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Nano-medicine based drug delivery system

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ABSTRACT:

Nanomedicine is the medical application of nanotechnology. Nanomedicine is defined as the monitoring, repair, construction and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures. Nanomedicine ranges from the medical applications of nanomaterials to nanoelectronic biosensors and even possible future applications of molecular nanotechnology. The aim of nanomedicine is the improvement of healthcare for the benefit of the patient. Nanomedicine is an important and rapidly growing field, which is emerging from the application of nanotechnology to healthcare. The generally recognized categories include diagnostics, imaging, medical devices, drug discovery, drug delivery and regenerative medicine. Nanomedicine can offer impressive resolutions for various life threatening diseases. Disease areas which can be expected to benefit most from nanotechnology within the next few years are cancer, diseases of the cardiovascular system, the lungs, blood, neurological (especially neurodegenerative) diseases, diabetes, inflammatory/infectious diseases, Parkinson's or Alzheimer's disease and orthopedic problems.

Keywords: Nanomedicine, nanoparticles, nanotubes, nanobiosensor, nanorobotics.

INTRODUCTION:

Nanomedicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve. Nanotechnology is a collective term referring to technological developments on the nanometer scale, usually 0.1-100 nm. A nanometer is one-billionth of a meter, too small to be seen with a conventional laboratory microscope. It is at this size scale - about 100 nanometers or less that biological molecules and structures inside living cells operate. Therefore, nanotechnology is engineering and manufacturing at the molecular scale.

Nanomedicine is the process of diagnosing, treating, and preventing disease and traumatic injury, of relieving pain and of preserving and improving human health, using molecular tools and molecular knowledge of the human body. It is the application of nanotechnology (engineering of tiny machines) to the prevention and treatment of disease in the human body. The most elementary of nanomedical devices will be used in the diagnosis of illnesses. In the relatively near term, nanomedicine can address many important medical problems by using nanoscale structured materials and simple nanodevices that can be manufactured today. This includes the interaction of nanostructured materials with biological systems. Nanomedicine seeks to deliver a valuable set of research tools and clinically useful devices in the near future. [1,2]

Nanomedicine increase the localization of therapeutic compounds, including imaging agents, radio sensitizers, small molecule therapeutics and gene medicines such as siRNA, to target tissues such as site of infection or inflammation or solid tumors through a passive targeting mechanism also called the enhanced permeability and retention (EPR) effect.

Key goals for nanomedicine:

The main objective for nanomedicine is to develop cure for traditionally incurable diseases like cancer through the utilization of nanotechnology and also to provide more effective cure with fewer side effects by means of targeted drug delivery systems.

Advantages and disadvantages of nanomedicine:

With the help of nanomedicine diseases can be easily cured with no side effects and no surgery is required. Its detection is also very easy. The disadvantage appeared with nanomedicine is its implementation difficulties and high cost.

Applications of nanomedicine:

1. Diagnosis using nanomedicine: Diagnostic nanoapparatus could be attached to keep check of the internal chemistry of the body. Mobile nanorobots with wireless transmitters could easily circulate in the blood and lymph systems and can send out alerts when chemical imbalances appear within the blood.

2. Nervous system tracking: Nanomedicine also helps in better understanding the phenomenal changes in the human nervous systems. Fixed nanomachines could be

inserted in the nervous system of the human body to monitor pulse rate, brain activity, and other important functions.

3. Drugs dispersion: Live saving drugs are one of the important ingredients in the latest medicines but its unusual and its excess usage could cause death. Nanomedicine also has successful applications for the reduction of extra drugs from human body.

4. Heart and ECG machine: Advanced and fully equipped nanomedical heart trackers are present to accurately track the heart beat and it's down falls and also for treating it as needed in the body. In human heart defibrillators and pacemakers, nanodevices could influence the behavior of individual cells.

5. Artificial antibodies: Nanomedicine was the first to conceptualize the artificial red and white blood cells and later on it successfully showed the positive results. Cancer patients are now treated by injecting artificial red blood cells to balance the human body blood level. Artificial antibodies, white and red blood cells and antiviral nanorobots could be considered as successful applications of nanomedicine.

Medical nanomaterials and nanodevices:

Nanoparticles:

Nanospheres and nanocapsules that can be either amorphous or crystalline. Nanopowders are agglomerates of ultrafine particles, nanoparticles or nanoclusters. They are specifically designed to absorb or encapsulate a drug, thereby protecting it against chemical and enzymatic degradation, for targeting particular organs/tissue and also as carriers of DNA in gene therapy, to deliver proteins, peptides and genes by oral route.

It focuses in the production of nanoscale particles or molecules to enhance the bioavailability of a drug. It also focuses on maximizing bioavailability and for prolonged period of time. The advantage is that cells can take up the nanoparticles because of their incredibly small size, avoidance of macrophage clearance, long resistant times.

Table 1: Basic information of some nanomaterials moving to market

Product	Type of Nanomaterial	Phase	Indication	Company
VivaGel	Dendrimer	Phase 2	Topical microbicide for HIV	Star pharma
MRX-952	Branching block copolymer self-assembled Nanoparticulate formulation of Irinotecan Metabolite	Preclinical	Oncology	ImaRx Therapeutics
Abraxane	Nanoparticle albumin	NDA filed	Lung cancer, breast cancer, others	American Pharmaceutical Partners
Cyclosertcamptothecin	Cyclodextrin nanoparticle	IND filed	Metastatic solid	Insert Therapeutics
TNT AntiEpCA	Polymer-coated iron oxide	Preclinical	Solid tumors	Triton BioSystems
Verigene Platform	DNA Functionalized Gold nanoparticles	On market	Diagnostics	Nanosphere
INGN-40	Liposome	Phase1	Metastatic lung cancer	Introgen

Biomedical application of nanoparticles:

- Iron oxide nanoparticles can used to improve MRI images of cancer tumors. The nanoparticles are coated with a peptide that binds to a cancer tumor once the nanoparticles are attached to the tumor the magnetic property of the iron oxide enhances the images from the Magnetic Resonance Imagining scan.
- Nanoparticles coated with proteins that attach to damaged portions of arteries. This could allow delivery of drugs to the damaged regions of arteries to fight cardiovascular disease.
- Quantum Dots (crystalline nanoparticles) that identify the location of cancer cells in the body.
- Gold nanoparticles that allow heat from infrared lasers to be targeted on cancer tumors.
- Porous silica nanoparticles used to deliver chemotherapy drugs to cancer cells.
- Nanoparticles, when activated by x-rays that generate electrons that cause the destruction of cancer cells to which they have attached themselves. This is intended to be used in place radiation therapy with much less damage to healthy tissue.
- A nanoparticle cream that releases nitric oxide gas to fight staph infections.

Nanopores:

One of the earliest therapeutically useful nanomedical devices, employing bulk micromachining to fabricate tiny cell-containing chambers within single crystalline silicon wafers. The chambers interface with the surrounding biological environment through polycrystalline silicon filter membranes which are micro machined to present a high density of uniform nanopores as small as 20 nanometers in diameter. These pores are large enough to allow small molecules such as oxygen, glucose, and insulin to pass, but are small enough to impede the passage of much larger immune system molecules such as immunoglobulin and graft-borne virus particles.

Quantum dot:

These dots are tiny particles measuring only a few nanometers across, about the same size as a protein molecule or a short sequence of DNA. They come in a nearly unlimited palette of sharply-defined colors which can be customized by changing particle size or composition. Particles can be excited to fluorescence with white light, can be linked to biomolecules to form long-lived sensitive probes to identify specific compounds up to a

thousand times brighter than conventional dyes used in many biological tests, and can track biological events by simultaneously tagging each biological component (e.g., different proteins or DNA sequences) with nanodots of a specific color.

Nanotube:

A nanotube is a nanometer-scale tube-like structure. It may be of following types:

- Carbon nanotube
- Inorganic nanotube
- DNA nanotube
- Membrane nanotube

Fullerenes:

One nanometer buckyballs made from just a few dozen carbon atoms. Nanoparticles such as C60 have many properties which make them attractive candidates for many therapies. These are of extremely small molecular size with high physiological and radiation stability. These are metabolically inert (negligible toxicity).

Soluble derivatives of fullerenes such as C60 have shown great utility as pharmaceutical agents. Fullerene compounds may serve as antiviral agents (most notably against HIV, where they have also been investigated computationally, antibacterial agents (E. coli, Streptococcus, Mycobacterium tuberculosis), photodynamic antitumor and anticancer therapies, antioxidants and anti-apoptosis agents which may include treatments for amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and Parkinson's disease. Single-walled and multi-walled carbon nanotubes are being investigated as biosensors, for example to detect glucose, ethanol [3], hydrogen peroxide, selected proteins such as immunoglobulin and as an electrochemical DNA hybridization biosensor.

Application of nanotubes:

- One of the important properties of nanotubes is that they can easily penetrate membranes such as cell walls. In fact, long and narrow shape makes them look like miniature needles, so it makes sense that they can function like a needle at the cellular level. Using this property by attaching molecules that are attracted to cancer cells to nanotubes to deliver drugs directly to diseased cells.

- Nanotubes bound to an antibody that is produced by chickens have been shown to be useful in lab tests to destroy breast cancer tumors. The antibody carrying nanotubes are attracted to proteins produced by a one type of breast cancer cell. Then the nanotubes absorb light from an infrared laser, incinerating the nanotubes and the tumor they are attached to.
- Improve the healing process for broken bones by providing a carbon nanotube scaffold for new bone material to grow on.

Nanovaccines:

Nanovaccines are created which in reality are specialized nanoemulsions made up of tiny Soya bean oil droplets suspended in water and studded with bits of pathogenic organisms. These can be ingested by swabbing in to the nose. Since they are swabbed they produce immunity not only in the blood stream but also in mucous lining making them relevant for varied disease. They have potential to change small pox vaccination process.

Nanobiosensor:

A biosensor [4] is a measurement system for the detection of an analyte that combines a biological component with a physicochemical detector and a nanobiosensor is a biosensor that on the nanoscale size.

Types of Nanobiosensor:

- Optical Biosensors
- Nanotube Based Biosensors
- Electrical Biosensors
- Viral Nanosensors
- Electrochemical Biosensors
- Nanoshell Biosensors
- Nanowire Biosensors

Applications of Nanobiosensor:

Medicinal uses of nanosensors mainly revolve around the potential of nanosensors to accurately identify particular cells or places in the body in need. By measuring changes in volume, concentration, displacement, velocity, gravitational, electrical and magnetic

forces, pressure or temperature of cells in a body, nanosensors may be able to distinguish between and recognize certain cells, most notably those of cancer, at the molecular level in order to deliver medicine or monitor development to specific places in the body. In addition, they may be able to detect macroscopic variations from outside the body and communicate these changes to other nanoproducts working within the body.

Nanoshell:

Nanoshells are extremely small beads of glass coated with gold. They can be fashioned to absorb light of almost any wavelength, but nanoshells that capture energy in the near-infrared, which can easily penetrate several centimeters of tissue.

Unlike carbon fullerenes, the slightly larger nanoshells are dielectric-metal nanospheres with a core of silica and a gold coating, whose optical resonance is a function of the relative size of the constituent layers. The nanoshells are embedded in a drug-containing tumor targeted hydrogel polymer and injected into the body. The shells circulate through the body until they accumulate near tumor cells. When heated with an infrared laser, the nanoshells (each slightly larger than a polio virus) selectively absorb the IR frequencies, melt the polymer and release their drug payload at a specific site.

Table 2: Different biosensors, principal, applications and relevant references

Biosensors	Principle	Applications	References
1. Optical biosensor	Colorimetric for color, Photometric for light intensity	Detection of disease like cancer, direct glucose determination in blood using reagent less optical biosensor	[5], [6]
2. Surface Plasmon resonance (SPR)biosensor (optical biosensor) (Invented: Biacore International AB (Biacore), 1990)	Evanescent wave phenomenon	Detection and identification of biological analyte and biophysical analysis of bimolecular interactions	[7]
3. Electrochemical biosensor	Immobilization of biomolecules	Use in Bioaffinity Assays for Determining DNA and Its Effectors, also Electrochemical measurement of blood glucose concentrations	[8], [9]
4. DNA biosensors	Nucleic acid hybridization rennealing between the ssDNA from different sources	DNA biosensors can detect the presence of genes or mutant genes associated with inherited human diseases	[10]
5. Nanotube based biosensor (Carbon nanotubes (CNTs) discovery by Iijima in 1991)	We report a system for bimolecular assays that uses carbon nanotubes as both an electrode and an immobilization phase in an electrochemiluminescence based sensing device	Detection of bio-molecules like Streptavidin and IgG, application in immunoassays, nucleic acid probe assays, assays for clinical chemistry analyte	[11]
6. Piezoelectric biosensor	based on nucleic acids interaction/DNA based	To point mutation detection in PCR samples.	[12]

Nanoshells offer advantages over traditional cancer treatments: earlier detection, more detailed imaging, fast noninvasive imaging and integrated detection and treatment. This technique could also prove useful in treating diabetes. Instead of taking an injection of

insulin, a patient would use a ballpoint-pen-size infrared laser to heat the skin where the nanoshell polymer had been injected. The heat from nanoshells would cause the polymer to release a pulse of insulin. Unlike injections, which are taken several times a day, the nanoshell-polymer system could remain in the body for months. A point-of-care whole blood immunoassay using antibody-nanoparticle conjugates of gold nanoshells [13] was developed. Varying the thickness of the metal shell allow precise tuning of the color of light to which the nanoshells respond near-infrared light penetrates whole blood very well, so it is an optimal wavelength for whole blood immunoassay. Successful detection of sub-nanogram-per-milliliter quantities of immunoglobulin was achieved in saline, serum and whole blood in 10–30 minutes.

Iron nanoparticles and monoclonal antibodies are bond into nanobioprobes about 40 nanometers long. The chemically inert probes are injected and circulate inside the body, whereupon the antibodies selectively bind to tumor cell membranes. Once the tumor (whether visible or micro metastases) is covered with bioprobes after several hours, a magnetic field generated from a portable alternating magnetic field machine (similar to a miniaturized MRI machine) heats the iron particles to more than 170 degrees, killing the tumor cells in a few seconds. Once the cells are destroyed, the body's excretion system removes cellular residue and nanoparticles alike. Test subjects feel no pain from the heat generated.

Nanococktail to target and kill tumor:

Nanococktail is defined as a "cocktail" of different nanometer-sized particles that work in concert within the bloodstream to locate, adhere to and kill cancerous tumors. It is a system containing two different nanomaterials the size of only a few nanometers, or a thousand times smaller than the diameter of a human hair, that can be injected into the bloodstream. One nanomaterial was designed to find and adhere to tumors, while the second nanomaterial was fabricated to kill those tumors.

When a single drug does not work in a patient, it is preferred to administer a cocktail containing several drug molecules. That strategy can be very effective in the treatment of cancer, where the rationale is to attack the disease on as many fronts as possible. Drugs may sometimes work together on a single aspect of the disease or they may attack separate functions. In either case, drug combinations can provide a greater effect than either drug alone.

While one type of nanoparticle improves detection of the tumor, the other is designed to kill the tumor. One type of responder particle was designed with strings of iron oxide, which they called "nanoworms," that show up brightly in a medical magnetic resonance imaging or MRI system. The second type is a hollow nanoparticle loaded with the anti-cancer drug doxorubicin. The nanoworms would be useful to identify the size and shape of a tumor in a patient before surgery, while the hollow nanoparticles might be used to kill the tumor without the need for surgery.

Nanorobotics:

Nanorobotics is the emerging technology field of creating machines or robots whose components are at or close to the microscopic scale of a nanometer (10^{-9} meters) [14]. More specifically, nanorobotics refers to the nanotechnology engineering discipline of designing and building nanorobots with devices ranging in size from 0.1-10 micrometers and constructed of nanoscale or molecular components. The names nanobots, nanoids, nanites, nanomachines or nanomites have also been used to describe these devices currently under research and development.

Applications of Nanorobotics:

Potential applications for nanorobotics in medicine include early diagnosis and targeted drug-delivery for cancer [15] biomedical instrumentation, surgery, pharmacokinetics monitoring of diabetes and health care. It offers targeted drug delivery with lesser side effects and improved bioavailability. It is also used to cure skin diseases via cream containing nanorobots which removes right amount of dead skin and excess oil.

Conclusion:

Nanomedicine, one of the important applications of the nanotechnology has made a revolutionary development in the medical field. The evolution is what will lead us to our new future and as in our past with medicine and how we were able to make certain disease obsolete like Typhoid Mary, T.B., smallpox, chicken pox and mononucleosis. This evolution will possibly be the end of cancer and aids which will greatly increase our chances for survival as well as our children.

Over the next 10–20 years, new nanotechnologies may revolutionize science, technology and society. However, if medical nanotechnology wants to realize its full potential, major impediments blocking serious steps forward have to be removed. The future of nanomedicine is undermined by the lack of financial profitability, consumer distrust, ineffective regulation of new and generic products, weak patent protection and insurance market failure. Nanomedicine impact on society and humans will continue to

take form. It will be our future because of the possibility's that are currently becoming available.

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