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Review Article

A Review on Status of Nanotechnology in Pharmaceutical Sciences

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ABSTRACT

The most important unit operation in pharmacy is the size reduction. Improved stability, reduced toxicity, increased bioavailability, increased rate of release and good drug formulation opportunities accomplished by size reduction. In present days, the performance of various dosage forms has been increased in nanometer size. The cargo size of a specified unit, for example nanometer is 10^{-9} meter. The process which occurs in nano-length size or molecular size level is referred as nanotechnology. It has shown great development in engineering, physics and electronics but pharmaceutical field and medical field needs more development. Although, it has vast application in medical field like immunology, cardiology, bioengineering, oncology, ophthalmology, cardiology etc. In pharmaceutical field, it also provides excellent materials, devices and system. The present status of nanotechnology in pharmaceutical field may be counted as development as biomarkers, biosensors, nano medicine, tissue engineering, nano-robots etc. For developing new technology, as old reaches up to the limits nanotechnology gives great opportunities.

Keywords: Nanoparticles, Nanotechnology, Pharmaceutical nanotechnology, Nanoscale,

INTRODUCTION

Nanoscience and nanotechnology has great approach in research and application in pharmaceutical field. In 1974, the term ‘‘nanotechnology’’ was being used. Any technology which works on nanoscale and has multidisciplinary application will be considered as nanotechnology. It deals with the nano length scale size (i.e. 10^{-9}) or molecular level process[1]. Materials in nanoscale showed big difference in properties as compared to large scale. The properties remained same on size reduction and great changes have been observed when size is below 100 nm. Size reduction may help in improving the bioavailability, reducing toxicity, solubility and good formulation properties of a drug. Performance of the drug in various dosage forms may be enhanced by nanometer size range of the drug. Various advantages of nano sizing are rapid therapeutic activity, low dose, increased surface area, solubility and oral bioavailability and decreased patient variance.

The structure is known as quantum well, if only one length of 3-dimenssional nanostructure is in nano-dimension; and if two lengths are in nano dimension then it will be quantum wire. If all three dimensions are in nano range, then it will be known as quantum dots. There are many advantages of nanotechnology based drug delivery system as compared to traditional system of drug delivery. The advantages may include good patient compliance, improved bio-distribution, decreased toxicity and increased efficacy. Pharmaceutical nanoparticles (NPs) have nano size structure, prepared in different sizes (5 nm to 300 nm) and different morphologies (amorphous, crystalline, spherical, needles) and contains drugs or bioactive materials in them[2].

SCOPE AND OPPORTUNITY

All the applications of nanotechnology are related to pharmacy, provides smart and intelligent drug delivery system, developed most helpful and powerful tool in pharmaceutical field. To fight against various diseases, pharmaceutical nanotechnology plays very important role. It helps in detecting the neurodegenerative diseases, diabetes mellitus, and cancer as well as detecting viruses and microorganism associated with any infection. The pharmaceutical nanotechnology starting from intelligent tools in drug delivery and diagnosis to smart material for tissue engineering, and artificial RBC etc[1]. Furthermore, nanotechnology uses in pharmacy like development of nanomedicines, nanorobots, advance diagnostics, tissue engineering and diagnostic agents like biomarkers, biosensors, image enhancement devices, implant technology etc.Moreover, many nanosystems being developed in pharmacy like carbon nanotubes, quantum dotes, dendrimers, nanofibers, liposomes, metallic nanoparticles, etc[3].

TYPES OF PHARMACEUTICAL NANOTOOLS

Quantum dots

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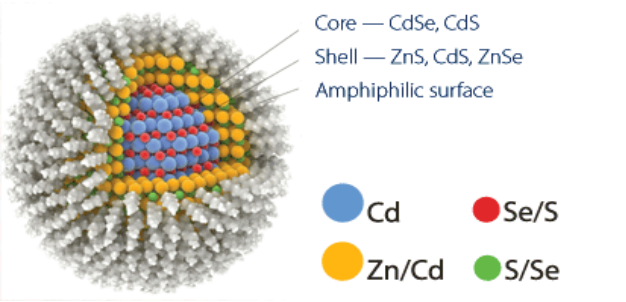

Figure 1: Structure of quantum dot[5].

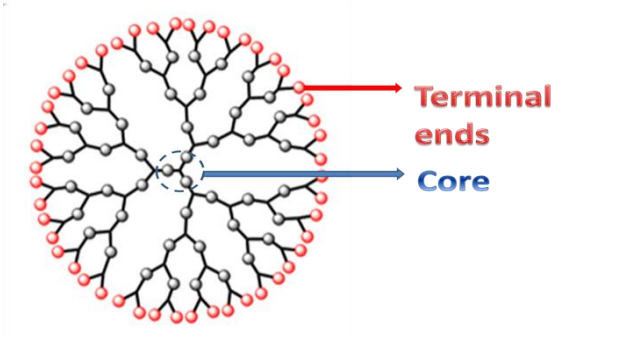

Figure 2: Schematic representation of dendrimer

Quantum dots (QDs) are consisting of shell, core and cap[4] as shown in Figure 1. The semiconducting material which contains semiconducting core (CdSe) and a shell (e.g. ZnS), helpful in improving solubility in aqueous buffer, improve optical properties. Quantum dots has wide application in medical as well as pharmaceutical area like DNA hybridization, time graded tissue fluorescence imaging, immunoassays, cells labelling, biomolecules analysis, DNA cells or drugs, transporting vehicle, and therapeutic tool for cancer management[5].

Dendrimers

From last few decades in addition to various nanocarriers a multitasking, versatile, leading candidate named 'dendrimers' appeared as rising star in the present horizon. A tree like structures having different compartment of chemical polymer and highly branched structure is known as dendrimers. Dendrimers have distinct domains in their structure named as central core, branches and terminal functional groups as shown in Figure 2. The core consists of single atom or an atomic group which contain at least one identical functionalized group. Though, branches are originated from core with repeated units and bridging amongst them with as a minimum one branch junction. Therefore, bridging amid the branching units structured a geometrical sequence and result in formation of a radially concentric layer known as "generation"[6].

The most promising characteristic of dendrimers is delivery of bioactive ranging from genes, metal, vaccines, and drugs to their desired site. Drugs and other bioactive are incorporated in it by physical or chemical interaction, because of the hollow space present in it, and act as drug delivery vehicle. Dendrimers shows great advantages in biomedical field like, encapsulates the less water dissolvable drugs in the inner cavities, size and short polydispersibility index of dendrimer, take-up by the reticuloendothelial framework can be kept away, improves solvency, retention effect and penetrability, neutral and anionic surface dendrimers have less cytotoxicity and visual irritation targeting efficacy. Furthermore, dendrimers mainly used in solublization, gene therapy, MRI contrast agent, immunoassay and dendrimer based drug delivery[7]. Various dendrimers like Triazine, polyamidoamine (PAMAM; i.e. Starburst™), poly(propylenemine) (PPI) and poly-L-lysine (PLL) and their conjugates extensively been explored as gene and drug delivery carriers for tumor imaging worldwide for improved diagnosis and cancer treatment[8].

Various FDA approved dendrimer-based products are VivaGel™ (Starpharma) as a topical microbicide for control of HIV transmission and other sexually transmitted diseases; SuperFect®, developed by Qiagen and used for gene transfection of a wide cell lines ranges. US Army Research Laboratory, developed Alert Ticket™ for detection of anthrax. Stratus® CS, for cardiac marker diagnostic and marketed by Dade Behring[9].

Carbon nanotubes

Carbon nanotubes (CNTs) are one of the most promising materials in the nanotechnology boom, and the development of CNT-based products is expected to offer enormous societal benefits. It has attracted the attention of various researchers worldwide. Their miniature size, fantastic strength, and incredible physicochemical features make them distinctively useful for various functions[10]. CNTs are hexagonally arranged network of carbon atom, 1-100 nm in length and 1nm in diameter, graphite layer rolled up into a cylinder. It is classified into two types: single walled nanotubes (SWNTs) and multi-walled nanotubes (MWNTs). The discovery of CNT is shown in Figure 3, with their respective years. The physicochemical properties associated with CNTs include an organized architecture with higher aspect ratio, surface area, mechanical strength, electrical and thermal conductivity, metallic or semi-metallic behavior, and ultra light weight. As a whole, these unique properties make them a promising material with tremendous biomedical potential[11].

Liposomes

When a dry phospholipid is hydrated and close vesicles are formed, these vesicles are called liposomes (Figure 4). Basically there are 3 types of liposomes based on the number and size of the vesicles such as: Multi lamellar vesicles (MLVs) with several vesicles separated by aqueous space, small uni-lamellar vesicles (SUVs), and large uni-lamellar vesicles (LUVs) consisting of single bilayer surrounding the entrapped space[13]. Cationic liposomes, employed as transfection agent in gene delivery by conquering the limitations linked with viral vector[14].

Polymeric nanoparticles

Due to some inherent properties like non-immunogenicity, nontoxicity, biocompatibility, biodegradability, polymeric nanoparticles used as

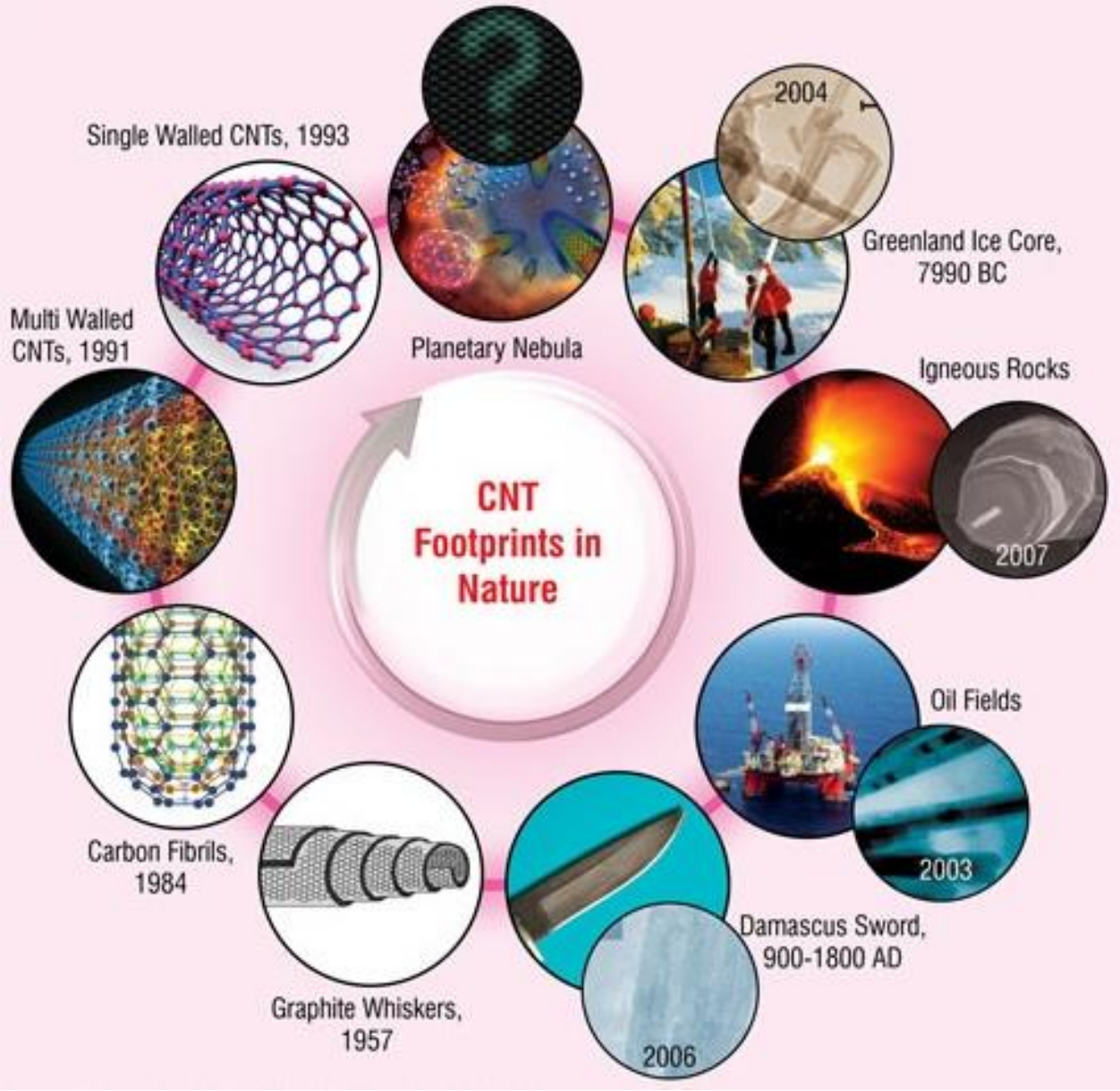

Figure 3: Development of CNT with their discovering year[12].

alternative in nano systems. The schematic representation of polymeric nanoparticles is shown in Figure 5. If the drug is confined to a cavity surrounded by a unique polymeric membrane, then the system is known as nano-capsules. If the drug is dispersed throughout the polymeric matrix, then the system is called nano-spheres. Some natural polymers are used to prepare the nanoparticles like albumin, gelatin, and alginate; but also have some disadvantages also like degradation, potential antigenicity, poor batch-to-batch reproducibility[15].

NANOPARTICLES: NANOTECHNOLOGY IN DRUG DELIVERY

Nanotechnology gained significant interest from analytical and biomedical researchers in recent years. Nanoparticles (NPs), result of their florescent properties shows their potential for application in biosensing, chemical sensing, biological and imaging monitoring[16]. Developing clinically useful formulation for the treatment of disease is the main goal of application of nano-drug delivery system. A particular amount of drug is to deliver which is therapeutically effective, and also over a long period of time with the help of clinically useful drug delivery system. All these requirements can be fulfilled by nano scale drug delivery system manufactured by nanotechnology. An approval from United States of Food and Drug Administration (USFDA), system is to be used by human being. Double emulsion method or solvent exchange method are methods which are currently used for the preparation of micro/nano systems[17].

There are various methods of preparing nano-design of the drugs like controlled precipitation, milling, high pressure homogenization, etc. These developed methods help to prepare drug nano-suspension, nanocrystals, nanoprecipitation and nanoparticles. Traditional drug delivery system has made a great impact in field of medicine. Generally, controlled release polymer system has some unique properties like increased patient

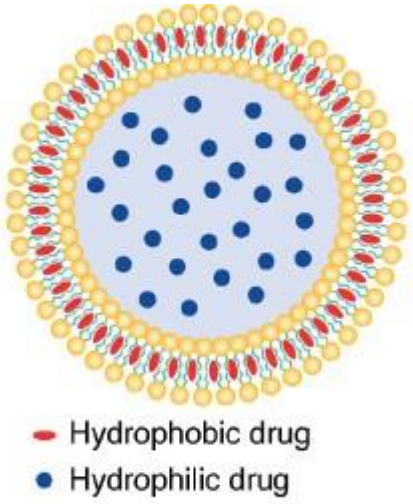

Figure 4: Schematic representation of liposomes.

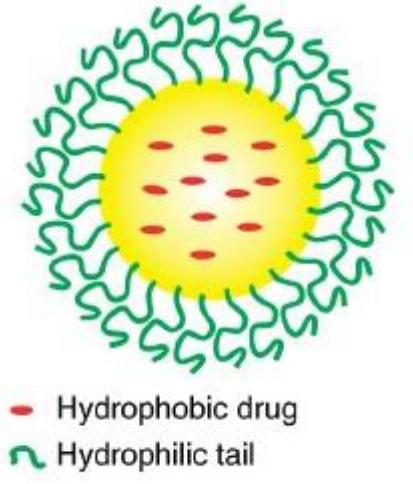

Figure 5: Schematic representation of polymeric nanoparticles.

compliance, increase in efficacy of drug, optimum dosage for longer period of time etc. For developing diagnostic modalities, highly effective and selective drug delivery system, nanoscale material can be used as drug delivery vehicle.

The main reasons of preparing nanoparticles as drug delivery system are to get pharmacologically active agent for site specific action of the drug at optimum rate and fix dose regimen, as well as controlling the particle size[19]. For e.g. solid lipid nanoparticles show various distinctive features such as low toxicity, prolonged drug release, large surface area, and superior cellular uptake in comparison to the traditional colloidal carriers also the capability to improve bioavailability and solubility of drugs[20].

PREPRATION OF NANOPARTICLES

Dispersion of performed polymers

a) Polymerization method
b) Salting-out/emulsification diffusion method
c) Solvent evaporation method
d) Production of nanoparticles by supercritical method
e) Spontaneous emulsification/solvent diffusion method
f) Nanoparticles prepared from hydrophilic method

Polymerization of monomers

There are various materials which are being used for the preparation of nanoparticles like polysaccharides, proteins and synthetic polymers. Various factors which may affect the selection of matrix material are: desired drug release profile, antigenicity of the final product, size of nanoparticles required, degree of biodegradability, biocompatibility and toxicity, surface characteristics (change and permeability) and inherent properties of the drug. Three most commonly used method for the preparation of nanoparticles is:

a) Dispersion of performed polymer
b) Polymerization of monomers
c) Ionic gelation or conservation of hydrophilic polymers

Polymerization method

It is methods of nanoparticles preparation in which monomers are polymerized in an aqueous solution to form nanoparticles. Drug may be introduced by two ways via adsorption on the nanoparticles after polymerization completed or by dissolving in the polymerization medium. The prepared nanoparticle suspension is then purified to remove the various surfactants and stabilizers used for the polymerization by re-suspending the particles in the isotonic surfactant free medium or ultracentrifugation[19].

Co-acervation or ionic gelation method

This is another preparation method of nanoparticles. First the positively charged amino group of chitosan reacts with negatively charged tri-polyphosphate to form co-acervates with the size range in nanometer. Due to electrostatic interaction between 2 aqueous phases co-acervates are formed. But, when ionic interaction at room temperature transition occurs from liquid to gel then it is called ionic gelation[21].

Dispersion of performed polymers

This is the most common method of preparation of nanoparticles. This method is used to prepare the biodegradable nanoparticles from poly (lactic acid) (PLA); poly (D, l-glycoside), PLG; poly (D, L-lactate-co-glycoside) (PLGA) and poly (cyanoacrylate) (PCA). The solvent evaporation method or spontaneous emulsification or solvent diffusion method are used for this method[19].

APPLICATIONS OF PHARMACEUTICAL NANOTOOLS

Various applications of pharmaceutical nanotechnology are given as follows:

As nanomaterials for tissue engineering

Nanotechnology provides various materials that are used for implant coatings, tissue regeneration scaffolds, structural implant materials, bone repair, tissue repair and replacement.

Nano-based drug delivery tools

These are polymeric nanoparticles, liposomes, polymeric micelles, antibody-drug conjugates and dendrimers which are classified as: functional system for delivery of bioactive, site specific targeting (intracellular, cellular, tissue), stimuli sensitive delivery system, sustained and

controlled delivery system and multifunctional system of combined delivery of therapeutics, bio-sensing and diagnostic.

Molecular diagnostics

The nanoscience of characterizing, representing, and quantifying subcellular biological in intact organism is called as molecular imaging. This process includes signal transduction, cellular metabolism, protein-protein interaction, intracellular trafficking and gene expression. It is successfully used in optical imaging, ultrasonic imaging, nuclear imaging and magnetic resonance imaging.

Drug discovery

Pharmaceutical nanotechnology has important application in the discovery of new drug. It helps to detect the biomarkers associated with specific disease or mechanism of action of drug. Nanotechnology helps to improve the drug discovery process through automation, speed and reliability of assay[22].

COMMERCIALLY AVAILABLE NANOPARTICLES

Gold nano-spheres

The particles are in narrow size distribution and available from 2 to 250 nm. Gold particles are good quality nano-spheres, used in conjugation studies of protein and antibody as well as in the production of diagnostic test[23].

Silver nano-spheres

These nanoparticles are in 1 to 100 nm size ranges. Silver nanoparticles are referred as AgNPs, widely exploited for use in biological labeling, photography, sensing, optoelectronics, photonics, and photovoltaic cells[24].

Silica nano-spheres

The silica particles are stable in organic solvents and water, and produced by new dying method. These are easy to disperse and separate as they have density of 2.0 g/cm^3. Silica particles are available as fluorescent particles and easy to functionalize. They are useful for coupling of oligopeptides, proteins, antibodies, oligonucleotides, DNA[25].

Magnetic Plain Dextran Nano-spheres

The biodegradable magnetic nanospheres are used in the magnetic field assisted radionuclide therapy. The superparamagnetic iron oxide cores are coated with hydrophilic polymers, such as dextran, chitosan, starch, polyethylene imine, ficoll and polyvinyl pyrrolidone (PVP). Their different surface properties were demonstrated via significant difference of particles electrophoretic mobility depending on the pH-value[26].

Melamine nano-spheres

The melamine nanospheres modified to achieve a high density of carboxy functional groups. These nanospheres with carboxy group terminated surfaces are utilised for different conjugation reactions in biomedical research, microarray technology, biotechnology in development of different assays, etc [27].

CONCLUSION AND FUTURE PROSPECTIVE

After the entry of nanotechnology in nanoscience world, researcher gained better realization of the different strategies. Although in future, it is highly complicated to predict the nano-medicine significance in our life having so many uncontrollable and uncertainties factors. Therefore, nano-medicine has the huge ability to multiply the medicine power and also to bring revolution in our everyday lives. Having some important properties like superior strength, high precision, and improved physical and chemical properties at the nanoscale, nanostructures and nanoparticles can significantly improve the efficacy of novel drug delivery for different kind of lethal diseases including cancer and AIDS.

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