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New Era of Nanotechnology In Pharmaceuticals: An Overview

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ABSTRACT

Nanotechnology belongs to the production and utilization of materials at the nanoscale up to 100nm in size. Nanotechnology is emerging technique has application in biology and biotechnology as well as medical technology. It is expected to provide reasonable products by this technology in various fields of application. Novel nanodevices, nano and bio-materials are fabricated by nanotechnology. Paramagnetic nanoparticles, nanoshells, quantum dots, nanosomes are some of the nanoparticles used in diagnosis. These are the targeted drug delivery system. It provides therapeutically active drug molecule only to the site of action, without affecting other tissues, at comparatively lower doses. The prospective medical applications are in detection, diagnosis, monitoring and treatment of disease. It is effective in the treatment of cancer, tuberculosis, Alzheimer's disease, Parkinson's disease and heart diseases. The clinical applications are in dentistry, ophthalmology, tissue engineering and surgery are discussed. The purpose is to improve the health by amplifying the safety and efficacy of nanodevices. Nanotechnology will have global impact in the development of future health systems.

Keywords: Nanotechnology, Nanoparticles, Nano-devices, Applications.

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INTRODUCTION

Nanotechnology is branch of science, engineering and technology conducted at the nanoscale which is about 1 to 100nm.is about 1 to 100nm. It deals with dimensions and tolerance at nanoscale. Nanotechnology is the study and application of very small things and can be used across all the others science like biology, chemistry, materials science and engineering. Nanoscience and nanotechnology comprise the ability to see and to control individual atoms and molecules. Physicist Richard Feynman: Father of nanotechnology [1]. The prefix "nano" is Greek word having meaning "dwarf"; it means very small size. Nanotechnology involves work from top down i.e. to decrease the size of large structure to smallest. It is treatment of single atoms, molecules or compound into structure to provide devices and materials with specific properties. Enhancement in the field of Nanotechnology and it's applications in the field of medicines and pharmaceuticals has revolutionized in the 20th century. [2]

Nanomedicine involves use of nanotechnology for the sake of human health and well being. The aim of nanomedicine may be broadly defined as the "comprehensive monitoring, control, construction, repair, defense and improvement of all human biological system, working from the molecular level using engineered devices and nanostructures, ultimately to achieve medicinal benefits. It is now possible to provide therapy at molecular level with use of the tools, thus treating and assisting in study of the pathogenesis of disease. Significant processes of living organism occur basically at nanometers scale, elementary biological units like DNA proteins or cell membranes are of these dimensions. [3]

Nanoscale devices could be 100 to 10,000 times smaller than human cells but are same in size to large biomolecules such as enzymes and receptors. The successful application of these products as treatment for human beings will need to overcome critical barriers. In this review, the prominent technology being developed for diagnosis and therapeutic purpose has been reviewed. [4]

NANOTECHNOLOGY AND MEDICAL APPLICATION

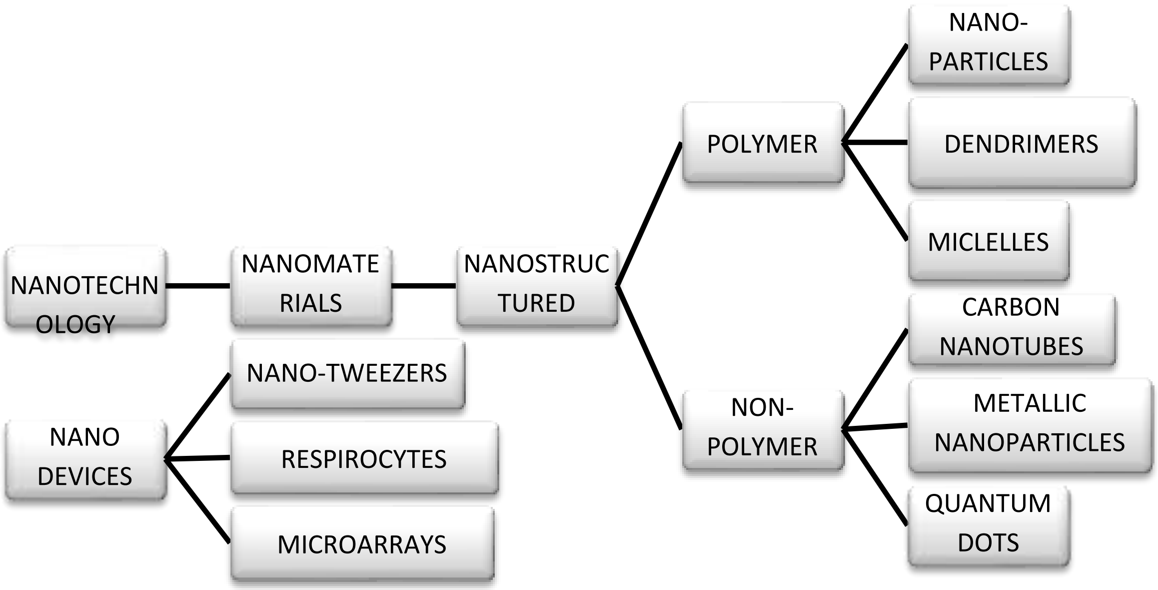

Figure 1: Schematic Diagram of Various Types of Pharmaceutical Nanosystem [2]

Liposomes

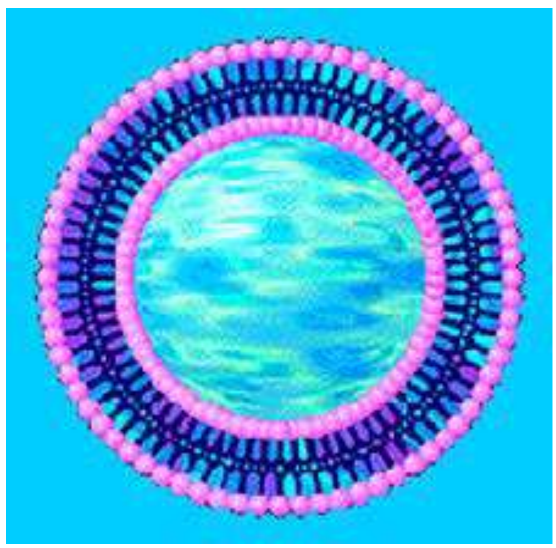

Figure 2: Structure of Liposomes

Liposomes are discovered in 1960s were the original models of nanoscaled drug delivery devices. These are the spherical nanoparticles made of lipid bilayer membranes with an aqueous interior but can be unilamellar with a single lamella of membrane or multilamellar with multiple membranes. Liposomes are usually composed of phospholipids or cholesterol, which are used to encapsulate various active drugs. These liposomes can be loaded with drugs either in the aqueous compartments. Usually polar drugs loaded in aqueous compartments and lipophilic drugs are incorporated in the liposomal membrane. Liposomes are ranging from 25nm to 10,000nm. The phospholipids used for making liposomes include phosphotidylcholines. These are versatile carriers for parenteral drug delivery systems. A large variety of drugs, peptides/ proteins and viruses and bacteria can be incorporated into liposomes. Liposomes can be use in the targeted drug delivery and cancer treatment. Some liposomes based pharmaceuticals such as Amphotericin B, Doxorubicin, Amikacin. Intramuscularly and SC injected liposomes deliver drug at a controlled rate. [5]

Nanopore

Nanopore comprise of silicon wafers with high density of pore (20nm in diameter). It is created by pore forming protein or as hole in synthetic materials such as silicon or grapheme. It permit entry of oxygen, glucose and other products such as insulin to pass through, but it does not allow immunoglobulin and cells to pass through them. It is a nanodevice to protect transplanted tissues from the host immune system. β cells of pancreas can be closed within the nanopore device and implanted in the recipient's body. Nanopores could serve as a newer modality of treatment for Type-I Diabetes mellitus. It can also be used in the sequencing of biopolymers specially, polynucleotide in the form of DNA or RNA. [6]

Fullerenes

A fullerene is a molecule of carbon in the form of a hollow sphere, ellipsoid, tube and many other shapes. It also called as “buckyballs”. The buckminsterfullerenes is the most common form of fullerene and measure about 0.7nm in diameter with 60 carbon atoms arranged in a shape known as truncated icosahedrons. It resembles a soccer ball with 20 hexagons and 12 pentagons and highly proportionate. Fullerenes have been widely used for several biomedical application including the design of high performance magnetic resonance imaging contrast agents and drug and gene delivery. [7]

Nanotubes

Carbon nanotubes are tubular structure like a sheet of graphic rolled into a cylinder capped at one or both ends by a buckyball. Nanotubes can be single walled or multiwalled carbon nanotubes in concentric fashion. Single walled nanotube has internal diameter of to 2nm whereas multiwalled nanotube has 2 to 25nm in diameter with 0.36nm distance between different layers. Carbon nanotube has mechanical, electric, electronic, thermal and optical properties. These are characterized by greater strength and stability and hence can be used as drug carriers. Specificity of cell can be obtained by conjugating antibodies to carbon nanotubes with radio labeling. Entry of nanotubes into the cell may be mediated through endocytosis or by insertion through the cell membrane. Indium-111 labelled carbon nanotubes are used for killing cancer cells specifically.

They act by transforming electromagnetic energy into heat, causing a temperature raise lethal to cancer cells. [8]

Quantum dots

Quantum dots are nano crystals of 2 to 10nm size they can made fluorescence if stimulated by light. Quantum dots are also known as “Nanorods”. They may be synthesized by semiconducting materials. A combination of ligands acts as shape controller and bond to different facets of the nanorod with different strengths. This allows different faces of the nanorod to grow at different rates, producing elongated objects. It consists of an organic core, the size of which determines the color emitted an inorganic shell and an aqueous organic coating to which biomolecules are conjugated. The biomolecules conjugation of the quantum dots can be modified to target various biomarkers.

Quantum dots have various biomedical applications in diagnosis and therapeutics. They can also be used for imaging of sentinel node in cancer patients for tumor staging and planning of therapy. Various malignancies like melanoma, lungs, breast and gastrointestinal tumors can be detected by this method. Quantum dots are used over conventional dyes as it produces brighter fluorescence with Near Infrared Fluorescence (NIR) system. [9]

Paramagnetic nanoparticles

Paramagnetic nanoparticles are commonly consisting of two components, a magnetic material, often iron, nickel and cobalt and a functional chemical component. Their size ranging from 1 to 100nm. Physical and chemical properties depends upon the synthetic route and chemical structure. Paramagnetic nanoparticles are used for diagnostic as well as therapeutic purposes. Paramagnetic iron oxide nanoparticles used as contrast agent for diagnosis in magnetic resonance imaging (MRI). Identification of specific organs and tissues can be done by targeting of these nanoparticles. This nanoparticles have been used with MRI to detect breast cancer cells which are expressed on cancer cells. Paramagnetic nanoparticles have application tissue specific targeting, magnetic particle imaging, optical filters and environmental remediation. [10]

Dendrimers

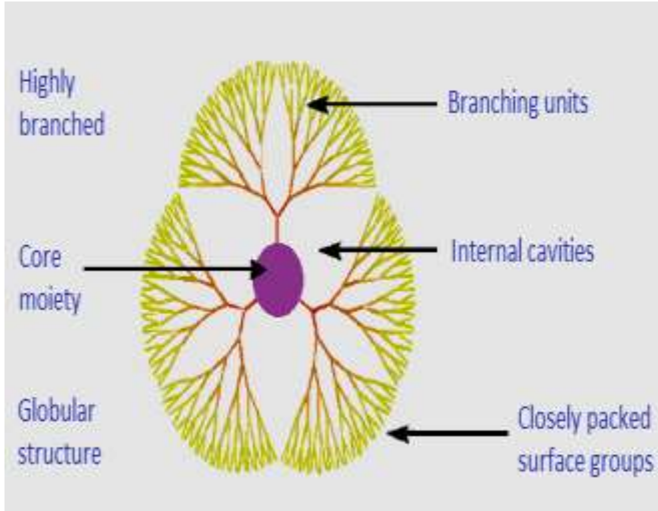

Figure 3: Schematic representation of dendrimer showing core, branches and surface

Dendrimers are nano-sized, radially symmetrical molecules with well defined, homogeneous and monodisperse structure that has a typically symmetric core, an inner shell and an outer shell. These are nanomolecules with regular branching structures. Dendrimers are hyper branched macromolecules with a carefully tailored architecture, the end-groups, which can be functionalized and thus modifying their physico-chemical and biological properties. The branches arise from the core in shape of a spherical structure by means of polymerization. This leads in formation of cavities within the dendrimers which can be useful in drug transport. The end part of dendrimer is attached with other molecules for transport.the complex of dendrimer is a tectodendrimer performing various functions such as targeting, diagnosis of disease state, delivery of drug and imaging.[11]

Nanoparticles

It can be further classified into various categories:

nanocrystals/nanosuspensions: Nanocrystals are crystals of poorly water-soluble drug in nanosize which when dispersed in water produce nanosuspension. Nanocrystalline drug suspensions have an advantage of higher loading.

nanoemulsions: It is clear, dispersed systems comprising of two immiscible liquids wherein the dispersed phase droplets are of nanosize. O/W nanoemulsions present the mosty important parenteral drug carrier systems where lipophilic drug are dissolved in the inner phase of the emulsion.

micelles, are the <5 nm they scatter little light and transparent.

nanocapsules: oil-containing nanocapsules differ from o/w nanoemulsions in providing a barrier made from polymers between the core and the surrounding environment. Nanospheres: They are also called as polymeric nanoparticles consist of drug dispersed in an amorphous form within a polymer matrix. Polymers suitable for the preparation of biodegradable nanoparticles include cellulose derivatives, polylactic acid and their co-polymers. cellulose derivatives, polylactic acid and their co-polymers.

solid lipid nanoparticles (sln): Melt-emulsifed nanoparticles based on lipids are solid at room temperature and generally prepared by not high pressure homogenization. Advantages of these SLN are:

- Use of physiological well-tolerable lipids.
- Avoidance of organic solvents in the preparation process.
- Wide potential application spectrum: dermal, peroral and intravenous.
- Improved bioavailability.
- Protection of sensitive drug molecules from the environment
- Controlled-release characteristics

nanosturctured lipid carries (nlc): they are oiilloaded soild-lipid nanoparticles. NLC offers several advantages over SLN such as-

- Greater degree of drug loading.
- Reduced burst release of drug.
- Better control of drug release.[12]

APPLICATION OF NANOTECHNOLOGY IN HEALTH CARE

In Cancer Therapy:

Nanoparticles are widely used in oncology due its small size, particularly in imaging. Nanotechnology can assist to have better diagnosis with less harmful substances as optical nanoparticles, to provide efficient drug delivery to tumor cells with liposomes and functionalized micelles. It can also be useful in molecular imaging with tomography of tumors and therapy of cancer as radiotherapy. [13]

The applications of various nano systems in cancer therapy are summarized as

1. Quantum dots are used to detect genes and proteins, tumors and lymph node visualization.
2. Nanowires are used to detect disease protein biomarkers, gene expression a DNA mutation.
3. Nanoparticles are used in MRI and ultrasonography image contrast agent and for targeted drug delivery, as permeation enhancers.
4. Carbon nanotubes are used to detect DNA mutation and disease protein biomarkers.
5. Nano shells have applications in tumor-specific imaging, deep tissue thermal ablation [14].

In Operative Dentistry

Nanodentistry can make maintenance of oral health by using nanomaterials and nanorobotics. In the local anaesthesia a colloidal suspension containing millions of active analgesics of micronsized dental robots will be instilled on the patient's gingiva. The dental robots is then commanded to shut down all sensitivity in any particular tooth that requires treatment. Orthodontic nanorobots can manipulate the periodontal tissues, allowing fast and painless straightening, rotating and vertical repositioning within minutes to hours. Carbon nanotubes are used improve tooth durability and appearance by replacing upper enamel layers with pure sapphire and diamond. Nanotechnology have application in diagnosis and treatment of oral cancer. [15]

In ophthalmology

Nanocarriers deliver ocular medicines to target sites specifically. Nanoparticles carry even the poorly water soluble drugs and improve the passage of topical application to the target tissues. Ex. Glucocorticoid drugs, cyclosporine etc for immunity related disorders. For retinal generative disorders, large unstable molecules like nucleic acids are also delivered using nanoparticles in gene therapy. Nanoparticles allow targeted drug delivery to types of cancer cells such as melanoma, thereby leaving retinal cells, unharmed by medication. Nanosurgical techniques helping preventing scarring of the bleb after glaucoma surgery. Nanotechnology found application in treatment of oxidative stress; measurement of intraocular pressure. [16]

In Neurodegenerative Disorders

Nanotechnology will play a key role in developing new diagnostic and therapeutic tools. Peptides and peptidic nanoparticles are newer tools for CNS diseases. Nanoparticles can be potentially revolutionise treatment for neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease and Strokes.

Biometric stimulation and optimization of an intracranial nano-enabled scaffold device (NESD) for the site-specific delivery of dopamine to the brain, this device will have designed for Parkinson's disease. It provides device to limit and reverse neuro pathological disease states and to support and promote physiological regeneration of damage neurons, to furnish neuronal protection and to facilitate drug delivery and small molecules across blood-brain barrier (BBB).

Nanoparticles have high affinity towards BBB for the circulating amyloid-β forms and hence it stimulates "sink effect" and improves Alzheimer's condition (AD). Nanoparticles can be directly administered into a brain *via* a bolus injection. [17]

In Tissue Engineering

Tissue engineering is the connecting discipline between engineering material science, medicine and biology. The technique is used to create repair and replace cells, tissues and organs by using cell or its combination with biomaterials and this helps to generate materials which resembles to indigenous tissues. Nanofibres, nanopatterns and controlled release nanoparticles are created by nanotechnology with the application in tissue engineering.

Electrospoon nanofibres used for bone, cardiac muscle tissue engineering. Nanostructures help to improve regulation of cell adhesion and vascularisation.

In stem cell tissue engineering electro spinning helps to improve adhesion and expansion of hematopoietic stem cell in bone marrow, this act as an efficient carrier for hematopoietic stem cells. Electro spinning also help in cell differentiation, orientation in neural cell tissue engineering. [18]

By using, NESD, artificially stimulated cell proliferation, in organ transplant and artificial implants therapy nanotechnology can be beneficial and can lead to life extension.

In surgery

With the help of nanotechnology, minute surgical instruments such as lab on chip, biochip and nanorobots can be created which are used to perform microsurgery on any part of the body. These instruments would be precise and accurate, targeting only the area of surgery without damaging large part of body. Computers can be used to control the nano-sized surgical instruments for the visualization of surgery instead of surgeon holding the instrument. "Nano cameras" can provide near visualization of surgery. Surgery could also be done on tissues, genetic and cellular level. [19]

FUTURE PROSPECTS OF NANOTECHNOLOGY

Theranostics

Theranostics is a combination of two words Therapeutic and Diagnostic, interchangeably referred to as "Theragnostics". This term is used in the context of molecular targeting vectors. ex. Peptides. Iodine isotopes is the first theranostic agent administered orally had been shown to cure neck swelling due to thyromegaly. Theranostics comprise of administration of diagnostic agent to determine localization in the site under study as a surrogate for a potential therapeutic agent with similar chemical properties. This combination therapy include in-vitro diagnostic technique and in-vivo nano-imaging can lead to targeted tumor disruption or removal.

Nanorobots

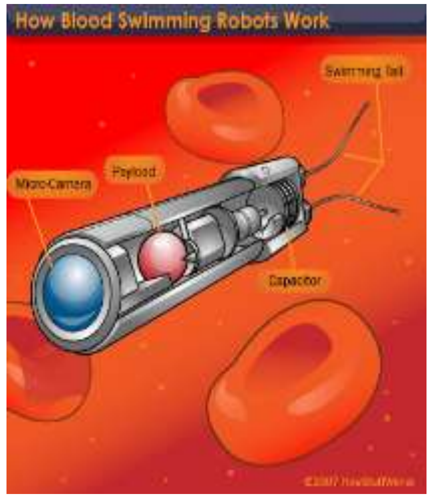

Figure 4: Structure of Nanorobots

Nanorobots may be defined as “swallow the doctor” the modern nanomedicine. The theoretical aspects of nanorobotics include specific design issues such as, sensing, navigation, movement, power communication. Nanorobotics can be applied to identify the specific chemicals or toxic materials and may provide early indications of organ failure or tissue rejection.

Recent research is finding their use in nanophotonics to produce light more efficiently.

In surgical robotics surgeon used their thumbs and fingers to move joystick handles on a control cabinet to move two arms containing miniature instruments that are inserted into ports in the patient.

Nanorobots enable to enter cells and correct DNA or a deficiency. It break downs blood clots and/or even kidney stones. Potential application includes early diagnosis and targeted drug delivery for tumors, diabetes, biomedical instrumentation, pharmacokinetics and health care. In future, nanorobots will be applied as injections to patient for treatment at cellular level. [20]

DNA Machine

It can be defines as “nucleic acid robot”. Which are basically organic molecular machines with nanoscale size DNA configuration can provide various means to form two dimensional and three dimensional nanomechanical devices. Biological circuit gates DNA materials have been manipulated as molecular machines to help drug delivery for targeting diseased cells. This type of material works smartly as biomaterial drug delivery. [21]

Respirocytes: a Mechanical Artificial RBC

It is hypothetical artificial RBCs, a type of nanodevices which can function as RBC with greater potential. It is a blood borne spherical 1-micron diamondoid 1000atm pressure vessel, it is able to deliver 236 times more oxygen to the tissue per unit volume than natural red cells and manage carbonic acidity. In the treatment of acute anemia caused by sudden loss of blood after injury or surgical intervention. It also used to treat low oxygen availability to nerve tissues as occurs in advanced atherosclerotic narrowing of arteries strokes low blood flow condition are observed in most organs of peoples as geriatrics. In the cardiovascular and neurovascular diseases such as coronary angioplasty, organ transplantation and in cardiopulmonary bypass solutions perfusion of respirocytes should be useful in tissue oxygenation. [22]

Microbivores

Microbivores is a oblate spheroidal nanodevice. These are the hypothetical devices which function as WBCs in the blood stream designed to trap circulating microbes. They have to be greater efficacy than that of cellular blood cells in phagocytosis. The surface of microbivores is arranged with processes which can extend in length and secure the microbe which gets contact with it. The microbe is then gradually moves towards the ingestion port and undergoes the process of morcellization and enzymatic degradation. The ends products are then released as amino acids, fatty acids, nucleotides and sugars. It theoretically expected to clear the blood stream in septicemia at higher rate than the natural defense mechanism with antibiotics. Microbivores are used in the drug delivery, various surgeries, cancer detection and treatment, gene therapy, diabetes treatment and body surveillance. It is 1000 times faster and 80 times more efficient than natural phagocytes and kills one pathogen in just 30seconds.[23]

Nanoscale Cantilevers

Figure 5: Nanoscale Cantilevers

Nanoscale cantilevers are microscopic, flexible beams resembling a row of diving boards. These are constructed as a part of larger diagnostic device. They are made by using semiconductor lithographic techniques. Cantilevers can be used as detectors of cancer-related molecules. They may be coated with molecules enable of binding specific substrate-DNA complementary to a specific gene sequence. They can detect single molecules of DNA or protein. Binding of cancer-specific molecules with cantilever acts as sensors. When the molecules binds to the cantilever it leads to the sensor to change its physical properties and that change can be detected. The molecular products secreted by cancer cell binds selectively to the antibodies coated on the cantilever fingers. Researchers can read the change in real time and provide not only information about the presence and the absence but also the concentration of different molecular expressions. [24]

CONCLUSION

Nanomaterials have increased surface area, therefore used as promising tool for advancement of drug and gene delivery and diagnostic biosensor. Nanomaterials have unique physicochemical and biological properties as compare to their larger counterparts. The properties of nanomaterials can greatly influences their interaction with biomolecules and cells, due to their particular size, shape, chemical composition, solubility and surface structure. There is a very bright future to nanotechnology, by its merging with other technology. By further research in this, it can be useful for every aspect of human life. Medicines, stem cell research, neutraceuticals and regenerative medicines are among the leading sectors that will be modified by nanotechnology innovations.

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