International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 1071-1079 www.ijprajournal.com ISSN: 2249-7781

A Review on Nanoparticles

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Submitted: 12-01-2023 Accepted: 24-01-2023

ABSTRACT
Interest in new drug development has increased dramatically in recent years.A delivery system using nanoparticles. nanoparticles arehigh stability, high specificity, high drug delivery capacity,Controlled release capability, ability and ability to be used in various routes of administration. It delivers both hydrophilic and hydrophobic drug molecules. This review focuses on classification.Manufacturing Processes, Characterization, Applications, Benefits and Health of Nanoparticlesperspective.Generally nanoparticles size ranges from 1 to 100 nm with one (or) more dimensions. Generally nanoparticles classified into inorganic, organic and particles based on carbon in nanometric scale that has properties improved compared to larger size of respective materials. They show properties which are enhanced such as strength, sensitivity, high reactivity, stability, surface area etc., due to their smaller size.They can also be designed to improve the pharmacological and therapeutic effects of the drugs5 . They also have a very high surface area and they permit many functional groups to be adhered to them which in turn, can bind to tumor cells6 . They have proven to be an excellent replacement for radiation and chemotherapy as they can easily assemble in the micro environment of the tumor.

KEYWORDS: nanoparticles, drug delivery, targeting, drug release

I. INTRODUCTION

Nanoparticles are defined as particulate dispersions or solid particles with a size in the range of 10-1000nm. The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Depending upon the method of preparation, nanoparticles, nanospheres or nanocapsules can be obtained. Nanocapsules are systems in which the drug is confined to a cavity surrounded by a unique polymer membrane, while nanospheres are matrix systems in which the drug is physically and uniformly dispersed. In recent years, biodegradable polymeric nanoparticles, particularly those coated with hydrophilic polymer such as poly(ethylene glycol) (PEG) known as long-circulating particles, have been used as potential drug delivery devices because of their ability to circulate for a prolonged period time target a particular organ, as carriers of DNA in gene therapy, and their ability to deliver proteins, peptides and genes.

Nanotechnology is the science of the small; the very small. It is the use and manipulation of matter at a tiny scale. At this size, atoms and molecules work differently, and provide a variety of surprising and interesting uses. 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. Nanotechnology should not be viewed as a single technique that only affects specific areas.

Structure of nanoparticle

The nanoparticle structure of a material is generally determined by the chemical composition of the material, the number of atoms in the particle, and the nature of the chemical interactions between the atoms. Nanoparticles can have a regular crystal structure, be amorphous, or form quasi-closest packing that cannot be explained by the crystallographic space group. For each of these structural states of nanoparticles, there is a certain number of atoms involved in the particle corresponding to the optimal stable configuration. These numbers are commonly called magic numbers.[32][34]

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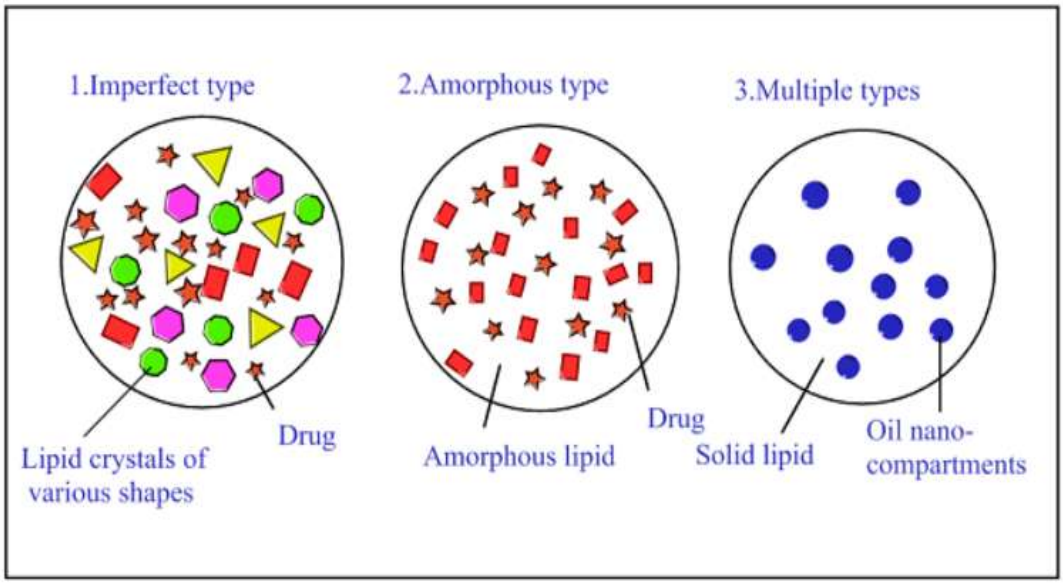

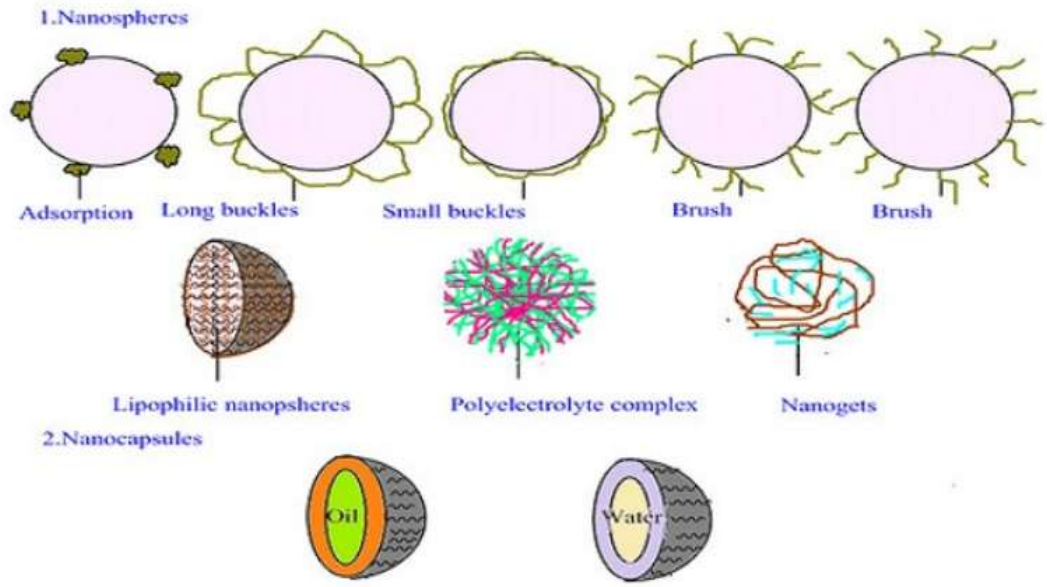

ADVANTAGE

- Large surface area to volume ratio makes them effective catalysts
- Nanoparticles in sun creams can be absorbed deeper into the skin
- So small they can enter the skin and therefore the bloodstream
- Nanoparticles in face creams cover better so you have to use less[9][10]

DISADVANTAGE

- Large surface can make them too reactive and explosive in some situations
- Changes the properties of a material
- They might be toxic to some types of cell, such as skin, bone, brain and liver cells
- Easily become airborne, breathing in can potentially damage the lungs[9][10]

EVALUATION

Yield of nanoparticle

The yield of nanoparticles was determined by comparing the whole weight of nanoparticles formed against the combined weight of the copolymer and drug. [15]

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$$\%\text{yield} = \frac{\text{amount of nanoparticle}}{\text{amount of drug} + \text{polymer}} \times 100$$

Drug Content/ Surface entrapment

After centrifugation amount of drug present in supernatant [w] determined by UV Spectrophotometery.[30]

After that standard calibration curve plotted. Then amount of drug present in supernatant subtracted from the total amount used in the preparation of nanoparticles (W). [W-w) is the amount of drug entrapped. %% drug entrapment calculated by[35]

$$\%\text{drug entrapment} = \frac{W - w}{W} \times 100$$

Surface Morphology

Surface morphology study carried out by Scanning Electron Microscopy (SEM) of prepared nanoparticle.[33]

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.[34]

II. CLASSIFICATION

The nanoparticles are generally classified into the organic, inorganic and carbon based.

1. Organic nanoparticles: micelles, Dendrimers, ferritin and liposomes etc. are commonly known polymers or organic nanoparticles. These nanoparticles are non-toxic, biodegradable, and some particles such as liposomes and micelles have a hollow core also known as nano capsules and are sensitive to thermal and electromagnetic radiation such as heat and light. [4] The organic nanoparticles are most widely used in the biomedical field for example drug delivery system as they are efficient and also can be injected on specific parts of the body which is also known as targeted drug delivery. Examples of organic nanoparticles are liposomes, dendrimers and micelles.

2. Inorganic nanoparticles: Inorganic nanoparticles are particles which are not made up of carbon. Metal and metal oxide-based nanoparticles are generally categorized as inorganic nanoparticles.[12]

a.Metal NPs:

Almost all the metals can be synthesised into their nanoparticles. [4] The commonly used metals for nanoparticle synthesis are aluminium (Al), cadmium (Cd), cobalt (Co), copper (Cu), gold (Au), iron (Fe), lead (Pb), silver (Ag) and zinc (Zn). These nanoparticles can be synthesized by chemical, electrochemical, or photochemical methods. In chemical methods, the metal nanoparticles are obtained by reducing the metal-ion precursors in solution by chemical reducing agents. These have the ability to adsorb small molecules and have high surface energy. These nanoparticles have applications in research areas, detection and imaging of biomolecules and in environmental and bioanalytical applications. For example, gold nanoparticles are used to coat the sample before analyzing in SEM. This was usually done to enhance the electronic stream, which helps us to get high quality SEM images. Due to their advanced optical properties, metal NPs find applications in many research areas.[11]

b. Ceramic NPs:

Ceramic nanoparticles are inorganic solids made up of carbides, carbonates, oxides, carbides, carbonates and phosphates synthesized via heat and successive cooling. They can be found in polycrystalline, dense, amorphous, polycrystalline, dense, porous or hollow forms.[13] Therefore, these NPs are getting great attention of researchers due to their use in applications such as catalysis, photocatalysis, photodegradation of dyes. By controlling some physical properties, these nanoparticles can be formulated in drug delivery system especially in targeting tumors, glaucoma, and some bacterial infections.[15]

c. Semiconductor NPs:

Semiconductor nanoparticles have properties like those of metals and non-metals. They are found in the periodic table in groups II-VI, IIIV or IV-VI. These particles have wide bandgaps, which on tuning shows different properties. They are used in photocatalysis, electronics devices, photo-optics and water splitting applications. Semiconductor materials possess properties between metals and nonmetals and therefore they found various applications in the literature due to this property. Some examples of

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semiconductor nanoparticles are GaN, GaP, InP, InAs from group III-V; ZnO, ZnS, CdS, CdSe, CdTe are II-VI semiconductors and silicon and germanium are from group IV. [5]

d. Polymeric NPs:

These are normally organic based NPs and in literature a special term polymer nanoparticle (PNP) is collectively used for it. Depending up on the preparation these are nanospheres or nano-capsular shaped. The former are matrix particles whose overall mass is generally solid and the other molecules are adsorbed at the outer boundary of the spherical surface. In the latter case the solid mass is encapsulated within the particle completely. The PNPs are readily functionalized and thus find bundles of applications in the literature.[16]
Some of the merits of polymeric nanoparticles are controlled release, protection of drug molecules, ability to combine therapy and imaging, specific targeting and many more. They have applications in drug delivery and diagnostics. The drug deliveries with polymericnanoparticles are highly biodegradable and biocompatible.[20]

e. Lipid-based NPs:

Lipid nanoparticles are generally spherical in shape with a diameter ranging from 10 to 100 nm. It consists of a solid core made of lipid and a matrix containing soluble lipophilic molecules.[18] The external core of these nanoparticles is stabilized by surfactants and emulsifiers. These nanoparticles have application in the biomedical field as a drug carrier and delivery and RNA release in cancer therapy.[17]

3. Carbon-based NPs:

Carbon-based nanoparticles include two main materials, namely, carbon nanotubes (CNTs) and fullerenes. CNTs are nothing but graphene sheets rolled into a tube. These materials are mainly used for the structural reinforcement as they are 100 times stronger than steel. CNTs can be classified into singlewalled carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs).[25] CNTs are unique in a way as they are thermally conductive along the length and non-conductive across the tube. Fullerenes are the allotropes of carbon having a structure of hollow cage of sixty or more carbon atoms. The structure of C-60 is called Buckminsterfullerene, and looks like a hollow football. The carbon units in these structures have a pentagonal and hexagonal arrangement. [6] These have commercial applications due to their electrical conductivity, structure, high strength, and electron affinity. The rolled sheets can be single, double or many walls and therefore they are named as single-walled (SWNTs), double-walled (DWNTs) or multi-walled carbon nanotubes (MWNTs), respectively. They are widely synthesized by deposition of carbon precursors especially the atomic carbons, vaporized from graphite by laser or by electric arc on to metal particles. Lately, they have been synthesized via chemical vapor deposition (CVD) technique. Due to their unique physical, chemical and mechanical characteristics, these materials are not only used in pristine form but also in nano-composites for many commercial applications such as fillers, efficient gas adsorbents for environmental remediation and as support medium for different inorganic and organic catalysts. [7]

Metal NPs

Metal NPs are purely made of the metals precursors. Due to well-known localized surface plasmon resonance (LSPR) characteristics, these NPs possess unique optoelectrical properties.NPs of the alkali and noble metals i.e. Cu, Ag and Au have abroad absorption band in the visible zone of the electromagnetic solar spectrum. The facet, size and shape controlled synthesis of metal NPs is important in present day cutting-edge materials. Due to their advanced optical properties, metal NPs find applications in many research areas. Gold NPs coating is widely used for the sampling of SEM, to enhance the electronic stream, which helps in obtaining high quality SEM images. There are many other applications, which are deeply discussed in applications section of this review.[21]

Ceramics NPs

Ceramics NPs are inorganic nonmetallic solids, synthesized via heat and successive cooling. They can be found in amorphous, polycrystalline, dense, porous or hollow forms. Therefore, these NPs are getting great attention of researchers due to their use in applications such as catalysis, photocatalysis, photodegradation of dyes, and imaging applications.[22]

Semiconductor NPs

Semiconductor materials possess properties between metals and nonmetals and therefore they found various applications in the literature due to this property. Semiconductor NPs possess wide bandgaps and therefore showed significant alteration in their properties with

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bandgap tuning.[23] Therefore, they are very important materials in photocatalysis, photo optics and electronic devices As an example, variety of semiconductor NPs are found exceptionally efficient in water splitting applications, due to their suitable bandgap and bandedge positions.[22]

Polymeric NPs

These are normally organic based NPs and in the literature a special term polymer nanoparticle (PNP) collective used for it. They are mostly nanospheres or nanocapsular shaped The former are matrix particles whose overall mass is generally solid and the other molecules are adsorbed at the outer boundary of the spherical surface. In the latter case the solid mass is encapsulated within the particle completely. The PNPs are readilyfunctionalize and thus find bundles of applications in the literature. [27]

PREPARATION OF NANOPARTICLES

For the preparation of nanoparticles,the selection of the appropriate method is based on the drug to be loaded and physicochemical properties of the polymer. The primary preparation methods of nanoparticles includes:

Double Emulsion and Evaporation Method

Poor entrapment of hydrophilic drugs is the main drawback of this method.Therefore to encapsulate hydrophilic drug the double emulsion technique is engaged, inwhich aqueous drug solutions is added to organic polymer solution with vigorous form w/o emulsions. With continuous stirring to form mixed emulsion (w/o/w), this w/o emulsion is added into another aqueous phase. Then by the evaporation solvent is removed and by centrifugation at high speed nano particles can be isolated. Before lyophilisation the prepared nanoparticles must be washed.[27] The variables used in this method are;incorporated quantity of hydrophilic drug, the amount of polymer, the volume of aqueous phase andthe stabilizer concentration. The characterization of nano particles also affected by these variables.[24]

Salting Out Method

By using salting-out from aqueous solution the water-miscible solvent is separated using this method.[29] Initially in a solvent, polymer and drug are dissolved which is consequently containing the saltingout agent (electrolytes, such as calcium chloride and magnesium chloride or sucrose as non-electrolytes) and polyvinylpyrrolidone(PVP) or hydroxyethylcellulose as a colloidal stabilizer into an aqueous gel increase the diffusion of solvent,which indicates the formation of nanospheres. Several parameters such as electrolyte concentration, concentration of polymers in the organic phase, type of stabilizer, stirring rate, internal/external phase ratio can be varied. [25] This technique leads to high efficiency and easily scaled up in the preparation of Ethyl cellulose, PLA and Poly(methacrylic) acids nanospheres. [30,31] Salting out may be useful for heat sensitive substances because an areemulsified.This oil in water emulsion is diluted with water or with an aqueous phase to increase of temperature does not require in this technique. An exclusive application to lipophilic drug and the extensive nanoparticles washing steps are the drawbacks of this method.

Emulsions Diffusion Method

To prepare nanoparticles, emulsions diffusion method is another method which iscommonly used. The encapsulating polymer is dissolvedin a solvent which is partially miscible with water such as propylene carbonate, benzyl alcohol and the initial thermodynamic equilibrium of both liquids saturated with water should be ensured. Subsequently, The polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and according to the oil-topolymer ratio nanospheres or nanocapsules are formed. Finally, according to boiling point the solvent is removed by evaporation or filtration. This technique has several advantages, such as high reproducibility (batch-to-batch), no requirement of homogenization, high encapsulation efficiencies (generally 70%),simplicity, narrow size distribution and ease of scale-up. But some drawbacks of this method are: the high volumes of water to be eliminated from the suspension and reduced encapsulation efficiencyduring emulsification becausein the saturated-aqueous external phase leakage of watersoluble drug. [31] Examples of some drug- loaded nano particles which were produced by this technique; cyclosporine (cy-A-); loaded sodium glycolate nanoparticles [30], mesotetra (hydroxyphenyl) porphyrin-loaded PLGA (p-THPP) nano particles[31]and nano particles of doxorubicin-loaded PLGA

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Solvent Displacement/Precipitation method

Solvent displacement includes from an organic solution, the precipitation of a preformed polymer and in the aqueous medium the diffusion of the organic solvent in the presence or absence of surfactant. In a semi-polar water miscible solvent such as acetone or ethanol, polymers, drug and lipophilic surfactant are dissolved. Then solution is poured or injected using the magnetic stirring, into stabilizer containing aqueous solution. By the rapid solvent diffusion nano particles are formed. Then under reduced pressure solvent is removed from the suspension. The particles size is also affected by rate of addition of the organic phase into the aqueous phase. It was observed that by increasing the rate of mixing, both particles size and drug entrapment decreases. [30] For most of the poorly soluble drugs nano precipitation method is well suited. By adjusting preparation parameters; nanosphere size, and drug release can be controlled effectively. While adjusting concentration of polymer results in good production of smaller sized nanospheres.

Polymerization method

In this method, polymerization of monomers is done in an aqueous solution andafter polymerization completed, drug is incorporated either by adsorption onto the nanoparticles or by being dissolved in the polymerization medium. To remove various stabilizers and surfactants, employed for polymerization by ultra centrifugation the nanoparticle suspension is then purified and in an isotonic surfactant-free medium re-suspending the particles. For making polybutyl cyanoacrylate or poly(alkylcyano acrylate) nanoparticles, this technique has been reported. [7] Formation of nanocapsule and their particle size affected by the surfactants and stabilizers concentration used.

Coacervation or ionic gelation method

On the preparation of nanoparticles much research has been focused using biodegradable hydrophilic polymers such as chitosan, sodium alginate and gelatin. A method for preparing hydrophilic chitosan nanoparticles by ionic gelation developed by Calvo and co-workers.39,40 The method contains two aqueousphases, in which one is the polymer chitosan and the other phase is a polyanioni.e. sodium tripolyphosphate In this method, interaction of positively charged amino group of chitosan with negative charged tri polyphosphate occurs which form coacervates with an anometer size range. Electrostatic interaction between two aqueous phases results in the formation of coacervates, while ionic interaction conditions at room temperature results in transition from liquid to gel due to ionic gelation.[26]

Drug	Company	Application	Date of first approval
Lipid-based			
Doxil	Janssen	Kaposi`s sarcoma, ovarian cancer, multiple myeloma	1995
DaunoXome	Galen	Kaposi`s sarcoma	1996
AmBisome	Gilead Sciences	Fungal/protozoal infection	1997
Visudyne	Bausch and Lomb	wet age-related macular degeneration, myopia, ocular histoplasmosis	2000
Marqibo	Acrotech Biopharma	Acute lymphoblastic leukimia	2012
Onivyde	Ipsen	Metastatic pancreatic cancer	2015
Vyxeos	Jazz Pharmaceutical	acute myelyd leukaemia	2017
Onpattro	Alnylam Pharmaceutical	Transthyretin-mediated amyloidosis	2018
Polymer-Based			
Oncasper	Servier Pharmaceutical	Acute lymphoblastic leukimia	1994
Copaxone	Teva	Multiple sclerosisi	1996
Peglntro	Merck	Hepatitis C Infection	2001

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Eligard	Tolmar	Prostate Cancer	2002
Neulasta	Amgen	Neutropenia, chemotherapy induced	2002
Abraxane	Celgene	Lung cancer, metastatic breast cancer, metastatic pancreatic cancer	2005
Cimiza	UCB	Crohn`s disease, rheumatoid arthritis, psoriantic arthritis, ankylosing spondylitis	2008
Plegridy	Biogen	Multiple sclerosisi	2014
ADYNOVATE	Takeda	Heaemophilia	2015
Ingorganic			1992
INFeD	Allergan	Iron-deficient anaemia	
DexFerrum	Amirican Regent	Iron-deficient anaemia	1996
Ferrlecit	Sanofi	Iron-deficiency in chronic kidney disease	1999
Venofer	American Regent	Iron-deficiency in chronic kidney disease	2000
Feraheme	AMAG	Iron-deficiency in chronic kidney disease	2009
Injectafer	American Regent	Iron-deficient anaemia	2013

Application of Nanoparticles

Nanomedicine has incredible prospects for the improvement of the diagnosis and treatment of human diseases. An environmentally acceptable procedure for the biosynthesis of nanoparticles is the use of microbes. To revolutionize a wide array of tools in biotechnology nanotechnology has potential so that they are more cheaper, personalized, safer, portable and easier to administer.[25]

III. CONCLUSION

Due to their incredible properties, nanoparticles have become significant in many fields in recent years such as energy, healthcare, environment, agriculture etc. Nanoparticle technologies have great potentials, being able to convert poorly soluble, poorly absorbed and labile biologically active substance.

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