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Nano Technology: A Review

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ABSTRACT

The recent research on bio-systems at the nano-scale and the nanotechnology has created one of the most dynamic science and technology domains at the confluence of physical sciences, molecular engineering, biology, biotechnology and medicine. This domain includes better understanding of living and thinking systems, revolutionary biotechnology processes, synthesis of new drugs and their targeted delivery, regenerative medicine, neuromorphic engineering and developing a sustainable environment. Nano bio-systems research is a priority in many countries and its relevance within nanotechnology is expected to increase in the future. The reduction of drug particles into the sub-micron range leads to a significant increase in the dissolution rate and therefore enhances bioavailability. There has been a considerable research interest in the area of developing drug delivery using nanoparticles (NP's) as carriers for small and large molecules. Targeting delivery of drugs to the diseased lesions is one of the most important aspects of drug delivery system. They have been used *in-vivo* to protect the drug entity in the systemic circulation, restrict access of the drug to the chosen sites and to deliver the drug at a controlled and sustained rate to this site of action. Various polymers have been used in the formulation of nanoparticles for drug delivery research to increase therapeutic benefit, while minimizing the side-effects. This review article presents the most outstanding contributions in the field of nanotechnology as drug delivery system. Pharmaceutical nanotechnology based systems, methods of preparation, applications, advantages and disadvantages.

Key words: *Nanotechnology, Nanoparticles, Nano-systems, Nanodevices, Nanotubes.*

INTRODUCTION

Over the past decades, there has been considerable research interest in the area of developing nano technology by using nano particles as carriers for small and large molecules. Various polymers have been used in the formulation of nano particles. This review presents the most outstanding contributions in the field of nanotechnology. The word 'Nano' is derived from Latin word, which means dwarf. Nano size refers to one thousand millionth of a particular unit thus nanometer is one thousand millionth of a meter (i.e. $1n=10^{9}m$).The term nanotechnology has been most commonly used in the fields of science like electronic, physics and engineering since many decades. However, bio medical and pharmaceutical fields remain yet to be explored. Nanotechnology is a multi disciplinary field, convergence of basic sciences and applied disciplines like biophysics, molecular biology, and bio engineering. Size reduction is a fundamental unit operation having important application in pharmacy. Major advantages of nano sizing include 1. Increase surface 2.Enhanced solubility 3. Increase rate of dissolution and oral bio availability 4.Rapid onset of action 5. Less amount of dose required in the field of pharmacy. For applications to medicine and physiology these materials and devices can be designed to interact with a high degree of functional specificity, thus allowing a degree of interaction between technology and biological systems not previously attainable. It should be appreciated that nanotechnology is not in itself a single emerging scientific discipline but rather a meeting of traditional sciences such as chemistry, physics material science and biology to bring together the required collective expertise needed to develop these noval technologies.

Addressing the associated opportunities, the revised also suggests how to manage far-reaching developments in these areas. As early as 1959, Richchard Feynman proposed building devices with each atom precisely placed. In 1986, Eric Drexler published an influential book, engines of creation, in which he described some of the benefits and risks of such a capability. If molecules and devices can be manufactured by joining individual atoms under computer control, it will be possible to build structures out of diamond,100times as strong as steel, to build computers smaller than a bacterium, and to build assembler and mini factories of various sizes, capable of making complex products and even of duplicating themselves. Drexler's subsequent book, nano-systems, substantiated these remarkable clams, and added still more. A self contained tabletop factory could produce its duplicate in one hour. Devices with moving parts could be incredibly efficient. Molecular manufacturing operations could be carried out with failure rate less than one in a quadrillion (Dinauer N et al., 2005 and Widder K et al., 1979).

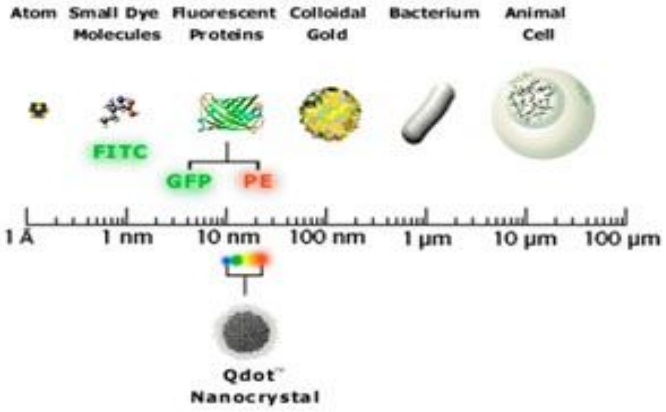

Figure 1: Representing the nano-particles with their approximate sizes

It seems clear that if advanced nanotechnology is ever developed, its products will be incredibly powerful. As soon as molecular manufacturing was proposed, risks associated with it began to be identified. Engines of creation described one hazard now considered unlikely, but still possible grey goo. A small nano-machine capable of replication could in theory copy itself too many times. If it were capable of surviving outdoors, and of using biomass as raw material it could severely damage the environment.

Four Generations

Mihail (Mike) Roco of the U.S. National Nanotechnology Initiative has described four generations of nanotechnology development (see chart below). The current era, as Roco depicts it, is that of passive nanostructures, materials designed to perform one task. The second phase, which we are just entering, introduces active nanostructures for multitasking; for example, actuators, drug delivery devices, and sensors. The third generation is expected to begin emerging around 2010 and will feature nano-systems with thousands of interacting components. A few years after that, the first integrated nano-systems, functioning (according to Roco) much like a mammalian cell with hierarchical systems within systems, are expected to be developed.

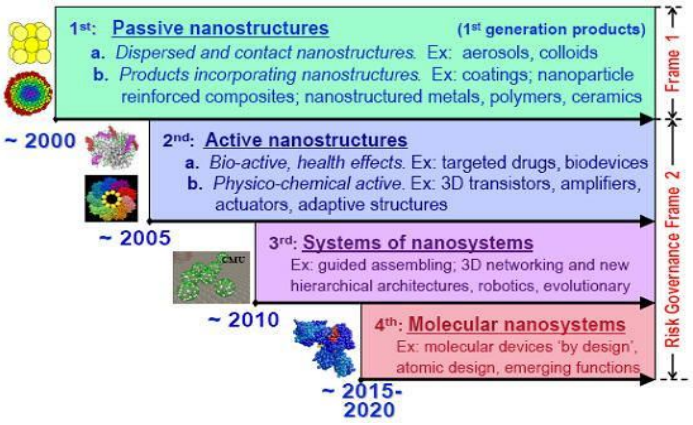

Figure 2: Representing the four generations of nanoparticles.

Some experts may still insist that nanotechnology can refer to measurement or visualization at the scale of 1-100 nanometers, but a consensus seems to be forming around the idea (put forward by the NNI's Mike Roco) that control and restructuring of matter at the nano-scale is a necessary element. CRN's definition is a bit more precise than that, but as work progresses through the four generations of nanotechnology leading up to molecular nano-systems, which will include molecular manufacturing, we think it will become increasingly obvious that "engineering of functional systems at the molecular scale" is what nanotech is really all about.

PHARMACEUTICAL NANOTECHNOLOGY BASED SYSTEMS

Pharmaceutical nanotechnology consisting of two basic types, which are nano-materials and nanodevices, which play a key role in pharmaceutical nanotechnology and other fields.

Nanomaterials

These are made from biomaterials; these are used in orthopedic or dental implants or as scaffolds for tissue engineered products. Their surface can be modified or coatings can be done which enhances biocompatibility with the living cells. These are further classified into two types nanocrystalline and nanostructure materials.

Nanocrystalline

These are readily manufactured and can substitute the less performing bulk material. These materials are directly used in drug encapsulation, bone replacement, protheces and implants.

Nanostructured materials

These are processed forms of nanomaterials with special shapes and functions. These include quantum dots, dendrimers, fullerenes and carbon nanotubes.

Nanodevices

These are the small devices in the nano scale. These include nano and micro electromechanical systems (NEMS/MEMS), micro fluidics and micro assays. These also include biosensors and detectors, which are used in diagnosis.

TYPES OF PHARMACEUTICAL NANOSYSTEMS:-

Carbon nanotubes

These are hexagonal networks of carbon atoms. Length and diameter of these tubes are 1nm and 1-100nm in length. Nanotubes are of two type's single walled nanotubes (SWNTS) and multi walled nanotubes (MWNTS). These are small macro molecules have unique size, shape and remarkable physical properties (Sinha N et al., 2005).

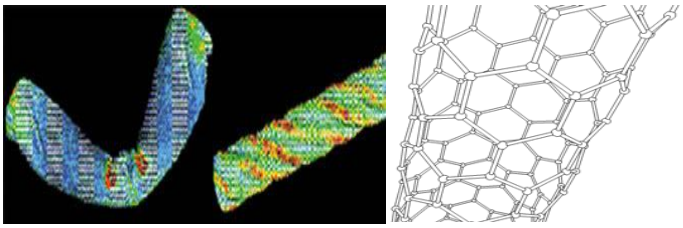

Figure 3: Carbon nanotubes

Quantum Dots

These are semi conducting materials consisting of a semi conductor core coated by a shell to improve optical properties. Their properties originate from their physical size which ranges from 10-100A^0 in radius. These have a large impact on imaging, in-vitro and in-vivo detection and analysis of biomolecules, immunoassay, and DNA hybridization and in non-viral vectors for gene therapy. It has main function in labeling of cells and therapeutic tools for cancer treatment (Bailey et al., 2004).

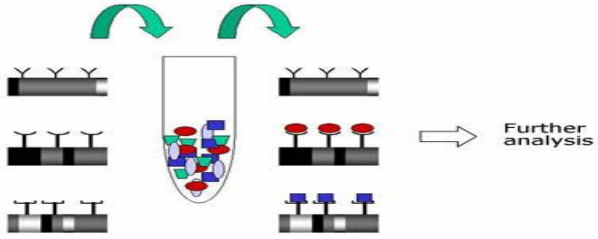

Figure 4: quantum dots.

Dendrimers

These are hyper branched, tree-like structures and have compartmentalized chemical polymer. It contains three different regions core, branches and surface. The core forms the central part and the branches radiates from it forming an internal cavity and a sphere of groups. The branches can be altered or modified according to requirements. The dendrimers can be made more biocompatible compounds with low cytotoxicity and high biopermeability according to the requirements. These can deliver bioactive s like drug, vaccines, materials and genes to desired sites. The space between the core and branches accommodates drugs or bioactive products (Kreuter and Speiser., 1976).

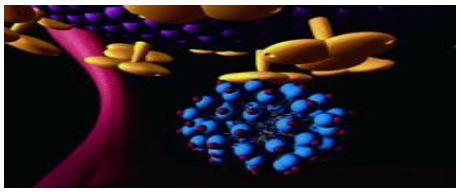

Figure 5: Dendrimers.

Polymeric nanoparticles

These are colloidal carrier, 10nm-1µm in size consisting of synthetic or natural polymers. These nanoparticles provide alternative to above mentioned nanosystems due to inherent properties like biocompatibility, non-immunogenicity, non-toxicity and biodegradability. Polymeric nanoparticles are classified and comprised of nanocapsules and nanosphere. Nanocapsules are systems in which drug is confined to a cavity surrounded by unique polymeric membrane, where as nanospheres are systems in which the drug is dispersed throughout the polymer matrix. Natural polymers used are gelatin, albumin and alginate in the preparation of nanoparticles synthetic polymers used for nanoparticles preparation of nanoparticles synthetic polymers used for nanoparticles of preparation may be in the form of preformed polymer. e.g.:- polyesters like polycarpolactone (Maincent P et al., 1992).

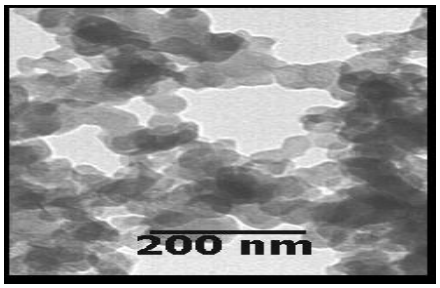

Figure 6: Nanoparticles.

Metallic nanoparticles

Metallic nanoparticles are more favor in the good delivery as carrier for drug and biosensor. Nanoparticles of various metals have been made yet silver and gold nanoparticles are of prime importance for biomedical use, a large number of ligands have been linked to nanoparticles such as sugar, peptides, proteins and DNA. These nanoparticles have surface Functionalization and are very easy to decorate ligands unto the surface. Due to this Functionalization ability, these are used for active delivery of bioactive, drug discovery, bioassays, detection, imaging and many more other applications.

Liposomes

These are the closed vesicles forms when dry phospholipids are hydrated. These are of 3 types based on size and number of bi-layers.

a) Multilamellar vesicles

These consists of several lipid bi-layers separated from one another by aqueous spaces. These are heterogeneous in size, ranging from few hundreds to thousands of nm in diameter.

b) Small unilamellar vesicles (SUV'S) and large unilamellar vesicles (LUV'S)

These consist of a single bi-layer surrounding the entrapped aqueous space. SUV'S are less than 100nm and LUV'S are more than 100nm. Drug is either entrapped in the aqueous space or intercalated into lipid bi-layer of liposome's, depending on physicochemical characteristics of the drug. Liposome's can be prepared with great diversity in structure, composition, size, flexibility and a variety of surface modification approaches for both active and passive delivery of bioactive. They are used in cancer therapy, carrier for antigens, pulmonary delivery, leishmaniasis, ophthalmic drug delivery (Jain S et al., 2004).

Polymeric micelles

Amphiphillic block copolymers assemble into nanoscopic supra molecular core shell structure known as 'polymeric micelles'. These are usually of less than 100nm and their hydrophilic surface protects their nonspecific uptake by reticulo-endothelial system. Micelles formed in solutions as aggregates in which the component molecules are arranged in a spherical structure with hydrophobic core shield from water by a mantle of hydrophilic groups. These are used for systemic delivery of water insoluble drugs. And drugs are trapped physically within the hydrophobic cores or can be linked covalently to component molecules of the micelles. These have high loading capacity, stability in physiological conditions, slower rate of dissolution, high accumulation of drug at target site and possibility of Functionalization of end group for conjugation of targeting ligands (Ferrari, M., 2005).

Polymer drug conjugate

The conjugation of low molecular weight drugs with polymer causes drastic change in pharmacokinetic disposition of drug in whole body and at cellular level. So, these are designed to increase the overall molecular weight, which facilitates their retention in cancer cells through EPR effect using passive delivery approach (Ferrari M., 2005).

Polyplexes or lipopolyplexes

These form spontaneously between nucleic acids and polycations or cationic conjugated to targeting ligands or hydrophilic polymers and are used in transfection protocols. The shape, size distribution and transfection capability of these complexes depends on their composition and charge ratio of nucleic acid to that of cationic lipid or polymer.

E.g.:- poly-l-lysine, linear and branched poly ethylene amine, poly amidoamine, poly-amino esters and cationic cyclodextrin (Ferrari M., 2005).

PREPARATION OF NANO PARTICLES

The appropriate method involved in the preparation of nano particles is selected depending mainly on two aspects. They are

1) Physicochemical characteristics of the polymer.
2) Drug to be loaded.

The preparation techniques determine the inner structure, In-vitro release profile and biological fate of polymeric delivery system. 2 types of systems with different inner structures are :-

1) **Matrix type:-** Entanglement of oligomer or polymer units. Nano particles and nano spheres.
2) **Reservoir type:-** Oily core and embryonic polymer shell. Nano capsules (J. Kreuter., 1978 and Gunter Schmid et al., 2004).

The different methods are

1) Ampiphillic macromolecule cross linking.
   a) Heat cross linking.
   b) Chemical cross linking.
2) Polymerization based methods.
   a) Polymerization of monomers in-situ.
   b) Emulsion (micellar) polymerization.
   c) Dispersion polymerization.
   d) Interfacial condensation polymerization.
   e) Interfacial complexation.
3) Polymer precipitation methods.
   a) Solvent extraction or evaporation.
   b) Solvent displacement (nano precipitation).
   c) Salting out.

1. Amphiphillic macromolecule cross linking:

The materials used are Amphiphillic macro molecules, proteins and polysaccharides. These should have affinity to both aqueous and lipid solubility. It occurs in 2 steps:-

1) Aggregation of amphiphillic.
2) Stabilization by heat denaturation or chemical cross linking.

The aggregation takes place in o/w or w/o emulsion type. These sub-divide the amphiphiles prior to aggregative stabilization. The aggregation may also takes place in-aqueous amphiphillic solution through removal, extraction, diffusion of solvent. The amphiphiles are aggregated as tiny particles and sub sequently rigidised via chemical cross linking (Gupta P.k et al., 1987 and Wickline S.A et al., 2002).

2. Polymerization based methods.

a. Polymerization of monomers in-situ.

The polymers used are polymethacrylate, polyacrylamide, polybutyl cyano acrylate, N-N' methylene- bis-acrylamide etc. The two different approaches generally adopted for the precipitation of nanospheres using in-situ technique are:-

1. The monomer to be polymerized is emulsified in a non-solvent phase (emulsion polymerization).
2. The monomer is dissolved in a solvent that is non-solvent for the resulting polymer (dispersion polymerization).

In emulsion polymerization, the monomer is dissolved in internal phase. In dispersion polymerization, it is taken in the dispersed phase. In both the cases the polymer is insoluble, thus results in a ordered suspension of nanospheres (Kreuter J., 1991 and Labhaasetwar V et al., 1995).

b. Emulsion polymerization:-

The process can be conventional or inverse, depending upon the nature of the continuous phase in the emulsion. In the conventional case, the continuous phase is aqueous (o/w emulsion), in the inverse case it is organic (w/o emulsion). The two different methods proposed for the emulsion polymerization process are (Jain NK., 2001, De Jaeghere F et al., 1999, Ibrahim H et al., 1992 and Kreuter J., 1994).

1. Micellar nucleation and polymerization.
2. Homogeneous nucleation and polymerization.

Micellar nucleation and polymerization

The monomer is emulsified in the non-solvent phase with the help of surfactant molecules. This leads to the formation of monomers – swollen micelles and stabilized monomer droplets. Swollen micelles exhibit size in nanometric range and this have more surface area than monomer droplets. The polymerization occurs in the presence of a chemical or physical initiator. The energy provided by the initiator creates free reactive monomers in the continuous phase, which collide with surrounding un-reactive monomers and initiative polymerization chain reaction. The monomer molecules reach the micelles by diffusion from the monomer droplets through continuous phase, allowing polymerization to progress with in the micelles. In this case, monomer droplets act as monomer reservoirs. In this the monomers are slightly soluble in the continuous phase (De Jaeghere F et al., 1999).

Homogeneous nucleation and polymerization

This process applies largely in case of where monomer is sufficiently soluble in the continuous outer phase. The nucleation and polymerization occurs directly in this phase, leading to the formation of primary chains called oligomers. Both micelles and droplets act as monomer reservoirs throughout the polymer chain length.When the oligomers have reached a certain length, they precipitate and form primary particles, which are stabilized by the surfactant molecules provided by the micelles and the droplets. Depending on bulk conditions and system stability, the end product nanoshperes are formed either by additional monomer input into the primary particles or by fusion of the primary particle (Gupta P.k et al., 1987 and Kreuter J., 1983).

C. Dispersion polymerization:-

The term emulsion polymerization is used when the monomer is emulsified in an immiscible (non-solvent) phase by means of surfactants. But in this monomer is dissolved in an aqueous medium, which acts as a precipitant for subsequently formed polymer. In in-situ controlled polymerization the drug may be added to monomeric phase or may be added to the formed polymeric nanoparticles dispersion for adsorptive loading. The monomer is introduced into the dispersion medium of an emulsion or an inverse emulsion into non-solvent based polymeric solution. The polymerization is initiated by adding a catalyst and proceeds with nucleation phase followed by a growth phase (propagation).
But in dispersion polymerization, the nucleation is directly induced in the aqueous monomer solution and the presence of stabilizer or surfactants is not absolutely necessary for the formation of stable nano spheres. This is used to prepare bio-degradable polyacrylamide and poly methyl- methacrylate (PMMA) nano particles.

D. Interfacial polymerization

In this the pre formed polymer phase is transformed to an embryonic sheath. The polymer that becomes core and drug molecule to be loaded are dissolved in a volatile solvent. The solution is then poured in to a non solvent for both polymer and core phase. The polymer phase is separated as a co-acervate phase at o/w inter phase. The resultant mixture turns milky due to formation of nano capsules. This is used for encapsulation of proteins, enzymes, anti bodies and cells were employed (Bertling W. M et al., 1989, Gupta P.k et al., 1987, Kreuter J., 1983, Kubik, T et al., 2005 and Wood R. W et al., 1986).

e. Interfacial complexation

This is based on micro-encapsulation. In this aqueous polyelectrolyte is dissolved in reverse micelles in an apolar bulk phase with the help of an appropriate surface-active agent. A competing polyelectrolyte is added to the bulk, which allows a layer of insoluble polyelectrolyte complex to co-acervate at the interface (Langer K., 1996).

3. Polymer precipitation method

In this, the hydrophobic polymer and or a hydrophobic drug is dissolved in a particular organic solvent followed by dispersion in a continuous aqueous phase, the polymer is insoluble. The external phase also contains the stabilizer. Due to the solvent miscibility techniques they are also known as solvent miscibility techniques they are also known as solvent extraction or evaporation method. The polymer precipitation occurs due to solvent extraction or evaporation. This can be done by.

1) Increasing the solubility of organic solvent in the external medium by adding an alcohol.
2) By incorporating additional amount of water into the ultra-emulsion (extract or diffuse solvent).
3) By evaporation of the organic solvent at room temperature or at accelerated temperature or by using vacuum.
4) Using an organic solvent that is completely soluble in the continuous aqueous phase (acetone) – nanoparticles (Ferrari, M., 2005 and Gupta P.k et al., 1987).

a. Solvent extraction method

This method involves the formation of a conventional o/w emulsion between a partially water miscible solvent containing the stabilizer. The subsequent removal of solvent (solvent evaporation method) or the addition of water to the system so as to affect diffusion of the solvent to the external phase (emulsification diffusion method) is two variance of the solvent extraction method. Recently emulsification-diffusion method has been used on a regular basis for the solvent extraction purpose. The solvent used for polymer is often poorly miscible with dispersion phase and thus diffuses and evaporates out slowly on continual stirring of the system. The dispersion medium miscible polymer solvent instantaneously diffuses into the aqueous phase and as a result polymer consolidates and precipitates as tiny nanospheres (Nahar M et al., 2006).

Double emulsion solvent evaporation method

The emulsion solvent evaporation technique has been further modified and a double emulsion multiple emulsion of water in oil in water type has been used. Following evaporation of the organic solvents nanoparticles are formed which are then recovered by ultracentrifugation, washed repetitively with buffer and lyophilized.

PLGA nanoparticles were prepared loaded with bovine serum albumin using double emulsion solvent evaporation method Due to the high solubility of protein in water, the double emulsion technique has been chosen as one of the appropriate methods (Labhaasetwar V et al., 1995 and Senthilkumar M et al., 2007).

b. Solvent displacement or nanoprecipitation

This is based on the interfacial disposition of a polymer following displacement of a semi-polar solvent miscible with water from a lipophilic solution. This method involves the use of an organic phase, which is completely soluble in the external aqueous phase, inducing immediate polymer precipitation because of the complete miscibility of both the phases. Separation and extraction of the solvent is not required for polymer precipitation. After nanoparticles preparation, the solvent is eliminated and the free-flowing nanoparticles can be obtained under reduced pressure. This method is useful for slightly soluble drugs in water. If the drug is highly hydrophilic, it diffuses out into the external aqueous phase, if the drug is highly hydrophobic, it may precipitate in the aqueous phase as nanocrystal, which further grow on storage (Fessi H et al., 1989 and Lukowski G et al., 1992).

In the case of hydrophilic polymer, an aqueous solution of polymer is dispersed or emulsified in oil phase. The precipitation of polymer proceeds on addition of acetone. By this technique ovalbumin loaded dextran nanospheres of approximately 1micrometer size were prepared. The nanospheres were fairly stable and uniform in size. However, the loading efficiency of lipophilic drugs, such as indomethacin, metripranol, betaxolol in nanoparticles of PLA, PLGA and PECL has been increased using a modified solvent displacement method. In this, the drug is dissolved in a small volume of appropriate oil and the n diluted in the polar organic solvent (acetone/ethanol/methanol). When the organic solution is dispersed in the aqueous, the polymer precipitates around the nanodroplets, forming a reservoir system (Molpeceres J et al., 1996 and Quintanar-Guerrero D et al., 1996).

C. Salting out

It is one of the most commonly adopted methods used to prepare nanoparticles. The method involves the incorporation of a saturated aqueous solution of polyvinyl alcohol (PVA) into an acetone solution of the polymer under magnetic stirring to form an o/w emulsion. The process differs from nanoprecipitation technique as in the latter the polymeric solution (acetone) is completely miscible with the external aqueous medium. But in the salting out technique, the miscibility of both the phases is prevented by the saturation of the external aqueous phase with PVA. The precipitation of the polymer occurs when a sufficient amount of water is added to external phase to allow complete diffusion of the acetone from internal phase into the aqueous phase. This technique is suitable for drugs and polymers that are soluble in polar solvents, such as acetone or ethanol (Allemann E et al., 1992 and Bindschaedler C et al., 1990).

APPLICATIONS OF PHARMACEUTICAL NANOTECHNOLOGY

Miniaturization is beneficial in pharmaceutical technology. Since It has increased complexity and It also imparts large number of benefits in drug delivery and diagnostic. The various pharmaceutical and biochemical areas where nanosystems are used are:-

I) Nano materials for tissue engineering

The nanomaterials are used for tissue repair and replacement, Implant coatings, Tissue regeneration, Structural implant materials, Bone repair, Bio-resoursable materials, Implantable devices (sensory aids, retina implants), Surgical aids, Operating tools and also in Smart instruments.

II) Drug carrier system

Nanotech enabled drug delivery system with optimized physical, chemical and biological properties, which can serve as effective delivery tools for currently available bioactives. Some nano-based carrier systems are polymeric nanoparticles, liposomes, dendrimer, polymeric micelles, polymer-drug conjugates, antibody-drug conjugates (Jain NK., 2001 and Song CX et al., 1995). These can be classified as

1. Sustained and controlled delivery system.
2. Stimuli sensitive delivery system.
3. Functional system for delivery of bioactives.
4. Multi-functional system for combined delivery of therapeutics, biosensing and diagnostic.
5. Site-specific targeting (intracellular, cellular, tissue).

The Carrier Systems are widely Used in the given Regions:-

1. Cancer treatment

Nanotech has a revolutionary impact on cancer diagnosis and therapy. Available therapies for cancer are surgery, chemotherapy, immunotherapy and radio therapy. Nanotech is used to improve these conventional therapies by virtue of its nanotools.

Carbon nanotubes:- D.N.A mutation detection, disease protein biomarker detection.

Dendrimers:- controlled release drug delivery, image contrast agents.

Targeting and localized delivery are the key challenges in cancer therapy. The approaches to treat cancer are basically attributed to the pathophisiology of diseased sites like leaky vasculature of the cancer tissues. The nanocarriers can alter the biodistribution and pharmacokinetic parameters of the anticancer drug. The nanotool identifies biomarkers or detects mutaton in cancer cell and treats the abnormal cells by,

1. Thermotherapy, photo thermal therapy using silica nanocells, carbon nanotubes. Magnetic field induced thermotherapy using magnetic nanoparticles. Photodynamic therapy- quantum dots.

2. Chemo therapy- nanostructural polymer nanoparticles, dendrimers and nanoshells.

3. Radio therapy- carbon nanotubes, dendrimers (Thomas Webster et al., 2007 and Ferrari, M., 2005).

2. Implantable delivery systems

Nanoparticles can act as the delivery systems by virtue of its size, controlled and approximately zero order kinetics, otherwise they may cause toxicity when compared to I.V. Carriers are liposome, ethosome and transferosome. These help in minimizing peak plasma levels and reduce risk of adverse reactions, allow for more predictable and extended duration of action, reduce the frequency of re-dosing and improve patient acceptance and compliance (Jain NK., 2002).

3. Site specific drug delivery

Liposomes, polymeric micelles, dendrimers, ironoxide, proteins using manipulation in passive and active uptake of drug.The tumor targeting of drugs is done by passive delivery using enhanced permeation and retention (EPR) effect of nanoparticles taking the advantages of nanoparicles taking the advantages of leaky vasculature of tumor. Surface modification using site-specific ligands via covalent binding or adsorption with carrier system enhanced their site specificity. In chemotherapy of tuberculosis with active delivery to lung cells is reported to have improved drug bioavailability, reduction in dose frequency and overcoming the non-adherence problem encountered (Jain NK., 2001).

4. Gene therapy:-

The normal gene is inserted in place of an abnormal disease causing gene using a carrier molecule. Nanotech enabled effective and promising tool in systemic gene treatment. Chitosan, gelatin and poly-1-lysine and modified silica nanoparicles are used in gene therapy. These have increased transfection efficiency and decreased cytotoxicity. Nano technology provides ideal vectors in gene delivery (Jain, K.K., 2005).

III) Molecular diagnostics:- (molecular imaging)

It is representing, characterizing and quantifying sub cellular biological processes include gene expression, protein-protein interaction, signal transduction, cellular metabolism. They are used in magnetic resonance imaging, optical imaging, ultrasonic imaging and nuclear imaging. Other applications are specific labeling of cells and tissues, useful for long-term imaging, multicolor multiplexing, dynamic imaging of sub cellular structures and fluorescence resonance energy transfer (FRET) and magnetic resonance imaging (MRI). MRI agents are replaced by nanomaterials like dendrimer, quantum dots, carbon nanotubes and magnetic nanoparticles. They are very efficient, stable, intense, clearer image due to high intensity, photostability, resolution, resistance (Gupta P.k et al., 1987).Quantum dots, iron oxide nanocrystal and metallic nanoparticles.

IV) Biosensor and bio-labels

These tools are employed for determination of various pathological proteins and physiological-biochemical indicator associated with disease or disrupted metabolic conditions of body. Biosensor is a measurement system that consists of a probe with a sensitive biological recognition element or bio-receptor, a physiochemical detector component and a transducer to amplify and transducer these signals into measurable form. A nanobiosensor or nanosensor is a biosensor that has dimensions on the nanometer size scale. Biosensors are used in target identification, validation, assay development, ADME, toxicity determination (Khopde AJ et al., 2001).

V) Drug discovery

Nanotech helps in identification and validation of target by identifying the protein present on the surface or target surface. Nanotech will enhance drug delivery process, through miniaturization, automation, aped and reliability of assays. Single walled nanotubes are successfully used to identify surface protein of pathogen. Quantum dots- track individual glycine receptors and to analyze their dynamics in the neuronal membrane of living cells, for periods ranging from milliseconds to minutes. Gold nano particles, nanobodies (smallest, available, intact antigen-antibody fragments) produced by ablynx are some commonly used nanomaterials in diagnosis[4]. The pharmaceutical nanotechnology is used in the biodetection of pathogens in humans, separation and purification of molecules and cells and detoxifying agents. Future nanomachine (respirocyte) is the nano-on-board mini computer,that can be used for detection of disease causing marker or antigen, to view the diseased site and to deliver the therapeutic agent at the site.

The main advantages of nano-technology in the pharmacy field are improved bioavailability, reduced toxicity, sustained and

controlled release, targeted delivery, do not occlude in blood capillaries, passes easily through most of the physiological biobarriers, provides effective delivery to brain and intracellular compartment, protects fragile drugs or proteins from harsh biological environment, faster, safer and more accurate disease diagnosis, more accurate less invasive surgery, inexpensive and the large-scale production is feasible.

Some of the main dis advantages of nanotechnology in the pharmaceutical field are high aggregation in biological system due to high surface energy, poor solubility and poor incompatibility in case of carbon nanotubes, quickly scavenged by RES system of body resulting in low biological half life, poor target and site specificity, high immunogenicity of foreignness, undefined and unpredictable safety issue and acute and chronic toxicity.

CONCLUSION

Pharmaceutical nanotechnology has emerged as a discipline having enormous potential as a carrier for spatial and temporal delivery of bioactives and diagnostics and provides smart materials for tissue engineering. It offers new tools, opportunities and scope , which are expected tohave a great impact on many areas in disease, diagnostics, prognostic and treatment of diseases through its nano-engineered tools.

Pharmaceutical nanotechnology provides opportunities to improve materials, medical devices and help to develop new technologies where existing and more conventional technologies may be reaching their limits. It raises new hope to industries by providing new patentive technologies in view of revenue loss caused due to off-patent drugs.

Pharmaceutical nanotechnology has a profound influence on disease prevention efforts because it offers innovative tools for understanding the cell as well as the difference between normal and abnormal cells. It could insights into molecular basis of disease.

Some of the advantages are:-

1. Identifying, defining and characterization of model nanomaterials.
2. Developing toxicity testing protocol.
3. Detecting and monitoring exposure level.
4. Assessing the impact of environment.
5. Developing the biocompatible hybrid system.

But still we lack the sufficient data and guidelines regarding safe use of these nanotechnology based devices and materials. There are several confounding unresolved issues, which warrant the application in its full boom.

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