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CONTEMPORARY INCLINATION OF NANOTECHNOLOGY- A REVIEW

[1]**Ms. Anju S Thej (Thej) *,[2]Dr. KEERTHI G S NAIR (Nair)**

[1]M.Pharm, Scholar, [2]Associate Professor and HOD, Department of Research and Development
[1]Pharmaceutics
[1]The Dale view College of Pharmacy and Research Centre, Trivandrum Kerala, India.

Abstract: One of the most fundamental unit operations that is crucial in pharmacy is size reduction. It aids in enhancing release, decreasing toxicity, increasing stability and bioavailability, and enabling improved drug formulation prospects. The performance of pharmaceuticals in the nanoscale size range has been observed to rise in a variety of dosage forms in recent trends. The Latin word "nano" means "dwarf" in English. Nano size refers to 10^{-9} of a particular unit thus nanometer is 10^{-9} of a meter. The field of study known as nanotechnology is concerned with molecular and nanoscale processes. Though it has had a significant influence on a wide range of medical domains, including biophysics, molecular biology, bioengineering, cardiology, cancer, ophthalmology, endocrinology, immunology, etc., biomedical and pharmaceutical sectors have not yet been fully explored. Better pharmaceutical applications are made possible by intelligent systems, gadgets, and materials provided by nanotechnology. Nanotechnology is now being used in the pharmaceutical industry to produce nanomedicine, tissue engineering, nanorobots, biosensors, and biomarkers etc. Where existing and more conventional technologies may be nearing their limits, pharmaceutical nanotechnology offers chances to enhance materials, medical devices, and aid in the development of new technology. Therefore, improvements in medication delivery as well as other prospects for medicine and pharmacy will result from this field's developments in the years ahead.

Keywords: Nanotechnology, Nanoparticles, Drug-delivery systems, Pharmaceutical nanotools.

INTRODUCTION

Size reduction is one of the basic unit operation having significant applications in pharmacy. It aids in enhancing solubility and bioavailability, minimizing toxicity, improving release and providing better formulation opportunities for drugs. A drug in the nanometer size range improves the performance in a wide variety of dosage forms. Significant benefits of nanosizing include:

1. Increased Surface Area
2. Enhanced Solubility
3. Increased Rate of Dissolution
4. Increased Oral Bioavailability
5. More Rapid Onset of Therapeutic Action
6. Less Amount of Dose Required
7. Decreased Fed/Fasted Variability
8. Decreased Patient-To-Patient Variability.

Nanotechnology and nano science are widely seen as having a great potential to bring advantages to many areas of research and applications. In 1974, the term "nanotechnology" was first used when Norio Taniguchi, a scientist at the University of Tokyo, Japan, referred to materials in nano meters. Nanotechnology is a multifaceted field which literally means any technology on a nanoscale that has applications in the real world.The study of processes at the molecular level and in the nanometer range is known as nanotechnology.

Materials characteristics on a smaller scale, known as the nano scale, can differ greatly from those on a larger size. When a material's dimension is reduced from a large size, its properties first remain the same, and then gradually alter little, and eventually, when the size falls below 100 nm, significant changes in properties may take place. If only one length of a three dimensional nanostructure is of nano dimension, the structure is referred to as a quantum well and if two sides are of nanometer length then the structure is referred to as a quantum wire. All three dimensions of a quantum dot are in the nano range [1].

Materials can be nanostructured to provide innovative performance and new characteristics. In comparison to conventional dosage forms, nano particle drug delivery systems may have a number of benefits, including improved efficacy, reduced toxicity, enhanced bio distribution and improved patient compliance. Pharmaceutical nanoparticles are sub nanoscale structures made up of several tens or hundreds of atoms or molecules with a range of sizes (from 5 nm to 300 nm) and morphologies (amorphous, crystalline, spherical, needles, etc).They include drugs or bioactive chemicals.

Nano scale materials and devices can be designed using either "bottom-up" or "top-down" fabrication approaches. Nano materials or structures are fabricated from build-up of atoms or a molecule in a controlled manner that is regulated by thermodynamic means such as self-assembly in case bottom-up methods. On the other hand, advances in micro technologies can be used to fabricate nanoscale structures and devices. These techniques are collectively referred to as top down nanofabrication technologies include photolithography, nanomolding, dippen lithography and nano fluidics [2].

Nano scale materials and devices are often fabricated using either "bottom-up" or "top-down" fabrication approaches. Nano materials or structures are fabricated from build from atoms or a molecule in a controlled manner that is regulated by thermodynamic means such as self-assembly in case bottom-up methods. On the other hand, advances in micro technologies are often used to fabricate nano scale structures and devices. These techniques are collectively mentioned as top down nanofabrication technologies; include photolithography, nano molding, dippen lithography and nano fluidic.

Scope and opportunity

Applications of nanotechnology in pharmacy, that offer intelligent and smart drug delivery systems is expected to emerge as most important and powerful tool as an alternative to conventional dosage form. Pharmaceutical nanotechnology is most innovative and highly specialized field, which will soon alter the pharmaceutical industry in near future. Pharmaceutical nanotechnology offers ground-breaking opportunities to fight against many diseases. It aids in detecting the antigen associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting the microorganisms and viruses associated with infections. It is anticipated that the market would be overrun with pharmaceuticals created using nanotechnology in the next ten years. Pharmaceutical nanotechnology has a very broad application range, ranging from smart material for tissue engineering to intelligent tools for delivery of drugs and diagnostics, and more recently, artificial RBC etc [3]. The development of nanomedicine, tissue engineering, nanorobots, advanced diagnostics, as carriers of diagnostic and therapeutic modalities, and as biosensors, biomarkers, image enhancement devices, implant technology, bioactive surfaces, among other uses, are current applications of nanotechnology in pharmacy. A large number of nano systems, which have been explored in pharmacy to date, are liposomes, dendrimers, metallic nano particles, polymeric nano particles, carbon nano tubes, quantum dots, nano fibres etc [4].

Pharmaceutical nanotechnology based systems

The two fundamental categories of nano tools offered by pharmaceutical nanotechnology are nano materials and nanodevices, which play a crucial role in the field of pharmaceutical nanotechnology and related fields.

Nanomaterials are biomaterials that are utilised in tissue-engineered products as orthopaedic or dental implants, or as scaffolds. Surface modifications or coatings might greatly promote the biocompatibility by favoring the interaction of living cells with the biomaterial. These materials can be sub divided into nanocrystalline and nano structured materials

Nanocrystalline materials are easily manufactured and can replace the less performing bulk materials. Raw nanomaterials can be used in case of drug encapsulation, bone replacements, prostheses, and implants.

Quantum dots, dendrimers, fullerenes, and carbon nanotubes are examples of nanostructured materials, which are treated versions of raw nanomaterials that have unique shapes or properties. Nanodevices are miniature devices in the nanoscale and some of which include nano- and micro electromechanical systems (NEMS/ MEMS)microarrays (different kind of biological assay e.g. DNA, protein, cell, and antibody) and microfluidics (control and manipulation of micro or nanolitre of fluids).Biosensors and detectors for detecting minute amounts of bacteria, airborne pathogens, biological hazards, and disease signatures are a few examples, as are certain intelligent devices like respirocytes.

Nanoparticulate drug-delivery systems [1]

An ideal drug-delivery system owns two elements:

A. The ability to target

B. To control the drug release.

When dealing with treatments that are administered to healthy cells but have the potential to harm cancer cells as well, targeting enables great drug effectiveness and a reduction in side effects. Controlled release of the medication to the target can also be used to minimize or avoid side effects. Nano particulate provides a far better penetration of the particles to the body as their size allows delivery through intravenous injection or other routes.

Lipid-Based Colloidal Nano drug-Delivery Systems

Lipid nanocapsules are submicron sized particles with a solid or semi-solid shell around an oily liquid centre. As drug delivery systems, colloidal drug carriers have a variety of potential benefits. The use of physiological lipids, the shunning of organic solvents in the preparation process, and a broad possible application range including oral, cutaneous, and intravenous are some benefits. Better bioavailability for poorly soluble medicines is another benefit. Particle growth, an unpredictable gelating tendency, unexpected dynamics of polymorphic transitions, and inherently poor integration abilities because of crystalline structure of the solid liquid nanoparticle are some of the frequent drawbacks [5].

Recent Trends in Solid–Lipid Nanoparticle Research

Recently, a method for synthesizing lipid nanocapsules in the nanometer range by a lipid-based solvent-free formulation process has been devised. This method takes advantage of how an ethoxylated hydrophilic surfactant's hydrophilic-lipophillic balance varies with temperature, resulting in an inversion phase.

Polymeric Micelles as Drug Carriers Systems

`Due to their ability to solubilize hydrophobic compounds, small particle size, strong thermodynamic solution stability, extended release of different drugs, and inhibition of rapid clearance by the reticuloendothelial system(RES), polymeric micelles have drawn attention in drug delivery [6]. Similar to low-molecular-weight surfactants, the critical micelle concentration (CMC) is the primary characterization factor for polymeric micelles. Additionally, a variety of drugs can be incorporated to the hydrophobic core of polymeric micelles by chemical conjugation or physical entrapolymeric micelles using a variety of contacts, including hydrophobic, ionic, or hydrogen bonding interactions. The hydrophobic core acts as a reservoir from which the drug is released gradually over time [7].

Polymer-based nanoparticulate drug delivery systems [8-9]

1. Hydro gel-Based Nanoparticulate Drug-Delivery Systems.
2. Dendrimer-Based Drug-Delivery Systems.
3. Calcium Carbonate Nanoparticles
4. Protamine-Based Nanoparticulate Drug Carriers (Proticles):

The most popular source of protamine is salmon, is nonantigenic and essentially nontoxic peptide from the sperm with a molecular mass of around 5000 g/mol. It serves as the cationic component and can be utilised as a delivery method for DNA or oligonucleotides.

5. Chitosan-Based Nanoparticulate Drug-Delivery System:

d- and N-acetyl d-glucosamine are joined by b-(1, 4)-glycosidic linkages to form the polycationic polymer chitosan, which is often employed in NPDDSs to deliver anticancer medications, genes, and vaccines. Chitosan is a biocompatible and natural polymer. Additionally, chitosan nanoparticles are being examined for use in ocular applications [10].

6. Silicone Nanopore-Membrane-Based Drug- Delivery System.
7. Albumin and Gelatin Nanospheres.
8. Polymeric Nanocapsules as Drug Carriers.
9. Polystyrene Nanospheres.

Types of pharmaceutical nanotools [2]

1. Carbon Nanotubes: These are hexagonal networks of carbon atoms with a diameter of 1 nm and a length of 1–100 nm that are formed when a sheet of graphite is rolled up into a tube. Single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs) are the two forms of nanotubes, and their graphene cylinder arrangements are different.

2. Quantum Dots: These are semiconducting materials containing a semiconductor core (CdSe), a coating with a shell (ZnS) to enhance optical characteristics, and a cap to enhance solubility in aqueous buffers. The development of diagnostic tools (magnetic resonance imaging, MRI) in vitro and in vivo detection and analysis of biomolecules is greatly influenced by quantum dots [11].

3. Dendrimers: These have various chemical polymer compartments and highly branching, tree-like shapes. The core, branches, and surface are the three distinct areas found in dendrimers. They offer favourable characteristics for delivering bioactives, raging from drug, vaccines, metals, and DNA, to targeted areas. Their hollow interior provides space to encapsulate drugs and other bioactive physically or

by various interactions to act as drug delivery vehicles. Dendrimer-based drug delivery, immunoassay, solubilization, gene therapy, and MRI contrast agents are some of their most significant uses.

4. Liposomes: When dry phospholipids are moistened, these closed vesicles are produced. According to the size and quantity of bilayers, liposomes may be divided into three fundamental categories. Multilamellar vesicles (MLVs) are composed of a number of lipid bilayers that are separated apart by aqueous spaces. A single bilayer encircles the confined aqueous region in both Small Unilamellar Vesicles (SUVs) and Large Unilamellar Vesicles (LUVs).

5. Polymeric Micelles: Amphiphilic block copolymers with supramolecular core-shell structures, they are typically have a diameter of less than100 nm.

6. Polyplexes/Lipopolyplexes: These are assemblies, which are utilised in transfection techniques; spontaneously form between nucleic acids and polycations or cationic liposomes (or polycations coupled to targeting ligands or hydrophilic polymers).

Engineering of pharmaceutical nanosystems

Nanosystems are the chemical entity, making them difficult to accept for drug bio delivery. They need to be altered in size and surface with biocompatible polymers and certain site-specific ligands in order to be suitable for biological delivery. Some are:

1. Functional Nanosystem:

Surface functionalization is the process of modifying the characteristics of nanosystems by incorporating, adsorbing, or covalently coupling substances like polymers and/or ligands to their surfaces. Polymers, carbohydrates, endogenous substances/ligands, peptides, proteins, nucleic acids, and polysaccharides are a few of the often used tools for surface modification. In compared to ordinary nanosystems, these tools transform nanosystems into intelligent tools that provide a wide range of properties including improved biostability, decreased aggregation, and higher target specificity [12].

2. Multifunctional Nanosystems:

There are three ways that multifunctional nanosystems can be produced. First, multifunctionality is imparted to the material's core to allow for the simultaneous delivery of two or more therapeutic active moieties; second, it is imparted to the surface to stabilise it with PEG (poly ethylene glycol) to modify the circulation time and use of a targeting moiety; and third, it is imparted to the material by using biomaterials that are thermally, pH, and stimulus sensitive [13].

Nanotechnology in drug delivery: nanoparticles

The production of therapeutically relevant formulations for the treatment of patient disorders is the ultimate objective of the application of nano-drug delivery systems. A particular quantity of a drug that can be therapeutically efficacious must be delivered through clinically appropriate drug delivery systems, often over a long period of time. The nanotechnology-produced micro size medication delivery devices can satisfy such needs. Little consideration has also been given to the systems' need for introduction into the human body, which demands Food and Drug Administration approval (FDA). The majority of the existing techniques for producing nano/micro particles are based on solvent exchange techniques or double emulsion methods.

To develop drug nano crystals, nano particles, nano precipitates, and nano suspensions, different approaches including milling, high pressure homogenization, controlled precipitation, etc. are being investigated. Strategies for controlled drug delivery have had a significant influence on medicine. At general, controlled-release polymer systems distribute drugs in the ideal dosage for extended periods of time thus promoting patient compliance, increasing the efficacy of drug and improving the use of especially toxic, poorly soluble, or relatively unstable drugs. To provide highly targeted and efficient therapeutic and diagnostic modalities, nanoscale materials can be utilized as drug delivery systems.

Nanoparticles are referred as the particulate dispersions or solid particles with a size between 10 and 1000 nm.. A nanoparticle matrix is used to dissolve, trap, encapsulate, or attach the drug. Nanoparticles, nanospheres, or nanocapsules can be produced depending on how they are prepared. Controlling particle size, surface characteristics, and the release of pharmacologically active substances are the main objectives when developing nanoparticles as a delivery system in order to accomplish the drug's site-specific activity at the therapeutically optimal rate and dosing regimen.

Applications of pharmaceutical nanotools

In order to get through various physiological, biochemical, and pharmacological obstacles, size reduction is crucial. Pharmaceutical nanotechnology offers a wide range of nanosize systems or devices that have several advantages. Some significant application areas include:

1. As nanomaterials for tissue engineering: Nanotechnology has produced a variety of specific product that are employed for bone healing, implant coatings, tissue regeneration scaffolds, and tissue repair etc.
2. Nanobased drug delivery tools: These include polymeric nanoparticles, liposomes, dendrimers, polymeric micelles, polymer-drug conjugates, and antibody-drug conjugates. These can be broadly categorised as:

A. Sustained and controlled delivery system
B. Stimuli sensitive delivery system
C. Functional system for delivery of bioactives
D. Multifunctional system for combined delivery of therapeutic, diagnostic and biosensing.
E. Site specific targeting (intracellular, cellular, tissue).

Additionally, nanobased drug delivery systems are being used to treat a number of ailments, including cancer treatments etc.

a) Cancer treatment: Nanotechnology has the potential to revolutionise cancer detection and treatment.

b) Implanted delivery systems: When compared to intravenous administration, implantable delivery devices have a smaller, more controlled, and nearly zero order release, which otherwise might induce toxicity.

c) Site-specific drug delivery: Various methods, including liposomes, polymeric micelles, dendrimers, iron oxide, and proteins using drug manipulation in passive and active uptake, are now being investigated for better site-specific drug delivery.

d) Gene therapy: Using a carrier molecule, a normal gene is substituted for with a defective disease-causing gene in gene therapy. Conventional usages of viral vectors are linked to diseases in host, inflammatory responses, and adverse immunologic effects. Delivery systems with nanotechnology capabilities are now being used as prospective vectors for systemic gene therapy, and they have been shown to be efficient and promising.

3. Molecular diagnostics: In intact organisms, subcellular biological processes may be represented, characterized, and quantified using molecular imaging, a branch of nanoscience. Gene expression, protein-protein interactions, signal transduction, cellular metabolism, and intracellular and intercellular trafficking are some of these processes. They have been used with success in a variety of nuclear imaging, optical imaging, magnetic resonance imaging, and ultrasonic imaging.
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4. Biosensor and biolabels: Using this innovative and promising technology, a variety of analytical tools have been designed. These instruments are used to identify different pathogenic proteins and physiological-biochemical indicators linked to disease or altered body metabolism .A biosensor is defined as a measurement system that consists of a probe with a sensitive biological recognition element, or bioreceptor, a physicochemical detector component, and a transducer in between to amplify and transduce the signals in to the measurable form.

5. Drug discovery: Pharmaceutical nanotechnology is essential in the process of discovering new drugs, which depends on a better understanding of the mechanism of drug action and the discovery of biomarkers linked to specific diseases. Through the identification of the protein that is present on the cell surface or target surface, nanotechnology aids in target identification and validation. The drug discovery process will be improved by nanotechnology through miniaturisation, automation, speed, and reliability of assays.

Commercially available nanoparticles

A. Melamine Nanospheres: Biodegradable Polylactide Nanospheres and Plain Polymethyl Methacrylate Nanospheres
B. Nanospheres made of magnetic plain dextran.
C. Gold Nanospheres: High grade gold nanospheres are employed in the development of diagnostic tests as well as investigations of the conjugation of proteins and antibodies. The particles range in size from 2 to 250 nm and have a relatively narrow size distribution.

D. Silver Nanospheres: High-quality silver nanospheres can be employed in the creation of diagnostic tests as well as studies on the conjugation of proteins and antibodies. The particles range in size from 2 to 250 nm and have a relatively narrow size distribution.

E. Silica Nanospheres: With a density of 2.0 g/cm3, these mono-disperse silica particles are simpler to disperse and separate. The silica particles, made using a novel dying technique, are stable in both water and organic solvents. Silica particles may be made into fluorescent particles and are simple to functionalize. They are helpful for coupling proteins, lectins, oligonucleotides, DNA, and oligopeptides [14].

Targeted Nano-Pharmaceuticals

"Targeted nano-pharmaceuticals" are created to more effectively target medications into diseased cells, tissues, and organs. Biomarkers are distinctive characteristics on the surface of diseased cells. Drugs are included in the targeted nano-pharmaceuticals, which attach to the cells' biomarkers and preferentially detect them. The drugs are then locally released, allowing for a more precise targeting of the diseased cells. Drug adverse effects in other body regions can be minimised with precise targeting. Better targeting also allows higher doses to be administered locally while minimising the adverse effects for the patient.

For instance, chemotherapy for cancer is known to have serious side effects; by utilising more precisely targeted nano-pharmaceuticals, it is expected to lessen these detrimental effects for the patient. A significant problem for medical research is identifying the right biomarkers to target for a particular condition. Nanopharmaceuticals may include contrast agents that help researchers identify the location of a disease (such as a tumour) on a body scan image, such as one performed using Positron Emission Tomography, X-Ray Computed Tomography, or Magnetic Resonance Imaging. Thus, the images can depict where the infection is located and how far it has spread. They can also be used for "treatment monitoring," or assessing how well a therapy is working over time.

Future perspective

At the compound annual growth rate (CAGR) of 13.5%, the size of the worldwide nanomedicine industry is expected to rise from an estimated $53 billion in 2009 to more than $100 billion in 2014. The potential for developing a system that is more effective for the creation of nanoproducts is constrained. It is critical to understand how nanomaterials are distributed inside the body. This is related to a second constraint that calls for imaging techniques to track the biodistribution of nanomedicine over time. The safety of nanomedicine has not yet been fully established, despite rigorous standards and ongoing identification of potential advantages. Nanotechnology is anticipated to be used in diagnostics, molecular research methods, and instruments as it advances concurrently in other areas [15-16].

Although Instead of investing in new and advanced nanotechnology applications, it should focus on fixing existing issues, such as availability of drugs to the poor, easy and cost-effective diagnostic solutions. The majority who require primary healthcare facilities will be served by it. In order to develop nanotechnology-based therapy options, further research is required with a stronger emphasis on transport processes, endocytosis, biological barriers, degradation routes, and control over its potential harmful effects.

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