The Emerging Therapy of Tomorrow with Nanomedicine: Present Status

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Abstract

Nanomedicine is new concept in combining nanotechnology and medicine. Nanotherapeutics is the use of nanomedicine in therapy. The definition of nanomedicine require attention as the nanotechnology represents a cluster of technologies. This article outlines present development in nanomedicine and prospect in nanotherapeutics. Health and safety issues also are discussed.

Richard Feynman a nobel Laurete predicted the emergence of a new science called nanotechnology in 1959, as this deals with structure of one to one hundred nanometers in scale [1] . Nanotechnology is term used to define the products, processes and properties at the nano/micro scale that have resulted from the convergence of the physical, chemical and life sciences. National Nanotechnology Initiative (NNI) defines nanotechnology as research and development at the atomic, molecular or macromolecular levels in the sub-100nm range (0.1-100nm) create structure, devices, and system that have novel functional properties [2,3] . Definition of nanotechnology as proposed by Bawa and Colleagues [4] . 'The design; characterization, production and application of structures, devices and systems by controlled manipulation of size and shape at the nanometer scale (atomic, molecular and macromolecular scale) that produces structures, devices and systems with at least one novel / superior characteristic or property. Nanotechnology is not new technology for eg. protein vaccines some peptiders and viruses also molecular medicine and biotechnology may be considered nanotechnology [2,3] . Nanotechnology will have a profound impact on the future of medical practice.

Nanomedicine is a combination of nanotechnology and medicine and it provide new direction in medical diagnosis, monitering and treatment at the level of single molecules or molecular assemblies at the “nano” scale of about 100nm or less. Nanomedicine defined as “the monitoring, repair, construction, and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures [5] . Nanomedicine is the application of nanoscale technologies to the practice of medicine. It is used for diagnosis, prevention and treatment of disease and to gain increased understanding of underlying disease mechanisms. Presently nanomedicine involves detection of particles, drug delivery system, emulsions, and carriers for delivering vaccines: and biomaterials with unusual properties and improved biocompatibility. Nanotechnology is also biomimicry i.e. to understand the natures solution towards biological system or to learn from nature [6] . Potential of nanomedicine market: “The market of nanobiotechnology has existed for only a few years, but it is expected to exceed $3 billion by 2008, reflecting on annual growth rate of 28%” [7] . “By 2014, 16% of goods in health care and life sciences (by revenue) will incorporate emerging nanotechnologies” [2] .

NANOMEDICINE TECHNOLOGIES AND TECHNIQUES: IN PROCESS OF PATENT ,,,,,,

Biopharmaceutics: Drug delivery (Drug encapsulation, Functional drug carrier), Drug discovery. Implantable materials: Tissue repaired and replacement (Implant coatings, Tissues regeneration scaffolds), Structural implant materials (Bone repair, Bioresorbable materials, Smart materials). Implantable devices: Assessment and treatment devices (Implantable sensors, Implantable medical devices), Sensory aids (Retina implants, Cochear implants). Surgical aids: Operating tools (Smart instrument, Surgical robots). Diagnostic tools: Genetic testing (Ultrasensitive labeling and detection technologies, High throughput arrays and multiple analyses), Imaging (Nanoparticle labels, Imaging devices), Understanding basic life processes. Areas of potential

development:

In the following areas of nanomedicine including drug delivery [14,15] :

- Synthesis and use of novel nanomaterials and nanostructures.
- Biomimetic nanostructures (synthetic products developed from and understanding of biologic systems).
- Devices and nanosensors for detection of diseases and pathogens (eg, polymerase chain reaction-coupled micro/nano-fluidic devices).
- Identification of novel biologic targets / receptors / ligands for imaging diagnosis, and therapy (eg, for cancers and for neurodegenerative and cardiovascular diseases).
- Theranostics – Construction of multifunctional biologic nanostructures, devices, and systems for diagnosis and combined drug delivery.
- Nanotechnology for tissue engineering, and regenerative medicine.
- Stimuli-sensitive nanodevices and physically targeted treatments.
- Miniaturized nanofluidic devices and systems that transport fluids more efficiently to the site of delivery.
- More efficient site-specific targeting by way of nanodrugs, resulting in with reduces systemic side effects and better patient compliance.
- Close-looped drug delivery nanodevices and implants containing sensors on the same chips.
- Microsurgical devices, molecular motors, or nanobots that are capable of navigating throughout the body to repair damaged sites, destroy tumors or viruses, and even perform gene therapy.

NANODEVICES AND CATEGORIES OF NANOMEDICINE

Quantum dots: Quantum dots are precisely design fluorophores whose emission is directly related to their size (Quantum-confinement). These colloidal semiconductors are single crystals with absorption and emission properties [16,17] , can be used as noninvasive indicators of tumors [18,19] .

Fluorescence resonance energy transfer (FRET): FRET between a donor and an acceptor molecule provides qualitative information about distance and quantitative information about the kinetics of changes in distance [20] . These sensor perform in living cells and when manipulated through genetic engineering permit visualization of a variety of uptake and transport processes eg. high capacity glucose transport pathway system was identified in the lumen of the endoplasmic reticulumn (ER) [21] .

Dendrimers: Dendrimers are major class of chemical polymer (in nanoscale) [22] in which the atoms are arranged in many branches and sub-branches radiating out from a central core [23] eg. MRI contrast agent in nanobased drug delivery. Dendrimers also known as “artificial proteins” synthesized as nanostructure and they are distinguished by their precise nanoscale scaffolding and nanocontainers properties. These are emerging nanomedicine. Polyamidoamine a multipurpose dendrimer prototype suitable for use as a targeted, diagnostic and for controlled delivery of cancer therapies [23,24] .

Nano-liposomes: The lipid based nanosystems eg. Nanoemulsions, lipid-core micelles and small unilamellar vesicles. This is to improve drug solubility to minimise adverse effect and to improve efficacy – useful strategy in cancer treatment [25] .

Other-Nanodevices / Nanostructures: Nanowires has potential in the treatment of parkinsonism and other neurodegnerative disorders [26] . Micelles – self assembling nanosized colloidal particles used to improve solubility of various pharmaceutical and act as drug carriers [27,28] . Nanotubes – carbon nanostructures, Shvedova AA et al [29] reported the unusual inflammatory and fibrogenic pulmonary responses to single walled carbon nanotubes in mice (inhaled form). The nanotubes retained their fluorescent and emissive properties inside the white blood cells [30] . Nanobombs: Boundle of carbon nanotubes its shockwave kills the cancerous cells useful in breast cancer [31] .

Nanoparticles and nanodevices eg. Nanobiosensors and nanobiochips are being used to improve drug discovery and development. Drug targeting by using nanoparticle should reduce systemic toxicity, encapsulation and nanocarriers protect drugs from metabolism and from excretion. Drug diffusion through pore (in organic aluminium oxide

nanoporous filter) – a novel method of administering antiangiogenic and antioxidant drugs. In the treatment of proliferative vascular disease.

Treatment modalities: are in various stages of development [32] . The goal of nanomedicine use is comprehensive monitoring, repair and important of all human biologic systems. Therapeutics of nanomedicine or Nanotherapeutics – The use of nanomedicine in therapy – the main areas of nanotherapeutics are - drug therapy, genetherapy and immunotherapy. In drug therapy because of size reduction or encapsulation of drug particle the therapeutic potential of water insoluble and unstable drug improve and also facilitate the delivery of drugs (small molecules) across blood brain barrier [33] . In genetherapy the DNA nanoparticle can deliver functional genes to correct genetic disorder such a haemophilia cyticfibrosis and muscular dystrophy [34] .

Nanomedicine in chemotherapy as diagnostic agent, in treatment, and to assess the progress of therapy [35] . Based on nanoparticle technology – a drug containing paclitaxel as albumin-bound particle (size of 100-200nm) in an injectable suspension form for the treatment of breast cancer. This overcome the problem of insolubility with paclitaxel [36] (see in box).

Figure 1

Box: Nanomedicines– Status

Product	Type of nanomaterial	Indication	Phase
VivaGel	Dendrimer	Topical microbicide for HIV	Phase – 3
MRX-952	Branching block copolymer self-assembled nanoparticulate formulation of irinotecan metabolite	Oncology	Preclinical
Abraxane	Paclitaxel-albumin Nanoparticle	Non-small cell lung cancer, breast cancer, others	On market
Cyclosertcamptothecin	Cyclodextrin nanoparticle	Metastatic solid tumors	IND field
TNT AntiEpCAM	Polymer-coated iron oxide	Solid tumors	Preclinical
Verigene platform	DNA-functionalized gold nanoparticles	Diagnostics	On market
INGN-401	Liposome	Metastatic lung cancer	Phase – 1
Combidex	Superparamagnetic iron oxide nanoparticle	Tumor imaging	NDA field

Abbreviations: IND, investigational new drug; NDA, new drug application.

Cardiovascular nanomedicine: The role of nanomedicine in cardiovascular area are in diagnosis, in evaluation of atherosclerotic diseases activity and in management of cardiovascular diseases. The nanocardioproduct and approaches promise to change the present medical strategy of “see and treat” to “detect and prevent” [37] . A variety of imaging devices i.e. supramagnetic nanoparticles and perfluorocarbon nanoparticle emulsion, for noninvasive MRI [38] . Nanosensors designed for measuring nitic oxide (NO) level at molecular level in a single endothelial cell [39] . The No nanosensors are porphyrinic molecular metals (specifically designed electrically conductive organic material) that can oxidize No selectively and generate a current proportional to its concentration with the use of No nanosensor “Real-time” detection is possible at the level of single cell or neuron. Hsieh PC et al [40] reported that the locally controlled intramyocardial delivery of platelet – derived growth factor (PDGF) with peptide nanofibers improve postinfarction ventricular function without pulmonary toxicity, and leads to long term improvement in cardiac function.

Neurologic nanomedicine: The role of nanomedicine in neurology is to investigate molecular, cellular and physiologic process [41,42,43] . To promote functional regeneration of the nervous system [44] . To facilitate the delivery of drugs across the blood brain barriers [45] and in neuroprotective strategies [46] . Flurescent indicator protein for glutamate (FLIPE) – a nanosensor developed to monitor glutamate level inside and at the surface of living cell [47] . This neurotransmitter, excitatory in nature influence all form of bahviour and influence learning and memory [48] also involved in the neurologic damage as in stroke and neurodegeneractive disorders [49] , to prevent excitotoxicity and spillover to other synapses its rapid removal from synaptic cleft is essential. Alzheimers disease (AD) is other target for diagnosis [50] .

The role of nanomedicine in dermatology, to provide, state of art patient care. Gold nanoparticle, quantam dot and magnetic nanoparticles are used in nanoimaging. In noninvasing imaging of skin high resolution dermoscopy, microscopy and spectroscopy offer advance diagnostic and therapeutic modalities.

To increase the efficacy of anticancer drug and to reduce the toxic effect, a polymeric misceller and liposome based delivery system conjugated to tumor specific ligands have been studied [51,52,53] . In prostatic tumor – the tumor cell overexpress transferring receptor and for targeting drug to tumor, ligand transferring has been investigated [54] . For the treatment of a localize prostatic tumor the approach is direct intertumoral delivery of biodegradable nanoparticles, a controlled release formulation, providing sustained drug effect [55] . The drugs intracellular adhesion molecular (ICAM-1) protect endothelial cell from oxidative damage by reactive oxygen species particle. ICAM-1 is a good target for

vascular immunotargeting of nanoparticle to the damage endothelium [56] . Carbon nanostructure - Fullerenes could be potential drugs in future. In the treatment of neurodegeneratic disorder like parkinsonism, multiple sclerosis and other disease that are associated with oxidative stress and damage. Fullerens can be use an alternative to chelating agent. Fullerenes also known as bulky ball (cluster of carbon C 60) [57] . Fullerenes are resistant to biochemical degradation within the body – produce less adverse effect, nanotechnology faciliate the drug delivery. “Pharmacies on a chip” [58] researcher at the Massachusetts institute of technology achieved a controlled release of drug from microchip. Poly (Liactic acid) microchip device were manufactured to contain 36 drug reservoir [59] .

An immunosuppresant agent sirolimus was approved by FDA as a solid dose formulation in year 2000 [60] .

Health and safety issues – a large proportion of the atoms that make up a nanoparticles because of their small size, are exposed to the exterior of the particle and may participate in many chemical processes. It may lead to the adverse consequences due to exposure in to the environment.

Studies in human showed that deposition of nanoparticle in the lungs increases with decreasing particle size and the toxicity of inhaled insoluble nanomaterials increases with decreases particle size and increasing particle surface area [61] . Certain classes of nanoparticle could be responsible for destructive inflammatory processes in the lungs eg. carbon black nanoparticle may induce a type-II alveolar epithelial cell line to release pro-inflammatory mediators.

Nanotechnology changes the properties of substance eg. Carbon as fullerens and nanotubes an attractive candidate for applications but also make them dangerous, when expose to environment. The measures for safety needs to be taken on environmental concern with the use of nanotechnology [62] . Nanomedicine have potential to cross blood brain barrier [63] may cause harm to the patient.

The verichip corporation has declared the availability of the world first and only patented, FDA – cleared radiofrequency identification implantable microchip [64] , with this ethical question arises about patient own personal detail which is available to other [64] . Privacy and confidentiality of the patients may be affected. Goldstcin [65] state that by eg. 2016 “-------- your doctor will be capable of scanning your entire genome within a few minutes”. The protection and maintenance of health information of the patient is the ethical issue, and while using nanotechnology in medical field ensuring privacy and confidentiality is of utmost importance.

SUMMARY

A clear definition of nanotechnology is an issue that require attention. Nanotechnology represents a cluster of technologies with different characteristic and applications. Nanomedicine related applications are under development and this is a long process of converting nanomedicine in to commercially viable products. The ultimate goal of nanotherapeutic is comprehensive monitoring repair and improvement of all human biologic system. There is great concern over the environmental and health risk with the use of nanomedicine. The protection and maintenance of health information of the patients is the ethical issue and ensuring privacy & confidentiality is of utmost importance while using nanomedicine.

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