

Nanotechnology: A Triumphant Leap in Health Care and Medicine

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Abstract: Nanotechnology is the study of extremely small structures, having size of 0.1 to 100 nm. Nano medicine is a relatively new field of science and technology. Brief explanation of various types of pharmaceutical nano systems is given. Nanotechnology with its entry in the field of biology medicine and health care has revolutionized this field and how we used to think about treating them. Application of Nanotechnology in various fields such as health and medicine, drug delivery, protein and peptide delivery and cancer treatment are future aspects of use of nanotechnology in medicine. The advancement in nanotechnology helps in the treatment of neurodegenerative disorders such as Parkinson's disease and Alzheimer's disease. In addition, early diagnosis, implants with improved properties are anticipated. The following review give an insight about the use of nano-biotechnology in drug delivery and notorious disease treatment.

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1. Introduction

A new weapon introduced recently in terms of creating resistance against microbial attacks and that most powerful weapon is nanotechnology. Nano-biotechnology refers to the science of integration between biology and nanotechnology (Sahoo and Labhassetwar, 2003). This technology has revolutionized the world and making world a place free from severe attacks of microorganisms and other powerful agents causing killing diseases. Nano biotechnology as defined in broad terms an interdisciplinary field, that includes fields such as diverse as molecular chemistry, molecular biology, material physics and quantum electronics (Ali et al., 2014). It basically relies on the idea of producing products that can penetrate into the organisms system whereby effectively carry out the function, it was meant for (Kayser et al., 2005). Many nanotech research strands are dedicated to finding alternatives or complements to antibiotic treatments, other projects are contributing to the fight against microbial resistance by developing new methods to detect and track antibiotic resistance in bacteria. Faster and more effective detection and diagnosis of drug-resistant infections is important because giving a patient access to the correct treatment earlier can have a major influence on the clinical outcome, not to mention continued transmission of the infection (Huh and Kwon, 2011). Nanotechnology is not only being envisioned as a replacement for antibiotic treatments, however, nanotechnology also holds the potential to

preserve and extend the effectiveness of existing antibiotics, primarily by acting as an enhanced drug delivery system to unleash a large and sustained payload of antibiotics to harmful bacteria in a more selective way. Breaking all the walls, Nanotechnology has demonstrated the potential to help detect AMR (antimicrobial resistance) faster, enhance and extend the effectiveness of existing antibiotics and offer alternative treatments when antibiotics fail (Ayala-Núñez et al., 2009).

Nanoparticles exist in the natural world and are also created as a result of human activities. Because of their submicroscopic size, they have unique material characteristics, and manufactured nanoparticles may find practical applications in a variety of areas, including [medicine](#), [engineering](#), catalysis, and environmental remediation (Stone et al., 2010). Many of the inner workings of cells naturally occur at the nanoscale. On the cellular level an ability to act as a gene vector has been demonstrated for nanoparticles (Mansouri et al., 2006). Carbon black nanoparticles have been implicated in interfering with cell signaling (Canesi et al., 2008).

Hence, it is now very well known that nano biotechnology can be used in many field for innovative results that can save life of human and provide human with better health and keep human save from life threatening diseases. No doubt, all of discovery has impacts and demerits too, same is with 10^9 particles. But a technology that has positive impact more than negative ones is considered to be

more than best technology. In this review, we discuss detail role of nanotechnology in curing of human diseases and tissue engineering.

Nanotechnology in Health and Medicine

Even today various disease like **diabetes**, HCV, Alzheimer's disease, Tuberculosis and multiple sclerosis as well as different kinds of serious inflammatory or infectious diseases (e.g. HIV) constitute a high number of serious and complex illnesses which are posing a major problem for the mankind. Nanomedicine is an application of nanotechnology which works in the field of health and medicine. Nano-medicine makes use of nano materials, and nano electronic biosensors. In the future, nano medicine will benefit molecular nanotechnology. The medical area of nano science application has many projected benefits and is potentially valuable for all human races.

Nanobiotechnology and the Cure of Diseases

Cure of AIDS

Besides little bit success in curing of HIV disease, there are various hidden aspects of these controlling processes which are needed to open. The major difficulty has been the failure of the treatment, typically due to poor patient compliance. Much different type of factors which cause failure of HIV treatment process such as need to take the medication daily for a lifetime, patients fail to adhere to the treatment schedule, leading to ineffective drug levels in the body and rebound of viral replication. Another most important cause of failure is the production of viral resistant against one or more drugs. These types of viral resistant were rose due to disturbance of genetic materials of virus lead to the production of mutation. In order to overcome these problems, different individual therapies were performed for selection of different combination of most effective drugs for each patient. The changes in combination of drugs may lead to the side effects on patients. Many studies reported that the changes in drugs may cause serial problems to HIV patient such as heart strokes, cancer, liver diseases and accelerating aging. Most of the scientist believe that such disease was happened when mutation occur in HIV retrovirus or combine with other virus. For complete eradication of HIV virus, scientist's required to explore new methods or approaches such as nanotechnology which is applied in order to avoid the needs of lifetime treatments.

Although at an earlier stage, applications of nanotechnology for prevention and treatment of HIV/AIDS have also gained attention in recent years. There are emerging novel approaches in which nanotechnology can enhance current treatment as well as advance new therapeutic strategies, such as gene therapy and immunotherapy (Mamo et al., 2010). Moreover, some nanomaterials have therapeutic

effects by themselves. Nanotechnology can also play a major role in preventive strategies for developing vaccines and microbicides.

Cure of Alzheimer's disease

Alzheimer defined "senile dementia" more than a century ago with a remarkable accuracy. It is now known as the Alzheimer's disease (AD), and is the main cause of the dementia syndrome (Hardy and Selkoe, 2002).

En route to very early diagnosis of a complex disease like AD we need to have an affordable, ultrasensitive and selective molecular detection method. The recently growing application of Nanotechnology in molecular detection of biomarkers is promising for very early diagnosis of Alzheimer's disease. From a practical point of view, one may perform a molecular detection process either inside the body (*in vivo*) or on the samples derived from the body (*in vitro*) (Georganopoulou et al., 2005). Nanotechnology may help us to achieve early diagnosis of AD by providing us with a highly potent signal transduction approach. Signal transduction refers to the process through which a biological signal (a biomarker) transforms to a recordable signal, and is amplified enough to be recorded (Haes et al., 2005). This potential application of nanotechnology in molecular diagnosis is mainly based on the special physical (optical, electrical or magnetic), chemical and biological characteristics of certain multifunctional nanoparticles (Yang et al., 2011).

In recent years, significant amount of research have been focused on finding the so called "neuroprotective agents", therapeutics that could stop the disease progress by targeting special molecular mechanisms in the AD pathology process (Beck et al.). However, more futuristic are approaches that could rebuild the damaged tissue, called as "regenerative agents". These two (neuroprotective and neuroregenerative) approaches together are known as "disease-modifying approaches" (Nazem and Mansoori, 2011). They are distinguished from symptomatic approaches by the fact that in addition to ameliorating the symptoms they are aimed to stop the disease progress and restore the dysfunctional or dead tissue (Apaolaza et al., 2014). The therapeutic potential of nanotechnology for AD includes both neuroprotective and neuroregenerative approaches (Suri et al., 2007). In addition, nanotechnology has shown promising applications in targeted drug delivery for AD, and several nano-carrier systems have been studied in recent years to increase the bioavailability and efficacy of different AD therapeutic agents (Suri et al., 2007).

Cure of HCV

Scanning surface confocal microscopy, simultaneous recording of high-resolution topography

and cell surface fluorescence in a single scan enables imaging of individual fluorescent particles in the nanometer range on fixed or live cells. This technique has been used to record the interaction of single virus-like particles with the cell. This method provides a technique for elucidating the interaction of individual viruses and other nanoparticles, such as gene therapy vectors, with target cell.

Nanoviricides (NanoViricides Inc) are polymeric micelles, which act as nanomedicines to destroy viruses (Barton et al., 2011). As defined by Nanoviricides Inc, & quot; nanoviricide is a polymeric single chemical chain with covalently attached ligands that specify the virus target (Diwan, 2012). The antiviral spectrum of the drug is determined by the specificity of the set of ligands attached to the chain. Nanoviricide is designed to seek a specific virus type, attach to the virus particle, engulf or coat the virus particle, thereby neutralizing the virus's infectivity, destabilize and possibly dismantle the virus particle, and optionally it may also be made capable of attacking the viral genome thereby destroying the virus completely. Active pharmaceutical ingredients are optional and can be hidden in the core of the nanoviricide missile (Jain, 2008).

Cure of Tuberculosis

Tuberculosis (TB) in humans has been described since ancient times and its causative agent, *Mycobacterium tuberculosis* (MTB) is widely disseminated. The WHO estimates that approximately one third of the global community is infected with *M. tuberculosis* (Jain et al., 2017). In 2006, an estimated 9.2 million incident cases and approximately 1.7 million deaths due to TB occurred worldwide making it the world's leading causes of mortality. Despite mass *Mycobacterium bovis* BCG vaccination and the development of antitubercular drugs, tuberculosis still remains a major global public health problem (Trunz et al., 2006).

Nanotechnology has provided a huge improvement to pharmacology through the designing of drug delivery systems able to target phagocytic cells infected by intracellular pathogens, such as mycobacteria. The increased therapeutic index of anti-mycobacterial drugs; the reduction of dosing frequency; and the improvement of solubility of hydrophobic agents, allowing the administration of higher doses, have been demonstrated in experimental infections (Pandey and Khuller, 2006). These advantages may lead to new therapeutic protocols that will improve patient compliance and, consequently, lead to a more successful control of mycobacterial infections. The Rising rates of tuberculosis and drug-resistant disease in developing countries have also amply illustrated the need for better diagnostic tools and effective vaccines. Because still we don't have a

highly efficient method in relation to diagnose tuberculosis.

Treatments with improved sustained release profiles and bioavailability can increase compliance through reduced drug requirements and there in minimize MDR-TB (Multi drug resistance tuberculosis) (Davies, 2004). Chemotherapy of TB is complex due to the requirement of multi drug regimens that need to be administered over long periods. The Poor patient compliance is the single most common reason for chemotherapy failure in TB (Gelperina et al., 2005). The micro-encapsulation of pharmaceutical substances in biodegradable polymers used in controlled drug delivery has seen as an emerging technology. Carrier or delivery systems such as liposomes and microspheres have been developed for the sustained delivery of anti-TB drugs and have found better chemotherapeutic efficacy when investigated in animal models (e.g. mice) (Barrow et al., 1998). Gelperina et al. summarizes major data on nano- particulate formulations of the anti-TB drugs (Galperin and Koonin, 1999).

Sharma et al. (2004), conducted a study to explore lectin-functionalized poly (lactide-co-glycolide) nanoparticles (PLG-NPs) as bio adhesive drug carriers against tuberculosis (TB), in order to reduce the drug dosage frequency of anti-tubercular drugs and thus improve patient compliance in TB chemotherapy. In this study they observed the presence of drugs in plasma for 6–7 days for rifampicin and 13–14 days for isoniazid and pyrazinamide after administration of lectin coated PLG-NPs through the oral/aerosol route. They also observed that upon administration of uncoated PLG-NPs (oral/aerosolized) rifampicin was detectable in plasma for 4–6 days, whereas isoniazid and pyrazinamide were detectable for 8–9 days. All three drugs were present in lungs, liver and spleen for 15 days (Sharma et al., 2004).

Johnson et al., (2005) evaluated the efficacy of nanoparticle-encapsulated anti-tuberculosis drugs administered every 10 days versus that of daily non encapsulated drugs against *Mycobacterium tuberculosis* aerosol infection in guinea pigs. In both cases the treatments significantly reduced the bacterial count (Johnson et al., 2005). This finding suggested that the nanoparticle drug delivery system has potential in intermitted treatment of tuberculosis.

Cancer and Nanotechnology

Cancer is one of the leading causes of deaths worldwide with an estimated 7.6 million individuals lost each year and accounting for 13% of all deaths. Cancer-related mortality is expected to rise to 13.1 million by 2030 (Bray et al., 2013). Cancer is not a single disease but a multitude of diseases with each organ or system developing a distinct set of diseases.

Many instances of cancer could be avoided, with some estimates indicating that about 30% of cancer deaths are associated with smoking or other lifestyle factors or dietary practices that could potentially be avoided by changes in human behavior. First of all, nanotechnology can be used for better cancer diagnosis (Schroeder et al., 2012). One of the main usage fields of optical nanoparticles is to allow better cancer detection (Choi et al., 2010). To start with, classical methods that are used in diagnosis have limitations. At their earliest stages, tumors lack blood vessels of their own; they take their nutrients such as oxygen and glucose from the surrounding tissue. Cells at the tumor's periphery get more of those nutrients than cells at the tumor core, so most small tumors grow at their edges while starving their cores. Cells in the tumor core release proteins to signal their oxygen-starved state. Two fundamental processes are involved in differentiating malignant and nonmalignant cells:

- Passive targeting
- Active targeting.

Passive targeting

It is well known that the tumor vasculature is leaky relative to the hierarchical structure of normal vasculature, in part, because malignant cells are not responsive to cell signaling required for orderly vasculogenesis. Macromolecules may enter the tumor through leaky vasculature and persist, in part, because of reduced lymph clearance in tumors by a phenomenon referred to as the enhanced permeability and retention effect. The efficiency of the EPR depends on tumor size, tumor type, and tumor heterogeneity, among other factors (Chauhan et al., 2011).

Active targeting

In principle, any ligand that displays preferential binding toward malignant relative to nonmalignant cells or that results in selective activation proximal to malignant cells can be used to actively target malignant cells (Srinivasan, 2008). In this regard, growth factor receptors such as epidermal growth factor receptor (EGFR), transferrin receptor (DR) complexes (e.g., DR5), and folate ligand as well as tumor-specific antigens (e.g., PSMA) have all been utilized to localize NPs to malignant cells via active targeting. A variety of chemical and biological molecules have been used to direct NPs to malignant cells expressing the molecular target receptor including monoclonal antibodies, small molecules, and nucleic acid aptamers (Sinha et al., 2006).

Advances in the treatment of diabetes

Nanotechnology is increasing importance in diabetics' research in the recent decade. Some of the applications of nanotechnology in treating diabetes mellitus are artificial pancreas, instead of pancreas transplantation use of artificial beta cells, for oral

delivery of insulin use of nanospheres as biodegradable polymeric carriers etc (Gu et al., 2013). Over the last few years, several methods have been proposed for non-invasive monitoring of blood glucose and this can be made possible by [nanotechnology](#). Various types of nanoparticles are currently studied for insulin delivery in [diabetes](#) treatment such as, Polymeric biodegradable nanoparticles, Polymeric micelles, Ceramic nanoparticles, Liposomes and Dendrimer (Panyam and Labhasetwar, 2003). Polymeric nanoparticles are found to be effective and efficient over traditional oral and intravenous administration methods. These are biodegradable polymers surrounded by nanoporous membrane and are used as carriers of insulin. pH change swell the polymer system resulting in release of insulin. Copolymers like N, N-dimethylaminoethylmethacrylate, polyanhydrides, polyurethanes, polyacrylic acids and polyacrylamide are being investigated for these applications (Kumari et al., 2010).

To overcome the problem of invasive and painful subcutaneous injections, oral insulin administration is considered to be the most convenient method for the [treatment](#) of diabetes mellitus. Gastric [enzymes](#) are major barrier for insulin when administered orally as they degrade insulin in the stomach. Therefore, it should be enveloped in a matrix in order to get protected from the harsh environment in the stomach. This can be achieved by using combination of calcium phosphate-polyethylene glycol-insulin with casein (Sarmiento et al., 2007).

Need of nanomaterials in Dentistry

Despite better understanding of the materials and chemistry, and recent improvements in physical properties, no material has been found that is ideal for any dental application. For example, silver amalgam has been used for dental restoration for more than a century; however, there has been a major concern about mercury toxicity from the amalgam restorations for many years. Another major issue is the color of amalgam for aesthetic considerations and alternative materials are being sought to replace (Eggleston and Nylander, 1987). Nature has arranged complex biominerals in the best way from the micro to the nano-scale and no one can yet combine biological and physical properties to get ideal structures. In addition, no synthetic material can be intelligent enough to respond to external stimuli and react like nature made tissues. There are a number of possible options to make smart materials for the construction and mimicking of nature. All these approaches are not possible without the intervention of nanotechnology. For example components required for designing such biomaterials (biomolecules, cells, tissue engineering

scaffolds and signal) involve the development of nanomaterials (Kumar and Vijayalakshmi, 2006).

Nanomaterials for Dental Tissue Regeneration

The applications of nanoscale scaffold materials for tooth tissue regeneration are well established. For pulp regeneration, pulp stem cells were purified in the laboratory and grown in sheets on scaffolds. The scaffolds used were composed of nanofibers of biodegradable collagen type I or fibronectin. Self-assembling polypeptide hydrogels have been used for pulp tissue regeneration (Zhang and Webster, 2009). There is a formation of a nanofiber mesh that supported the growing cells. Puramatrix (containing amino acids repeats of alanine, arginine and aspartate) has been proven to enhance cell growth. Natural silk based nanomaterials are being used for various tissue regeneration applications and have promising scope for dental applications. Injectable self-assembly collagen I scaffold loaded with exfoliated teeth stem cells resulted in the formation of pulp like tissue and functional odontoblasts. Collagen type I is the most abundant fibrous protein found in the form of nanofibers in dentin (~80%–90% of organic matrix) and bone. Odontogenic differentiation and mineralization was promoted in the presence of type I collagen scaffolds. The tissue regeneration approached are not in practical implementation at present, however further research is expected to overcome the challenges to fancy tissue engineering products available for clinical applications in the field of dentistry in near future.

Advances in cardiovascular diseases

Cardiovascular diseases are the major cause of non-communicable illness in both developing and developed nations, representing 30% of global deaths. New therapeutic approaches are desperately needed. Nanomedicine represents one such approach, and involves using molecular entities on the scale of 10-150 nanometers, for purposes of diagnosing, treating, and preventing disease (Iverson et al., 2008).

Nanotechnology in hypertensive disease

Most antihypertensive drugs have significant disadvantages, such as low bioavailability, relatively short half-life, low permeability and adverse side effects. For effective and safe administration of these drugs, delivery systems that can provide a low frequency of dosing, increased bioavailability, increased selectivity and reduced undesirable effects, are needed. For this, nanotechnology provide alternative strategies to achieve those objectives (Wickline and Lanza, 2003). One example is the design of a formulation of curcumin in a nanoemulsion system with the aim of reducing its unfavorable solubility and bioavailability properties, the curcumin nanoemulsion system can improve its

activity by enhancing its solubility, which results in increased bioavailability (Sood et al., 2014).

Nanotechnological advances in atherosclerosis and hyperlipidemia

On the base of different studies, some nanocarriers can be used as drugs delivery devices for reduction of major landmarks in the development of atherogenesis, including intimal hyperplasia, has led to advancing the use of nanotechnology as an appropriate tool for delivering bioactive agents to the vessel wall, which have potential benefit for the treatment of atherosclerosis. Besides its previously mentioned antihypertensive properties, curcumin encapsulated in a nanoemulsion also shows significant activity in reducing cholesterol, as compared to pravastatin (Caruthers et al., 2007). Therefore, it has been suggested that curcumin could also have a potential to use as alternative therapeutic compound for the treatment of hyperlipidemia. Some estrogens, like 17 β -estradiol (17- β E), also interfere with the progression of coronary atherosclerosis (Ray and Lahiri, 2009).

Moreover, monocyte inflammatory activity plays a crucial role in the destabilization and rupture of atherosclerotic plaques. The administration of nanoparticles loaded with pitavastatin exerts its effect on circulating monocytes which are recruited to the site of inflammation, thereby inhibiting the destabilization and avoiding or delaying plaque rupture. Furthermore, the nanoparticles of a new nanoparticulate delivery drug system formulated from poly-(lactic-co-glycolic) acid (PLGA) were incorporated to a variety of relevant cells, such as monocytes, vascular smooth muscle cells, and endothelial cells. This new system enhances the therapeutic efficacy of pitavastatin at least 20 times compared with conventional daily oral administration of this drug. Nanoparticulate delivery system was suggested that this formulation could become an attractive therapy to achieve regression of atherosclerotic plaques (Makadia and Siegel, 2011).

Nanomedicine applied to the treatment of stroke

Oxidative stress is the common underlying mechanism of damage in ischemic stroke. Another novel nanotechnology application for the treatment of ischemic stroke consists of nanoparticles that can easily cross the blood brain barrier (BBB) without compromising its integrity (Quan et al., 2013). Studies show that cytidine 5'-diphosphate has neuroprotective capacity in ischemia-reperfusion. Incorporation of this drug in suitable nanoparticles could allow the drug to exert its effect in the CNS by passage of said nanoparticles through the blood brain barrier (BBB), increasing its therapeutic activity in the required site. Another class of drugs that may allow rescue neuronal cells after brain ischemia/reperfusion injury is, again,

statins. A recent *in vitro* study evaluating the efficacy of statins as neuroprotective active ingredients concluded that both atorvastatin and rosuvastatin were effective in mitigating neuronal cell death. However, both drugs have very low permeability through the BBB. This obstacle can be overcome by formulating statins nanoparticulate carrier systems which greatly facilitate the penetration of these drugs in the central nervous system (CNS), a fundamental step that determines its usefulness in the treatment of ischemic stroke (Patel et al., 2012).

Nanoparticles Delivery Systems

Nanoparticles Drug delivery

Nanoparticle drug delivery systems are nanometric carriers used to deliver drugs or biomolecules. Generally, nanometric carriers also comprise sub-micron particles with size below 1000 nm and with various morphologies, including nanospheres, nanocapsules, nano-micelles, nanoliposomes, and nanodrugs (Kumari et al., 2010). Nanoparticle drug delivery systems have outstanding advantages, some of which include:

- They can pass through the smallest capillary vessels because of their ultra-tiny volume and avoid rapid clearance by phagocytes so that their duration in blood stream is greatly prolonged.
- They can penetrate cells and tissue gap to arrive at target organs such as liver, spleen, lung, spinal cord and lymph.
- They could show controlled- release properties due to the biodegradability, pH, ion and/or temperature sensibility of materials.
- They can improve the utility of drugs and reduce toxic side effects.

As drug delivery system, nanoparticles can entrap drugs or biomolecules into their interior structures and/or absorb drugs or biomolecules onto their exterior surfaces. Presently, nanoparticles have been widely used to deliver drugs, polypeptides, proteins, vaccines, nucleic acids, genes and so on. Over the years, nanoparticle drug delivery systems have shown huge potential in biological, medical and pharmaceutical applications (Cappel and Kreuter, 1991). Currently, the researches on nanoparticle drug delivery system focus on:

- The selectness and combination of carrier materials to obtain suitable drug release speed.
- The surface modification of nanoparticles to improve their targeting ability.
- The optimization of the preparation of nanoparticles to increase their drug delivery capability, their application in clinics and the possibility of industrial production.

- The investigation of *in vivo* dynamic process to disclose the interaction of nanoparticles with blood and targeting tissues and organs, etc.

One type of nanoparticle, which is differentiated from any of the above terms, is a solid lipid nanoparticle (SLN) with a lipid core that is solid at room temperature. During formation of SLNs the solid lipid is first melted, then emulsified as a liquid to form an o/w emulsion, and cooled to allow the lipid to solidify. Due to the similarity in formation and content, these particles have been referred to as “emulsions with solid fat globules” (Birdi, 2013).

Nanotechnology and Protein delivery

Development of effective protein delivery strategies is essential to further enhance therapeutic outcomes to enable widespread medical applications. Biodegradable polymeric microparticles are promising parenteral depot formulations for long-term protein drug release (from weeks to months), in particular when the maintaining of protein concentration in therapeutic range is required for more than 1 week (Yan et al., 2010). They enable sustained release of proteins by both diffusion from the polymer matrix and the degradation/erosion of the polymer. One of the most widely used materials for the encapsulation of proteins is poly (lactic-co-glycolic acid) (PLGA), as it is biocompatible, biodegradable with favorable degradation rates, and already approved by the FDA for use in humans. Encapsulation of proteins into polymeric microparticles can be achieved by several methods such as double emulsion (the most widely used technique), single emulsion, phase separation (coacervation), ultrasonic atomization, spray-drying, and microfluidics. Once the proteins are encapsulated into microparticles, their release kinetics depend on the microparticle size, molecular mass of the polymer, degradation rate, charge property of the polymers, ratio of hydrophilicity to hydrophobicity, polydispersity of microparticle size, protein loading amount, as well as the surrounding microenvironment (Yu et al., 2016). Currently, there are a number of microparticle protein-delivery formulations (e.g., Trelstar depot) on the market, and various microparticles are under preclinical development for delivering therapeutic proteins such as bone morphogenetic protein-2, insulin, recombinant human epidermal growth factor, and recombinant human erythropoietin (EPO). However, these clinically successful microparticle systems may cause blockage of the needle required for administration, and the bioactivity of the released proteins under physiological conditions need to be considered for long-term delivery. Extended protein stability is still challenging, and in addition, degradation and erosion of biodegradable polymers including PLGA can lower the pH inside the microparticles, which can further

lead to denaturation of the protein as well as aggregate formation (Asuri et al., 2006).

Conclusion:

Nanotechnology in modern medicine and nanomedicine is in infancy, having the potential to change medical research dramatically in the 21st century. Nanomedical devices can be applied for analytical, imaging, detection, diagnostic and therapeutic purposes and procedures, such as targeting cancer, drug delivery, improving cell-material interactions, scaffolds for tissue engineering, and gene delivery systems, and provide innovative opportunities in the fight against incurable diseases. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. The vision is to improve health by enhancing the efficacy and safety of nanosystems and nanodevices.

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References

- Sahoo SK, Labhasetwar V (2003) Nanotech approaches to drug delivery and imaging. *Drug discovery today* 8: 1112-1120.
- Ali MA, Rehman I, Iqbal A, Din S, Rao AQ, et al. (2014) Nanotechnology, a new frontier in Agriculture. *Adv life sci* 1: 129-138.
- Kayser O, Lemke A, Hernandez-Trejo N (2005) The impact of nanobiotechnology on the development of new drug delivery systems. *Current pharmaceutical biotechnology* 6: 3-5.
- Huh AJ, Kwon YJ (2011) "Nanoantibiotics": a new paradigm for treating infectious diseases using nanomaterials in the antibiotics resistant era. *Journal of controlled release* 156: 128-145.
- Ayala-Núñez NV, Villegas HHL, Turrent LdCI, Padilla CR (2009) Silver nanoparticles toxicity and bactericidal effect against methicillin-resistant *Staphylococcus aureus*: nanoscale does matter. *Nanobiotechnology* 5: 2-9.
- Stone V, Hankin S, Aitken R, Aschberger K, Baun A, et al. (2010) Engineered nanoparticles: Review of health and environmental safety (ENRHES). Project final report.
- Mansouri S, Cuie Y, Winnik F, Shi Q, Lavigne P, et al. (2006) Characterization of folate-chitosan-DNA nanoparticles for gene therapy. *Biomaterials* 27: 2060-2065.
- Canesi L, Ciacci C, Betti M, Fabbri R, Canonico B, et al. (2008) Immunotoxicity of carbon black nanoparticles to blue mussel hemocytes. *Environment international* 34: 1114-1119.
- Mamo T, Moseman EA, Kolishetti N, Salvador-Morales C, Shi J, et al. (2010) Emerging nanotechnology approaches for HIV/AIDS treatment and prevention. *Nanomedicine* 5: 269-285.
- Hardy J, Selkoe DJ (2002) The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *science* 297: 353-356.
- Georganopoulou DG, Chang L, Nam J-M, Thaxton CS, Mufson EJ, et al. (2005) Nanoparticle-based detection in cerebral spinal fluid of a soluble pathogenic biomarker for Alzheimer's disease. *Proceedings of the National Academy of Sciences* 102: 2273-2276.
- Haes AJ, Chang L, Klein WL, Van Duyne RP (2005) Detection of a biomarker for Alzheimer's disease from synthetic and clinical samples using a nanoscale optical biosensor. *Journal of the American Chemical Society* 127: 2264-2271.
- Yang C-C, Yang S-Y, Chieh J-J, Horng H-E, Hong C-Y, et al. (2011) Biofunctionalized magnetic nanoparticles for specifically detecting biomarkers of Alzheimer's disease in vitro. *ACS chemical neuroscience* 2: 500-505.
- Beck A, Beck-Sickinger A, Langer R, Clozel M DRUG DISCOVERY AND NEW THERAPEUTICS.
- Nazem A, Mansoori GA (2011) Nanotechnology for Alzheimer's disease detection and treatment. *Insciences J* 1: 169-193.
- Apaolaza PS, Delgado D, del Pozo-Rodriguez A, Gascón AR, Solinís MÁ (2014) A novel gene therapy vector based on hyaluronic acid and solid lipid nanoparticles for ocular diseases. *International journal of pharmaceutics* 465: 413-426.
- Suri SS, Fenniri H, Singh B (2007) Nanotechnology-based drug delivery systems. *Journal of occupational medicine and toxicology* 2: 16.
- Barton RW, Tataka JG, Diwan AR (2011) Nanoviricides-A Novel Approach to Antiviral Therapeutics. *Bionanotechnology: Global Prospects*, D Reisner ed In press, CRC Press, Boca Raton, FL.
- Diwan AR (2012) Nanoviricides: Novel Antiviral Nanomedicines-A Customizable Platform Technology.
- Jain KK (2008) Nanomedicine: application of nanobiotechnology in medical practice. *Medical Principles and Practice* 17: 89-101.
- Jain D, Ghosh S, Teixeira L, Mukhopadhyay S. Pathology of pulmonary tuberculosis and non-

- tuberculous mycobacterial lung disease: Facts, misconceptions, and practical tips for pathologists; 2017. Elsevier.
22. Trunz BB, Fine P, Dye C (2006) Effect of BCG vaccination on childhood tuberculous meningitis and miliary tuberculosis worldwide: a meta-analysis and assessment of cost-effectiveness. *The Lancet* 367: 1173-1180.
 23. Pandey R, Khuller G (2006) Nanotechnology based drug delivery system (s) for the management of tuberculosis.
 24. Davies PD (2004) Multi-drug-resistant tuberculosis. *Tuberculosis: Springer*. pp. 809-837.
 25. Gelperina S, Kisich K, Iseman MD, Heifets L (2005) The potential advantages of nanoparticle drug delivery systems in chemotherapy of tuberculosis. *American journal of respiratory and critical care medicine* 172: 1487-1490.
 26. Barrow EL, Winchester GA, Staas JK, Quenelle DC, Barrow WW (1998) Use of microsphere technology for targeted delivery of rifampin to *Mycobacterium tuberculosis*-infected macrophages. *Antimicrobial agents and chemotherapy* 42: 2682-2689.
 27. Galperin MY, Koonin EV (1999) Searching for drug targets in microbial genomes. *Current opinion in biotechnology* 10: 571-578.
 28. Sharma A, Sharma S, Khuller G (2004) Lectin-functionalized poly (lactide-co-glycolide) nanoparticles as oral/aerosolized antitubercular drug carriers for treatment of tuberculosis. *Journal of antimicrobial chemotherapy* 54: 761-766.
 29. Johnson CM, Pandey R, Sharma S, Khuller G, Basaraba RJ, et al. (2005) Oral therapy using nanoparticle-encapsulated antituberculosis drugs in guinea pigs infected with *Mycobacterium tuberculosis*. *Antimicrobial agents and chemotherapy* 49: 4335-4338.
 30. Bray F, Ren JS, Masuyer E, Ferlay J (2013) Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *International journal of cancer* 132: 1133-1145.
 31. Schroeder A, Heller DA, Winslow MM, Dahlman JE, Pratt GW, et al. (2012) Treating metastatic cancer with nanotechnology. *Nature Reviews Cancer* 12: 39.
 32. Choi Y-E, Kwak J-W, Park JW (2010) Nanotechnology for early cancer detection. *Sensors* 10: 428-455.
 33. Chauhan K, Manchanda A, Khurana JK, Jain P, Sharma D, et al. (2011) Nanotechnology: the nano soldiers in the war against cancer. *J Pharm Res* 4: 4420-4423.
 34. Srinivasan C (2008) Carbon nanotubes in cancer therapy. *CURRENT SCIENCE-BANGALORE*-94: 300.
 35. Sinha R, Kim GJ, Nie S, Shin DM (2006) Nanotechnology in cancer therapeutics: bioconjugated nanoparticles for drug delivery. *Molecular cancer therapeutics* 5: 1909-1917.
 36. Gu Z, Aimetti AA, Wang Q, Dang TT, Zhang Y, et al. (2013) Injectable nano-network for glucose-mediated insulin delivery. *ACS nano* 7: 4194-4201.
 37. Panyam J, Labhasetwar V (2003) Biodegradable nanoparticles for drug and gene delivery to cells and tissue. *Advanced drug delivery reviews* 55: 329-347.
 38. Kumari A, Yadav SK, Yadav SC (2010) Biodegradable polymeric nanoparticles based drug delivery systems. *Colloids and Surfaces B: Biointerfaces* 75: 1-18.
 39. Sarmiento B, Ribeiro A, Veiga F, Sampaio P, Neufeld R, et al. (2007) Alginate/chitosan nanoparticles are effective for oral insulin delivery. *Pharmaceutical research* 24: 2198-2206.
 40. Eggleston DW, Nylander M (1987) Correlation of dental amalgam with mercury in brain tissue. *The Journal of prosthetic dentistry* 58: 704-707.
 41. Kumar SR, Vijayalakshmi R (2006) Nanotechnology in dentistry. *Indian J Dent Res* 17: 62-65.
 42. Zhang L, Webster TJ (2009) Nanotechnology and nanomaterials: promises for improved tissue regeneration. *Nano today* 4: 66-80.
 43. Iverson N, Plourde N, Chnari E, Nackman GB, Moghe PV (2008) Convergence of nanotechnology and cardiovascular medicine. *BioDrugs* 22: 1-10.
 44. Wickline SA, Lanza GM (2003) Nanotechnology for molecular imaging and targeted therapy. *Am Heart Assoc*.
 45. Sood S, Jain K, Gowthamarajan K (2014) Optimization of curcumin nanoemulsion for intranasal delivery using design of experiment and its toxicity assessment. *Colloids and Surfaces B: Biointerfaces* 113: 330-337.
 46. Caruthers SD, Wickline SA, Lanza GM (2007) Nanotechnological applications in medicine. *Current opinion in biotechnology* 18: 26-30.
 47. Ray B, Lahiri DK (2009) Neuroinflammation in Alzheimer's disease: different molecular targets and potential therapeutic agents including curcumin. *Current opinion in pharmacology* 9: 434-444.
 48. Makadia HK, Siegel SJ (2011) Poly lactic-co-glycolic acid (PLGA) as biodegradable

- controlled drug delivery carrier. *Polymers* 3: 1377-1397.
49. Quan L, Zhang Y, Crielaard BJ, Dusad A, Lele SM, et al. (2013) Nanomedicines for inflammatory arthritis: head-to-head comparison of glucocorticoid-containing polymers, micelles, and liposomes. *ACS nano* 8: 458-466.
 50. Patel T, Zhou J, Piepmeier JM, Saltzman WM (2012) Polymeric nanoparticles for drug delivery to the central nervous system. *Advanced drug delivery reviews* 64: 701-705.
 51. Cappel MJ, Kreuter J (1991) Effect of nanoparticles on transdermal drug delivery. *Journal of microencapsulation* 8: 369-374.
 52. Birdi K (2013) *Surface chemistry essentials*: CRC Press.
 53. Yan M, Du J, Gu Z, Liang M, Hu Y, et al. (2010) A novel intracellular protein delivery platform based on single-protein nanocapsules. *Nature nanotechnology* 5: 48.
 54. Yu M, Wu J, Shi J, Farokhzad OC (2016) Nanotechnology for protein delivery: Overview and perspectives. *Journal of controlled release* 240: 24-37.
 55. Asuri P, Karajanagi SS, Yang H, Yim T-J, Kane RS, et al. (2006) Increasing protein stability through control of the nanoscale environment. *Langmuir* 22: 5833-5836.

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