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Revolutionizing Healthcare and Medicine with Nanotechnology: A Comprehensive Review of its Benefits, Safety Concerns, and Environmental Risks

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Abstract
The usage of nanoparticles has proven to be effective and beneficial across an array of applications.However, the unequivocal implications of exposure to nanoparticles on human health and as well as the environmental dangers connected to their manufacturing and usage are still under-exploredNanotechnology deals with the invention and application of technologies on a scale of 1 to 100 nm at the molecular and atomic levels. It is an exceptionally versatile and multifaceted science that touches various aspects and fields like medicine, chemistry, physics, biology, and healthcare, it is gaining attention from researchers all over the world day after day. Nanoparticles have great and special optical and electromagnetic properties at nanoscale dimensions, thereby providing opportunities to continue with developments in the areas of health sciences and medicine, such as targeted delivery of drugs, medical diagnostics, tissue engineering, cancer treatments, regenerative medicine, and development of vaccines. However, because of the instabilities and inconsistencies in the size, shape, and chemical makeup of some nanoparticles can impose deleterious effects on the environment and human health. As a result, questions have been raised concerning the transportation, fate, and modification of nanoparticles discharged into the ecosystem. To determine the importance of nanotechnology and to direct its progress in different fields. The governments, civil society organizations, scientists, and the general public must work together toachieve this goal.This critical review assesses the knowledge ofthe exposure, application, safety concerns, risks, and impacts of nanoparticles on the environment and human health.

Keywords
Human health, nanoparticles, risks and impacts, safety concerns, healthcare, targeted drug delivery, medicine, nanotechnology, medical diagnosis, and environment.

Introduction

The invention and application of technologies on the scale of 1 to 100 nm isknown as nanotechnology (1). Nanotechnology and the science of nanomaterials provide great scope for material engineering and currently, they are rapidly expanding and developing scientific technologies. It involves the study of regulating, modifying, and constructing systems depending on their molecular and atomic parameters (2). The core of nanotechnology lies in the ability to generate bigger components with basically innovative molecular organizationat these levels. Nanostructures are the tiniest man-made objects constructed from fundamentally understood components and exhibit unique chemical, physical, and biological

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characteristics and activities. The main objective of nanotechnology is to package all the knowledge into techniques to understand, discover, and effectively produce and use these nanostructures(3). Nobel prize winner Richard P. Feynman,a physicist, outlined his vision for nanotechnology,by emphasizing the benefits of application of larger objects and mechanistic tools at a smaller tool and particle scale, proposing that since “there was quite some room at the bottom”(4). Nanotechnology has proven to be a major draw since it is well known that nanotechnology and biotechnology work together to create a platform of immense potential and significance in terms of heterogeneity in application. Diagnostics kits, dental medicine, diagnostic tests, environmental remediation, skincare products, sun protection products, medical imaging (X-ray), sterilization of healthcare gadget surfaces, sport gear, biological sensors, textiles, and gene inactivation are some of the applications of nanotechnology in healthcare(5). The practice of diagnosis and treatment has been revolutionized completely, through the application of nanotechnology in various forms through nanodiagnostics, nanosensors, nanomedicine, drug delivery systems, and nanoimplants (figure 1)(6). Nano-biomaterials are being rapidly used in several industries, which include food, medicine, textiles, pharmaceuticals, agriculture, and crop protection tactics(7).

Nanomedicine is undoubtedly one of the newest social technical practices aiming to stake a claim in the rapidly emerging field of personalized medicine. As a result, nanomedicine’s proponents have made their claims, if not exaggerated,its expected advantages. For example, advocates of nanomedicine have positioned it as the most “patient-friendly approach,” as therapies are tailored to the patient’s needs, thereby minimizing the risk of unwanted side effects from the drugs(8).

The possible risks associated with materials based on nanotechnology remain a significant concern. Previous studies have shown that nanoparticles can harm DNA in vitro and there arenegative consequences of nanomaterials in vivo such as increased inflammation and weakened immunity. That is why it is important to figure out the toxicity of nanomaterials in healthy and prone animal populations, including humans. More efforts should be put into acquiring additional information regarding environment, health, and safety (EHS)consequences of nanomaterials for the benefits of the public and the environmentto assess and control risks as well as creating regulations that promote wise investment in innovations on nanotechnology.(9).

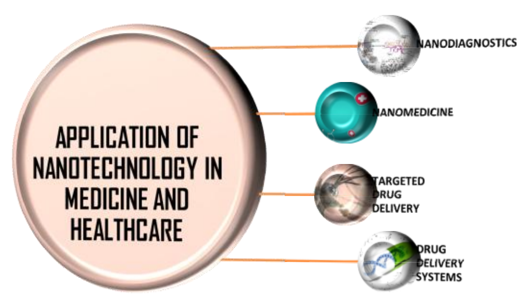

Figure 1: Some applications of nanotechnology in medicine.

Benefits And Application Of Nanotechnology In Healthcare And Medicine.

Diagnosis And Treatment Of Cancer

A Greek philosopher, Hippocrates (460-370 B.C), was the first to coin the word cancer to the disease, and he used the terms carcinoma and carcinos, which describe tumors that develop an ulcer and those that don’t(10). The utilization ofnanoparticles in clinical diagnosis is referred to as nanodiagnostics(11). The early detection of Cancer and imaging of umor tissue has now been made possible by using nanoparticles. For

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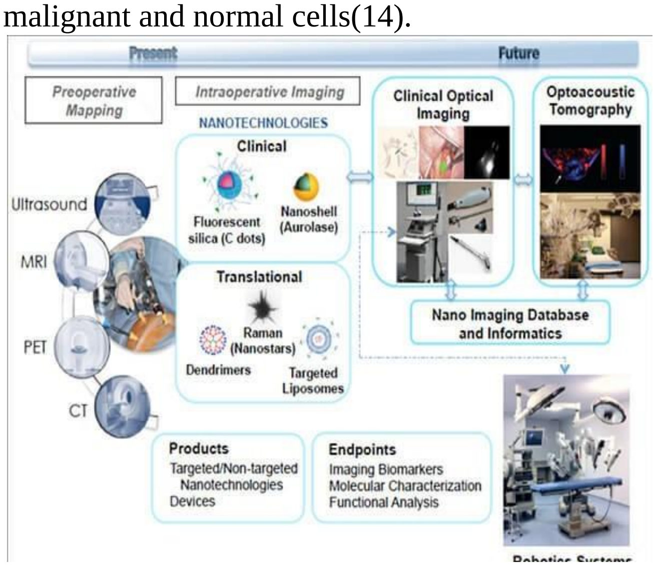
instance, the development of immune Tera magnetic iron oxide nanoparticles (SPIONs) for MRI imaging to detect metastasis in lung cancer, where the cancerousstem cells are the main target of the immune Tera magnetic iron oxide nanoparticles. These SPIONs have demonstrated excellent specificity and no adversereaction, which makes them the ideal building blocks for aerosols in lung tumor imaging using MRI(12). Superparamagnetic, and magnetized nanoparticles are in use and of great importance in hyperthermia and photodynamic therapy for cancer, magnetized cardiac stents, and imaging of liver metastasis. AuNPs are also used in cancer treatment and have found good application in Raman spectroscopy techniques, imaging of cells using CT (figure.2), dark-field light scattering techniques, and photo-thermal heterodyne scans(13).Polymeric nanoparticles, quantum dots, carbon nanotubes, and dendrimers are the several types of nanoparticles that have been applied in cancer diagnosis. Nanoparticles can be coupled with some agents such as peptides, carbohydrates, aptamers, antibodies, and other small molecules that can bind specifically to a target molecule to reach the right site or organ and improve the cancer detection capabilities of nanoparticles(11). Nanoparticles' ligand-mediated particles target cancer cells,and aid these particles to differentiate between malignant and normal cells(14).



Source: [Nanotechnology and Early Cancer Detection and Diagnosis - NCI]

Figure 2: Methods used in earlydetection of tumors with several nanoparticles by using nanotechnology.

An increasing focus is being placed in the present day on the role of calcium in cancer. Calcium has been shown to have a significant role in angiogenesis, tumor formation, migration, and cell death. The expression of calcium signal related proteins in tumor cells are different from that of normalcells,and the pathophysiology of some specific cancers,including lung, liver, breast, colon, and so forth is associated with the regulation of calcium signaling. Defects in calcium channels directly linked to the initiation and spread of cancer in the body(15). Combining Gadolinium and liposomal irinotecan combined with convection enhanced delivery(clinicalTrials.gov identifier: NCT02022644) are currently being studied in phase 1 clinical research. Application of Gd will offer real-time delivery imaging, while the formulation of liposomal therapy will allow delivery across the blood-brain barrier. CED enhances intraparenchymal administration of chemotherapy to brain cancer through the use of fluid convection (16).

Figure 3: Nanomedicines approved by FDA for cancer treatment.

The extraordinary behavior flexibility in the behavior of nanomaterials accounts for the advance in the diagnosis of cancer. Currently, Lanthanide-based upconversionnanomaterials are used in nanotechnology to confirm tissue, cell, and molecular-level imaging of cancer cells. These nanoparticles have the capability to upconvert low energy photons to high energy, which can penetrate deep into tissues, as detectable via the use of autofluorescence. In addition, nanotechnology is being used to identify fibroblast activation protein-a on the outermost layer of tumor-associated cells by using a responsive fluorescence nanoprobe(17).

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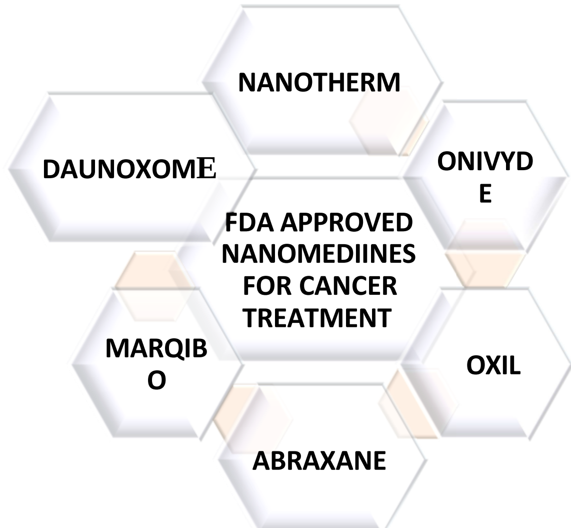
TARGETED DRUG DELIVERY



The use of nanotechnology in drug delivery is generally anticipated to have major significant shifts in the biotechnology and pharmaceutical industries soon. The prospective outcomes of nanotechnology application in drug delivery are delivering medications to the intended tissue or cell, improved delivery of poorly water-soluble medications, transcytosis of medicines across tightly packed endothelial and epithelial barriers, transportation of big macromolecule medications to the intracellular sites of action, combined use of more than medications or therapeutic methods for combination treatment, and co-delivers the medications with imaging modalities since the sites have been visualized, and finally some combination therapy is intended to have real-time effects(18). Recently, various anticancer medications such as paclitaxel, dexamethasone, doxorubicin, and 5-fluorouracil have been effectively developed using nanoparticles. Drug delivery systems have been effective because of their small size, less toxicity, modification of drug pharmacokinetics, and regulated drug release time. Chemotherapy usually fails in the successful treatment of cancer because certain tumor cells become resistant to several anticancer medications. Recent studies have shown that anticancer drugs may be delivered into cells using nanoparticles without turning on the p-glycoprotein pumps, which can transport anticancer medications out of the cell as quickly as they cross the cell's outer membrane, and causing resistance to several anticancer medications.(19)

- **CNS Drug Delivery By Lipid Nan particles**
  The encapsulation of medications in lipid nanoparticles prolongs their duration in circulation in the bloodstream, reduces the side effects associated with the medication, and improves its therapeutic effects concerning the CNS disorders. Liposomes are quickly taken up by the macrophages, microglia, and the steroids of the central nervous system, which can be deposited selectively or non-selectively onto the surfaces and release their contents into the cytoplasm of the cell. Thesepropertiesmake lipid nanoparticles valuable classes of nanocarriers for medication delivery to or within the CNS(20). However, delivery of drugs to central nervous system diseases is a tough challenge, since there exists the natural blood-brain barrier and the blood-cerebrospinal fluid barrier, which makes it difficult or hinders the delivery of medications to the site of CNS disorders. Nanotechnologybased drug delivery platformsare amongthe new strategies that have been seen to overcome these obstaclesand effectively deliver these drugs to the central nervous system, a promising therapeutic strategy for the treatment of certain prevalent diseases of the brain, which includes Huntington's illness, Alzheimer's disease, amyotrophic lateral sclerosis,frontotemporal dementia, and Parkinson's Illness.(21).

- **Nanogels In Drug Delivery**
  Nanogels are known as networks of polymers that have nanoscale compounds, forming ionic or non-ionic chain combinations like PEG or polyacrylic acid, pluronics, and polyethylene amine. The hydrogel nanoparticles are one of the unique drug delivery techniques, because they both have hydrogelic and nanoparticle properties at the same time. The most peculiar feature of these nanogels is their very high loading capacity (ranging from 40 to 60%)

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which is mostly not achieved with any other nanoparticles(20).

- **DNA Nanotechnology In Drug Delivery**
The remarkable nomenclature of DNA nanotechnology is a straightforward yet powerfully effective design scheme for the self-assembly of such distinct nanostructures, with a great deal of promise for improving therapeutic efficiency and drug toxicity reduction. There are diverse sequence programming and optimization techniques developed so far to create DNA nanostructures to make them fine in controllability concerning engineered size, shape,function, and surface chemistry. Powerful anticancer therapeutic compounds, which includeCpGoligonucleotides, and doxorubicin are being incorporated into DNA nanosystems to improvetheir absorption by cells. All these developments highlight that DNA nanotechnology holds great promise for future applicationsin nanomedicine.(22).

- **Nanotechnology In Renal Delivery System**
Renal-targeted therapy is cardinal for enhancing the therapeutic index in kidney diseases. The treatment of kidney disease, in recent years, has been targeted therapy which involves the use of macromolecular carriers, prodrugs, small molecule-therapeutic conjugation, antibody-drug combination, antisense/siRNA, and low molecular weight peptide and protein therapeutic combination techniques.(23). Additionally, nanoparticles can be considered an innovative way or tool for administering medications to treat chronic kidney disease, generally known as CKD. It is currently that nanoparticles were introduced in the treatment of renal cancer. Currently, phase 1 clinical trials (NCT04260360) for kidney cell cancers are actively conducted using submicron particle docetaxel (NanoDoce). In vivo, preclinical studies have shown good results because of thespecial nanoscale composition of the drug in which an invented biosynthesis technologyproduces identical nanomaterials with an average diameter of about 900 nm. When NanoDoce was given locally, it demonstrated a tumor decrease in the xenograft model of 786-O carcinoma of the renal cells in humans(24).

Nanomedicine
The application of nanotechnology in medicine is known as nanomedicine, and it's creating its way into therapeutic diagnostic tools to treat many kinds of medical conditions. The early detection, treatment, evaluation, and diagnosis of disease have all been linked to nanomedicine and most of the inventions mentioned are currently being used in everyday clinical practice. The targeting capacity of nanomedicine makes it possible to provide doses that are significantly greater than the maximum acceptable dose of the unformulated medication. It can, therefore, tailor doses based on individualized patient situation(25).
Nanomedicine has the potential to overcome two key factors that affect customized drug response related to the variations in cytochrome P enzymes (CYPs) and medication transporters in different individuals. Therefore, the nanomedicine medication formulation can make the formulated medications highly stealthy against metabolizing enzymes, and also intracellularly via endocytic processing that is transporter independent(25).
In the long run, the main objective of nanomedicine research is to improve our knowledge of and ability to manipulate the molecular scale elements referred to as nanomachinery within living cells. This could completely change the way we detect and manage diseases by allowing us to precisely modify nanomachinery to enhance human health and further expand our understanding of cellular systems. In the past, one of the major limiting factors has been the evaluation of single-molecule characteristics in living cells, hampered by problems, such as probe size and the photobleaching of fluorescent labels. The potential of nanomedicine lies in the

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development of platform technologies interfacing with nanoscale imaging techniques to reveal molecular mechanisms probing into living cells more enhanced. This may open the door to the next generation for early diagnosis and targeted treatment of many diseases (26).

Safety Concerns In Nanotechnology

The industrial production and application of nanotechnology bear a significant risk of exposure to nanoparticles to the environment and the workers. These exposures can have harmful effects to the environment and human health. Therefore, the toxic effects on living organisms due to nanoparticles make them very hard to detect.The vast majority of the nanoparticles' effects are yet to be determined, which could havegreater adverse implications for both the environment and living organisms. Furthermore, there isn't a systematic database of toxic effects of occupational exposure limits (OEL) and nanoparticles globally. The most significant challenge is to evaluate the risk that nanotechnology poses to the natural environment, animals, and humans, which may result in more severe circumstances(27).

Humans are unknowingly contaminated with nanomaterials in the environment or purposely through the use of biomedical substances. Humans maybe exposed to nanoparticles from their environment invarious ways such as air, food supply, or water.Biological sources of nanoparticles like ultrafine particles from eruptions of volcanoes or the earth's biological geological weathering events, are present in the air,which is contaminated to human beings. Consumption of food or water is another possible way of getting exposed to these nanoparticles. Studies on rats have revealed that nanoparticles can be absorbed by the mammalian gut, which makes human exposure through the food they consume a great concern.(28).

Even though not all nanoparticles are harmful, on industrial levels, it is crucial that risk evaluation, risk management, and risk communication must be clearly defined as a necessary industrial standard practice for all compliance. At the consumer level, toxicity at ambientand consumption levels must be clearly described as a labeling norm with easily comprehensible codes in color or images that illustrate the toxicity level. Public concerns about nanoparticles can be addressed with the help of carefully designed communication plans that inform consumers of the true nature and dangers associated with nanoparticles(29). Certainly, nanoparticles' safety demands further investigation regarding their potential harmtopublic health and the environment (30).

Risks of Nanotechnology to the Environment

Chemical and hazardous materials are naturally discharged into the environment by various activities, such as daily human activities, industrial operations, and agricultural practices. These chemicals and hazardous compounds destabilize the ecosystem whenever they attain sufficient concentration, hence causing effects on human life and other organisms within the environment. To address environmental concerns and risks arising from pollution, several methods for environmental remediation have been invented and bioremediation has proven to be more reliable and highly effective due to its environmentally friendly characteristics(31). Conclusions regarding the ecological effects of nanoparticles and their environmental interactions are extremely challenging to draw becausetheenvironmental impacts of nanoparticles cannot be accurately diagnosed due to multiple factors such as complexity in identification, minimal detection limits, and undetected environmental concentrations. Changes in nanoparticles' chemical makeupeven to a slight extent, have the potential to drastically alter their characteristics, thereby turning them into dangerous substances.The United States Environmental Protection Agency noted "Toxicity identification is difficult due to their distinct chemical properties, high reactivity, and low solubility. In some instances, determining the source of the nanoparticles in the samples might be quite challenging sometimes. Recently, ecological effect studies concerning Ag2S nanoparticles has been carried out by researchers. In doing so, it was discovered that plants such as monocotyledonous wheat and dicotyledonous cucumber may take up nanosilver if found in soil(32).

It's necessary to tacklethe safety issues identified by researchers,including the general population concerning nanotechnology to ensure the technology is safe and reliable for all. The concernsarticulated by the general public and researchers are environmental contamination, having harmful impacts rather than anticipated health and medical benefits, changing human life and lifestyle for good or bad use by criminals, other misguided people, and so on. The most likely risks include catalytic effects (increasing the rate of reactions), poisonous impacts, and explosion and fire by nanopowder and nanofibers. In humans, nanofibers found in asbestos are connected to human health problems. Regarding this, the risks of nanoparticles to human health can be evaluated by considering possible and probable exposures, the power and capacity of nanoparticles to pass through the body's internal and external defenses, and the toxic implications after penetration should all be considered. Some studies have shown that nanoparticles can pass through barriers that large particles cannot penetrate because of their small size (31).

Conclusion

Nanotechnology is driving the healthcare revolution by focusing on the preventive management of public health,thereby helping to resolve the complications of localized treatment administration, minimizing the risk of side effects, and increasing the effectiveness of treatment. Nanotechnology is suitable for tumor detection, treatment, and gene therapy. Nanomedicine remains the main area of application for nanorobotics. The development of vaccinations, diagnostic and imaging devices, drug delivery, wearable technology, and antimicrobial products. Growthineffective drug development, better medical devices, and early-stage disease detection is expected with the rise of nanotechnology. The best way to create plans for protecting the environment, particularly for those that have adverse effects on human well-being and different biogeochemical implications on diverse natural resources should be studied and understood. It's clear and alarming that nanomaterials are present in the water sources, air, and soils used to grow food crops. One important feature that hinders all attempts to comprehend their fate in the environment is their nanoscale size. The potential toxicity of increasing influx of nanoparticles into the environment especially ENMS, requires a better understanding to predict long-term effects. Preventive actions could reduce the impact of nanoparticles entering the environment, thereby reducing the impact on human health and the environment. It is still not well understood what toxic effects the presence and exposure of synthetic, incidental, and biological nanomaterials might cause. Modern-day analysis techniques are not advanced enough to study nanoparticles in intricate biological and ecological systems. Recent scientific endeavors have shed further light on how nanoparticles interact with organs, tissues, and cells. In this regard, similar to any class of dangerous pollutants, various exposure routes should be carefully examined, and further research is required to assess the human health implications of nanoparticle occurrence in the environment.

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