NANOTECHNOLOGY APPLICATIONS IN NOVEL DRUGS DELIVERY

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ABSTRACT

Nanoscience is the study of the underlying laws governing molecules with dimensions between 1 and 100 nanometers. The field of nanotechnology is highly broad, and in recent years, its developing fields have made significant advancements in areas such as the environment, energy, defence, agriculture, food, chemicals, pharmacy, and health care. With its most significant uses in diagnosis, medicine delivery, and other areas, nanotechnology is playing an increasingly significant role in healthcare. It has shown successful in treating serious diseases like cancer, tuberculosis, diabetes, brain targeting, and others. Many compounds are now being researched for medication delivery, and more particularly for cancer therapy. It's interesting to note that pharmaceutical sciences are also utilising nanoparticles to lessen the toxicity and adverse effects of medications. Drug delivery into the brain has become more accessible thanks to the capacity to pass the Blood Brain Barrier (BBB). One of the top research areas where nanomedicines are crucial is targeted drug or gene delivery for the treatment of cancer. In conclusion, novel therapeutic and diagnostic techniques have been steadily developed using nanoparticles for imaging and medication administration. The review demonstrates how nanotechnology is playing a growing role in novel drug delivery.

Keywords: Nanotechnology, Nanomedicines, Nanorobots, Therapeutic purposes, Drug delivery, Nanoparticles.

INTRODUCTION

The word Nano is originated from the Greek word 'Nanos', which means dwarf. In science, the prefix 'nano' means one billionth part of any measurement i.e. for time, it is a nanosecond (1/1,000,000,000th part of a second), for length, it is a nanometer and so on. So, Nanoscience is the study of phenomena and manipulation of material at the Nano scale. Nanoparticles have been created as a result of the discovery of nanomedicines, allowing for more precise medication and gene delivery to the intended target. To manipulate different diseases and their metabolic pathway, we can deliver drugs using nanotechnology in the form of dendrimers, liposomes, nanoshells, emulsions, nanotubes, quantum dots, etc. In the diagnosis and treatment of cancer, it is crucial. Effective target therapy utilised in pre-sympathomimetic and diagnostic techniques is one of the most recent advances in medication delivery.

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NANOTECHNOLOGY IN INDIA: PAST AND PRESENT

India is the land of knowledge. As it is well known, no stream of science is untouched by Indian scholars since the beginning of ancient history. Nanotechnology is neither an exception. Various evidences prove that Indian scientists were aware of the fact that the tiniest size of a matter is the most powerful in various aspects. They also knew about the uses and benefits of nanotechnology. In *Rasa-meemansa*, an epic of Ayurveda, formation and usage of various types of *avalehas* and *bhasmas* is well described. These include the alteration of matter into a newer kind of material which comprises of very different medicinal qualities from that of the original matter. Two examples are listed below:

1) *Swarna bhasma* (Gold ash) – When gold ash is heated up to a particular temperature through a special procedure and a pill is formed with it, it is said that by just keeping this pill in mouth, one is capable of flying into the skies i.e., this pill gives the man the capability of flying just like air.

2) *Paarad bhasma* (Mercury ash) – Similarly, super refined *paarad bhasma* is said to have the power of making human body as strong as steel. Not only this, it is also said that the special miraculous powers that could be acquired by the use of *paarad bhasma* are only known to Lord Shiva.

In this way, it is proved that old Indian scholars were aware of the fact that on reaching to the tiniest form of matter, its qualities are altered very much, and those special qualities can be utilized in the welfare of human being. The same principle is now worked upon by the scientists worldwide.

Presently, researches in the field of nanotechnology are underway in premier research institutes of India. JNCAR, IITs, Tata Institute of Fundamental Research, Indian Institute of Science and various national laboratories are the torch bearers. Some of the premier universities in India, such as Cochin University of Science and Technology, University of Pune, University of Bombay, University of Madras, University of Delhi, and JNU New Delhi are on to carry out research in this frontier area. The Ministry of Science and Technology has identified this as a core thrust area and liberal funding is available for research under the 'Nanoscience and Technology Initiative Programme' started by the DST, Govt. of India.

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APPLICATIONS OF NANO TECHNOLOGY IN HEALTHCARE:

Nanoscience and Nanotechnology have a great impact on the field of drug delivery where controlled release of drug is needed. At nanoscale, materials have novel properties like increased strength, resiliency, and electrical conductivity. Some of the most common examples of nanodevice are:

- The iPod Nano which uses microscopic memory chips for increasing the storage capacity
- Use of nanoparticles in lotion helps in easy absorption
- Silver nanoparticles can be used in eliminating fungus and preventing odors in shoes and refrigerators
- Nanomaterials are used in treating glaucoma patients also
- Miniature biochips are used to detect increase in glucose level
- Nanotechnology is also used for creating artificial skin, cartilage and bone for human use etc.

Nanomedicines in Diabetes

A state of disordered metabolism, or hyperglycemia, or abnormally high blood sugar levels, can be referred to as diabetes. It is typically brought on by a combination of inherited and environmental factors. New treatment options for diabetes mellitus are provided by nanotechnology. Artificial pancreas, artificial beta cells, and boxes with nanopores that shield transplanted beta cells from immune system attack are all possible alternatives to pancreas transplantation. The development of nanospheres as biodegradable polymeric carriers for oral insulin administration. Nanomedicines have enormous potential, and nanotechnology has the potential to revolutionise medical practise.

Nanoparticles in Tuberculosis

Drug delivery methods based on nanoparticles are effective against recurrent intracellular diseases like TB. Intermittent chemotherapy in experimental tuberculosis has showed promise when using polymeric nanoparticles made of polylactide-co-glycolide. Compared to liposomes and microparticles, which are more common drug carriers, it has definite advantages. Future studies may significantly rely on natural carrier systems, even though their use, for example, in solid lipid nanoparticles and alginate nanoparticles, is still in its infancy. In the meanwhile, intermittent chemotherapy based on nanotechnology offers a cutting-edge and reliable platform for the fight against tuberculosis.

Nanotechnology in brain targeting

The blood-brain barrier (BBB) guards the brain against toxins that travel through the bloodstream. The BBB is a vital barrier that keeps the brain alive, but it severely restricts the ability of most medications to reach the brain since they cannot pass it in sufficient quantities. Many potentially helpful medications, including cytostatics and medicines that

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act on the central nervous system (CNS), either do not cross the BBB at all or do so in insufficient amounts. To transfer pharmaceuticals to the brain, which are typically hindered from doing so by BBB, however, ways to improve the bioavailability of drugs in the brain are required for therapeutic reasons. One approach of accomplishing this objective is to bind medications to nanoparticles and then transfer them. Drugs are either attached to the surface of or incorporated into poly (butylcyanoacrylate) particles using the highly beneficial nanoparticle technology. This drug-particle complex is then coated with an appropriate surfactant (like polysorbate 80). The combination is then administered orally or intravenously. Some other vital uses of nanotechnology are:

1. **Nanodevices**: Single walled carbon nanotubes are being used to create extremely selective electrical biomolecule detectors as well as to study surface-protein and protein-protein binding. The method, when paired with the sensitivity of nanotube-based electronics, creates highly focused electronic sensors for identifying clinically significant biomolecules, such as antibodies linked to autoimmune disorders in humans.
2. **Biosensors**: These are currently used in areas of target identification, validation, assay development, lead optimization and absorption, distribution, metabolism, excretion and toxicity (ADMET).
   a) **Nanobiosensors**: Nanobiosensors are nanosensors containing immobilised bioreceptor probes that are selective for target analyte molecules. To make molecular diagnostics easier, these can be included into other technologies like lab-on-a-chip. They can be used for a variety of purposes, such as the detection of microbes in various samples, the monitoring of metabolites in bodily fluids, and the identification of tissue disease like cancer. They can be used in lab settings but are most suited for Point-of-Care (POC) applications due to their portability.
   b) **Nanowire biosensors**: Since the surface features of these are easily modifiable, they can be adorned with almost any imaginable molecular recognition unit, whether chemical or biological, making the wires themselves analyte independent. Highly sensitive, real-time electrically based sensors for biological and chemical species are made using silicon nanowires that have been doped with boron.
   c) **Viral nanosensors**: The term "biological nanoparticles" essentially describes the viral particles. As a nanosensor for therapeutically important viruses, magnetic nanobeads have been constructed in response to HSV and adenovirus. In a 10 ml serum sample, as few as five virus particles can be easily found using a magnetic field.
   d) **PEBBLE nanosensors**: Encapsulated Probes By Biologically Localised Embedding (PEBBLE), which creates spherical sensors with a size range of 20 to 200 nm, nanosensors are made of sensor molecules that are trapped in a chemically inert matrix. These are immune to protein interference and can image ions and molecules in real time both within and outside of cells. **Optical biosensors**: Many

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biosensors which are currently marketed rely on the optical properties of lasers to monitor and quantify interactions of biomolecules that occur on specially derived surface or biochips. Example: Surface Plasmon.

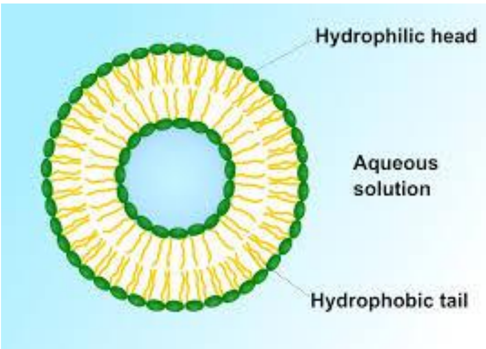
e) **Laser nanosensors**: In this method, laser light is fired into the fibre, creating an evanescent field that is utilised to excite target molecules attached to antibody molecules at the fiber's tip. When a laser strikes them, they emit optical signals that a photometric detecting system codes. The study of proteins and biomarkers in human live cells is done using this technique.

Drug Delivery System

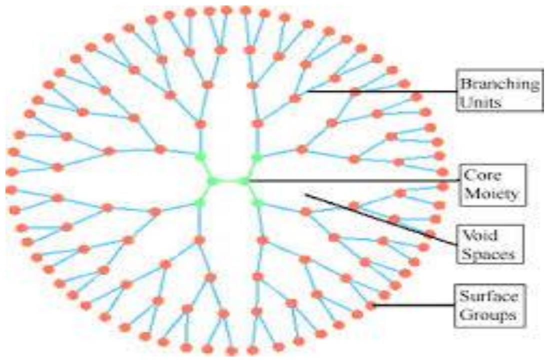
Currently, 95% of all novel treatment systems exhibit subpar biopharmaceutical characteristics and Pharmokinetics. There is no known medical mechanism that can distribute and transport therapeutically active medication molecules to an inflammatory or action site without causing any negative effects. These issues are solved by medication delivery systems based on nanotechnology, which have several appealing qualities. Nanomedicine is small enough to be injected without obstructing capillaries and needles, allowing for precise drug administration and medical imaging. For this reason, nanoscale Liposomes, Micelles, Nanoemulsions, and Nanogels are employed.

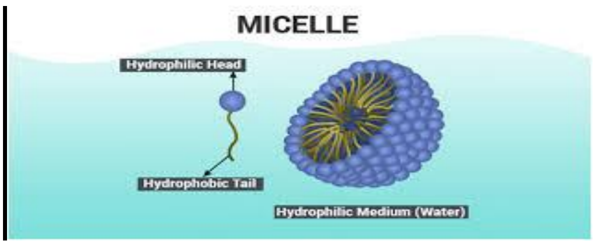
Figures of Liposome, Dendrimer and Micelle as given bellow:

Liposome



Dendrimer





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Liposomes:

Using liposomes dates back to the 1960s. They contain an aqueous core inside a single phospholipids membrane organelle. They range in size and form from 30 nanometers to several micrometres. They are utilised as a technique for targeted medication administration due to their size, hydrophobic, hydrophilic, and biocompatibility properties. Because liposomes are so tiny, they can pass through vascular holes and penetrate solid tumours. To enhance the delivery of medicines to target cells, they have had their surface changed with active targeting ligands. A multicomponent liposome that contains doxorubicin and an antisense oligonucleotide has recently been created, and it targets the mRNAs for MRP-1 and BCL-2 to inhibit both pump resistance and non-pump resistance.

Micelles for drug delivery

Micelles are amphibian self-assemblies that create supramolecular core-shell structures in water. The assembly of amphiphiles in aqueous media is driven by hydrophobic interactions when the concentration reaches CMC, or critical micelle concentration. Today's micelles are made of amphiphile polymers and are in the nanosized range. Amphiphile polymers comprised of polyethylene glycol (PEG) and low molecular weight hydrophobic core forming blocks make up the majority of the nanosized miceller delivery systems. This system has the benefit of lower toxicity and is thermodynamically resilient to dilution due to their low monomer content in equilibrium with micelles. There are four types of micelles used for medication delivery:

- Phospholipid micelles
- Pluronic micelles
- Poly (L-amino acid) micelles
- Polyester micelles

Dendrimers:

Dendrimers, which have been around since the 1980s, are macromolecules made up of a core of ABn (where n = 2 or 3), and a sequence of branches that form a tree-like structure surrounding the core. Due to their nanosize, simplicity in preparation, functionalization, and polymorphism, they are excellent candidates for targeted drug administration. Their structure allows for the incorporation of therapeutic agents with medicinal activity. Example: The anticancer drug fluorouracil (FU) also causes negative effects. The reduction of harmful effects is made possible by the acetylation of polyamidoamine (PAMAM) dendrimers, which results in dendrimer - 5 FU conjugates that, upon hydrolysis, release 5 FU.

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Nanoemulsions for drug delivery:

The dispersion of two immiscible liquids, such as oil and water, is known as a nanoemulsion. Surface-active films made of surfactant and co-surfactant stabilise the dispersed phase droplets, which are of the order of nanometers in size. Because of their optical transparency, thermodynamic stability, and simplicity of preparation, they significantly increase in relevance. The rate of drug release at the site of action can be impacted by nanoemulsion structure. They have a substantially longer oil-water contact area due to their nanosize, which helps the drug release from the dispersed phase droplets. To prepare it, homogenizers must be used for sonication and high- and low-energy emulsification. Amphotericin B, a low-dose antifungal antibiotic, has already been provided via IV injection to mice, rats, dogs, and monkeys.

Implications of nanotechnology:

Implanting nanotransmitters and nanosensors inside of people has made it possible to employ nanodevices to monitor and treat people at the tiny level. However, this goes beyond the confines of typical hospital care because one can receive treatment while lounging in his own house. Homebound patients may have access to information sent by biochips that track diseases like hypercholesterolemia and warn them when critical levels are reached. Individual duties have expanded as a result of education, with implications for patients' safety as well. When nanotechnology is widely used, healthcare consumers will play entirely different roles. They will have the authority to select their prescription, but there will also be obligations on their end. Modifications to the clinician's decision-making and productivity are some of the immediate repercussions for his or her role. Clinicians can discover that their position is shifting from one of specialists to one of participants, coordinators, or coaches. Diseases may potentially be caused by software issues with nanodevices that are implanted in humans. Care that is highly individualised may be required. Since these devices will be used to control the entire body's metabolism, patients and clinicians will need to have a full understanding of device interfaces. The day when insurance refuses to pay us because of early monitoring of our health at the cellular level may not be too far off. Nanotechnology will increase our reliance on technology.

Robotics and Nanorobots:

Scientists anticipate the creation of biocompatible surgical nanorobots that would be able to find and destroy isolated cancerous cells, remove microvascular obstructions and rehabilitate vascular endothelial cells, perform 'noninvasive' tissue and organ transplants, carry out molecular repairs on damaged extracellular and intracellular structures, and even exchange new whole chromosomes for old ones.

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Nanotechnology based drug delivery tools:

1) **Quantum Dots** (QDs) are tiny, nanometer-sized light-emitting particles. It exhibits a unique variety of spherical nanocrystals with diameters ranging from 1 to 10 nm. Semiconductors, insulators, metals, magnetic materials, metallic oxides, and other materials can all be developed into QDs. These fluorescent probes are being developed as a novel class for molecular imaging and medical diagnostics. The development of diagnostic tools like magnetic resonance imaging (MRI), in vitro and in vivo detection and analysis of biomolecules, immunoassays, DNA hybridization, the creation of non-viral vectors for gene therapy, transporters for DNA, protein, drugs, or cells, time-graded fluorescence imaging of tissue, cell labelling, and therapeutic tools for the treatment of HIV, cancer, and diabetes are just a few of the important developments that QDs have a significant influence on.

2) **Dendrimers** are chemical polymers that have been compartmentalised and are hyperbranched, like trees. The core, branches, and surface are the three distinct regions found in dendrimers. The surface area is substantial as a result of their branching forms. Dendrimers have the ability to link treatment with detection and diagnostics since they can store therapeutic materials like DNA in their hollow. Dendrimer-based drug delivery, solubilization gene therapy, immunoassay, and MRI contrast agent are among the dendrimer's most significant applications.

3) **Nanoshells** are tiny beads that have a gold coating. They work by absorbing particular light wavelengths. Because they may quickly and deeply permeate human tissues, beads that can absorb near infrared light have been produced. Heat is produced, which kills malignant cells while protecting healthy neighbouring cells.

4) **Nanotubes** have a diameter that is half of a DNA's diameter. They therefore aid in the identification of DNA alterations linked to cancer. They can be made of coaxial cylinders with increasing diameter along a common axis that are either single-layered (like straw) or multiple-layered (like a poster wrapped in a tube). These are tiny macromolecules that are distinct in terms of their size, shape, and exceptional physical characteristics. Due to their highly intriguing physicochemical characteristics, such as their ordered structure with high aspect ratio, ultra-light weight, high mechanical strength, high electrical conductivity, high thermal conductivity, metallic or semi-metallic behaviour, and high surface area, nanotubes have some distinct advantages over other drug delivery and diagnostic systems.

5) **Cantilevers** help in detection of cancer. They are tiny bars which through their one end bind to molecules associated with cancer. These molecules may bind altered DNA proteins that are present in certain types of cancer, which result in change in surface tension and lead to bending of cantilever. By monitoring the bending of cantilever, cancer can be detected and treated at the beginning stage.

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Advantages of Applications of Nanotechnology in Healthcare

The last two decades of 21th century saw tremendous efforts by scientists in this field and these efforts are bearing fruits now. Along with drug delivery some very important applications of nanotechnology include detection of defected genes, targeting and improving the efficacy. Most significant advantages of nanotechnology are as following:

- Targeted drug delivery with nanoparticles has been observed to be very effective e.g. PEG-coated nanoparticles.
- Bio-compatible polymeric micelles with polysorbate 80 for use in brain targeting.
- Nanoemulsion used in drug delivery and in food industries for the development of nutraceuticals.
- Albumin conjugated Paclitaxel as a nanoparticle is used for treatment of taxane-refectory metastatic breast cancer.
- Doxorubicin bounded to polysorbate coated nanoparticles crosses blood brain barrier (BBB) and is used in treatment of human glioblastoma.
- Sunscreens are developed containing titanium dioxide & zinc oxide nanoparticles.
- Silver nanoparticles prevent HIV from binding host cell surface.
- Many anticancer drugs have been developed in the form of nanoencapsulation, enclosing drugs in lipid nanocapsules and encapsulating drug in hydrogel nanoparticles.

CONCLUSION:

The use of nanotechnology in cell biology and physiology enables focused interactions at a fundamental molecular level. Nanotechnology has revolutionised the production of materials, the development of several new technologies, the administration of drugs, and the monitoring and diagnosing of systems. Numerous nanotechnological items are now undergoing research. Some have begun mainstream use while others are undergoing clinical testing. However, this technology has a wide range of effects that affect consumers, doctors, and the practise of informatics. The ethical application of nanomaterials is a significant topic of worry for medical professionals. Clinical professionals may discover that their positions as subject-matter experts are eroded once this technology is widely used and approved. The development of this new era in healthcare will require overcoming many challenges and implications, but nanotechnology has already ushered in one. In the areas of genomics, proteomics, molecular diagnostics, and high throughput screening, new opportunities have given us a potent instrument. The most adaptable materials for creating diagnostics could be nanoparticles because of their unique features. Nanotechnology advancements will provide us a better understanding of our body systems. With the development of various potential strategies for therapeutic agent delivery and imaging that take advantage of nanoscale carriers, it has a bright future. Future research will now focus on a variety of difficulties in the use of nanomedicines.

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While pre-clinical and clinical research are receiving more funding, the current studies already lack safety safeguards like toxicity testing. Additionally, the price of nanomedicines must be kept below a reasonable level in order to achieve widespread acceptance. Because it is believed that such technologies could generate product delays due to technical or regulatory issues, actual implementation of innovative drug delivery systems based on nanotechnology. Therefore, oral drug delivery is still the favoured method. Additionally, the expense becomes a barrier to regular use. This paper discusses the benefits and potential applications of nanotechnology in the pharmacy industry, including its broad use in the realms of genetics, imaging diagnosis, medication delivery, and the treatment of various diseases. However, much more research is required before "nano" may be used frequently in the pharmacy industry.

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