"NANOTECHNOLOGY" CURRENT STATUS IN PHARMACEUTICAL SCIENCE: A REVIEW

Varshney H. M.[1], Mohan Shailender*[1]

[1]Department of Pharmaceutics, Faculty of Pharmacy, Jaipur College of Pharmacy, Jaipur, Rajasthan-302022, India

ABSTRACT

Size reduction is one of most fundamental unit operation which is of prime importance in pharmacy. It helps in improving stability and bioavailability, reducing toxicity, enhancing release and providing better formulation opportunities for drug.

In the recent trends, the drugs in nanometer size range have found to increase the performance in variety of dosage forms. The word 'nano' is a Latin word, which means 'dwarf'. Nano size refers to 10^{-9} of a particular unit thus nanometer is 10^{-9} of a meter.

Nanotechnology is the science that deals with the processes that occurs at molecular level and of nanolength scale size. Nanotechnology has shown tremendous progress in physics, electronics and engineering but biomedical and pharmaceutical fields are yet to be explored, although, it has powerful impact in various medical fields such as biophysics, molecular biology, bioengineering, cardiology, oncology, ophthalmology, endocrinology immunology etc. Nanotechnology provides intelligent system, devices and materials for better pharmaceutical applications.

The current status of nanotechnology in pharmaceutical field includes development of Nanomedicine, tissue engineering, nanorobots, biosensors, biomarkers etc. Pharmaceutical Nanotechnology provides opportunities to improve materials, medical devices and help to develop new technology where existing and more conventional technologies may be reaching their limits.

Thus in the coming years advancements in this field will led to the improved form of drug delivery as well as other prospects of medicine and pharmacy.

Keywords: Nanotechnology, Pharmaceutical Nanotechnology, Nanoscale, Nanoparticles, Bionanotechnology.

INTRODUCTION

Size reduction is one of the fundamental unit operation having important applications in pharmacy. It helps in improving solubility and bioavailability, reducing toxicity, enhancing release and providing better formulation opportunities for drugs. Drugs in the nanometer size range enhance performance in a variety of dosage forms. Major advantages 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 nanoscience are widely seen as having a great potential to bring benefits to many areas of research and applications. The term "nanotechnology" was first used in 1974, when Norio Taniguchi, a scientist at the University of Tokyo, Japan, referred to materials in nano meters [1].

Nanotechnology is a multidisciplinary field which literally means any technology on a nanoscale that has applications in the real world. Nanotechnology is the science that deals with the processes that occur at molecular level and of nanolength scale size (*i.e.* 10^{-9}) [2].

The properties of materials at the nanoscale can be very different from those at a larger scale. When the dimension of a material is reduced from a large size, the properties remain the same at first, and then small changes occur, until finally when the size drops below 100 nm, dramatic changes in properties can occur. If only *one length*

Corresponding author:
Email: shailendra1903@gmail.com

of a three-dimensional nanostructure is of nanodimension, the structure is referred to as a **quantum well**; if *two sides are of nanometer length*, the structure is referred to as a **quantum wire**. A **quantum dot** has all *three dimensions in the nano range*. Materials can be nanostructured for new properties and novel performance [3].

Nanoparticulate drug delivery system may offer plenty of advantages over conventional dosage forms, which includes improved efficacy, reduced toxicity, enhanced biodistribution and

photolithography, nanomolding, dip-pen lithography and nanofluidics [5, 6]. (Figure 1)

NANODEFINITIONS

'Nanoscience' can be defined as study of phenomenon and manipulation of materials at atomic and molecular scales.

'Nanotechnology' is related to design characterization, production and applications of structures, devices and systems by controlling

Table 1: Nanosystems in Tissue Engineering

Nanosystems	Property	Applications
Nanoengineered prosthetics	Increased miniaturization; increased prosthetic strength & weight reduction; improved biocompatibility.	Retinal, auditory, spinal and cranial implants.
Cellular manipulation	Manipulation of cellular systems.	Persuasion of lost nerve tissue to grow; growth of body parts.

improved patient compliance. Pharmaceutical nanoparticles are subnanosize structure, which contain drug or bioactive substances with in them and are constituted of several tens or hundreds of atoms or molecules with a variety of sizes (size from 5 nm to 300 nm) and morphologies (amorphous, crystalline, spherical, needles, etc) [4].

Nanoscale materials and devices can be fabricated using either "*bottom-up*" or "*top-down*"

shape and size at nanometer scale.

'Nanomedicine' is defined as submicron size (<1um) modules, used for treatment, diagnosis, monitoring, and control of biological system.

'Pharmaceutical nanotechnology' embraces applications of nanoscience to pharmacy as nanomaterials, and as devices like drug delivery, diagnostic, imaging and biosensor.

Fig.1. Bottom-Up and Top-Down Techniques in Manufacturing Nanoparticles
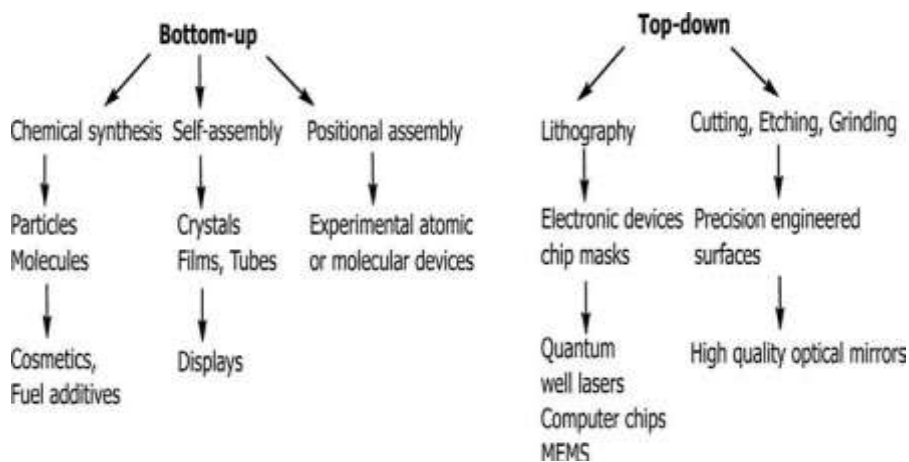
fabrication approaches. In *bottom-up methods*, nanomaterials or structures are fabricated from buildup of atoms or molecules in a controlled manner that is regulated by thermodynamic means such as self-assembly. Alternatively, advances in microtechnologies can be used to fabricate nanoscale structures and devices. These techniques are collectively referred to as *topdown nanofabrication technologies*, include

'Nanometrology' is the science of measurements at the nanoscale. Four commonly used techniques are: transmission electron microscopy (TEM), scanning electron microscopy (SEM), and scanning probe techniques [scanning probe microscopy (SPM)], and optical tweezers (single-beam gradient trap) [1].

'Nanotoxicology' refers to the study of the interactions of nanostructures with biological systems with an emphasis on the relationship between the physical and chemical properties of nanostructures with induction of toxic biological response.

'Bionanotechnology' generally refers to the study of how the goals of nanotechnology can be guided by studying how biological "machines" work and adapting these biological motifs into improving existing nanotechnologies or creating new ones [7].

'Nanobiomechanics' (also bionanomechanics) is an emerging field in nanoscience and biomechanics that combines the powerful tools of nanomechanics to explore fundamental science of biomaterials and biomechanics. For example, it has been shown that red blood cells infected by

associated with infections. It is expected that in next 10 yrs. market will be flooded with nanotechnology-devised medicine [1].

The scope of pharmaceutical nanotechnology is very wide from smart material for tissue engineering to intelligent tools for delivery of drugs and diagnostics, and more recently, artificial RBC etc. Current applications of nanotechnology in pharmacy are development of nanomedicine, tissue engineering, nanorobots, advance diagnostic, as carrier of diagnostic and therapeutic modalities and as biosensor, biomarker, image enhancement device, implant technology, bioactive surfaces etc. A large number of nanosystems, which have been investigated in pharmacy todate, are liposomes, dendrimers, metallic nanoparticles, polymeric nanoparticles, carbon nanotubes, quantum dots, nanofibres etc.[9].

Fig. 2. Schematic Diagram of Various Types of Pharmaceutical Nanosystem
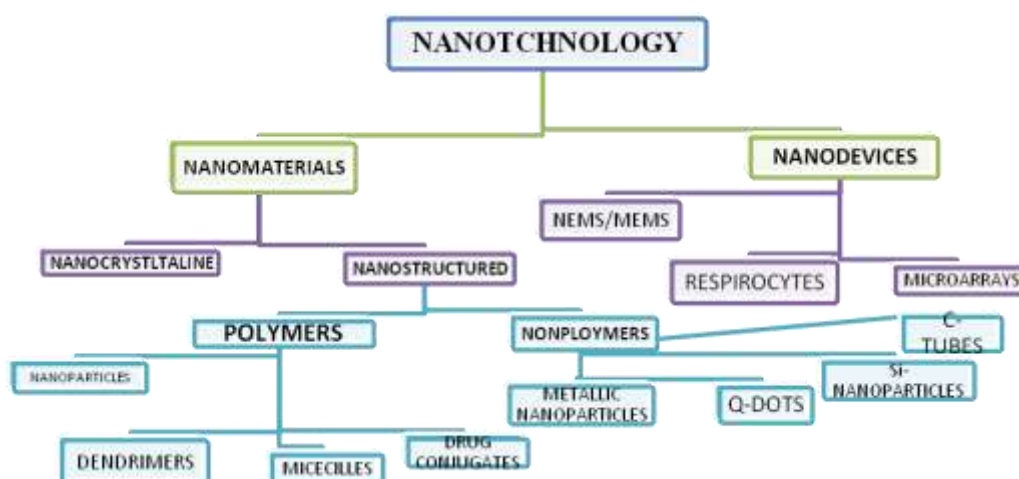
malaria are 10 times stiffer than normal cells [8].

SCOPE AND OPPORTUNITY

Applications of nanotechnology to pharmacy, that provide 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 revolutionize the pharmaceutical industry in near future. Pharmaceutical nanotechnology presents revolutionary opportunities to fight against many diseases. It helps in detecting the antigen associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting the microorganisms and viruses

PHARMACEUTICAL NANOTECHNOLOGY BASED SYSTEMS

Pharmaceutical nanotechnology provides two basic types of nanotools viz. nanomaterials and nanodevices, which play a key role in region of pharmaceutical nanotechnology and related fields. (Figure 2)

Nanomaterials are biomaterials used, for example, in orthopedic or dental implants or as scaffolds for tissue-engineered products. Their surface modifications or coatings might greatly enhance the biocompatibility by favoring the interaction of living cells with the biomaterial. These materials can be sub classified into nanocrystalline and nanostructured materials.

Nanocrystalline materials are readily manufactured and can substitute the less performing bulk materials. Raw nanomaterials can be used in drug encapsulation, bone replacements, prostheses, and implants.

to them. The reduction or prevention of side effects can also be achieved by controlled release of the medicament to the target. Nanoparticulate provides a better penetration of the particles to the body as their size allows delivery through

Table 2: Nanotools for Cancer Therapeutics.

Nanosystem	Applications in cancer therapeutics
C-Nanotubes	DNA mutation detection, disease protein biomarker detection.
Dendrimers	Controlled release drug delivery, image contrast agents.
Nanocrystals	Improved formulation for poorly-soluble drugs.
Nanoparticles	MRI and ultrasound image contrast agents, targeted drug delivery, permeation enhancers, reporters of apoptosis, angiogenesis, etc.
Nanoshells	Tumor-specific imaging, deep tissue thermal ablation.
Nanowires	Disease protein biomarker detection, DNA mutation detection, gene expression detection.
Quantum Dots	Optical detection of genes and proteins in animal models and cell assays, tumor and lymph node visualization.

Nanostructured materials are processed forms of raw nanomaterials that provide special shapes or functionality, for example quantum dots, dendrimers, fullerenes and carbon nanotubes. Nanodevices are miniature devices in the nanoscale and some of which include nano- and micro-electromechanical systems (NEMS/ MEMS), microfluidics (control and manipulation of micro or nanolitre of fluids), and microarrays (different kind of biological assay e.g. DNA, protein, cell, and antibody). Examples include biosensors and detectors to detect trace quantities of bacteria, airborne pathogens, biological hazards, and

intravenous injection or other routes.

Lipid-Based Colloidal Nanodrug-Delivery Systems

Lipid nanocapsules are submicron particles which are made up of an oily liquid core surrounded by a solid or semisolid shell.

Colloidal drug carriers have a number of potential advantages as drug delivery systems. Some advantages are better bioavailability for poorly soluble drugs, use of physiological lipids, the shunning of organic solvents in the preparation process, a wide potential application

Table 3: Nanomaterials for Molecular Diagnosis.

Modality	Compound	Status	Uses
Imaging Agents			
Endorem®	Superparamagnetic iron oxide nanoparticles	Market,	MRI agent
Gadomer®	Dendrimer-based MRI agents.	Phase III clinical trial.	MRI agent-cardiovascular.
Drug delivery	Albumin nanoparticle containing	Market.	Breast cancer.
Abraxane®	paclitaxel.		

disease signatures and some intelligent machines 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.

Targeting ensures high efficiency of the drug, reduction in the side effects, especially when dealing with drugs that are presumed to kill cancer cells but can also kill healthy cells when delivered

spectrum including oral, dermal, and intravenous.

The common disadvantages include: particle growth, unpredictable gelating tendency, unexpected dynamics of polymorphic transitions, and inherently low incorporation capabilities because of crystalline structure of the solid-liquid nanoparticles [10].

Recent Trends in Solid–Lipid Nanoparticle Research

Recently, a lipid-based solvent-free formulation process has been developed to prepare lipid nanocapsules in the nanometer

range [11]. This process takes advantage of the variation of the hydrophilic–lipophillic balance of an ethoxylated hydrophilic surfactant as a function of the temperature, leading to an inversion phase.

Polymeric Micelles as Drug Carriers Systems

Polymeric micelles have attained attention in drug delivery, partly due to their ability to solubilize hydrophobic molecules, their small particle size, good thermodynamic solution stability, extended release of various drugs, and prevention of rapid clearance by the reticulo-endothelial system (RES).

Critical micelle concentration (CMC), similar to low-molecular-weight surfactants, is the key characterization parameter for polymeric micelles.

Furthermore, various types of drugs can be loaded into the hydrophobic core of polymeric micelles by chemical conjugation or physical entrapolymeric micelles by utilizing various interactions such as hydrophobic interactions, or ionic interactions, or hydrogen bonding. The hydrophobic core serves as a reservoir from which the drug is released slowly over a longer period of time.

POLYMER-BASED NANOPARTICULATE DRUG-DELIVERY SYSTEMS

1. Hydrogel-Based Nanoparticulate Drug-Delivery Systems.

2. Dendrimer-Based Drug-Delivery Systems.

3. Calcium Carbonate Nanoparticles.

4. Protamine-Based Nanoparticulate Drug Carriers (Proticles): Protamine is a non-antigenic and virtually nontoxic peptide from the sperm, the compound derived from salmon, the most widely used source, and has a molecular mass around 5000 g/mol. It can be used as a carrier system for delivery of DNA or oligonucleotides and it is being used as the cationic component.

5. Chitosan-Based Nanoparticulate Drug-Delivery System: Chitosan, a polycationic polymer, consisting of d-glucosamine and *N*-acetyl-dglucosamine linked by b-(1, 4)-glycosidic bonds, has been widely used for NPDDSs for delivering anticancer drugs, genes, and vaccines [14-15]. Chitosan is a natural polymer and biocompatible. Chitosan nanoparticles also have being evaluated for ocular applications.

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, 1 nm in diameter and 1–100 nm in length, as a layer of graphite rolled up into a cylinder. There are two types of nanotubes: single-walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs), which differ in the arrangement of their graphene cylinders. (Figure 3).

Fig. 3. Structure of Nano Carbon Tubes

(a) Single walled (SWNTs) (b) Multi walled (MWNTs)

2. **Quantum Dots:** Quantum dots (QDs) are semiconducting materials that have a semiconductor core (CdSe), coated with a shell (e.g., ZnS) to improve its optical properties, and a cap that helps improving solubility in aqueous buffers. Quantum-dots have a large impact on some important development in different medical areas like diagnostic tools (magnetic resonance imaging, MRI), *in vitro* and *in vivo* detection and analysis of biomolecules etc.

3. **Dendrimers:** These are highly branched, tree-like structures and have different compartments of chemical polymer. Dendrimer contain three different regions: core, branches, and surface. They have promising properties for delivery of bioactives ranging from drugs, vaccines, metal, and genes to desired sites. Their hollow interior provides space to incorporate drugs and other bioactive physically or by various interactions to act as drug delivery vehicles. Most important applications of dendrimers are solubilization, gene therapy, dendrimer based drug delivery, immunoassay and MRI contrast agent. (Figure 4).

4. **Liposomes:** These are closed vesicles that are formed when dry phospholipids are hydrated.

Fig. 4. Schematic Representation of Dendrimer
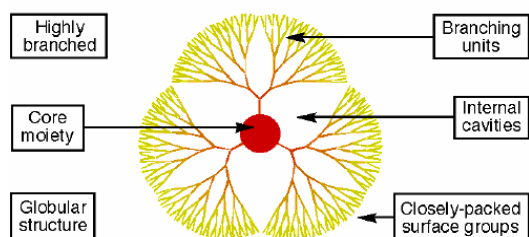
Liposomes are classified into three basic types based on their size and number of bilayers. Multilamellar vesicles (MLVs) consist of several lipid bilayers separated from one another by aqueous spaces. Small unilamellar vesicles (SUVs) and Large unilamellar vesicles (LUVs) consist of a single bilayer surrounding the entrapped aqueous space. (Figure 5).

5. **Polymeric Micelles:** Polymeric micelles are usually of <100 nm and are amphiphilic block copolymer having supramolecular core-shell structure.

6. **Polyplexes/ Lipopolyplexes:** These are assemblies, which form spontaneously between nucleic acids and polycations or cationic liposomes (or polycations conjugated to targeting ligands or hydrophilic polymers), and are used in transfection protocols [2].

ENGINEERING OF PHARMACEUTICAL NANOSYSTEMS

Since nanosystems are the chemical entity, they are not easily accepted for bio-delivery of the drug. They need some modifications to make them compatible for biological delivery, by altering their size and surface by biocompatible polymers and with some site specific ligands.

Some modifications are

1. **Functional Nanosystem:** The modification in the properties of nanosystems by the incorporation, adsorption or covalent coupling of components like polymers and/or ligands to their surface is known as surface functionalization. Some commonly employed tools for surface modification are polymers, carbohydrates, endogenous substances/ligands, peptide, protein, nucleic acid and polysaccharides. These tools make the nanosystems an intelligent tool and that offers large varieties of properties like higher biostability, lower aggregation and high target

specificity in comparison to conventional nanosystems.

2. **Multifunctional Nanosystems:** Multifunctional nanosystems can be developed in three ways firstly *multifunctionality imparted to the core* for the simultaneous delivery of two or more therapeutic active moieties; secondly as *multifunctionality imparted to surface* for stabilization by PEG (poly ethylene glycol) for the modification in circulation time, and use of targeting moiety and thirdly as *multifunctionality imparted to material* by using thermal sensitive, pH and stimuli sensitive biomaterials.

NANOTECHNOLOGY IN DRUG DELIVERY: NANOPARTICLES

The ultimate goal of application of nano-drug delivery systems is to develop clinically useful formulations for treating diseases in patients. Clinically useful drug delivery systems need to deliver a certain amount of a drug that can be therapeutically effective, and often over an extended period of time. Such requirements can be met by the micro scale drug delivery systems

Fig. 5. Structure of Liposomes
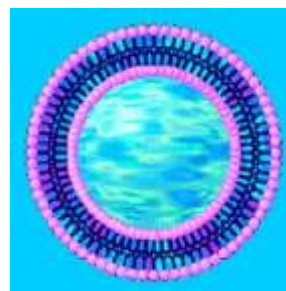
manufactured by nanotechnology.

In addition, little attention has been paid to the fact that the systems have to be introduced into the human body, requiring approval from the Food and Drug Administration (FDA). The current methods of preparing nano/micro particles are mainly based on double emulsion methods or solvent exchange technique [14-15].

Nano-design of drugs by various techniques like milling, high pressure homogenization, controlled precipitation etc., are explored to produce, drug nanocrystals, nanoparticles, nanoprecipitates, nanosuspensions (which for ease of understanding commonly mentioned as nanocrystals).

Controlled drug-delivery strategies have made a dramatic impact in medicine. In general, controlled-release polymer systems deliver drugs in the optimum dosage for long periods, thus increasing the efficacy of the drug, maximizing patient compliance and enhancing the ability to use highly toxic, poorly soluble or relatively unstable drugs. Nanoscale materials can be used as drug delivery vehicles to develop highly selective and effective therapeutic and diagnostic modalities.

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10 -1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. The major goals in designing nanoparticles as a delivery system are to control particle size, surface properties and release of pharmacologically active agents in order to achieve the site-specific action of the drug at the therapeutically optimal rate and dose regimen.

PREPARATION OF NANOPARTICLES

A. Dispersion of preformed polymers by:

i.   Solvent evaporation method.

ii.   Spontaneous emulsification/solvent diffusion method.

iii. Salting-out/ emulsification diffusion method.

iv.   Production of nanoparticles using supercritical technology.

v.   Polymerization methods.

vi.   NPs prepared from hydrophilic polymers.

B. Polymerization of monomers:

Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including [18]:

i.   Size of nanoparticles required;

ii.   Inherent properties of the drug;

iii. Surface characteristics such as charge and permeability;

iv.   Degree of biodegradability, biocompatibility and toxicity;

v.   Drug release profile desired;

vi.   Antigenicity of the final product.

Nanoparticles have been prepared most frequently by three methods:

(1) Dispersion of preformed polymers;

(2) Polymerization of monomers;

(3) Ionic gelation or coacervation of hydrophilic polymers.

Dispersion of preformed polymers: Dispersion of preformed polymers is a common technique used for the preparation of biodegradable nanoparticles from poly (lactic acid) (PLA); poly (D, L-glycolide), PLG; poly (D, L-lactide-co-glycolide) (PLGA) & poly (cyanoacrylate) (PCA).

1. *Solvent evaporation method:* In this method, the polymer is dissolved in an organic solvent such as dichloromethane, chloroform or ethyl acetate which is also used as the solvent for dissolving the hydrophobic drug. The mixture of polymer and drug solution is then emulsified in an aqueous solution containing a surfactant or emulsifying agent to form oil in water (o/w) emulsion. After the formation of stable emulsion, the organic solvent is evaporated either by reducing the pressure or by continuous stirring. In order to produce small particle size, often a high-speed homogenization or ultrasonication may be employed.

2. *Spontaneous emulsification or solvent diffusion method:* In this method, the water miscible solvent along with a small amount of the water immiscible organic solvent is used as an oil phase. Due to the spontaneous diffusion of solvents an interfacial turbulence is created between the two phases leading to the formation of small particles. As the concentration of water miscible solvent increases, a decrease in the size of particle can be achieved.

Both solvent evaporation and solvent diffusion methods can be used for hydrophobic or hydrophilic drugs. In the case of hydrophilic drug, a multiple w/o/w emulsion needs to be formed with the drug dissolved in the internal aqueous phase.

Polymerization method: In this method, monomers are polymerized to form nanoparticles in an aqueous solution. Drug is introduced either by dissolving it in the polymerization medium or by adsorption onto the nanoparticles after polymerization completed. The nanoparticle suspension is then purified to remove various stabilizers and surfactants employed for polymerization by

ultracentrifugation and re-suspending the particles in an isotonic surfactant-free medium. Nanocapsules formation and their particle size depend on the concentration of the surfactants and stabilizers used [18].

Coacervation or Ionic Gelation Method: In this method, positively charged amino group of chitosan interacts with negative charged tripolyphosphate to form coacervates with a size in the range of nanometer. Coacervates are formed as a result of electrostatic interaction between two aqueous phases, whereas, ionic gelation involves the material undergoing transition from liquid to gel due to ionic interaction conditions at room temperature.

Production of nanoparticles using *Supercritical Fluid Technology*: Conventional methods such as solvent extraction-evaporation, solvent diffusion and organic phase separation methods require the use of organic solvents which are hazardous to the environment as well as to physiological systems. The supercritical fluid technology has been investigated as an alternative for the preparation of biodegradable micro- and nanoparticles because supercritical fluids are environmentally safe [19].

Supercritical CO_2 ($SC CO_2$) is the most widely used supercritical fluid because it has mild critical conditions (T_c = 31.1 °C, P_c = 73.8 bars), nontoxicity, non-flammability, and low price. The most common processing techniques involving supercritical fluids are *supercritical anti-solvent* (SAS) and *rapid expansion of critical solution* (RESS). This technique is more expensive.

APPLICATIONS OF PHARMACEUTICAL NANOTOOLS

Size reduction is helpful in overcoming various physiological, biochemical and pharmaceutical barriers. Pharmaceutical nanotechnology provides wide array of systems or device of nanosize, which offer numerous benefits. Some important applications areas are:

1. ***As nanomaterials for tissue engineering:*** Nanotechnology offered numerous smart materials that are used for tissue repair and replacement, implant coatings, tissue regeneration scaffolds, structural implant materials, bone repair etc. some other uses are given in table 1.

2. ***Nanobased drug delivery tools:*** These are polymeric nanoparticles, liposome, dendrimer, polymeric micelles, polymer-drug conjugates, antibody- drug conjugates, which can broadly be classify 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 therapeutics, biosensing and diagnostic.

   e. Site specific targeting (intracellular, cellular, tissue).

   Furthermore, nanobased drug delivery tools are now being employed in the treatment of various diseases such as in cancer therapy etc.

   a) ***Cancer treatment:*** Nanotechnology can have a revolutionary impact on cancer diagnosis and therapy. (Table 2)

   b) ***Implantable delivery systems:*** Nanotechnology is opening up new opportunities in implantable delivery systems because of its size, controlled and approximately zero order release which other wise may cause toxicity when compared to intravenous administration (due to first order drug kinetics).

   c) ***Site specific drug delivery:*** Several approaches are now being tested for better site-specific delivery using liposomes, polymeric micelles, dendrimers, iron oxide, proteins using manipulation in passive and active uptake of drug.

   d) ***Gene therapy:*** In gene therapy, a normal gene is inserted in place of an abnormal disease-causing gene using a carrier molecule. Conventional uses of viral vectors are associated with adverse immunologic, inflammatory reactions and diseases in the host. Nanotechnology enabled delivery systems have currently emerged as potential vector and are shown to be effective and promising tool in systemic gene treatment.

3. ***Molecular Diagnostics:*** Molecular imaging is the nanoscience of representing, characterizing, and quantifying subcellular biological processes in intact organisms. These

processes include gene expression, protein-protein interaction, signal transduction, cellular metabolism, and both intracellular and intercellular trafficking. They have been successfully utilized in various magnetic resonance imaging, optical imaging, ultrasonic imaging and nuclear imaging. (Table 3)

4. ***Biosensor and Biolabels:*** A number of analytical tools have been developed with application of this smart and potential technology. These tools are used for determination of various pathological proteins and physiological-biochemical indicator associated with disease or disrupted metabolic conditions of body.

   A **biosensor** is generally 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 these signals in to measurable form.

   A nanobiosensor or nanosensor is a biosensor that has dimensions on the nanometre size scale.

5. ***Drug discovery:*** Pharmaceutical nanotechnology is playing crucial role in drug discovery that rely on better understanding of mechanism of the drug action and identification of biomarker associated with specific disease. Nanotechnology helps identification and validation of target by identifying the protein present on the cell surface or target surface. Nanotechnology will enhance the drug discovery process, through miniaturization, automation, speed and reliability of assays.

COMMERCIALLY AVAILABLE NANOPARTICLES

a) *Melamine Nanospheres:* Plain Polymethyl Methacrylate and Biodegradable Polylactide Nanospheres.

b) *Magnetic Plain Dextran Nanospheres.*

c) *Gold Nanospheres:* Gold particles are high quality nanospheres that can be used in the production of diagnostic tests as well as conjugation studies of proteins and antibodies. The particles have a very narrow size distribution and are available from 2 to 250 nm.

d) *Silver Nanospheres:* Silver nanospheres are high quality nanospheres that can be used in the production of diagnostic tests as well as

conjugation studies of proteins and antibodies. The particles have a very narrow size distribution and are available from 2 to 250 nm.

e) *Silica Nanospheres:* This mono-disperse silica particles having a density of $2.0g/cm^3$ are easier to dispense and to separate. The silica particles are stable in water and organic solvents, produced under a new dying method. Silica particles are easy to functionalize and available as fluorescent particles. They are useful for coupling of DNA, oligonucleotides, oligopeptides, proteins, lectins, and antibodies.

Targeted Nano-Pharmaceuticals

'Targeted nano-pharmaceuticals' are designed to better target drugs towards diseased cells, tissues and organs. Diseased cells tend to have specific features on their surface named biomarkers. The targeted nano-pharmaceuticals contain drugs and selectively recognize and bind to the biomarkers on the cells. The drugs are then released locally, resulting in more effective targeting of the diseased cells. Precise targeting of the drugs can reduce side-effects in other parts of the body.

Better targeting also allows higher doses to be administered locally while minimizing the side-effects for the patient. Chemotherapy treatment for cancer for example is known to have severe side effects, and the aim is to reduce such negative consequences for the patient by using more precisely targeted nano-pharmaceuticals. Discovering the right biomarkers to target for a certain disease is a key challenge for medical research.

Nano-pharmaceuticals may include contrast agents that allow the physician to see the location of the disease (e.g. tumour) on the image of a body scan, for instance with Magnetic Resonance Imaging (MRI), X-Ray Computed Tomography (CT) or Positron Emission Tomography (PET). The images can thereby show the location and extension of the disease and can also be used for 'therapy monitoring', i.e. monitoring the effectiveness of the therapy over time [20].

CHALLENGES TO PHARMACEUTICAL NANOTECHNOLOGY

Pharmaceutical nanotechnology has provided refined diagnosis and focused treatment of disease. However some ethical, scientific, social and regulatory issues posing various challenges in practical realization of pharmaceutical

nanotechnology. Some major health risk associated with such devices includes cytotoxicity, translocation to undesired cells, acute and chronic toxicity; some unknown, unpredictable and undefined safety issues, environmental impacts of nanomaterials and non-biocompatibility. There are no specific FDA directives to regulate pharmaceutical nanotechnology based products and related issues. Although some FDA approved nanotechnology based products, which have entered the market are liposome, nanoparticles, monoclonal antibody based product, polymer drug conjugate, polymer–protein conjugate and some polymeric drugs.

All-together these challenges caused urgent need to regulate these nanotechnology based products and delivery devices.

FUTURE PROSPECTS OF PHARMACEUTICAL NANOTECHNOLOGY

Pharmaceutical nanotechnology is an emerging field that could potentially make a major impact on human health. Nanomaterials promise to revolutionize medicine and are increasingly used in drug delivery or tissue engineering applications.

A modular approach to construct delivery systems that combine targeting, imaging and therapeutic functionalities into nanoplateforms is emerging as intelligent concept. These multifunctional nanoplateforms would localize to target cells, enable diagnostics and subsequently deliver therapeutics with great precision.

One very interesting and novel future strategy is to device a nanomachine, which can detect and attack pathogen simultaneously, detect the change in molecular event during diseased state, and also monitor the efficacy of treatment. However such intelligent machine (also knows as 'nanorobots' which can serves as mini onboard computer in human body) is very far reaching concept.

In short, recent development, market realization of various pharmaceutical nanotools and global interest shown by scientists, governments and industries ensure that there is tremendous potential and scope of nanobased drug delivery system in near future.

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