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Review Article

The Nanotechnology Revolution in Human Health

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Abstract

Nanotechnology is a field of applied science and technology covering a broad range of topics, such as materials science, chemistry, physics, engineering, and biology. Nanotechnology offers new opportunities in improving human care and disease treatment and control. Many medical challenges need to be overcome by the specific structure and properties at nanoscale. A great number of studies have reported on the applications of nanotechnology in human health care.

In this review, we discuss the current potential applications of nanotechnology for human health and we also suggest the advancement in the development of nanomedicine.

***Keywords:** Nanomedicine; Human Health; Nanoparticles; Medicine; Emerging Nanotechnology*

Abbreviations

NPs: Nanoparticles; CNTs: Carbon Nanotubes; FGO: Fluorinated Grapheme Oxide; MRI: Magnetic Resonance Imaging; SPECT: Single Photon Emission Computed Tomography; PET: Positron Emission Tomography; CT: Computed Tomography; AuNPs: Gold Nanoparticles; MNPs: Magnetic Nanoparticles; QDs: Quantum Dots

Introduction

Nanotechnology is defined as the science and engineering included in the design, production and application of devices and structures by controlling size and shape at nanometer scale.

Nanotechnology research in human health care can result in immense health benefits [1]. The genesis of nanotechnology can be traced to the promise of revolutionary developments in fields such as robotic, communications, genomics, and medicine. The application of nanotechnology in human health is called nanomedicine and it is based on the use of nanoparticles (NPs). Today, nanomedicine is defined as the science that uses nanomaterials to the development of diagnostics, treatment and prevention of specific medical applications [2,3].

However, materials and devices designed by nanotechnology, which are applied in medicine, can be interacting with tissues and cells at molecular scales with high degree of specificity, thus, allowing integration between technology and biological systems not previously attainable [4]. Nanotechnology not in itself a single scientific discipline but rather a meeting of several sciences to bring together the required collective expertise needed to develop these new technologies [4]. There are some advantages of nanotechnology in the field of medicine like surgical instruments, devices for diagnostic and treatment of diseases, implanted devices, the ability of some organs replacement, and the rapid suspension of novel diseases [5]. The nanoscale related to surface can provide powerful functionalizing strategies, through organic or inorganic shell, superficial binding biomolecules, natural or synthetic coatings, and encapsulated composites and hybrid [6-8]. Thus, the special properties of these nanostructures recommend them to be used in new diagnostics tools in medicine.

This review focuses on the potential applications of nanotechnology in human health and developments to realize the full potential of medicine.

Applications of nanotechnology in human health

Nanotechnology has great potential applications in human health care, as presented in the figure 1.

Figure 1: *Schematic representation of nanotechnology applications in human health.*

Nanotechnology as a risk to human health

NPs with size smaller than 100 nm could pose potential health risks, such as carbon nanotubes (CNTs) which have damaging effects on the respiratory system. Thus, CNTs are a materials consisting of nanotube agglomerates, metal catalyst and non-tubular forms of carbon such as fullerenes, can effect on the toxicity. In fact, there are several parameters which effect on the toxicity of nanomaterials including particle shape, size, chemical composition, surface charge, surface roughness, surface energy, specific surface area, coatings, medium, biological interaction, dissolution, and structure.

However, CNTs may damage DNA and harmful impacts on the organs if introduced into the human body [9-12]. Recent studies revealed that some nanomaterials interface with cell viability assays [13]. Subsequent studies demonstrated that classical dye based assays produce invalid results by using some nanomaterials because of interactions of nanoparticles with dye [14]. Moreover, several works confirmed the toxicity of nanoparticles [15]. The duration of the nanomaterials in the human body plays a major effect in causing the disease [16]. In addition, CNTs have harmful effects on the biological system. Moreover, titanium oxide nanoparticles, which are used in consumer products, possess the ability to transfer from pregnant mice to offspring affecting the genital systems and central nerve [17]. Müller., *et al.* [18] found that iron oxide nanoparticles Ferumoxtran-10 has no toxic influences on human monocyte-macrophage interactions at low value of concentrations (up to 1 mg/ml) for duration greater than 72 hours and possibly only toxic at high value of concentrations (10 mg/ml). In contrast, Cengelli., *et al.* [19] reported that iron oxide nanoparticles coated with various PVAs and dextran were not cytoxic to brain derived endothelial EC219 cells and murine N9 and N11 microglial cells.

Nanotechnology in orthopedics

Nanotechnology offers a powerfully platform with higher enhanced bioactivity and higher mechanical strength in improving the quality of life of patients. Thus, several studies were reported on the applications of nanotechnology in orthopedics field. For example, some studies [20] showed that alumina nanometer fibers significantly stimulate osteoblast responses compared with conventional alumina. Additionally, helical rosette nanotubes, as new developed materials, showed enhanced osteoblast adhesion compared with conventional uncoated titanium because these nanotubes mimic the dimensions of the nanostructure of collagen and other bone components [21]. Similarly, other studies concluded that adsorption of proteins was improved on nanospaced materials such as three dimensional (3D) nanofibrous scaffolds [22]. All these works have demonstrated that nanomaterials represent a powerful tool to improve orthopedic implants efficacy in human health. Some studies suggest that cells responses might be more sensitive to changes in surface roughness, in nanometer scale, as compared with conventional regimes, which lead to enhanced osteoblast and osteoblast activity, thus improving the degree of osseintegration [23].

Nanotechnology in gene therapy

Gene therapy is an experimental technique that uses genes to treat or prevent disease. It is based on the replacement of incorrect genes or the delivery of repaired ones genes or the [24]. The common approach in gene therapy used for correcting defective (faulty) genes by inserting a normal gene into a nonspecific location within the genome to replace a nonfunctional gene. In this context, the abnormal gene could be repaired through selective reverse mutation or swapped for a normal gene through homologous recombination, returning the gene to its normal function [25]. However, the application of nanotechnology in gene therapy has been extensively reviewed by Davis [26]. He reported that nanoparticles-based non-viral vectors (50 - 500 nm) were tested to transport plasmid DNA. He also suggested that nanotechnology, in gene therapy, could replace currently used viral vectors with potentially less immunogenic nanosize gene carriers. Zhang., *et al.* [27] also illustrated and described the methods used for the preparation of nanoparticles (2 - 200 nm in diameter) comprises a plurality of silane moieties, wherein each silane moiety is covalently coupled to the surface, wherein at least a portion of the plurality of silane moieties comprises a targeting agent, and wherein the silane moieties comprise a polyalkylene oxide moiety intermediate the targeting agent and the surface.

Nanotechnology in targeted drug delivery

Since 1960, researchers have been developing drug delivery systems [28]. Their miniscule dimensions mean that all kinds of nanoparticles are suitable for use in systems of this kind [29]. The active substance can be encapsulated and/or attached to the surface depending on the type of particle. This means that even if they dissolve poorly in water, they can be transported in an aqueous solution (e.g. a blood sample) and are also better protected against enzyme degradation. In addition, a suitable coating on the nanoparticles can avoid recognition and removal by the immune system [30].

Over the past two decades, researchers working in the development of pharmaceutical industry have concluded that drug delivery is an integral part of drug development, and a wide range of drug delivery systems has been designed. Thus, these systems would improve the absorption, stability and therapeutic concentration of the drug within the target tissue, as well as permit reproducible and long term release of the drug at the target site [31,32]. To improving patient comfort and reducing the frequency of drug administration, new drug delivery systems would offer protection and improve the pharmaco-kinetics of easily degradable proteins and peptides, which often have short *in vivo* half-life [33]. The drug delivery techniques represent a strategic tool for expanding drug markets in pharmaceutical industry because new delivery technologies could repackage classical drugs, offering a competitive edge after the expiry of patents and avoiding competition from generics. In this context, 13% of the current global pharmaceutical market is related to the sale of products that include a drug delivery system [34]. However, drug delivery accounts for 78% of sales and 58% of patent filing worldwide [35].

Nanofactories are other more futuristic target drug delivery approaches where biological molecules found *in vivo* may be converted into active biotherapeutics in response to a localized medical condition.

Nanotechnology offers new opportunities to treating brain disorders by using the numerous chemical entities. Nanoparticles can be powerfully used to deliver relevant drugs to the brain [36].

Nanotechnology in medical imaging

Over the past 25 years, medical imaging has progressed considerably. It involves Optical imaging, MR imaging, CT imaging, PET imaging, and SPECT imaging. Thus, the schematic diagram of the different nanomaterials used in medical imaging is illustrates in figure 2.

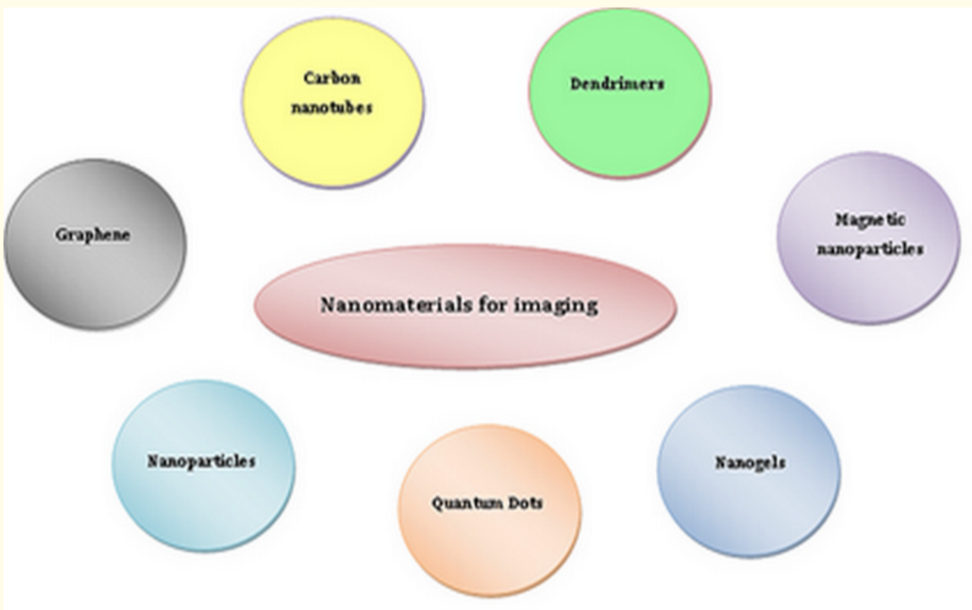

Figure 2: *Schematic diagram of the different nanomaterials used in medical imaging.*

Nanomaterials have several applications in field of medicine and related science because their unique physicochemical properties. However, nanotechnology offers new opportunities for molecular imaging, sensing clinically relevant biomarkers, tissue regeneration, and tools for therapeutic intervention [37].

Currently, the development of medical imaging techniques like magnetic resonance imaging (MRI), fluorescence, X-ray, and radio nuclides aim at enhance contrast agents and spatial resolution.

Evaluating the therapeutic efficacy of transplanted stem cells in diabetes, it is very important to track their migration, survival, fate and regenerative impact *in vivo*. After transplantation, stem cells may be tracked by using various labeling processes like magnetic nanoparticles (gold, iron oxide) or fluorescent dyes. Thus, the visualization of the labeled cells can be done by using medical imaging such as magnetic resonance imaging [38]. Medical imaging of the human body requires some form of energy. For example, the energy used in radiology must be able to penetrate the human tissues [39].

Nanoparticles (NPs)

Nanoparticles are advanced materials used in the field of biomedical based on inorganic and polymeric preparations.

Nanoparticles have many advantages for tumor imaging applications, such as high resistance to photo degradation, the possibility of biofunctionalization of their surface, the ability to be detected in biological tissues, and stable emission. Therefore, research shows that nanoparticles based imaging contrast agents like gadolinium can improve the specificity and sensitivity of magnetic resonance imaging [40]. It has also been shown that nanoparticles of gadolinium oxide are promising candidates for use in future paramagnetic contrast agent formulations, thus, the size of nanoparticles play a significant role in cellular uptake [41]. Additionally, Gold nanoparticles (AuNPs) have several advantages like low viscosity and negligible osmolarity (7.2 mM) [42].

Magnetic nanoparticles (MNPs)

Magnetic nanoparticles are a class of nanoparticles that can be controlled under the application of an external magnetic field, which are composed of magnetic elements, such as cobalt or iron.

Weissleder., *et al.* [43] showed that superparamagnetic nanoparticles of iron oxide are used clinically as contrast agents in magnetic resonance imaging. Laurent., *et al.* [44] found that magnetic iron oxide nanoparticles have proven highly effective as contrast agents in nuclear magnetic resonance imaging and treatment of hyperthermia. Harisinghani., *et al.* [45] also reported that superparamagnetic magnetite particles with dextran are used as image enhancement agents in magnetic resonance imaging. Similarly, Bouchard., *et al.* [46] concluded that pure metals can be used to develop magnetic particles due to their highest saturation magnetization, but they are not used for biomedical application. Muldoon., *et al.* [47] demonstrated that iron oxide nanoparticle represents one of the major successes in the class of nanoparticles. Combidex is in late stage clinical trials for the detection of lymph node metastases. Bhattacharyya., *et al*. [48] found that iron oxide nanoparticles induce genotoxicity and cytotoxicity by DNA damage and elevating oxidative stress in human breast cancer cell. Similarly, it has been shown that silica coated gold nanoparticles may both active agent and deliver excess heat to the tumor cells to reach a high efficacy [49]. Moreover, Haik [50] patented a medical imaging technique enables visualization of the malignant tissues by using contrast agents from magnetic nanoparticles. Thermal contrast agents can control magnetic nanoparticles that can be encapsulated in a biocompatible coating. It can be also loaded on attenuated strains of bacteria to detect tumor tissue when placed in a bloodstream of a patient. Thus, a device of alternating magnetic field can be used to induce heating of magnetic nanoparticles and a thermal scan can be used to identify tumors.

Nanogels (NGs)

Nanogels are materials in the range of nanoscale formed by polymer network. They are hydrogel nanoparticles.

Studies have shown that size optimization of biodegradable fluorescent nanogels for cell imaging [51]. Additionally, other studies have demonstrated with gel electrophoresis that completely charged nanogels form a strong complex with DNA [52]. Similarly, it has been reported that the synthesis of the nanomagnetogel offer powerful technological potential because it is simple and easy to scale up [53]. Some recent studies developed new nanogels made by the hydrophobized polysaccharides like dextran and pullulan [54].

Carbon nanotubes (CNTs)

Carbon nanotubes have several applications due to their attractive properties, such as strength and good electrical properties. Recent studies showed that CNTs have various physical features like high surface area, high mechanical strength, and high aspect ratio as well as interesting optical properties due to their good arrangement of molecular structure [55]. It has been also reported that CNTs have excellent electrical conductivity [56]. In addition, it has concluded that the detection of human cervical cells overexpressing folate receptors was improved by using a peptide nanotube folic acid modified grapheme electrode [57].

Quantum dots (QDs)

The first application of QDs as biolabels reported in 1998 [58]. Jin., *et al.* [59] found that QDs are bright, can emit the whole spectrum, and having a low degradation compared with traditional organic dyes used in biomedical. True., *et al.* [60] concluded that, due to their unique properties, when sensitivity increases QDs endow them and render them suitable for multicolored imaging. In recent studies [61], it was suggested that QDs have unique properties and become powerful tools for the biomedical field in particular for quantitative and long term detection and fluorescence imaging. Recent studies found that hyaluronic acid polymer-covered QDs have interesting qualities for both *in vivo* and *in vitro* cancer imaging field [62].

Graphene

Graphene and its derivatives seem the most promising materials for the future because of their attractive properties, such as high dispersibility in aqueous solutions, superior photo and pH stability, broad absorption, biocompatibility [63]. Recent studies found that fluorinated grapheme oxide (FGO) without magnetic nanoparticles (MNPs) was a highly effective MRI contrast agent [64]. In addition, other studies also showed that FGO can efficiently convert absorbed light into heat, raising local temperature and constituting its ability as efficient therapeutic tools [65].

Dendrimers

Since 1980, the first dendritic molecules were produced. Dendrimers are widely used in medicine due to the multiple molecular hooks on their surfaces that can be used to fluorescent dyes, enzymes and molecules, and attach cell identification tags. However, there as two structural types of dendrimers: the first type has a central core from which branches radiate and the second has no central core and formed of a series of polymers. Dendrimers are nanosized, radially symmetric molecules with well defined, homogenous, and monodisperse structure reforming tree like branches or arms [66]. Studies also demonstrated the usefulness of dendrimers containing gadolinium ions chelated on the surface [67]. Thus, it can be concluded that the presence of chelators is necessary due to the toxicity of gadolinium ions accumulated in the body [68].

Nanotechnology in cardiac therapy

The use of nanotechnology in cardiac therapy has gained great success. It can provided novel techniques in therapies. Thus, there are many types of nanomaterials used in cardiovascular applications.

Nanotechnology applications for advances in nanomedicine can enable the design and creation of nanomaterials and level nanoscale devices for therapeutic like reservoirs for drugs [69] or cells [70]. Recent studies have developed nanocomposites based on nanoparticles in order to enhance the biological and mechanical properties of current cardiovascular implants and devices [71]. Similarly, some studies showed that smooth muscle cells play a critical role during wound healing and in the initiation of endothelial layer formation and inhibits neointimal formation, thus, selective cells formation can powerfully lead to a faster and better endothelialization [72]. In another work, Korin., *et al.* [73] investigated the effects of biodegradable poly(lactic-co-glycolic) acid nanoparticles laden with the enzyme tissue plasminogen activator responsible for the dispersion of clots. Thus, these nanoparticles were used to free and separate the drug including high shear stress caused by the narrowing of the surrounding vascular. Studies have found that the new formulation showed good therapeutic effects *in vivo* and *in vitro* and it can have great potential on atherosclerosis [74]. Currently, it has been shown that the applications of nanotechnology in relation to medicine are concentrated especially on the approaches of cancer treatment and diagnosis [75].

Nanotechnology in dentistry

Nanotechnology will have future medical applications in nanodentistry (nanodental techniques) by using nanomaterials and various biotechnologies such as tissue engineering and nanorobotics.

In 1959, Richard P. Feynman, winner of the Nobel Prize in Physics, gave a famous presentation entitled "There's Plenty of Room at the Bottom" [76]. He proposed employing machines tools to make smaller machines tools and down to the atomic level. In addition, Feynman offered the first known proposal for a nanomedical procedure to cure heart disease: "A friend of mine (Albert R. Hibbs) suggests an interesting possibility for relatively small machines. He says that, although it is a very wild idea, it would be interesting in surgery if you could swallow the surgeon. You put the mechanical surgeon inside the blood vessel and it goes into the heart and looks around. It finds out which valve is the faulty one and takes a little knife and slices it out. Other small machines might be permanently incorporated in the body to assist some inadequately functioning organ". However, nanodentistry will make possible the maintenance of comprehensive oral health by employing nanomaterials [77], biotechnology [78] and nanorobotics. As with all technologies, nanotechnology has achieved tremendous progress, but ethical and social issue, safety, risks, and regulation should to be considered before the nanotechnology can be seen as the option of providing high quality dental care [79]. Table 1 illustrates the two types of approaches used in nanodentistry. The top-down approaches are mainly used to produce functional micro and nanostructures by using plasma laser or chemical vapor deposition, etc [80]. However, these techniques were used in coatings of medical implants for improving bioactivity, biocompatibility, and blood flow [81].

Top-down approach	Bottom-up approach
Nano-encapsulation	Nanorobots
Nano-needles	Nanodentifrice
Nanocomposites and nanoclusters	Hypersensitivity cure
Nanosolutions	Tooth repair
Nanoparticles as antimicrobial agents	Nanodiagnosis
Nano-impression materials	Local anesthesia
Nano-based bone replacement	Impression materials
Nano light-curing glass ionomer	Dental durability and cosmetic

Table 1: *Two approaches used in nanodentistry.*

They are several types of pure nanoparticles or nanocomposites used in the field of dentistry (Table 2). As can be seen, some materials, with biological characteristics, have shown the ability to form an interfacial chemical bond with bone. The hydroxyapatite/collagen (Hap/Col) nanocomposites are used for implants coatings [82]. These materials have a high wear resistance, an excellent biocompatibility, and designed to better serve as bone grafts [83].

Nanoparticles	Chemical properties	Physical properties	Mechanical properties
Ag NPs	- Very stable with catalytic activity Unique surface chemistry	- High surface area - High electrical conductivity - High thermal conductivity - Non-linear optical behavior	- High ductility - High malleability - Good conductors
TiO_2 NPs	- Insoluble in water and organic solvent	- High surface area - Exhibit magnetic properties	- Null ductility - Elastic limit of 367.5 MPa - Compressive strength of 3675 MPa
SiO_2 NPs	- Molar mass of 59.96 g/mol	- Specific surface area of 180 m^2/g - Density of 2.4 g/cm^3 - There are two type of structure: S-type (spherical particles) and P-type (porous particles) that exhibit a higher UV reflectivity	- Null ductility - Elastic limit of 155 MPa - Compressive strength of 1600 MPa

ZrO_2 NPs	- Molar mass of 231.891 g/mol White surface area High resistance to corrosion Available in different forms (nanocrystals, nanofluids, and nanodots)	- Density of 6.05 g/cm^3 Lighter and less susceptible to embrittlement by hydrogen	- High resistance to corrosion Hardness of 1200 HV Compressive strength of 2000 MPa High ductility Soft - High malleability
CNTs	- Heat transmission of about 6 KW/m.K - Stable - Hexagonal structure - Strongest and stiffest nanomaterials	- High surface area - Density of 2 g/cm^3 - High thermal conductivity - Powerful semiconductors - Heat stability - Ultra-light weight	- High strength of 60 GPa - Young's Modulus of 1 TPa - High tensile ductility (8 - 13%) - It has the malleability of rubber
Graphene	- The most reactive form of carbon (allotrope of carbon) - Acquired a number of unique and exceptional characters - Highest ratio of edge atoms of any allotrope, defects within a sheet increase its reactivity	- High specific surface area of 2630 m^2/g - High conductivity of 2500 W/mK - High thermal conductivity of 5000 W/m.K - Remarkable electronic properties - Good optical properties: able to transmit 97.7% of light	- Young's Modulus of 1 TPa - Tensile strength of 1100 GPa - High ductility - High malleability - Transparent - High stability
HAp NPs	- Molar mass of 502.31 g/mol - Hexagonal structure - It is a calcium phosphate - It is quite stable - Poorly soluble in water - Melting point of 1614°C	- High surface area - Density of 3.16 g/cm^3	- Hardness of 800 HV - Young's Modulus of 120 GPa - Tensile strength of 100 MPa - Compressive strength of 900 MPa

Table 2: *Properties of different nanoparticles used in nanodentistry.*

Conclusion

Nanotechnology and nanomedicine aimed at the improvement of human life by developing applications for novel therapeutic and diagnostic modalities. Therefore, several works are required for the detailed understanding about the nanotechnology for the human health. To better understand the role of nanotechnology in the future, it is necessary to improve antioxidant therapy and better understand the molecules bases of diseases. In addition, the comparisons of nanomaterials used in the field of medicine will also help to new proposed advanced nanotechnology and thus better nanoparticles. In fact, the major challenges in nanotechnology are safety and regulatory.

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Conflict of Interest

The author declares that there is no conflict of interest.

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