provides cell support and plays a vital role in storing, releasing and activating a wide range of biological factors thus providing successful regeneration of tissues. Nanotopographic surfaces and nanofeatured scaffolds are the recent advancement in the field of nanotissue engineering as they encapsulate and control the spatiotemporal release of drugs.[32]

CONCLUSION:

Nanomedicine plays an important role in health systems by focusing on patient treatment with efficient case management but also on development of innovative health policies. On a recent research, to control the administration of insulin doses, nanopumps are generally used. They control the delivery at nanolitre level which is very close to physiological delivery of insulin. Nanomedicine also helps in reducing the amount of precious reagents required to carry out screening of potential drugs. They help in the identification of targeted protein and drugs. The main objective for nanomedicine is to develop cure for diseases like cancer through the utilization of nanotechnology and with fewer side effects by means of targeted drug delivery systems. Nanotechnology will bring out revolutionary changes in the field of medical sciences over the coming next 10-20 yrs.Nanomedicine lags behind because of lack of financial profit, consumer distrust and ineffective regulation of new and genetic products. But overall nanomedicine as a part of nanotechnology is a boon to the present and future generation of mankind.

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