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Review Article

Medical Applications of Nanomedicine

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Abstract

Nanomedicine is the Applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems as per National Institutes of Health. Research into the rational delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents is at the forefront of projects in nanomedicine. Applications to medicine and physiology imply materials and devices designed to interact with the body at subcellular (i.e., molecular) levels with a high degree of specificity. This can potentially translate into targeted cellular and tissue specific clinical applications designed to achieve maximal therapeutic affects with less side effects. This article presents a brief review of Nanomedicine with an emphasis on its various aspects associated i.e. introduction, definition, medical and clinical application especially in drug delivery, diagnosis**,** targeting, cancer, neurology, nephrology, cvs, respiratory diseases etc.

Key words: Nanomedicine, nanotechnology, nanoparticles, drug delivery.

Introduction

Nanomedicine is the medicinal diligence of nanotechnology (is the branch of engineering that deals with things smaller than 100 nanometers (especially with the manipulation of individual molecules)). The range of Nanomedicine from medical applications of nano-materials (is a field that takes a materials science-based approach to nanotechnology. It studies materials with morphological features on the nanoscale, and especially those that have special properties stemming from their nanoscale dimensions) to nano-electronic ((physics) the use of nanotechnology to create electronic components) biosensor (is an analytical device for the detection of an analyte that combines a biological component with a physicochemical detector component). The range can also be possible

for future applications of molecular nanotechnology (a technology based on the ability to build structures to complex, atomic specifications by means of mechanosynthesis).[1] Nanomaterials have been designed with chemically modifiable surfaces to attach a variety of legends that can turn these nanomaterials into biosensors, molecular-scale fluorescent tags, imaging agents, targeted molecular delivery vehicles, and other useful biological tools (Figure 1)[2].

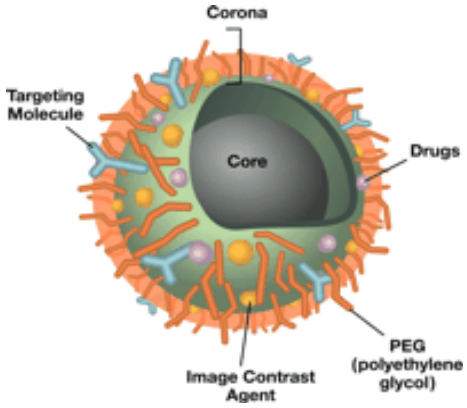

Figure 1: Multifunctional Nanoparticle[2]

Artificial nanostructures, such as nanoparticles and nanodevices, being of the same size as biological entities, can readily interact with biomolecules on both the cell surface and within the cell (see Figure 2). Nanomedical developments range from quantum dots for molecular diagnostic and imaging to therapy using nanocarrier and integrated medical nanosystems, which may perform complex repair actions at the cellular level inside the body in the future.[3]

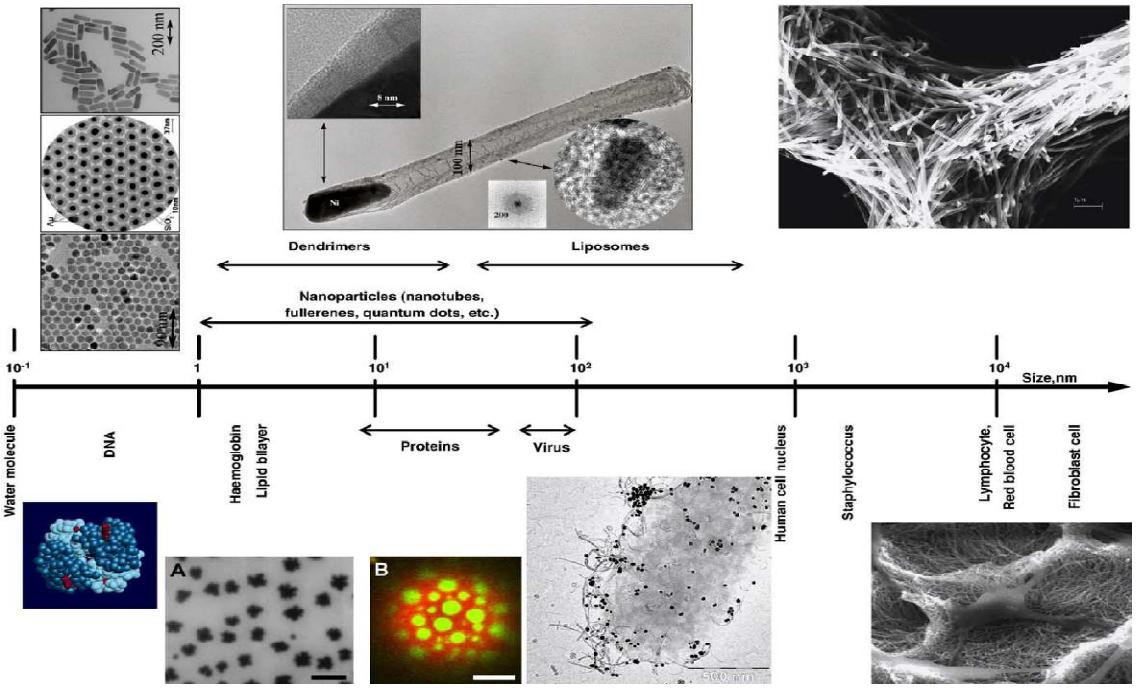

Figure 2: Nanotechnology structures that have the same size than biological systems[3]

Artificial nanostructures are given at the top, biological nanostructures at the bottom of the figure. Nanostructured material from left to right: gold nanoparticles, 37 nm diameter, and nanorods 200 nm length; carbon nanotubes, 200 nm diameter, with incorporated Ni particle of 8 nm; carbon nanotubes scaffolds. Biological structures from left to

right: DNA; pulmonary surfactant vesicles and liposomes; Gram negative bacteria transfected with gold nanoparticles via carbon nanotubes; fibroblast growing on scaffold made of carbon nanotubes.

Applications of nanotechnology for treatment, diagnosis, monitoring, and control of biological systems has recently been referred to as "Nanomedicine" by the National Institutes of Health. Research into the rational delivery and targeting of pharmaceutical, therapeutic, and diagnostic agents is at the forefront of projects in nanomedicine.[4] There is a huge range of Nanomedicine devices which involves medical applications of nanomaterials, nanoelectronic biosensors, and even more useful and practical future applications of molecular nanotechnology. In the field of medical and biological world nanomedicine has greater significance as this application has facilitated the mankind so well. Potential nanodrugs will work by very specific and well-understood mechanisms; one of the major impacts of nanotechnology and nanoscience will be in leading development of completely new drugs with more useful behavior and less side effects. It is one of the major technologies which have highly supported the entire field of medicine.

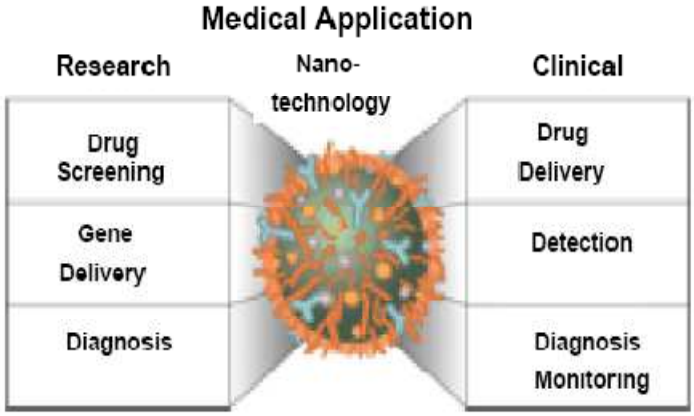

Figure 3: Medical Applications of Nanotechnology[5]

Medical Applications of Nanomedicine

Drug Delivery

Nanomedical approaches to drug delivery center on developing nanoscale particles or molecules to improve drug bioavailability. Bioavailability refers to the presence of drug molecules where they are needed in the body and where they will do the most good. Drug delivery focuses on maximizing bioavailability both at specific places in the body and over a period of time. This can potentially be achieved by molecular targeting by nanoengineered devices. It is all about targeting the molecules and delivering drugs with cell precision. More than $65 billion are wasted each year due to poor bioavailability. *In vivo* imaging is another area where tools and devices are being developed. Using nanoparticle contrast agents, images such as ultrasound and MRI have a favourable distribution and improved contrast. The new methods of nanoengineered materials that are being developed might be effective in treating illnesses and diseases such as cancer. Drug delivery systems, lipid- or polymer-based nanoparticles, can be designed to improve the pharmacological and therapeutic properties of drugs.

The strength of drug delivery systems is their ability to alter the pharmacokinetics and bio distribution of the drug. Nanoparticles have unusual properties that can be used to improve drug delivery. Where larger particles would have been cleared from the body, cells take up these nanoparticles because of their size. Complex drug delivery mechanisms are being developed, including the ability to get drugs through cell membranes and into cell cytoplasm. Efficiency is important because many diseases depend upon processes within the cell and can only be impeded by drugs that make their way into the cell. Triggered response is one way for drug molecules to be used more efficiently. Drugs are placed in the body and only activate on encountering a particular signal.[6]

Diagnosis

Nanotechnology has the potential to revolutionise molecular diagnostics to elucidate the key molecular defects for a particular disease. This process will require high-throughput detection devices that require nanogram quantities of analytics and reagents. With the current cost of molecular diagnostics escalating, it may be that increased use will inevitably expose these sophisticated tests to the economies of scale and decrease costs, making such testing

available at the bedside[7]. In the field of urology, several posters at annual meetings of the American Urological Association reported the use of nanotests as tools to measure prostate-specific antigen (PSA). In 2002, Azzourzi et al. reported the use of a PSA blotting paper nanotest assay. They found good correlation between the novel test and conventional PSA testing. However, the reliability decreased inversely to the PSA value[8].

Telomerase activity, a marker of limitless replicative potential, is often elevated in malignancy. Grimm et al have developed nanoparticles that switch on their magnetic state by annealing with telomerase-synthesized TTAGGG sequences, which can then be detected by bench top magnetic resonance relaxometers. They commented that these nanoparticles are biocompatible and may be able to detect molecular lesions in vivo[9]. Several groups have successfully imaged angiogenesis with MRI in animal models using nanoparticles by targeting avb3-integrin[10]. In addition, biosensing with implantable nanotubes could revolutionise the continuous monitoring of electrolytes or glucose in chronic diseases states such as diabetes. The mainstay of nanotechnology applications in imaging is the ability to confer in vivo localization and external detectability with high sensitivity and specificity. Quantum dots are fluorescent semiconductor nanocrystals with possible applications in biomolecular and cellular imaging. Although hydrophobic and toxic properties have until recently limited their use in vivo by altering the surface structure and limiting the use of toxic semiconductors such as selenium and cadmium, clinical potential may become a reality[11].

Nanoparticles Targeting

It is greatly observed that nanoparticles are promising tools for the advancement of drug delivery, medical imaging, and as diagnostic sensors. However, the biodistribution of these nanoparticles is mostly unknown due to the difficulty in targeting specific organs in the body. Current research in the excretory systems of mice, however, shows the ability of gold composites to selectively target certain organs based on their size and charge. These composites are encapsulated by a dendrimer and assigned a specific charge and size. Positively-charged gold nanoparticles were found to enter the kidneys while negatively-charged gold nanoparticles remained in the liver and spleen. It is suggested that the positive surface charge of the nanoparticle decreases the rate of opsonization of nanoparticles in the liver, thus affecting the excretory pathway. Even at a relatively small size of 5 nm, though, these particles can become compartmentalized in the peripheral tissues, and will therefore accumulate in the body over time. While advancement of research proves that targeting and distribution can be augmented by nanoparticles, the dangers of nanotoxicity become an important next step in further understanding of their medical uses.[12]

Nanomedicine in Cancer Treatment

The small size of nanoparticles endows them with properties that can be very useful in oncology, particularly in imaging. Quantum dots (nanoparticles with quantum confinement properties, such as size-tunable light emission), when used in conjunction with MRI (magnetic resonance imaging), can produce exceptional images of tumor sites. These nanoparticles are much brighter than organic dyes and only need one light source for excitation. This means that the use of fluorescent quantum dots could produce a higher contrast image and at a lower cost than todays organic dyes used as contrast media. The downside, however, is that quantum dots are usually made of quite toxic elements. Another nanoproperty, high surface area to volume ratio, allows many functional groups to be attached to a nanoparticle, which can seek out and bind to certain tumor cells. Additionally, the small size of nanoparticles (10 to 100 nanometers), allows them to preferentially accumulate at tumor sites (because tumors lack an effective lymphatic drainage system). A very exciting research question is how to make these imaging nanoparticles do more things for cancer. For instance, is it possible to manufacture multifunctional nanoparticles that would detect, image, and then proceed to treat a tumor. This question is under vigorous investigation; the answer to which could shape the future of cancer treatment. Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells, could enable the detection and diagnosis of cancer in the early stages from a few drops of a patient's blood.[13]

Nanomedicine for Neurology

The role of nanomedicine in neurology is to investigate molecular, cellular and physiologic process. To promote functional regeneration of the nervous system. To facilitate the delivery of drugs across the blood brain barriers and in neuroprotective strategies. Flurescent indicator protein for glutamate (FLIPE) – a nanosensor developed to monitor glutamate level inside and at the surface of living cell. This neurotransmitter, excitatory in nature influence all form of bahviour and influence learning and memory also involved in the neurologic damage as in stroke and neurodegeneractive disorders, to prevent excitotoxicity and spillover to other synapses its rapid removal from synaptic cleft is essential. Alzheimers disease (AD) is other target for diagnosis.[14]

Nanonephrology

Nanonephrology is a branch of nanomedicine and nanotechnology that seeks to use nano-materials and nano-devices for the diagnosis, therapy, and management of renal diseases. It includes the following goals:

1. The study of kidney protein structures at the atomic level
2. nano-imaging approaches to study cellular processes in kidney cells
3. nano medical treatments that utilize nanoparticles to treat various kidney diseases

Advances in Nanonephrology are expected to be based on discoveries in the above areas that can provide nano-scale information on the cellular molecular machinery involved in normal kidney processes and in pathological states. By understanding the physical and chemical properties of proteins and other macromolecules at the atomic level in various cells in the kidney, novel therapeutic approaches can be designed to combat major renal diseases. The nano-scale artificial kidney is a goal that many physicians dream of. Nano-scale engineering advances will permit programmable and controllable nano-scale robots to execute curative and reconstructive procedures in the human kidney at the cellular and molecular levels. Designing nanostructures compatible with the kidney cells and that can safely operate in vivo is also a future goal. The ability to direct events in a controlled fashion at the cellular nano-level has the potential of significantly improving the lives of patients with kidney diseases.

Nanoparticle solutions, acting as nanocarriers could enhance ocular drug delivery, thereby assisting the treatment of both AMD and primary open angle glaucoma. Nnanoparticles are structures smaller than 100 nm (i.e. 10-9 metres). As potential drug carriers, the active ingredient can be dissolved, entrapped/encapsulated or absorbed. Apparently different nanoparticles afford different drug-release kinetics, capacities and stability. These particulate delivery systems are also foreseen to improve patient compliance and reduce systemic side effects.[15]

Cardiovascular nanomedicine:

Cardio-nanomedicine has elicited much excitement from the point of view of diagnostics as well as that of therapeutics, although FDA-approved nano-cardio products are not available. Currently nanotechnology offers a broad platform in the field of cardiovascular science by offering tools to explore the frontiers of cardiac science at the cellular level. Nanotechnology-based tools can be effectively used to treat the cardiovascular diseases. These tools can be used in the areas of diagnosis, imaging, and tissue engineering. Miniaturized nanoscale sensors like QDs, nanocrystals, and nanobarcodes can sense and monitor biological signals such as the release of proteins or antibodies in response to cardiac or inflammatory events. Nanotechnology can also help in revealing the mechanisms involved in various cardiac diseases. It also helps in designing atomic-scale machines by imitating or incorporating biological systems at the molecular level. The use of these newly designed nanomachines can have a paradigm-shifting impact in the treatment of the dreaded cardiovascular diseases.[16]

Nanomedicine for Respiratory diseases

Applied nanotechnology to medical problems – nanomedicine– provides new concepts for diagnoses and therapies that could be described using the three interrelated themes molecular imaging, targeted drug delivery including controlled release and regenerative medicine (Table 1).[3]

Table 1: Potential Applications of Nanotechnology in Respiratory medicine

Therapy	Diagnostics	Research
Drug delivery and controlled release	Molecular imaging	Probing of DNA structure
Gene delivery	MRI contrast enhancement	Detection of proteins
Regenerative medicine and tissue engineering	Bio detection of pathogens	Pharmacokinetic studies
Tumor destruction	Fluorescent biological labels	Separation and purification of biological molecules and cells

Because nanocarrier systems may be administered to the airways easily, a number of respiratory diseases may be approached using nanoparticles: obstructive lung diseases, genetic disorders affecting the airways, infectious diseases including tuberculosis, and cancer.

Obstructive lung diseases:

The obstructive airway diseases chronic obstructive pulmonary disease (COPD) and bronchial asthma represent one of the major global causes of disability and death. For bronchial asthma, experimental studies have already been conducted to assess the use of such nanosystems. Nanoparticle technology was applied to discover a potent nanoparticles P-selectin antagonist with strong anti-inflammatory effects in a murine model allergic asthma.[17] A further study used chitosan/interferon (IFN)-γ pDNA nanoparticles. These particles were established to analyze the quantity of in situ IFN-γ production. The reason for this approach is that adenovirus-mediated IFN-γ gene transfer reduces airway hyperresponsiveness in mice but is limited so far by the frequency of gene delivery required. The nanocarriers were given to ovalbumin-sensitized mice to assess their efficacy to modulate ovalbumin-induced inflammation and airway hyperresponsiveness. On the molecular level, the treatment with nanocarriers involved signal transducer and activator of transcription 4 (STAT4) signaling because STAT4-deficient mice did exhibit reduced airway hyperresponsiveness and inflammation.[18]

Pulmonary tuberculosis:

Next to the experimental studies addressing its role for the treatment of allergic asthma nanoparticle technology has also been evaluated for its potential use in antimicrobial therapy. One of the first studies addressed the issue of nanoparticle-encapsulated antitubercular drugs as potential oral drug delivery systems against murine tuberculosis (TB)[19]. One of the major problems with long-duration TB chemotherapy is patient non-compliance. A reduction in the frequency of dosing using nanoparticle-encapsulated compounds might therefore lead to a significant improvement in the therapy. To assess this issue, poly (DL-lactide-co-glycolide) (PLG) nanoparticle-encapsulated formulations of the three frontline antitubercular drugs rifampicin, isoniazid and pyrazinamide were studied in mice.

Lungs Cancer therapy

Cancer gene therapy for the treatment of lung cancer has recently been demonstrated to have beneficial effects in experimental and in preclinical trial. The lung cancer gene therapy is currently limited to treating localized tumors since there is a host-immunity response against the gene delivery vector and the transgene. In this respect, studies are currently performed to develop novel gene delivery vectors that are non-immunogenic. One attractive vehicle is the non-viral vector, N-[1- (2,3-dioleoyloxy)propyl]-N,N,N-trimethylammonium chloride (DOTAP):cholesterol (DOTAP:Chol) nanoparticle that has been shown to be an effective systemic gene delivery vectors in preclinical studies[20].

Anemia

Anemia is a common complication of chronic kidney disease (CKD), with erythropoietin deficiency being the major contributing factor. The availability of erythropoiesis-stimulating agents (ESAs) has been a seminal advance in the treatment of anemia related to chronic kidney disease. Over the course of the last decade and a half, newer generations of ESAs have become available. The first-generation ESAs or epoetins have a relatively shorter half-life and have traditionally been administered up to 3 times per week intravenously or subcutaneously to maintain adequate hemoglobin (Hb) levels. At the turn of the century, darbepoetin alfa, a hyperglycosylated form, became available for clinical use. It conferred greater metabolic stability in vivo owing to two additional N-linked carbohydrate chains attached to the protein backbone and has a half-life 3 times longer than that of epoetin.[21]

The Future of Nanomedicine

Nanotechnology is beginning to change the scale and methods of vascular imaging and drug delivery. In future, the earliest molecular machine systems and nanorobots may join the medical armamentarium, finally giving physicians the most potent tools imaginable to conquer human disease, ill health, and aging. What nanoscientists will be able to achieve in the future is beyond current imagination. This might accomplished by self assembled biocompatible nanodevices that will detect, evaluate, treat and report to the clinical doctor automatically.

Conclusion

Nanotechnology has its applications in treatment, diagnosis, monitoring, and control of biological systems. Nanomedicine can be developed either as drug delivery systems or biologically active drug products. The technology is expected to create innovations and play a critical role in various biomedical applications, not only in drug delivery, but also in molecular imaging, biomarkers and biosensors. Target-specific drug therapy and methods for early diagnosis of pathologies are the priority research areas where nanotechnology would play a vital role. Concepts of nanomedicine offer numerous novel therapeutic options in pharmacotherapy.

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