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NANOPARTICLES - THE FUTURE OF DRUG DELIVERY

Arjun Sai Sreekar Aeila*, Tirandi.Manohara Sai, A.Rohit kumar

GITAM Institute of Pharmacy, GITAM (Deemed To Be University) Rushikonda, Visakhapatnam, 530045, Andhra Pradesh, India.

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ABSTRACT

There has been considerable interest in drug delivery research over the past few decades using Particulate delivery systems as carriers of small and large molecules. Particulate structures such as nanoparticles have been used as a physical tool to modify and improve the pharmacokinetic and pharmacodynamic properties of different types of drug molecules. They were used *in-vivo* to Protect the drug entity in the systemic circulation, restrict the drug's access to the selected locations, and deliver the drug to the site of action at a controlled and sustained rate. Different carriers have been used to increase therapeutic benefit in the formulation of nanoparticles for drug delivery research, while minimizing side effects. Here we review different aspects of the formulation of nanoparticles, their characterization, their effects and their applications in the delivery of drug molecules.

Corresponding author
Arjun Sai Sreekar Aeila
GITAM Institute of Pharmacy,
GITAM (Deemed To Be University) Rushikonda,
Visakhapatnam,
530045, Andhra Pradesh, India.
arjun.aeila1@gmail.com

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INTRODUCTION: [1,2]

Nanotechnology is a science field that involves both synthesis and the production of different nanomaterials. Nanoparticles are classified as objects of 1-100 nm size that may vary from the bulk material because of their volume. Copper, zinc, titanium, magnesium, gold, alginate and silver are used to produce various metallic nanomaterials. For purposes from various branches of industrial production such as solar and oxide fuel batteries for energy storage, nanoparticles are used for large integration into various everyday materials such as cosmetics or clothes, medical treatment. Nanoparticles are an important component in the manufacture of a nanostructure and are much smaller than the universe of everyday objects defined in Newton's laws of motion, but larger than an atom or a simple molecule controlled by quantum mechanics. Nanoparticles are organic solid organic particles (from Greek nanos–dwarf). The dimensions of nanoparticles are not specified in a uniform manner. They differ according to the field they are used in.

Nanoparticles: [3,4,5]

Since ancient times, nanoparticles have been used in pottery and medicine. There are various ideal methods for synthesizing nanoparticles. The following things are neutral pH, low cost and environmentally friendly fashion for synthesizing nanoparticles. The production of nanoparticles by plants is more stable and the synthesis rate is higher than in other species. Mainly these methods for synthesizing nanoparticles have been developed in different methods in the coming days due to cost-effectiveness and need little or no maintenance. Nanoparticles are generally divided into two classes of organic nanoparticles and inorganic nanoparticles. Organic nanoparticles are carbon nanoparticles and magnetic nanoparticles are inorganic nanoparticles.

Various types of nanoparticles

1. Polymeric nanoparticles.
2. Nanocrystal.
3. Inorganic nanoparticles.
4. Solid lipid nanoparticles.
5. Liposomes.
6. Nanotube.
7. Dendrimers.

Polymeric nanoparticles:

It is also a type of nanoparticle of polymeric nanoparticles. There has been a significant growth in the field of research in the recent year of polymer nanoparticles. The dispersion of preformed polymers and the polymerization of monomers are two strong strategies that are mainly involved in preparation.10 1000 nm is the size range of solid particles involved.

Nanocrystal:

A nanocrystal is a form based on material particles with at least one dimension of less than 100 nanometers and consisting mainly of atoms in a single or poly-crystalline arrangement. Nanocrystals are aggregates of about hundreds or thousands of molecules that combine in a crystalline form, consisting of a pure substance with a thin coating consisting of a surfactant or a surfactant mixture.

Inorganic nanoparticles:

The function of Inorganic nanoparticles has been established in the field of Modern Material Science based on their unique physical properties and particularly in biotechnology. Based on these two factors of inorganic nanoparticles, they have certain physical properties that include optical, magnetic, electrical, and catalytic properties mainly based on volume. For the preparation of these fascinating nanoparticles, such as iron oxides, gold, silver, silica, quantum dots, etc. Due to their size, novel physical properties mainly apply to the dimension of the nanometer scale.

Solid lipid nanoparticles:

Solid lipid nanoparticles played a dominant role in regulating drug delivery in the 1990s. As a colloidal carrier system, there are also alternative carrier systems for emulsions, liposomes, and polymeric nanoparticles.

Liposomes:

Liposomes are one of the methods focused on nanoparticles of different types.Liposome structure consists of one or more bilayers of phospholipids and are sphere-shaped vesicles to hold fascinating compounds. Today liposomes have been useful in various scientific disciplines in the field of reagents and tools. We have found their own way in the market since many features used in liposome. Numerous molecules serve as a carrier in the cosmetic and pharmaceutical industries, and liposomes are used in encapsulation in the food and farming industries to create a delivery system that can capture volatile compounds.

Nanotube:

A nanotube is a structure-like tube on a nanometer scale. Nanotubes belong to the structural fullerene family. Their name derives from their thin, hollow structure with walls created by carbon sheets called graphene that are one-atom-thick. Such sheets are rolled at different and distinct angles ("chiral") and the combination of rolling angle and radius defines the properties of the nanotube; for example, whether the shell is a metal or a semiconductor.Nanotubes are graded as single-walled and multi-walled nanotubes (SWNTs).

Dendrimers:

Dendrimers are derived from two Greek words: tree meaning Dendron and part meaning Meros. Dendrimers structure has a well-defined length, shape and molecular weight, and Dendrimers are also hyper-branched, globular, monodisperse, synthetic polymers with three-dimensional nanoscales. There are well-defined properties of Dendrites in both molecular chemistry and polymer chemistry.

Strategies used to synthesize nanoparticles: [6,7]

Nanoparticles have traditionally only been produced by physical and chemical methods.

The ion sputtering, solvothermal synthesis, and sol gel technique are some of the widely used physical and chemical methods. There are essentially two methods for the synthesis of nanoparticles, namely the approach from the bottom up and the approach from the top down.

Scientists attempt to formulate nanoparticles using larger ones to guide their assembly in the Top down method. At molecular level and with precise molecular structural power. In Top-down process bulk material is converted into fine particle in Bottom-up process atom is processed into nuclei and eventually into nanoparticles this is the process used for nanoparticles synthesis.

SYNTHESIS OF NANOMATERIAL: [8,9,10]

Vacuum Deposition and Vaporization:

Elements, alloys or compounds are vaporized and deposited in a vacuum during the vacuum deposition process. The cause of vaporization is the only method that vaporizes materials by thermal processes. The system is done at less than 0.1 Pa (1 m Torr) pressure and 10 to 0.1 MPa vacuum levels. The temperature of the substratum varies from 500 ° C to 500 ° C. A material's saturation or vapor pressure equilibrium is defined as the material's vapor pressure in harmony with the solid or liquid surface. If the vaporization rate is fairly high, a good deposition rate can be achieved for vacuum deposition.Vapor phase nucleation can occur by multi-body collisions in dense vapor cloud, the atoms move through a gas to provide the required nucleation collision and cooling. Such particles range from 1 to 100 nm and are referred to as ultra fine particles or clusters.

Gas Condensation:

The first method of synthesizing nanocrystalline metals and alloys was gas condensation. In this process, in an atmosphere of 1-50 m bar, a metallic or inorganic material is vaporized using sources of thermal evaporation such as Joule heated refractory crucibles, electron beam evaporation devices. A high residual gas pressure allows ultra-fine particles (100 nm) to form through a gas-phase collision in this process. The ultrafine particles are formed by collision with residual gas molecules of evaporated atoms. This gas requires pressures of more than 3 mPa (10 torr). Used sources for vaporization can be resistive heating, high-energy electron beams, low-energy electron beams and heating induction. Clusters produced by homogenous nucleation in the gas phase in the vicinity of the origin evolved through the incorporation of atoms in the gas phase. It consists of a source of evaporation equipped with ultra high vacuum (UHV) unit, a cluster collection device of cold finger scrapper assembly and compaction device filled with liquid nitrogen. During heating, atoms condense near Joule heating device in the super-saturation region. The nanoparticles are removed as a metallic plate by scrapper. Evaporation of refractory metal crucibles from W, Ta or Mo.If the metals interact with crustaceans, the evaporation method of electron beams is to be used. The process suffers from drawbacks including incompatibility of a source precursor, temperature ranges and dissimilar levels of evaporation in an alloy. For example, Fe is evaporated into an atmosphere of inert gas (He). The evaporated Fe atoms loose kinetic energy by collision with the atoms and condense in the form of small crystallite crystals that accumulate as a loose powder. In place of thermal evaporation, sputtering or laser evaporation can be used.

Chemical Precipitation:

The size is regulated by arrested precipitation technique in this technique. The basic thing was to synthesize and study the nanomaterial in situ, i.e. in the same liquid medium, avoiding physical changes and tiny crystallite aggregation. At lower temperatures for synthesis, thermal coagulation and Oswald ripening were controlled by double-layer crystallite repulsion using non-aqueous solvents.The synthesis involved the reaction of constituents in an appropriate solvent. Surfactant is used to keep the particles separate. Thus formed nanocrystal is separated, washed and dried by centrifugation.In order to impart true quantum containment, the dried material was further subjected to UV curing for possible polymerization of surfactant capping film on the nano cluster surface.

Sol-Gel Techniques:

Colloidal particles are much larger than normal nanoparticles or molecules. Nevertheless, it appears voluminous when combined with a liquid colloid while the nanosized molecules still remain transparent. This technique involves network construction by forming colloidal suspension (sol) and gelatin to create a continuous liquid (gel) phase network. Thalcoxides ions and aloxye precursor to synthesize these colloids is made up of metal silans. Tetramethoxysilane (TMOS) and tetraethoxysilanes (TEOS) which form silica gels are the most commonly used. In liquid, alcoxides are immiscible of copper, silica, zirconium, titanium, and many others, they are organo-metallic precursors. Mutual alcohol is used as a solvent.

Chemical Vapor Deposition (CVD) and Chemical Vapor Condensation (CVC):

CVD is a process where a solid is deposited on a heated substrate through a vapor or gas phase chemical reaction.CVC reaction requires energy to continue with the activation. Several methods can be used to provide this energy. The reaction takes place at a high temperature of 900oC in thermal CVD. A standard unit consists of a gas supply system, an exhaust system and a deposition chamber. For plasma CVD, plasma induces the reaction at temperatures ranging from 300 to 700 ° C. Pyrolysis occurs in laser CVD when an absorbing surface is warmed by laser thermal energy. For photo-laser CVD, ultraviolet light, which has enough photon power, causes the chemical reaction to sever the chemical bond in the reactant molecules. The reaction is triggered in this process and deposition occurs at room temperature. CVD has prepared nano composite powders. SiC / Si3N composite powder was prepared as a gas source at 1400 ° C using SiH4, CH4, WF6 and H2. Another process was developed in Germany in 1994, known as chemical vapor condensation (CVC). It involves pyrolysis of organic metal precursor vapors at a lower atmosphere of pressure.

Biosynthesis of nanoparticles: [11,12]

For nanoparticle biosynthesis-Preparation of botanical extracts, bioreduction depends on reaction mixture and incubation period, formation of nanoparticles analyzed by UV-Visible spectroscopy, characterization of nanoparticles by TEM, SEM, FTIR, EXD, XRD, purification and its application. There are basic steps involved in nanoparticle biosynthesis.

Characterization of nanoparticle: [13,14]

X-ray diffraction (XRD) analysis:

X-ray diffraction is a conventional method of determining the structure and morphology of crystallography. With the sum of constituent, there is an increase or decrease in frequency. This method is used to determine the metallic existence of particles provides information on the size and shape of the unit cell's translational symmetry from peak positions and information on electron density within the unit cell, namely where the atoms are from peak intensities. XRD patterns were calculated using X per flex diffraction meter with Cu K and= 1.5406 Å. Crystallite length is determined using Scherrer equation CS= K / os Where CS is the crystallite volume Constant[K]= 0.94 is the full width at half maximum[FWHM] Full width at half maximum in radius = FWHMx 180= 1.5406x 10-10, Cos= Bragg angle. Various scientists have conducted X-ray diffraction analysis with various nanoparticles to identify the high crystallinity of the prepared sample.

UV-visible absorption spectroscopy:

Absorption spectroscopy is used to determine a solution's optical properties. A Light is transmitted through the solution of the sample and the amount of light absorbed is measured. When the wavelength is varied and the absorption is measured at each wavelength. Use Beer-Lamberts Law, absorbance can be used to determine a solution's concentration. When treated with the Nerium Obander plant extract after application of aqueous 1mM Silver nitrate solution, the optical measurement of UV-visible spectrophotometer has specific absorbance peaks such as 410 nm. In the case of *Azadirachta indica*, synthesize with Iron nanoparticles by indicating suitable surface Plasmon resonance with high band intensities and peaks was found in 216-265 nm UV-visible spectroscopy

Transmission electron microscopy (TEM):

Transmission electron microscopy is a microscopy technique in which an ultra-thin sample transmits a beam of electrons communicating with the material as it passes through. An image is formed from the interaction of the transmitted electrons through the specimen; the image is magnified and focused on an imaging device such as a fluorescent screen, a photographic film layer, or a sensor such as a CCD camera can detect it. In both physical and biological sciences, TEM forms a major method of analysis in a variety of scientific fields. TEMs are used in research into virology, cancer, pollution, materials science, semiconductor research and nanotechnology.

Microscopic techniques:

Both methods are primarily used for morphological nanoparticles studies, including SEM and TEM. Many researchers used these techniques to demonstrate the more or less uniform size and shape of the synthesized nanoparticles.

Scanning electron microscope:

Scanning electron microscope analysis characterization is used to determine the size, shape and morphology of shaped SEM nanoparticles, and provides high-resolution images of the desired surface of a sample. The scanning electron microscope works on the same principle as an optical microscope, but it detects rather than photon the electrons scattered from the sample. Since electrons can be accelerated by an electrical potential, the wavelength of the photons can be made shorter. This helps the SEM to magnify up to 200,000 frames. Measures particle size and characterization, involving conductive or sputter-coated sample, and sensitivity up to 1 nm.

Fourier Transform Infrared [FTIR] spectroscopy:

Measures infrared strength vs. light wavelength, it is used to determine the nature of the related functional groups and structural characteristics of nanoparticles biological extracts. The spectra measured clearly reflects the well-known importance of optical properties of nanoparticles. Using Fourier Transform Infrared[FTIR] Spectroscopy, the green synthesized silver nanoparticle was analyzed using different leaf extracts with characteristic peaks.

EVALUATION OF NANOPARTICLES [15]

Particle Shape:

Until going for analysis, SEM characterizes the nanosuspension; lyophilizes the nanosuspension to form solid particles. Using a sputter coater, solid particles are coated with platinum alloy.

Drug Entrapment Efficiency:

Using ultracentrifugation at 10,000 rpm for 30 min at 50C, the nanoparticles are isolated from the aqueous medium. The resulting supernatant solution was then decanted and dispersed into the saline pH 7.4 phosphate buffer. Therefore, the process was repeated twice in order to completely remove the drug molecules that had not been captured. The amount of drug caught in the nanoparticles was determined as the difference between the total amount of drug used in the preparation of the nanoparticles and the amount of drug present in the aqueous medium.

Drug Entrapment Efficiency (percent)= Amount of release from lysed nanoparticle X 100 Amount of drug originally taken for the preparation of nanoparticles.

Zeta potential:

A nanoparticle's Zeta potential is widely used to describe nanoparticles ' surface charging properties. This represents the particle's electrical potential and is determined by the particle structure and the medium in which it is distributed. Nanoparticles with a zeta potential above (±) 30 mV were shown to be stable in suspension because the surface load prevents particle aggregation.

Particle size:

The most important characteristics of nanoparticles structures are particle size and size distribution. They determine the nanoparticles system's in vivo distribution, biological fate, toxicity and targeting ability. Furthermore, they can also influence nanoparticles ' drug loading, drug release and stability. Currently, photon-correlation spectroscopy or dynamic light scattering is the fastest and most routine method of determining particle size. Scanning or transmission of electron microscopy (SEM or TEM) typically verifies the results obtained by photon-correlation spectroscopy.

APPLICATIONS:[16]

Application of nanoparticles in cancer treatment:

There are a variety of currently under investigation nanoparticles systems to be applied in biomedicine with a focus on cancer treatment. There are a variety of nanoparticle systems currently being investigated and explored for biomedical applications with some particular emphasis on cancer therapy; hence some precious metals (mainly gold and silver systems) and some magnetic oxides (especially magnetite Fe3O4) received a lot of attention including quantum dots and some of the so-called natural nanoparticles.

Applications of nanoparticles in food:

Nanofoods is a term used to describe foods that are introduced during development, growth, storage or packaging using nanotechnology techniques, tools or generated nanomaterials. Nanofood is being developed for a number of purposes. These include improving food safety, improving nutrition and flavor and reducing costs of production and consumption. Nano-food also offers a range of advantages including healthy additives, longer shelf life and new types of flavor. Nanotechnology has rapidly appeared in food applications and encompasses all aspects of the food chain, from agriculture to food processing and nutrient bioavailability.

Application of nanoparticle in gene delivery:

Gene delivery is a technique that plays an essential role in the efficient execution of the gene in an appropriate host or host cell of its encoded protein. Nowadays, there are various types of primary gene delivery systems which use viral vectors such as retroviruses and adenoviruses, electroporation of nuclear acid and transfection of nucleic acid.

Targeted Drug delivery:

The precise placement of the medicine to cells or tissue of choice is a key area of drug delivery. Medication targeting mechanisms should be in a position to control the fate of a drug entering the body. Today's delivery systems are far from creating a "magical bullet," which was suggested at the beginning of the 20th century by Paul Ehrlich, in which the drug is specifically directed at the exact side of action. Nanotechnology poses another challenge here to get a little closer to this target and produce the medication in the right place at the right time.

CONCLUSION

The engrossment towards controlled drug delivery seeks to develop appropriate drug carriers that can transmit an adequate dose of the drug to diseased lesions. Various nanostructures have been tested as carriers in drug delivery, including liposomes, polymers, dendrimers, and magnetic nanoparticles. Nanoparticles enable improved delivery of poorly soluble drugs. The most widely used nano particles include gold nano particles, magnetic nanoparticles, silver nano particles in various drug delivery systems.

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