World Inventia Publishers

Journal of Pharma Research

http://www.jprinfo.com/

Vol. 8, Issue 9, 2019 ISSN: 2319-5622 USA CODEN: JPROK3

Review Article

A REVIEW ARTICLE ON NANOPARTICLES AND IT'S APPLICATIONS

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Received on: 31-07-2019; Revised and Accepted on: 11-09-2019

ABSTRACT

Nanoparticle is novel approach for drug delivery which can achieve better therapeutic action, better bioavailability and reduce toxicity. Nanoparticles are tiny materials whose size ranges from 1-100nm.They can be classified into different classes based on their properties, shapes or sizes. In this review we presented a detailed review about nanoparticles, their types, preparation techniques, evaluation parameters and applications of nanoparticles. Today nanoparticles are successfully used in brain targeting, in cancer therapy etc., nanoparticles gives us an opportunity to enhance patient compliance for better therapy. Several techniques are used for the preparation of Nanoparticles like Solvent Evaporation, Double Emulsification Method, Emulsion – Diffusion method, Nanoprecipitation Method, Coacervation Method, Salting out Method, Dialysis and Supercritical fluid technology. Nanoparticles are subjected to several evaluation parameters such as Zeta potential, Particle size and shape, Drug entrapment efficiency, Yield of nanoparticles, In-vitro, kinetic study, and Stability of Nanoparticles.

KEYWORDS: *Nanoparticle, Bio availability, Preparation, Evaluation.*

INTRODUCTION

Nanotechnology has gained huge attention over time. The fundamental component of nanotechnology is the nanoparticles. Nanoparticles are particles between 1 and 100nm in size and are made up of carbon, metal, metal oxides or organic matter. Nanotechnology employs knowledge from the fields of physics, chemistry, biology, materials science, health sciences, and engineering. It has immense applications in almost all the fields of science and human life. Nanoparticles can be defined as particulate dispersions or solid particles with a size in the range of 10-1000nm [1]. There have been made various revolutionary developments in the field of nanotechnology. Nanotechnology produced materials of various types at nanoscale level. Nanoparticles (NPs) are wide class of materials that include particulate substances, which have one dimension less than 100 nm at least [2].

Nanoparticles (NPs) are defined as particulate dispersions or solid particles drug carrier that may or may not be biodegradable. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. The term nanoparticle is a combined name for both nanosphares and nanocapsules. Drug is confined to a cavity surrounded by a unique polymer membrane called nanocapsules, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed [3].

Presently, different metallic nanomaterials are being produced using copper, zinc, titanium, magnesium, gold, alginate and silver. Nanoparticles are being used for diverse purposes, from medical treatments, using in various branches of industry production such as solar and oxide fuel batteries for energy storage, to wide incorporation into diverse materials of everyday use such as cosmetics or clothes [4].

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. Though liposomes have been used as potential carriers with unique advantages including protecting drugs from degradation, targeting to site of action and reduction toxicity or side effects, their applications are limited due to inherent problems such as low encapsulation efficiency, rapid leakage of water-soluble drug in the presence of blood components and poor storage stability [5].

Nanotechnology and Nanoscience studies have emerged rapidly during the past years in a broad range of product domains. It provides opportunities for the development of materials, including those for medical applications, where conventional techniques may reach their limits [6].

Definition: A Nanoparticle is a microscopic particle whose size is measured in nanometres (nm). It is defined as a particle with

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DOI: https://doi.org/10.5281/zenodo.3557300

at least one dimension <200nm.or nanoparticles are solid colloidal particles ranging in size from 10nm to 1000nm. They consist of macromolecular materials in which the active principle is dissolved, entrapped or encapsulated, and/or to which the active principle is absorbed or attached. Nanoparticle can be formulated, as injections consisting of spherical amorphous particles which do not aggregate; hence they can be safely administered by the intravenous route. Since no cosolvent is used to solubilize the drug, the overall toxicity of the formulation is decreased.

Nanoparticles represent very promising carrier system for the targeting of anti-cancer agents to tumors. Nanoparticles exhibit a significant tendency to accumulate in a number of tumors after iv injection. Nanoparticles can also be used in Brain Drug targeting.Poly (butyl cyanoacrylate) nanoparticles represent the only nanoparticles that were so far successfully used for in vivo delivery of drugs to brain. This polymer has the advantage that it is very rapidly biodegradable. The first drug that was delivered to brain using nanoparticles was the HexapeptideDalargin (Tyr-D-Ala-Gly-Phe-Leu-Arg), a Leu-enkephalin analogue with opioid activity. Other drugs that have successfully been transported into the brain are loperamide, tubocurarine, and doxorubicin. Nanoparticles mediated drug transport to the brain depends on the over coating of the particles with polysorbates, especially polysorbate 80 [7].

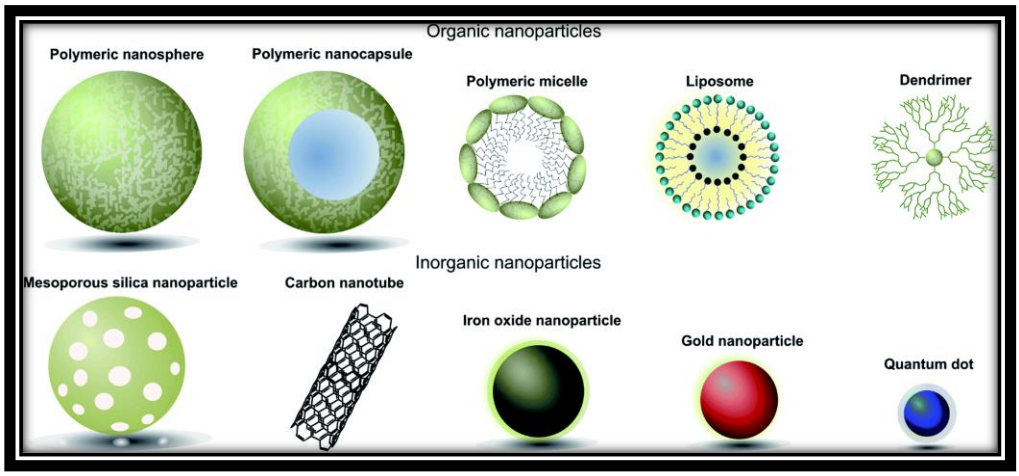

Fig. 1: Types of nanoparticles used in biomedical applications

2.1 Classification of Nanoparticles: Most current NPs can be organized into four material-based categories.

Carbon-based nanomaterials: Generally, these NMs contain carbon, and are found in morphologies such as hollow tubes, ellipsoids or spheres. Fullerenes (C60), carbon nanotubes (CNTs), carbon nanofibers, carbon black, graphene (Gr), and carbon onions are included under the carbon-based NMs category. Laser ablation, arc discharge, and chemical vapor deposition (CVD) are the important production methods for these carbon-based materials fabrication (except carbon black) [8].

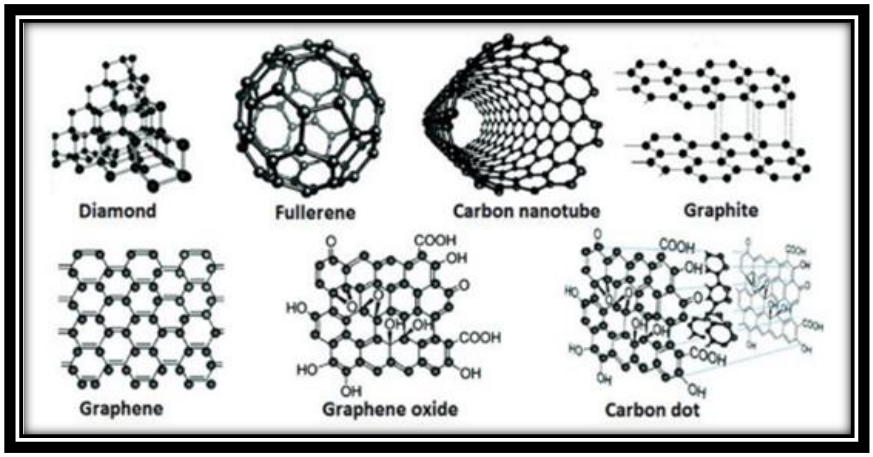

Fig. 2: Carbon based nanoparticles

Organic nanoparticles: Dendrimers, micelles, liposomes and ferritin, etc. are commonly knows the organic nanoparticles or polymers. These nanoparticles are biodegradable, non-toxic, and some particles such as micelles and liposomes has a hollow core (Fig3), also known as nanocapsules and are sensitive to thermal and electromagnetic radiation such as heat and light [4]. These unique characteristics make them an ideal choice for drug delivery. The drug carrying capacity, its stability and delivery systems, either entrapped drug or adsorbed drug system determines their field of applications and their efficiency apart from their normal characteristics such as the size, composition, surface morphology, etc. The organic nanoparticles are most

widely used in the biomedical field for example drug delivery system as they are efficient andalso can be injected on specific parts of the body that is also known as targeted drugdelivery [9].

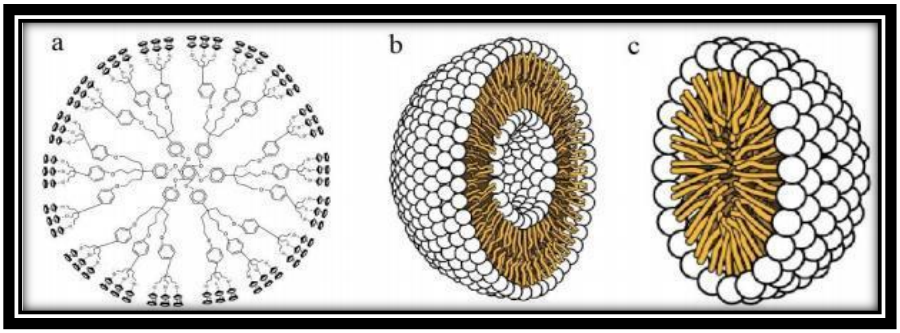

Fig. 3: Organic nanoparticles: a – Dendrimers, b – Liposomes and c – micelles.

Inorganic nanoparticles: Inorganic nanoparticles are particles that are not made up of carbon. Metal and metal oxide based nanoparticles are generally categorized as inorganic nanoparticles.

Metal based: Nanoparticles that are synthesized from metals to nanometric sizes either by destructive or constructive methods are metal based nanoparticles. Almost all the metals can be synthesized into their nanoparticles [10]. The commonly used metals for nanoparticle synthesis are aluminum (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). The nanoparticles have distinctive properties such sizes as low as 10 to 100nm, surface characteristics like high surface area to volume ratio, pore size, surface charge and surface charge density, crystalline and amorphous structures, shapes like spherical and cylindrical and colour, reactivity and sensitivity to environmental factors such as air, moisture, heat and sunlight etc.

Metal oxides based: The metal oxide based nanoparticles are synthesized to modify the properties of their respective metal based nanoparticles, for example nanoparticles of iron (Fe) instantly oxidizes to iron oxide (Fe2O3) in the presence of oxygen at room temperature that increases its reactivity compared to iron nanoparticles. Metal oxide nanoparticles are synthesized mainly due to their increased reactivity and efficiency [11]. The commonly synthesized are Aluminum oxide (Al2O3), Cerium oxide (CeO2), Iron oxide (Fe2O3), Magnetite (Fe3O4), Silicon dioxide (SiO2), Titanium oxide (TiO2), Zinc oxide (ZnO). These nanoparticles have possess an exceptional properties when compared to their metal counterparts.

Composite nanoparticles:

In the past two decades, composite nanoparticles have attracted great attention for their special and multiple properties. The synthesis of composite nanoparticles has not been confined to simply integration of some categories with special effects. The structure has become much more complex, and the scale of composite has been reduced to less than 1–20 nm, which can be referred to as quantum dots. According to the structural features, composite nanoparticles can be mainly grouped into three categories: simple hybrid, core/shell structured composite nanoparticles, and multifunctional quantum dots, as shown in In the past two decades, composite nanoparticles have attracted great attention for their special and multiple properties. The synthesis of composite nanoparticles has not been confined to simply integration of some categories with special effects. The structure has become much more complex, and the scale of composite has been reduced to less than 1–20 nm, which can be referred to as quantum dots. According to the structural features, composite nanoparticles can be mainly grouped into three categories: simple hybrid, core/shell structured composite nanoparticles, and multifunctional quantum dots, as shown in Composite nanoparticles are defined as the nanomaterials with composite structure which are constituted by two or more components of nanoscale with special physical and chemical properties. In the past two decades, composite nanoparticles have attracted great attention for their special and multiple properties. The synthesis of composite nanoparticles has not been confined to simple integration of some categories with special effects. The structure has become much more complex, and the scale of composite has been reduced to less than 1–20 nm, which can be referred to as quantum dots. According to the structural features, composite nanoparticles can be mainly grouped into three categories: simple hybrid, core/shell structured composite nanoparticles, and multifunctional quantum dots, as shown in fig 4 [12].

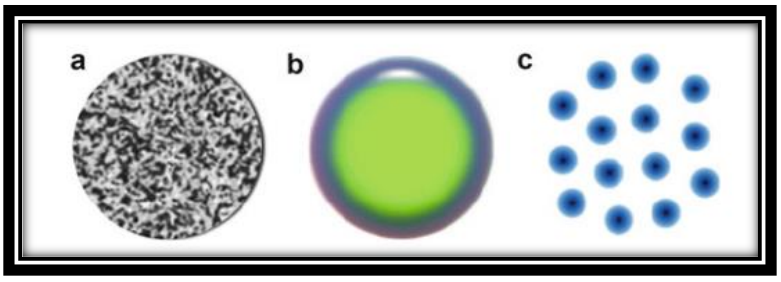

Fig. 4: Schematic representation for the basic structures of composite nanoparticles
(a) Simple hybrid (b) core/shell structured (c) multifunctional quantum dots.

Types of nanoparticles: [13]

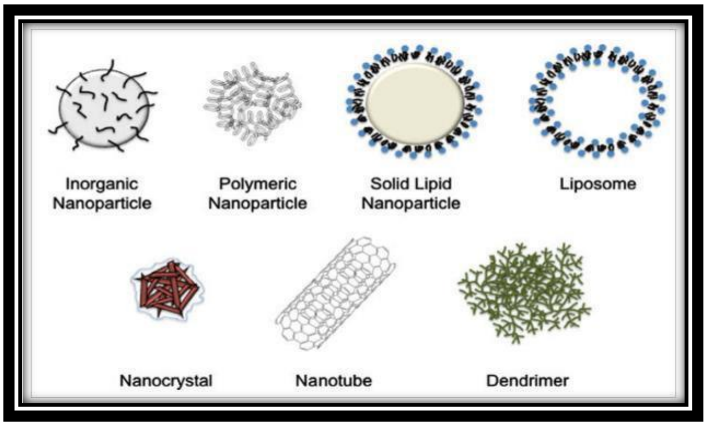

Fig. 5: Types of nanoparticles

Inorganic nanoparticles: In the field of Modern material science Inorganic nanoparticle has been developed the role based upon their unique physical properties and particularly in biotechnology. Based upon these two factors of inorganic nanoparticles they have certain physical properties that mainly include size- dependent optical, magnetic, electronic, and catalytic properties. Bio related application are involved for the preparation of these interesting nanoparticles like iron oxides, gold, silver, silica, quantum dots etc. Novel physical properties mainly related because of their size approaches nanometer scale dimension.

Polymeric nanoparticles: Polymeric nanoparticle it is also a type of nanoparticle. In the recent year polymeric nanoparticle has a tremendous development in the field of research. The dispersion of preformed polymers and the polymerization of monomers are two strong strategies mainly involved for preparation .10- 1000nm it is the range of size involved with solid particles.

Solid lipid nanoparticles: For controlling the drug delivery in 1990 s Solid lipid nanoparticles played a dominant role. There are certain alternate carrier systems to emulsions, liposomes and polymeric nanoparticles as a colloidal Carrier system.

Liposomes: Liposomes are one of the methods based upon the different types of nanoparticles. Structure of liposomes consists of one or more phospholipid bilayers and they are sphere-shaped vesicles to carry compound of interest. Today liposomes have been useful in the field of reagent and tool in various scientific disciplines. Since many features involved in liposome they made their own way in the market. Cosmetic and pharmaceutical industries numerous molecules act as a carrier, and in the field of Food and farming industries liposomes involved in encapsulation to grow delivery system that can entrap unstable compounds.

Nanocrystal: A Nanocrystal is a type based upon material particle having at least one dimension smaller than 100 nanometers and mainly composed of atoms in either a single or poly-crystalline arrangement. Nanocrystals are aggregates of around hundreds or thousands of molecules that combine in a crystalline form, composed of pure drug with only a thin coating comprised of surfactant or combination of surfactants.

Nanotube: A nanotube is a nanometer scale tube like structure. Nanotubes are members of the fullerene structural family. Their name is derived from their long, hollow structure with the walls formed by one-atom-thick sheets of carbon called graphene. These sheets are rolled at specific and discrete ("chiral") angles and the combination of the rolling angle and radius decides the nanotube properties; for example, whether the individual nanotube shell is a metal or semiconductor. Nanotubes are categorized as single-walled nanotubes (SWNTs) and multi-walled nanotubes.

Dendrimers: Dendrimers arise from two Greek words: Dendron meaning tree and Merosmeaning part. Structure of dendrimers has a well-defined size, shape and defined molecular weight and also dendrimers are hyper-branched, globular, monodisperse, three dimensional nanoscales synthetic Polymers. Molecular chemistry and polymer chemistry both exhibit well-defined characteristics features of Dendrites.

Preparation of nanoparticles:

Nanoparticles are aimed to be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection criteria of matrix materials depend on many factors such as: [14]

(a) Size of nanoparticles required;
(b) Inherent properties of the drug, e.g., aqueous solubility and stability;
(c) Surface characteristics such as Charge and Permeability;
(d) Degree of biodegradability, biocompatibility and toxicity;
(e) Drug release profile desired;
(f) Antigenicity of the final product;

Nanoparticles preparation is most frequently by three methods:

(1) Dispersion of preformed polymers;
(2) Polymerization of monomers;
(3) Ionic gelation or coacervation of hydrophilic polymers.

However, other methods such as supercritical fluid technology 8 and particle replication in non-wetting templates have also been described in the literature for production of nanoparticles. The latter was claimed to have absolute control of particle size, shape and composition, which could set an example for the future mass production of nanoparticles in industry.

Dispersion of preformed polymers: Dispersion of preformed polymers is a common technique used to prepare biodegradable nanoparticle from poly (lactic acid) (PLA); poly (D, L-glycolide), PLG; poly (D, L-lactide-coglycolide) (PLGA) and poly(cyanoacrylate) (PCA),This technique can be used in various ways [15, 16].

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. Particle size was found to be influenced by the type and concentrations of stabilizer, homogenizer speed and polymer concentration. In order to produce small particle size, often a high-speed homogenization or ultra-sonication may be employed [17].

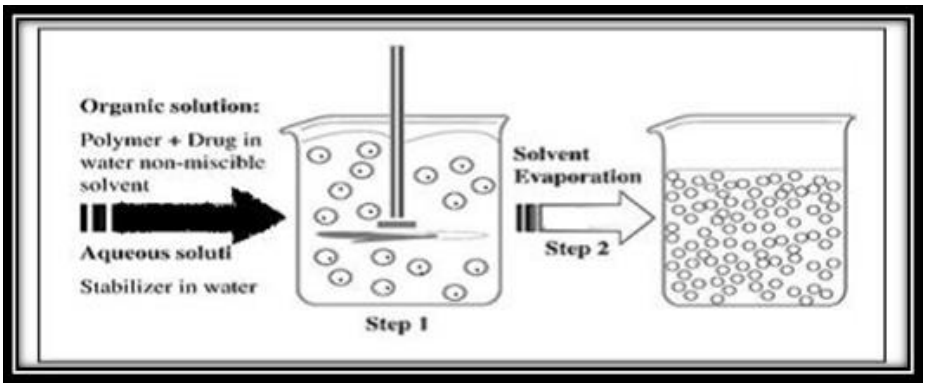

Fig. 6: Representation of the solvent-evaporation technique

Spontaneous emulsification or solvent diffusion method: This is a modified version of solvent evaporation 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 [18].

Emulsions-Diffusion Method: This method patent by Leroux et al it is modified form of salting out method. Polymer dissolved in water-miscible solvent (propylene carbonate, benzyl alcohol), this solution saturated with water. Polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer. Then solvent removed by evaporation or filtration. Advantages of this method are high encapsulation efficiencies (generally 70%), no need for homogenization, high batch-to-batch reproducibility, ease of scaleup, simplicity, and narrow size distribution. Some disadvantage of this method is reported high volumes of water to be eliminated from the suspension and the leakage of water-soluble drug into the saturated aqueous external phase during emulsification, reducing encapsulation efficiency [19-21].

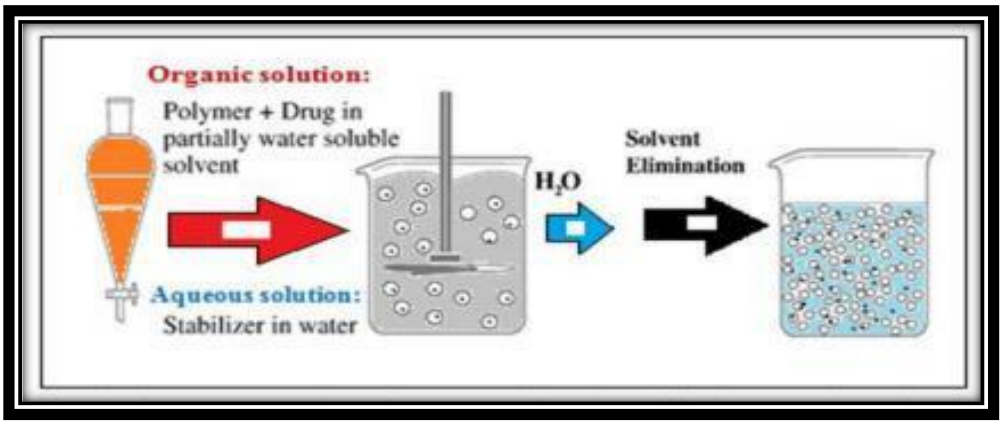

Fig. 7: Representation of the emulsification-diffusion technique

Polymerization method: In this method, monomers are polymerized to form nanoparticle in an aqueous solution. Drug is incorporated either by being dissolved 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. This technique has been reported for making polybutylcyanoacrylate or poly (alkyl cyanoacrylate) nanoparticles [22-24].

Coacervation or ionic gelation method: The nanoparticles preparation is carried by using biodegradable hydrophilic polymers such as chitosan, gelatin and sodium alginate. Developing a method for preparing hydrophilic chitosan nanoparticles by ionic gelation. 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 [25].

Nanoprecipitation method: In this method precipitation of polymer and drug obtained from organic solvent and the organic solvent diffused in to the aqueous medium with or without presence of surfactant [26]. This is another method which is widely used for nanoparticle preparation which is also called solvent displacement method. This technique was first described by Fessi at al. 1989 [27]. Tamizhrasi at al prepared Lumivudine loaded nanoparticles. Firstly drug was dissolved in water, and then cosolvent (acetone used for make inner phase more homogeneous) was added into this solution. Then another solution of polymer (ethyl cellulose, eudragit) and propylene glycol with chloroform prepared, and this solution was dispersed to the drug solution. This dispersion was slowly added to 10 ml of 70% aqueous ethanol solution. After 5 minutes of mixing, the organic solvents were removed by evaporation at 35° under normal pressure, nanoparticles were separated by using cooling centrifuge (10000 rpm for 20 min), supernatant were removed and nanoparticles washed with water and dried at room temperature in a desicator [28].

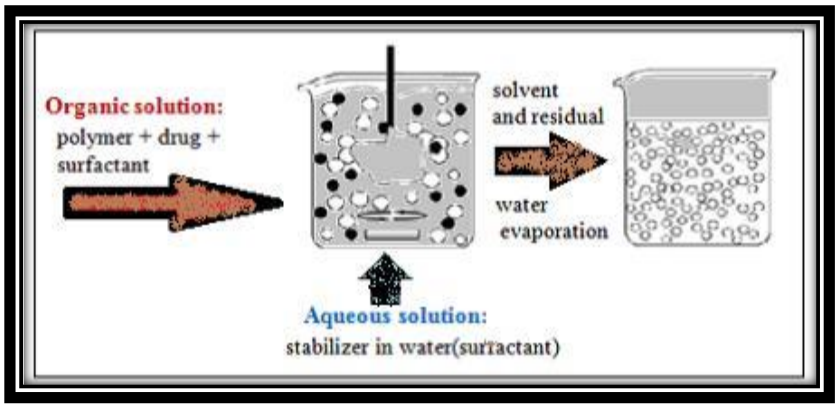

Fig. 8: Representation of the nanoprecipitation technique

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. Therefore, the supercritical fluid technology has been investigated as an alternative to prepare biodegradable micro- and nanoparticles because supercritical fluids are environmentally safe. A supercritical fluid can be generally defined as a solvent at a temperature above its critical temperature, at which the fluid remains a single phase regardless of pressure. Supercritical CO2 (SC CO2) is the most widely used supercritical fluid because of its mild critical conditions (Tc = 31.1 °C, Pc = 73.8 bars), nontoxicity, non-flammability, and low price [29, 30]. The most common processing techniques involving supercritical fluids are supercritical antisolvent (SAS) and rapid expansion of critical solution (RESS). The process of SAS employs a liquid solvent, e.g. methanol, which is completely miscible with the supercritical fluid (SC CO2), to dissolve the solute to be micronized; at the process conditions, because the solute is insoluble in the supercritical fluid, the extract of the liquid solvent by supercritical fluid leads to the instantaneous precipitation of the solute, resulting the formation of nanoparticles. RESS differs from the SAS process in that its solute is dissolved in a supercritical fluid (such as supercritical methanol) and then the solution is rapidly expanded through a small nozzle into a region lower pressure , Thus the solvent power of supercritical fluids dramatically decreases and the solute eventually precipitates. This technique is clean because the precipitate is basically solvent free. RESS and its modified process have been used for the product of polymeric nanoparticles. Supercritical fluid technology technique, although environmentally friendly and suitable for mass production, requires specially designed equipment and is more expensive.

Salting Out Method: This technique was introduced and patented by Bindschaedler et al. and Ibrahim et al. Salting out method is very close to solvent-diffusion method. This technique based on the separation of water-miscible solvent from aqueous solution by salting out effect (Catarina PR et al., 2006). In this method toxic solvents are not used. Generally acetone is used because it is totally miscible with water and easily removed. Polymer and drug dissolved in a solvent which emulsified into a aqueous solution containing salting out agent (electrolytes, such as magnesium chloride and calcium chloride, or nonelectrolytes such as sucrose) but salting out can also be produced by saturation of the aqueous phase using colloidal stabilizer/ emulsion stabilizer/ viscosity increasing agent such as polyvinylpyrrolidone or hydroxyethylcellulose, PVA, Poly(ethylene oxide), PLGA and poly(trimethylene carbonate). After preparation of o/w emulsion diluted with addition of sufficient water to allow the complete diffusion of acetone into the aqueous phase, thus inducing the formation of nanospheres. This technique does not require an increase in temperature and stirring energy required for lower particle size. Disadvantage of this technique is exclusive application to lipophilic drug and the extensive nanoparticles washing Steps [31-33].

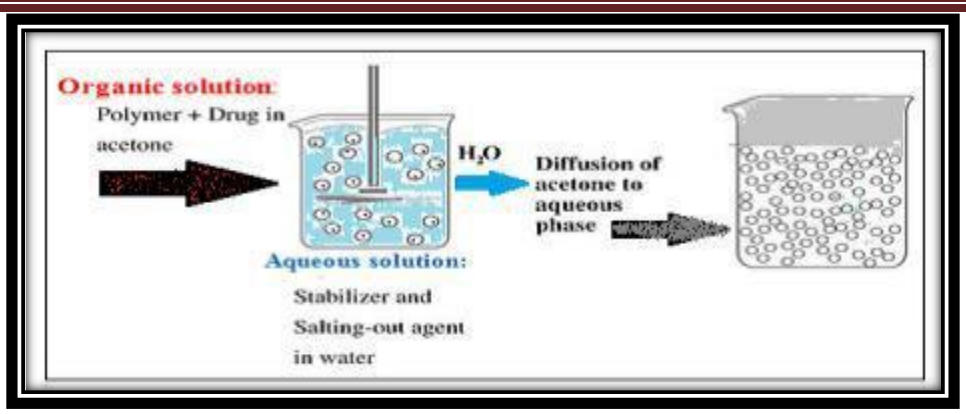

Fig. 9: Representation of the salting out technique

Evaluation parameters of Nanoparticles:

Zeta potential: The Zeta potential of a nanoparticle is commonly used to characterized the surface charge property of nanoparticles. It reflects the electrical potential of particles and is influenced by the composition of the particle and the medium in which it is dispersed. Nanoparticles with a zeta potential above (±) 30 mV have been shown to be stable in suspension, as the surface charge prevents aggregation of the particles [34].

Particle Shape: SEM characterizes the nanosuspension before going for evaluation; the nanosuspension is lyophilized to form solid particles. The solid particles are coated with platinum alloy using a sputter coater [35].

Particle size: Particle size and size distribution are the most important characteristics of nanoparticle systems. They determine the in vivo distribution, biological fate, and toxicity and targeting ability of nanoparticle system. In addition, they can also influence the drug loading, drug release and stability of nanoparticles. Currently, the faster and most routine method of determining particle size is by photon-correlation spectroscopy or dynamic light scattering. The results obtained by photon-correlation spectroscopy are usually verified by scanning or transmission electron microscopy (SEM or TEM) [36].

Drug Entrapment Efficiency: The nanoparticles were separated from the aqueous medium by ultra-centrifugation at 10,000 rpm for 30 min at 50C. Then the resulting supernatant solution was decanted and dispersed into phosphate buffer saline pH 7.4. Thus the procedure was repeated twice to remove the unentrapped drug molecules completely. The amount of drug entrapped in the nanoparticles was determined as the difference between the total amount of drug used to prepare the nanoparticles and the amount of drug present in the aqueous medium. Drug Entrapment efficiency (%) = Amount of released from the lysed nanoparticle X 100 Amount of drug initially taken to prepare the Nanoparticles [37].

Yield of nanoparticles: The yield of nanoparticles was determined by comparing the whole weight of nanoparticles formed against the combined weight of the copolymer and drug [38].

$$\%\text{yield} = \frac{\text{amount of nanoparticle}}{\text{amount of drug} + \text{polymer}} x100$$

In-vitro release Study: In-vitro drug release studies were performed in USP Type II dissolution apparatus at rotation speed of 50 rpm. The prepared immersed in 900ml of phosphate buffer solution in a vessel, and temperature was maintained at 37±0.20°C. Required quantity 5ml of the medium was withdrawn at specific time periods and the same volume of dissolution medium was replaced in the flask to maintain a constant volume. The withdrawn samples were analyzed using UV spectrophotometer [39].

Surface Morphology Surface morphology study carried out by Scanning Electron Microscopy (SEM) of prepared nanoparticle [40].

Kinetic Study For estimation of the kinetic and mechanism of drug release, the result of in vitrodrug release study of nanoparticles were fitted with various kinetic equation like zero order (cumulative % release vs. time), first order (log % drug remaining vs time), Higuchi‟s model (cumulative % drug release vs. square root of time). R_2 and k values were calculated for the linear curve obtained by regression analysis of the above plots [41].

Drug Delivery Therapy of Nanoparticles:

Liposome-based Drug Delivery Therapy:

Liposomes: Definition, Classification & Methods of Preparation: Liposomes are self-closed vesicular structures composed of phospholipids that entrap water in their interior. These structures result from self-assembly of the amphiphiles in an aqueous medium forming single or multiple concentric bilayers, where the polar head groups are in contact with the aqueous media and the fatty acids form the hydrophobic core of the bilayers that are shielded from the water.

Liposomes are commonly prepared by hydration of a dry phospholipid film above the main phase transition temperature of the lipid. The diameter of liposomes ranges from 20 nm to several hundreds of nanometers, whereas the thickness of the phospholipid bilayer membrane is approximately 4–7 nm. The classification of liposomes is generally based upon their size and number of lipidic bilayers. Liposomes resultant from the thin film hydration method are multilamellar vesicles (MLVs), which consist of many concentric bilayers in a single particle with diameters that vary between a few hundred to thousands of nanometers. MLVs can be processed by sonication or by extrusion, through a filter, to form unilamellar vesicles (ULVs), which are liposomes with a single membrane bilayer. ULVs can be further classified, regarding their size, into small unilamellar vesicles (SUVs) and large unilamellar vesicles (LUVs). Accordingly, SUVs show a diameter inferior to 100 nm while LUVs present a diameter superior to 100 nm [42].

Targeted Drug Delivery for Cancer: Cancer drug delivery is no longer simply wrapping the drug in new formulations for different routes of delivery. Knowledge and experience from other technologies such as nanotechnology, advanced polymer chemistry, and electronic engineering, are being brought together in developing novel methods of drug delivery. Advances in our knowledge of molecular biology of cancer and pathways involved in malignant transformation of cells are revolutionizing the approach to cancer treatment with a focus is on targeted cancer therapy. There is a vast range of strategies available for drug delivery in cancer.

Targeted Drug Delivery: The current focus in development of cancer therapies is on targeted drug delivery to provide therapeutic concentrations of anticancer agents at the site of action and spare the normal tissues. Vasir and Labhasetwar present an overview of the problems related to targeted drug delivery in cancer, and to provide an insight into the issues related to the development of targeted drug delivery systems for cancer. The authors have described several technologies for targeted drug delivery in cancer and suggest that combination of some of these approaches may provide solutions to some of the problems encountered.

Drug Delivery Using Monoclonal Antibodies: Monoclonal antibodies (MAbs) are used both for diagnosis and therapy in cancer. Several MAbs are in the market for cancer therapy. MAbs are being paired with powerful toxins and radiopharmaceuticals to create specific agents that seek out cancer cells and kill them. Describe targeted cancer therapy with radiolabeled and drug/toxin-conjugated MAbs and methods of producing these conjugates [43]. The clinical potential of these therapies in hematological malignancies is promising. For the treatment of solid tumors, the authors suggest application of combination therapies and use in residual disease rather than in bulky tumors. Bethge and Sandmaier have shown how radioimmunotherapy combines the advantages of targeted radiation therapy and specific immunotherapy using MAbs to target tumor cells [44]. Radiolabeled MAbs enable the reduction of toxicity of conventional strategies of radiation therapy and enhance the efficacy of MAbs. The authors provide an overview of available radionuclides and radioimmunoconjugates and discuss clinical results in hematological malignancies [45].

Applications of nanoparticles:

Cosmetics and Sunscreens:

The conventional ultraviolet (UV) protection sunscreen lacks long-term stability during usage. The sunscreen including nanoparticles such as titanium dioxide provides numerous advantages. The UV protection property of titanium oxide and zinc oxide nanoparticles as they are transparent to visible light as well as absorb and reflect UV rays found their way to be used in some sunscreens. Some lipsticks use iron oxide nanoparticles as a pigment [46].

Electronics:

The higher necessity for large size and high brightness displays in recent days that are used in the computer monitors and television is encouraging the use of nanoparticles in the display technology. For example nanocrystalline lead telluride, cadmium sulphide, zinc selenide and sulphide, are used in the light emitting diodes (LED) of modern displays [47]. The development inportable consumer electronics such as mobile phones and laptop computers led to the enormous demand for compact, lightweight and high capacity batteries. Nanoparticles are the ideal choice for separator plates in batteries. A considerable more energy can be stored compared to traditional batteries due to their foam like (aerogel) structure. Batteries made from nanocrystalline nickel and metal hydrides, due to their large surface area require less recharging and last longer [48]. The increase in electrical conductivity of nanoparticles is used to detect gases like NO_2 and NH_3 [49]. This is due to increase in the pores of nanoparticles due to charge transfer from nanoparticles to NO_2 as the gas molecules bind them together making them better gas sensors.

Catalysis:

Nanoparticles contain high surface area that offers higher catalytic activity. Due to their extremely large surface to volume ratio the nanoparticles function as efficient catalyst in the production of chemicals [50]. One of the important application is the use of platinum nanoparticles in the automotive catalytic converters as they reduce the amount of platinum required due to very high surface area of the nanoparticles thus reducing the cost significantly and improving performance. Some chemical reactions for example, reduction of nickel oxide to metal nickel (Ni) is performed using nanoparticles.

Medicine:

Nanotechnology has improved the medical field by use of nanoparticles in drug delivery. The drug can be delivered to specific cells using nanoparticles [51]. The total drug consumption and side effects are significantly lowered by placing the drug in the required area in required dosage. This method reduces the cost and side effects. The reproduction and repair of damaged tissue (Tissue engineering) can be carried out with the help nanotechnology. The traditional treatments such as artificial implants and organ transplants can be replaced by tissue engineering. One such example is the growth of bones carbon nanotube scaffolds [52]. The use of gold in medicine is not new. In Ayurveda an Indian medical system, gold is used in several practices. One common prescription is the use of gold for memory enhancement. To enhance the mental fitness of baby gold is included in certain medical preparations [53].

Food:

The improvement in production, processing, protection and packaging of food is achieved by incorporating nanotechnology. For example a nanocomposite coating in a food packaging process can directly introduce the anti-microbial substances on the coated film surface [54].

Tumor targeting using Nanoparticulate delivery system:

The rational of using nanoparticles for tumor targeting is based on:

(1) Nanoparticles will be able to deliver a concentrate dose of drug in the vicinity of the tumor targets via the enhanced permeability and retention effect or active nanoparticles.

(2) Nanoparticles will reduce the drug exposure of health tissues by limiting drug distribution to target organ. An experiment demonstrated in mice treated with doxorubicin incorporated into poly (isohexylcynoacrylate) nanospheres that higher concentration of doxorubicin manifested in the liver, spleen and lungs than in mice treated with free doxorubicin [55].

Nanoparticles for oral delivery of peptides and proteins:

Significant advances in biotechnology and biochemistry have led to the discovery of a large number of bioactive molecules and vaccines based on peptides and proteins. Development of suitable carriers remains a challenge

due to the fact that bioavailability of these molecules is limited by the epithelial barriers of the gastrointestinal tract and their susceptibility to gastrointestinal degradation by digestive enzymes [56].

Nanoparticle for gene delivery:

Polynucleotide vaccines work by delivering genes encoding relevant antigens to host cells where they are expressed, producing the antigenic protein within the vicinity of professional antigen presenting cells to initiate immune response. Such vaccines produce both humoral and cell mediated immunity because intracellular production of protein, as opposed to extracellular deposition, stimulates both arms of the immune system [57].

Nanoparticles using plant extracts: Nanoparticles synthesis can be carried out by various chemical and physical methods, but use of such methods are harmful in one or the other way. The photosynthesis of nanoparticles is emerging as the intersection of nanotechnology and biotechnology. Due to a growing need to develop environmentally benign technologies in material synthesis, it has received increased attention. This has motivated the researchers to synthesis the nanoparticles using this route that allow better control of shape and size for various applications [58].

Gold nanoparticles using plant extracts: Synthesis of gold nanoparticles using plant extract is useful not only because of its reduced environmental, but also because it can be used to produce large quantities of nanoparticles. Plant extracts may act both as reducing agents and stabilizing agents in the synthesis of nanoparticles. The properties of gold nanoparticles are very different from that of bulk, as the gold nanoparticles are wine red solution while the bulk gold is yellow solid. The gold nanoparticles can be manufactured into a variety of shapes including nanorods, nanospheres, nanocages, nanostars, nanobelts and nanoprisms [59].

Silver nanoparticles by plant extracts: The major advantage of using plant extracts for silver nanoparticle synthesis is that they are easily available, safe, and nontoxic in most cases, have a broad variety of metabolites that can aid in the reduction of silver ions, and are quicker than microbes in the synthesis. The main mechanism considered for the process is plant-assisted reduction due to phytochemicals. The main phytochemicals involved are terpenoids, flavones, ketones, aldehydes, amides, and carboxylic acids. Flavones, organic acids, and quinones are water-soluble phytochemicals that are responsible for the immediate reduction of the ions. Studies have revealed that xerophytes contain emodin, an anthraquinone that undergoes tautomerization, leading to the formation of the silver nanoparticles.

CONCLUSION

Nanoparticle technologies have great potentials, being able to convert poorly soluble, poorly absorbed labile biologically active substance into promising deliverable substances. Due to their tiny size, NPs have large surface area, which make them suitable candidate for various applications. Synthetic technique can be useful to control the specific morphology, size and magnetic properties of NPs. Though NPs are useful for many applications but still there are some health hazard concerns due to their uncontrollable use & discharge to natural environment, which should be considered to make the use of NPs more convenient & environmental friendly. Nanotechnology enabled drug delivery is opening prospective future in pharmaceutics. The emergence of nanotechnology is likely to have a significant impact on drug delivery sector, affecting just about every route of administration from oral to injectable.

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How to cite this article:

D. Shirisha, et al. A REVIEW ARTICLE ON NANOPARTICLES AND IT'S APPLICATIONS. J Pharm Res 2019;8(9):638-648.
DOI: https://doi.org/10.5281/zenodo.3557300

Conflict of interest: The authors have declared that no conflict of interest exists.

Source of support: Nil