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REVIEW ARTICLE

NANOTECHNOLOGY TO REVOLUTIONIZE MEDICINE

Shrestha Mohan

Bachelor of Pharmacy final year student, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Maharajgunj, Kathmandu, Nepal

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ABSTRACT

One of the most promising technologies of 21st century is nanotechnology. Nanotechnology is a collective term referring to technological developments on the nanometer scale, usually 0.1-100 nm. A nanometer is one-billionth of a meter, too small to be seen with a conventional laboratory microscope. It is at this size scale - about 100 nanometers or less - that biological molecules and structures inside living cells operate. Therefore, nanotechnology is engineering and manufacturing at the molecular scale. Nanomedicine is new concept in combining nanotechnology and medicine. Nanotherapeutics is the use of nanomedicine in therapy. The definition of nanomedicine requires attention as the nanotechnology represents a cluster of technologies. Nanomedicine, an offshoot of nanotechnology, refers to highly specific medical intervention at the molecular scale for curing disease or repairing damaged tissues, such as bone, muscle, or nerve Utilities of nanotechnology to biomedical sciences implies creation of materials and devices designed to interact with the body at sub-cellular scales with a high degree of specificity. This could be potentially translated into targeted cellular and tissue-specific clinical applications aimed at maximal therapeutic effect with very limited adverse-effects. Nanomedicine can offer impressive resolutions for various life threatening diseases. Disease areas which can be expected to benefit most from nanotechnology within the next few years are cancer, diseases of the cardiovascular system, the lungs, blood, neurodegenerative diseases, diabetes, inflammatory/infectious diseases, and orthopaedic problems. This article presents an overview of some of the applications of nanotechnology in nanomedicine.
Key Words: Nanotechnology, Nanomedicine, Quantum Dots (QDs), Nanoparticles

INTRODUCTION:

Nanotechnology is the engineering of functional system at molecular scale. Nanotechnology entails the measurement, prediction and construction of materials on the scale of atoms and molecules. A nanometer is one-billionth of a meter, and nanotechnology typically deals with particles and structures larger than 1 nanometer, but smaller than 100 nanometers. Hence, nanotechnology can be defined as the science and engineering involved in the design, synthesis, characterization and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale. A growing interest in the medical applications of nanotechnology has led to the emergence of a new field called nanomedicine.

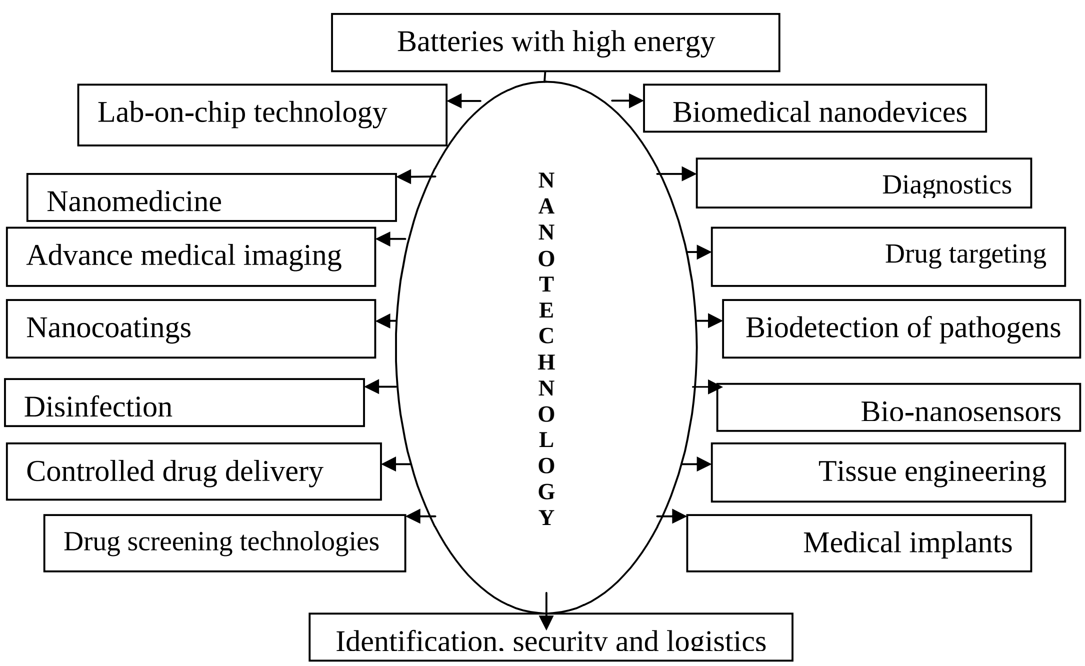


Figure 1: Schematic representation of nanotechnologic revolutionizing biomedical sciences

Nanomedicine is defined as the application of nanobiotechnology to medicine and is based on the use of nanoscale materials and devices for diagnosis and drug delivery as well as for the development of advanced pharmaceuticals referred to as nanopharmaceuticals. Human health-care nanotechnology research can definitely result in immense health benefits through newer and effective drug development. Nanomedicine offers the prospect of powerful new tools for the treatment of human diseases and the improvement of human biological systems using molecular Nanotechnology.

Nanomedicine uses nano-sized tools for the diagnosis, prevention and treatment of disease and to gain increased understanding of the complex underlying pathophysiology of disease. The ultimate goal is to improve the quality of life. The aim of nanomedicine may be broadly defined as the comprehensive monitoring, repairing and improvement of all human biological systems, working from the molecular level using engineered devices and nanostructures to achieve medical benefit.

Nanotechnologic Materials in Nanomedicine:

Nanostructured materials

Carbon nanotubes
Cyclic peptides
Dendrimers
Detoxification agents
Drug encapsulation
Fullerenes
Functional drug carriers smart drugs
MRI Scanning (nanoparticles)
Nanobarcodes
Molecular medicine
Nanoemulsions
Nanofibers
Nanoparticles
Quantum Dots (QDs)

Nanotherapeutics

Antibacterial and antiviral nanoparticles
Fullerence-based pharmaceuticals
Photodynamic therapy
Radiopharmaceuticals

Other commonly used nanomedicine technologic taxonomy

Biochips
BioMEMS
(Biomedical Microelectromechanical Systems)
Biorobotics and Biobots
Biosensors and Biodetection
DNA-based devices and nanorobots
Drug delivery
Drug encapsulation
Genetic therapy
MEMS/ Nanomaterial based prosthetics
Microarrays
Microneedles
Nanobiotechnology
Nanofiltration membrane
Nanopores
Nanosensors
Pharmacogenomics

APPLICATIONS:

Nanotechnology in drug delivery:

Nanotechnology helps in monitoring, repair, construction and control of human biological systems at the molecular level, using engineered nanodevices and nanostructures. Ideally, these technologies would improve the stability, absorption 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. Disease diagnosis, drug delivery targeted at specific sites in the body and molecular imaging are investigated and some products undergoing clinical trials. Recent advances suggest that nanotechnology will have a profound impact on disease prevention, diagnosis and treatment. Nanoparticle formulations provide protection for agents susceptible to degradation/denaturation in regions of harsh p^H. It also prolongs the duration of exposure of a drug by increasing retention of the formulation through bioadhesion. Another broad application is the delivery of antigens for vaccination. Mucosal immunity is extremely important in disease prevention but continues to be limited by both degradation of the vaccine and limited uptake.

Recent advances in encapsulation and development of suitable animal models have demonstrated that micro particles and nanoparticles are capable of enhancing immunization.[4,11]

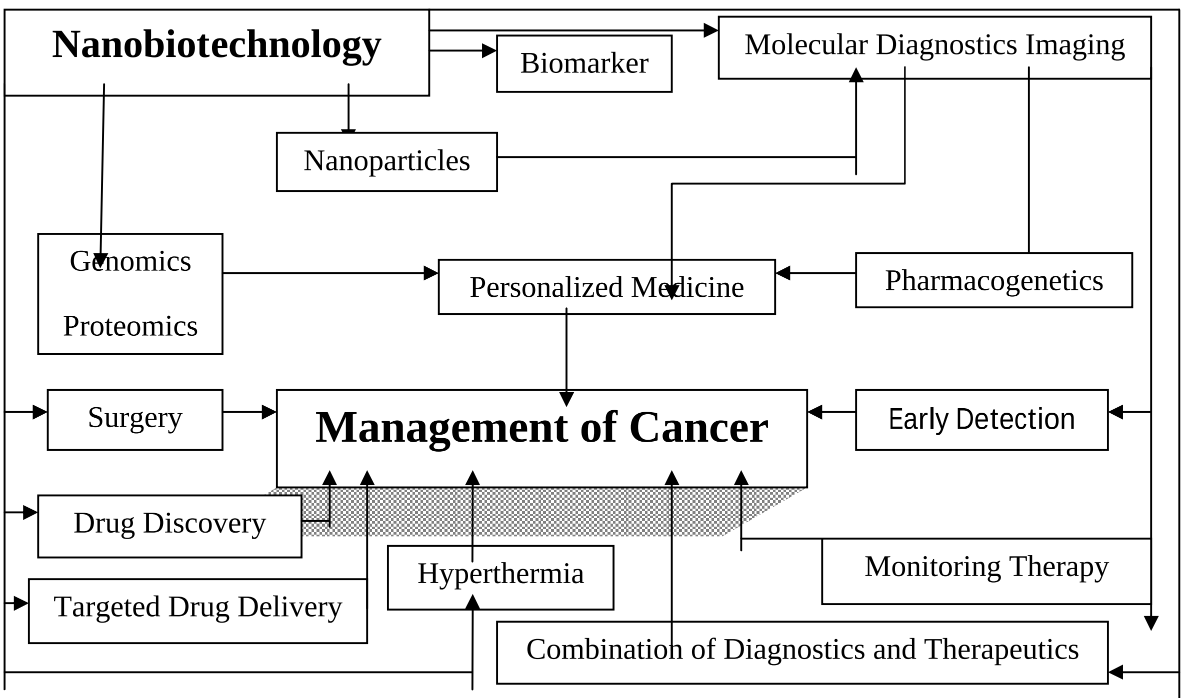
Nanotechnology against Cancer (Nanooncology):

The application of nanobiotechnology is currently the most important sector of Nanomedicine. Nanobiotechnology has refined and extended the limits of molecular diagnosis of cancer through the use of gold nanoparticles and quantum dots. Gold nanoparticles are non-toxic to human cells. Gold nanoparticles conjugated to anti-epidermal growth factor receptor (anti-EGFR) monoclonal antibodies (mAbs) specifically and homogeneously bind to the surface of the cancer cells with 600% greater affinity than the noncancerous cells. This specific and homogeneous binding is found to be helpful in recognizing a specific cancer cell in cancer detection.[7, 14]

A quantum dot is a portion of matter (eg. Semiconductor), whose excitons are confined in all three spatial dimensions. Quantum dots (QDs) have broad excitation spectrum from ultraviolet to red, which can be tuned, depending on their size and composition. The best characteristics of QDs and magnetic iron oxide nanoparticles can be combined to create a single nanoparticle probe that can yield clinically useful images of both tumors and the molecules involved in cancer. In magnetic resonance imaging (MRI) experiments, this combination nanoparticle generated on MRI signal that was over threefold more intense than the same number of iron oxide nanoparticles.[1,4,6]

Nanoparticles enable targeted drug delivery in cancer that increases efficacy and decreases adverse effects through reducing the dosage of cancer drugs administered. Nanoparticulate anticancer drugs can cross some of the biological barriers and achieve therapeutic concentrations in tumor and spare the surrounding normal tissues from toxic effects.

The rationale for using nanotechnology in oncology is that nanoparticles have optical, magnetic or structural properties that are not available from larger molecules or bulk solids. When linked with tumor-targeting ligands such as mAbs, peptides or small molecules, these nanoparticles can be used to target tumor antigens (biomarkers) as well as tumor vasculatures with high affinity and specificity.[12, 15, 16]



Nanotechnology in personalized therapy of cancer:

Personalized medicine means the prescription of specific therapeutics best suited for an individual. In cancer cases, the variation in behaviour of cancer of the same histological type from one patient to another is also taken into consideration. Personalized management is usually based on pharmacogenetic, pharmacogenomic, pharmacoproteomic and pharmacometabolic information, but other individual variations in patients and environmental factors are also taken into consideration. Personalization of cancer therapies is based on a better understanding of the disease at the molecular level, and nanotechnology will play an important role in this area.[16]

Nanotechnology as a tool in imaging:

It offers novel opportunity for sensing clinically relevant markers, molecular disease imaging, and tools for therapeutic intervention. Possibility is due to intracellular imaging through attachment of quantum dots (QDs) or synthetic chromophores to selected molecules, for eg. Proteins, or by the incorporation of naturally occurring fluorescent protein that with optical techniques such as confocal microscopy and correlation imaging, allow intracellular biochemical processes to be investigated directly.

QDs are semiconductor nanocrystals with unique optical and electrical properties. Fluorescence spectrum renders their optimal fluorophores for biomedical imaging. Thus, QDs are more appealing as in vivo and in vitro fluorophores in a variety of biological investigations. By nanotechnology, we can detect and diagnose cancer. QDs can allow the detection of tens to hundreds of cancer biomarkers in blood assays, on cancer tissue biopsies, or as contrast agents for medical imaging. Recent advances in nanosensor includes nanosensor based on fluorescence resonance energy transfer, which is capable of detecting low concentrations of DNA in a separate free format.[13, 14]

Nanotechnology in gene delivery:

Gene therapy is a recently introduced method for the treatment or prevention of genetic disorders by correcting defective genes responsible for disease development based on the delivery of repaired genes or the replacement of incorrect ones. Common approach for correcting faulty gene is insertion of a normal gene into a nonspecific location within the genome to replace a nonfunctional gene. An abnormal gene could also be swapped for a normal gene through homologous recombination or repaired through selective reverse mutation, which returns the gene to its normal function.

Nanotechnology in cardiac therapy:

Miniaturized nanoscale sensors like QDs, nanocrystals and nanobarcodes can sense and monitor biological signals such as the release of protein or antibiotics in response to cardiac or inflammatory events. Nanotechnology helps in revealing the mechanism involved in various cardiac diseases and also helps in designing atomic-scale machines by incorporating biological systems at the molecular level. The use of newly designed nanomachines can have a paradigm-shifting impact in the treatment of the dreaded CV disease. These machines have 3 key elements meant for sensing, decision making and carrying out the intended purpose of diagnosis and treatment. Eg. Abciximab, a chimeric mouse-human antibody used to lessen the chance of heart attack in people who need percutaneous coronary intervention (a procedure to open blocked arteries of the heart). [11, 16]

Nanotechnology for molecular diagnosis:

DNA microarrays and enzyme-linked immunosorbent assays rely on the labeling of samples with a fluorescent or radioactive tag, a highly sensitive procedure i.e. time-consuming and expensive. The chemical modifications and global amplification of the nucleic acid samples are achieved by polymerase chain reaction (PCR), which can introduce artifacts caused by the preferential amplification of certain sequences. Thus, nanotechnology is applied to overcome some of the limitation of biochip/microarray technology.

Nanotechnology in dental care:

Nanotechnology will have future medical applications in the field of nanodentistry. Nanodentistry will make it possible to maintain near perfect oral health through the use of nanomaterials, biotechnology and nanorobotics. It will be possible to induce local anesthesia. A colloidal suspension containing millions of active analgesic dental nanorobotic particles could be instilled on the patients' gingivae. Nanorobotics, after containing the surfaces of the crown or mucosa reach the dentin by migrating into the gingival sulcus and pass painlessly to the target site.[11, 14]

Nanotechnology for antibacterial activity:

Recent advances in antibacterial activity shows that silver nanoparticles (AgNPs) of a small size were successfully synthesized using the wet chemical reduction method into the lamellar space layer of montmorillonite/chitosan (MMT/Cts) as an organomodified mineral solid support in the absence of any heat treatment. Silver/ montmorillonite / chitosan bionanocomposite (Ag/MMT/Cts BNC) systems were examined and the antibacterial activity of AgNPs in MMT/Cts was investigated against Gram-positive bacteria, i.e., *Staphylococcus aureus* and methicillin-resistant *S. aureus* and Gram-negative bacteria, i.e., *Escherichia coli*, *E. coli* O157:H7, and *Pseudomonas aeruginosa* by the disc diffusion method using Mueller Hinton agar at different sizes of AgNPs. All of the synthesized Ag/MMT/Cts BNCs were found to have high antibacterial activity. These results show that Ag/MMT/Cts BNCs can be useful in different biological research and biomedical applications, including surgical devices and drug delivery vehicles. Other studies investigate the bactericidal effect of iron oxide nanoparticles of *S. aureus* and bactericidal effect of iron oxide nanoparticles on other types of bacteria for potentially widening such antibacterial applications.[5,8]

Nanotechnology on orthopedic applications:

Current treatment modalities include orthopedic implants used for internal fixing of fracture bones, but these are limited by the large number of implant failures. Nanotechnology can provide an alternative platform with higher mechanical strength, enhanced bioactivity and resorbability in improving the quality of life of patients who suffer from debilitating bone fractures.

Nanostructure materials with sizes 1 to 100nm can act as new and effective constituents of bone materials, because bone is also made up of nanosized organic and mineral phases. Several studies have reported improved osseointegration on nanostructure surfaces created from a wide range of chemistries including ceramics, metals, polymers and composites.

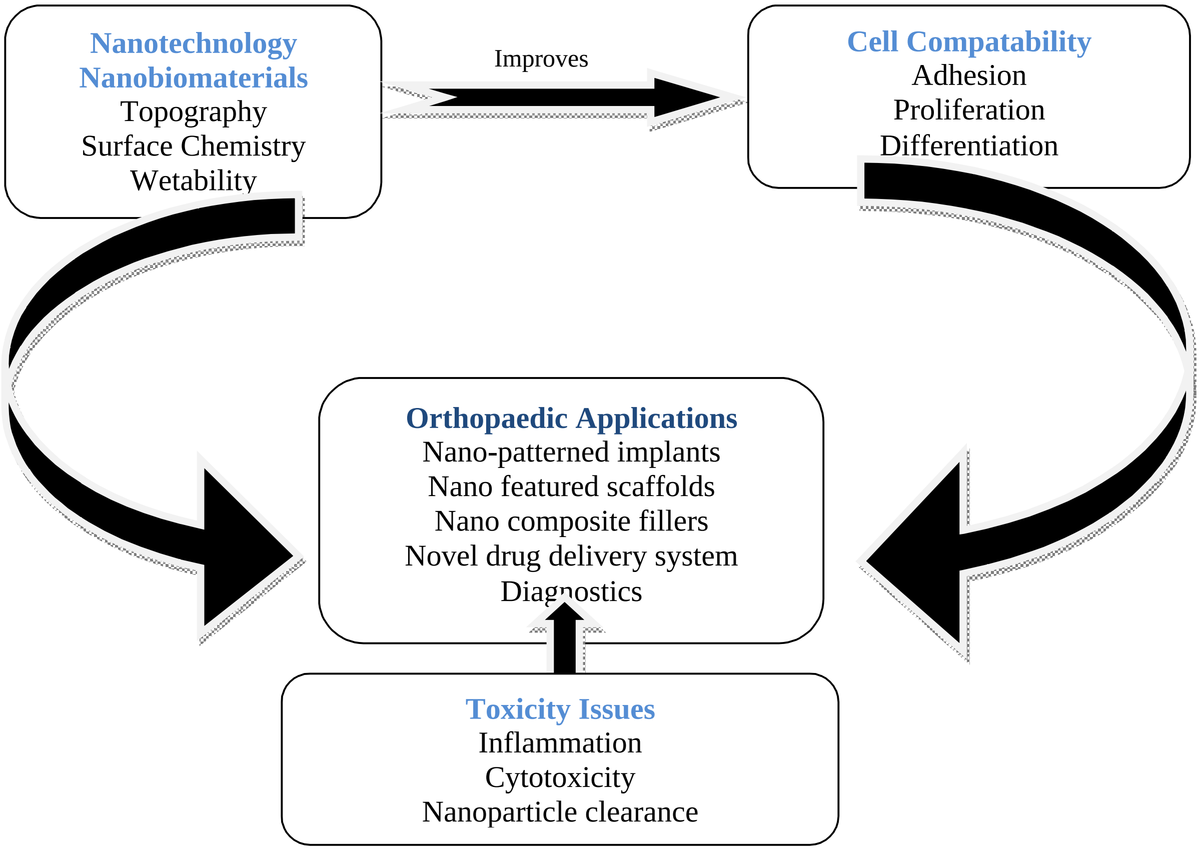


Figure 2: Nanoorthopedics [13]

Approved anticancer drugs using nanocarriers: [16]

Trade Name/Compound	Nanocarriers
Abraxane/ Paclitaxel	Albumin-bound paclitaxel
Bexxar/ anti-CD20 conjugated to iodine-131	Radioimmunoconjugate
Daunorubicin	liposome
Doxil/ Caelyx/ Doxorubicin	liposome
Zinostatin	Polymer-protein conjugates
Oncapsar/ PEG-L-asparaginase	Polymer-protein conjugate
Myoset/ Doxorubicin	Non pegylated liposome
Ontak/ IL-2 fused to diphtheria toxin	Immunotoxic fusion protein
Zevalin/ anti-CD20 conjugated to yttrium-90	Radioimmunoconjugate
Zoladex/ goserelin acetate	polymer rods

The Future of Nanotechnology:

The future of nanotechnology is completely uncharted territory and could improve the outlook for medical patients with serious illnesses or injuries. Physicians could theoretically study nanosurgery and be able to attack illness and injury at the molecular level. This, of course, could eradicate cancer as the surgical procedures would be done on the cellular base. Cancer cells would be identified, removed, and the surgical implantation of healthy cells would soon follow. Moreover, there would be an entire nanosurgical field to help cure everything from natural aging to diabetes to bone spurs. There would be almost nothing that couldn't be repaired (eventually) with the introduction of nanosurgery. In near future many other changes will appear in the field of medicine.[3, 10]

Today, nanotechnology is among the fastest growing areas of science and technology, with exponential progress being made. Within 10-15 years, nanotechnology is expected to be a mature industry, with countless mainstream products. Further into the future, nanotechnology will play a major role in medicine and longevity.[2, 14]

CONCLUSION:

The multidisciplinary field of nanotechnology is bringing the science of the almost incomprehensibly small device closer and closer to reality. The effects of these developments will at some point be so vast that they will probably affect virtually all fields of science and technology. As such, nanotechnology holds the promise of delivering the greatest technological breakthroughs in history. Over the next couple of years it is widely anticipated that nanotechnology will continue to evolve and expand in many areas of life and science, and the achievements of nanotechnology will be applied as a key component of the human health system in medical sciences, including diagnostics, drug delivery systems, and patient treatment.

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