International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 462-467 www.ijprajournal.com ISSN: 2249-7781

Nanoparticles: An Overview of Their Types, Preparation And Application

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Submitted: 15-01-2022 Accepted: 27-01-2022

ABSTRACT: Nanoparticles are solid colloidal particles the size of the particles ranges from 10 to 1000nm in which the active ingredient (drug) is dissolved, entrapped, encapsulated and or to which the active principle is absorbed or attached. Nanoparticles are classified into one dimension, two dimensions, three dimension. The nanoparticles show the enhanced properties such as strength, surface area, sensitivity, stability,efficacy etc. because the particle are smaller in size. Nanoparticles have their unique properties when compared to micro particles and macro particles. The nanoparticles are prepared by i) Ionotropic gelation Method ii) Micro emulsion iii) Emulsification solvent diffusion iv) Polyelectrolyte complex. Different types of nanoparticulate materials were used in electronics, pharmaceuticals, cosmetics, catalytic and materials industries. In this review the methods of preparation of nanoparticles and their applications has been discussed.

KEY WORDS: Nano particles, Micro particles, Bio availability, Efficacy

INTRODUCTION:

Nanotechnology plays a important role, especially in drug delivery system (1), Their nanosized particles have a high surface area to a volume ratio which helps to penetrate the cells more rapadily and gives more efficacy, whem compared to micro sized particles(2,3). It has immense applications in all the fields of science and human life(1). Nanoparticles represent a promising controlled and targeted drug delivery system. They are especially designed to release the drugs to a target site. Nanoparticles are solid colloidal particles the size of the particles ranges from 10 to 1000nm in which the active ingredient (drug or biologically active material) is dissolved, entrapped, encapsulated and or to which the active principle is absorbed or attached(1). Nanoparticles had been used as a physical approach to adjust and enhance the pharmacokinetic and pharmacodynamics effects for several types of drug molecules(4,5).

The Particulate drug carriers are, nano carriers, lipid based carriers, Micro particulate and colloidal carriers.

1. It has Better drug delivery system to a certain impermeable sites of body
2. Owing to their small size, these carriers have better bridged the gaps between the structure and function of bio-molecules.
3. Reaching the micron or nano range with these particles enables them to be highly potential carriers in many biological molecules as proteins. e.g. DNA.
4. Site specific target.
5. Targeted drug carriers reduce drug toxicity and provide more efficient drug distribution.

ADVANTAGES AND FEATURES OF NANOPARTICLES

- Nano particles have Increased bioavailability.
- Dose proportionality.
- Decreased toxicity.
- Smaller dosage form (i.e., smaller tablet)
- Stable dosage forms of drugs which are either unstable or have unacceptably low bioavailability in non-nanoparticulate dosage forms.
- Increase in surface area of active ingredient results in a faster the dissolution of an active ingredient in an aqueous environment, such as the human body.
- Faster dissolution shows the greater bioavailability, less toxicity.
- Controlled rate of drug release.
- Greater patient convenience and/ or better patient compliance.
- Easy handling of nanoparticles prepared in the powder form (6).

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LIMITATIONS OF NANOPARTICLES

- Drug carrier's exhibits difficulty in handling, storage, and administration because of susceptibility to aggregation.
- Nano particles are not suitable for less potent drugs.
- It can cross the nuclear envelope of the cell and it cause unintended genetic damage and mutation.

CLASSIFICATION OF NANOPARTICLES

1**) ONE DIMENSION**
2) TWO DIMENSIONS
3) THREE DIMENSION

1) ONE DIMENSION

One-dimensional systems such as thin films.

2) TWO DIMENSIONS

a) CARBON NANOTUBES

A Carbon nanotubes are a new form of carbon molecule. A wound in the hexagonal network of carbon atoms, these hollow cylinders have diameters as small as 0.7 nm and reach several millimeters in length. Each end can be opened or closed by a fullerene half-molecule. These nanotubes have a single layer or many layers (like a poster rolled in a tube) of co-axial cylinders of increasing diameters in a common axis.

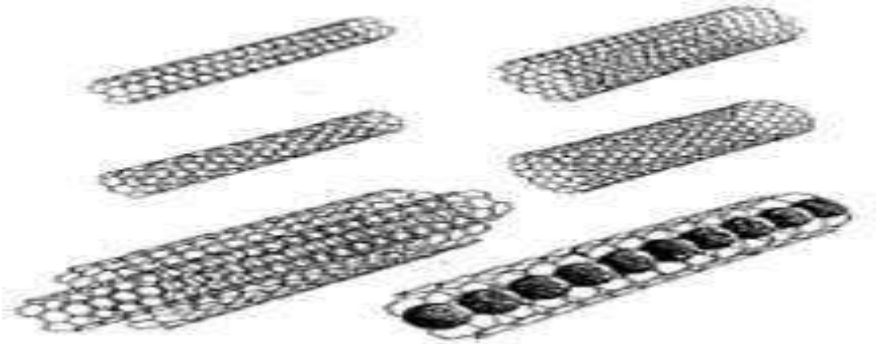

Fig:1:Schematic representation of monolayer or multilayer carbon nanotubes.

3) IN THREE DIMENSION

a) FULLERENCES (Carbon 60)

Fullerenes are spherical cages containing from 28 to more than 100 carbon atoms (see schematic representation opposite Fullerenes are a class of materials showing a unique physical properties). It can be subjected to extreme pressures and attains their original shape when the pressure is released from it. These molecules do not combine with each other, so giving them as major potential for application as lubricants.

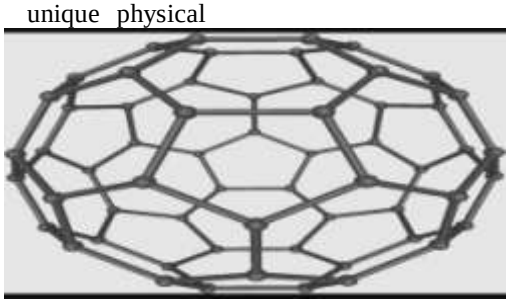

Fig:2:Schematic representation of Fullerenes

b) DENDRIMERS

A Dendrimers represent the new class of controlled-structure polymers with nanometric dimensions. They are considered to be basic elements for large-scale synthesis of organic and inorganic nanostructures with dimensions of 1 to 100 nm then showing a unique properties. It is Compatible with organic structures such as DNA, they can be fabricated to interact with metallic nanotubes and nanocrystals or to possess an encapsulation capacity

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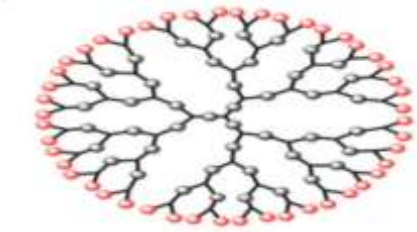

Fig:3:Schematic representation of Dendrimers

c) QUANTUM DOTS

It represents a special form of spherical nanocrystals,it has diameter. from 1 to 10 nm. They have been developed in the form of semiconductors, insulators, metals, magnetic materials or metallic oxides.

Parameters Influence Effectiveness Of Nanoparticles Formulation

- Drug incorporation and desired release
- Improved formulation stability and shelf life
- High drug loading capacity
- Effective bio-distribution and targeting
- Compatibility of the carrier less bio-accumulation & desired degradation rate.
- Less acute and chronic toxicity
- Acceptable scaling up of production

POLYMERS USED IN PREPARATION OF NANOPARTICLES

The naturals and synthetic source of polymers have been used. Polymer based systems in the submicron size range include water soluble polymer, drug conjugates, polymer nano-capsules and nano-spheres. A certain advantage of polymer systems is the wealth of possible chemical modifications, including the synthesis of block and combination of polymers.

Water soluble polymers offer mild and simple preparation methods without the use of organic solvent and high shear force. The water soluble polymers are available example; chitosan is the one of the most extensively studied. This is because chitosan posses some ideal properties of polymeric carriers for nanoparticles such as biocompatible biodegradable, nontoxic and inexpensive. Furthermore

It posses positively charge and exhibits absorption enhancing effect. These properties render chitosan a very attractive material as a drug delivery carrier. In the last two decades, Chitosan nanoparticles have been extensively developed and explored for pharmaceutical application

Formulation Aspects Of Nanoparticles

The nanoparticles are prepared by following techniques5

i) Ionotropic gelation Method
ii) Micro emulsion
iii) Emulsification solvent diffusion
iv) Polyelectrolyte complex

1) Ionotropic gelation method

Chitosan NP prepared by Ionotropic gelation technique was first reported by Calvo et al and has been widely examined and developed. The mechanism of chitosan NP formation is based on electrostatic interaction between amine group of chitosan and negatively charge group of polyanion such as tripolyphosphate. This technique offers a simple and mild preparation method in the aqueous environment. First, chitosan can be dissolved in acetic acid in the absence or presence of stabilizing agent, such as poloxamer, which can be added in the chitosan solution before or after the addition of polyanion. Polyanion or anionic polymers was then added and nanoparticles were spontaneously formed under mechanical stirring at room temperature. The size and surface charge of particles can be modified by varying the ratio of chitosan and stabilizer.

ii) Micro emulsion method

Chitosan NP prepared by micro emulsion technique was first developed by Maitra et al. This technique is based on formation of chitosan NP in the aqueous core of reverse micellar droplets and subsequently cross-linked through glutaraldehyde. In this method, a surfactant was dissolved in N-hexane. Then, chitosan in acetic solution and glutaraldehyde were added to surfactant/hexane mixture under continuous stirring at room temperature. Nanoparticles were formed in the presence of surfactant. The system was stirred overnight to complete the cross-linking process, which the free amine group of chitosan conjugates with glutaraldehyde. The organic solvent is then removed by evaporation under low pressure. The yields obtained were the cross-linked chitosan NP and excess surfactant. The excess surfactant was then removed by precipitate with CaCl2 and then

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the precipitant was removed by centrifugation. The final nanoparticles suspension was dialyzed before lyophilization. This technique offers a narrow size distribution of less than 100 nm and the particle size can be controlled by varying the amount of glutaraldehyde that alter the degree of cross-linking. Nevertheless, some disadvantages exist such as the use of organic solvent, time-consuming preparation process, and complexity in the washing step.

iii) Emulsification solvent diffusion method

This method is based on the partial miscibility of an organic solvent with water. An o/w emulsion is obtained upon injection an organic phase into chitosan solution containing a stabilizing agent (i.e. poloxamer) under mechanical stirring, followed by high pressure homogenization (7). The emulsion is then diluted with a large amount of water to overcome organic solvent miscibility in water. Polymer precipitation occurs as a result of the diffusion of organic solvent into water, leading to the formation of nanoparticles. This method is suitable for hydrophobic drug and showed high percentage of drug entrapment. The major drawbacks of this method include harsh processing conditions (e.g., the use of organic solvents) and the high shear forces used during nanoparticles preparation.

iv) Polyelectrolyte complex (PEC) formation

Polyelectrolyte complex or self assemble polyelectrolyte is a term to describe complexes formed by self-assembly of the cationic charged polymer and plasmid DNA. Mechanism of PEC formation involves charge neutralization between cationic polymer and DNA leading to a fall in hydrophilicity. Several cationic polymers (i.e. gelatin, polyethylenimine) also possess this property. Generally, this technique offers simple and mild preparation method without harsh conditions involved. The nanoparticles spontaneously formed after addition of DNA solution into chitosan dissolved in acetic acid solution, under mechanical stirring at or under room temperature. The complexes size can be varied from 50 nm to 700 nm.

Characterization Of Nanoparticles

- Physicochemical characterization
- Drug loading analysis
- drug release
- degradation of nanoparticles

PHYSICOCHEMICAL CHARACTERIZATION:

Nano particles can evaluated by physicochemical and chemical methods, which are exist for the characterization of nanoparticles(8,9).The methods are listed in Table

Physiochemical Methods of Nanoparticles

PARAMETERS	CHARACTERIZATION METHODS
Particle size & size distribution	photon correlation spectroscopy, Scanning electron microscopy (SEM), Transmission electron microscopy (TEM), Atomic force microscopy (AFM), Mercury porositometry, Laser defractrometry
Charge determination	Laser droplet anemometry, Zeta potentiometer
Surface hydrophobicity	Water contact angle measurements, rose bangle (dye) binding, hydrophobic interaction chromatography, X-ray photoelectron spectroscopy
Chemical analysis of surface	Static secondary ion mass spectrometry, sorptometer
Carrier drug interaction	Differential scanning calorimetry
Nanoparticle dispersion stability	Critical flocculation temperature(CFT)
Release profile	In-vitro release characteristic under physiologic & sink condition
Drug stability	Bioassay of drug extracted from nanoparticle, chemical analysis of drug
Crystalinity	Differential scanning calorimetry, X – ray diffraction
Molecular weight	Gel chromatrography
Density	Helium compression pycnometry

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Size is the most prominent of nanoparticles. However, other parameters such as density, molecular weight and crystallinity will largely influence their release and degradation properties. whereas surface characteristics such as surface charge and hydrophillicity or hydrophobicity will significantly influence the interaction with the biological environment after administration to human and animals and thus will influence the resulting body distribution (10).

DRUG LOADING ANALYSIS

Drug may be loaded by addition prior to the preparation of nanoparticles or by addition to previously prepared. The drug exists in one or more of the following forms13.

- A solid solution of the drug in the polymer
- A solid dispersion of the drug in the polymer
- Surface adsorption of the drug
- Chemical binding of the drug to the polymer.

NANOPARTICLES DEGRADATION

Nanoparticles due to their small size degrade faster than larger microspheres. The degradation of poly (alkyl cyanoacrylate) exists in two degradation pathways. One pathway is degradation by erosion of the polymer backbone under formation of formaldehyde. The second pathway is cleavage of the ester under formation of a soluble polymer acid. Some types of nanoparticles may degrade in a different manner. Polylactic acid nanoparticles, hydrolysis result in the erosion of the polyester backbone. Human serum albumin nanoparticles of a mean size of 1.45 nm definitely degrade from the center after their phagocytosis by human macrophages. The degradation is mostly terminated after about 3 – 4 days, only small number of intact nanoparticle fragments was found in the cytoplasm of the cells after 7 days14, 15.

DRUG RELEASE

Nanoparticles exhibit their special drug delivery effects in most cases by direct interaction with their environment (Biological environment). Drug from the nanoparticles is released by one or more following mechanism.

Desorption of surface bound drug

- Diffusion through the nanoparticles matrix
- Diffusion through the polymer wall (in case of nanocapsules)
- Nanoparticles matrix erosion
- A combined erosion diffusion process.

The release mechanism based on diffusion coefficient and the biodegradation rate are the main factors governing the drug release rate. The release rate of drugs from nanoparticles is also strongly influenced by the biological environment. The following methods have been used for the determination of in- vitro study(11,12)

- Dialysis bag diffusion technique.
- Reverse dialysis sac technique.
- Ultra centrifugation.
- Ultra filtration
- Centrifugal ultra filtration technique

APPLICATION OF NANOPARTICLES

Applications of nanotechnology in the different field can be summarized as follows:

1) Nanomedicnes medical devices, tissue engineering, for sustained ocular delivery etc.

2) Chemicals and cosmetics: nanoscale chemicals and compounds, paints, coating, etc.

3) Materials: nanoparticles, carbon nanotubes, biopolymers, paints, coating

4) Food science: processing, nutraceuticals food, nanocapsules ,

5) Environment and energy: water and air purification filters, fuel cells.

6) The thermo sensitive nanoparticles may be used for selective release of the content after specific localization like photodynamic therapy e.g.: doxorubicin nanoparticles

7) Industrially feasible multifunctional formulation technology for poorly soluble actives(13,14).

8) The self-assembling nanoparticles for paclitaxel delivery in ovarian cancer. PTX loaded nanoparticles had prolonged circulation time and accumulated preferentially in ovarian tumors via EPR effects, which resulted in enhanced therapeutic efficacy with better safety profiles in our subcutaneous and orthotropic ovarian cancer.

9) Ceramic based nanoparticles for entrapping therapeutic agents for photodynamic therapy. In this method the photosensitive drug/dye is entrapped with ceramic carrier. This ceramic nanoparticles widely used for skin and site specific therapeutic purpose (15,16)

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