Review Article

Review on Nanoparticle Drug Delivery System

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ABSTRACT

The most emerging branch in pharmaceutical sciences known as "Pharmaceutical nanotechnology."Nanoparticles are sub-nanosized colloidal structures composed of synthetic or semi-synthetic polymers. Their size ranges from 10–1000 nm. In which the drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Drugs that are transformed in to nano range offer some unique features which can lead to prolonged circulation, improved drug localization, enhanced drug efficacy. Various pharmaceutical nanotechnology based systems which can be termed as nanopharmaceuticals like polymeric nanoparticles, magnetic nanoparticles, liposomes, carbon nanotubes, quantum dots, dendrimers, metallic nanoparticles, polymeric nanoparticles, etc. Recently particulate systems like nanoparticles have been used as a physical approach to alter and improve the pharmacokinetic and pharmacodynamics properties of various types of drug molecules Nanotechnology is therefore emerging as a field in medicine that is expected to elicit significant therapeutic benefits.

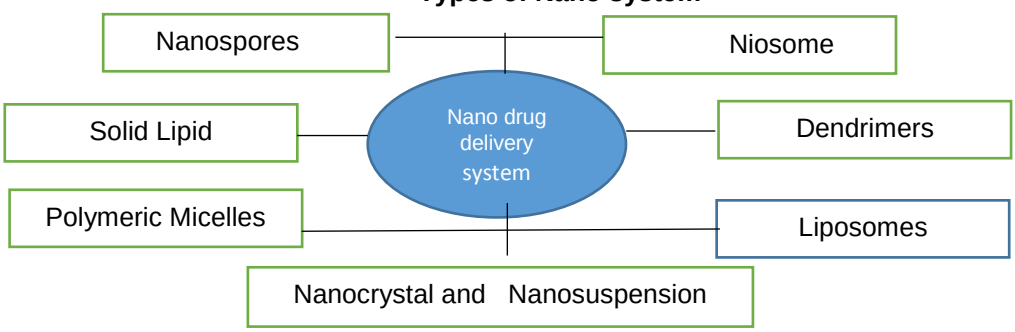
Keywords: Nanoparticle, Nonotechnology, Nanocarriers.

INTRODUCTION

Nanotechnology is the science of material featuring between 10 −9 and 10 −7 of a meter[1]. Or in another words it's the science of materials and devices whose structures and constituents demonstrate novel and considerably altered physical, chemical and biological phenomenon due to their nanoscale size.

Nanoparticles are sub-nanosized colloidal structures composed of synthetic or semi-synthetic polymers. Size ranges from 10–1000 nm.The drug is dissolved, entrapped, encapsulated or attached to a nanoparticle matrix. Nanotechnology employs knowledge from the fields of physics, chemistry, biology, materials science, health sciences, and engineering. Depending upon to 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 carrier of DNA in gene therapy, and their ability to deliver proteins, peptides and genes.

Types of Nano system



1. Niosome

Niosome is a class of molecular cluster formed by self-association of non-ionic surfactants in an aqueous phase. The unique structure of niosome presents an effective novel drug delivery system (NDDS) with ability of loading both hydrophilic and lipophilic drugs. Niosomes are vesicles composed of non-ionic surfactants, which are biodegradable, relatively nontoxic, more stable and inexpensive, an alternative to liposomes. Niosomes behave in vivo like liposomes, prolonging the circulation of entrapped drug and altering its organ distribution and metabolic stability. As with liposomes, the properties of niosomes depend on the composition of the bilayer as well as method of their production. It is reported that the intercalation of cholesterol in the bilayers decreases the entrapment volume during formulation, and thus entrapment efficiency.

2. Dendrimers

Dendrimers are a unique class of polymers, are hyper branched, tree-like structures, whose size and shape can be precisely controlled and have compartmentalized chemical polymer. Dendrimers are fabricated from monomers using either convergent or divergent step growth polymerization. Size of these regular branching polymeric nanostructures is dependent on the number of branching which can be controlled. These nanostructures arise several branches from the core in shape of a spherical structure by means of polymerization, resulting in formation of cavities 2 Nanoparticles Types, Classification, Characterization, Fabrication Methods within the dendrimer molecule which can be used for drug transport. Free ends of dendrimer can be utilized for conjugation or attachment to other molecule. These end groups that can be tailored according to requirements. Such interconnecting networks transport the attached molecules at desirable site and give dendrimers various functional applications[13].

3. Nanopores

Nanopores were designed in 1977, consist of wafers with highly dense pore of size 20 nm (diameter). Main advantage of these nanopores that they doesn't allow the entry of oxygen glucose and other products. They can be potentially utilized to protect transplanted tissues from the host immune system.

4. Nanocrystals and Nanosuspension

These are aggregated structures that are formed by the combination of various particles of drug in crystalline form coated with surfactant or combination of surfactants. To achieve static and electrostatic surface stabilization a minimum quantity of surfactants needs to be added in nanocrystals. These aggregated forms reduce limitations of several drugs that are suffering from bioavailability and absorption problems. In addition problems of preparing the parenteral dosage form may be resolved by formulation as nanocrystals. Loading capacity especially in carrier-based nanoparticles is quite low however administration of high drug levels with depot release can be achieved if dissolution is sufficiently slow. Nanocrystal technology can be utilized for many dosage forms.

5. Solid Lipid Nanoparticles

Solid lipid nanoparticles were developed as an alternative carrier system to liposomes, polymeric nanoparticles and emulsions as a colloidal carrier system for controlled drug delivery. Solid lipid nanoparticles carry distinct advantages that make them unique carriers systems than others like liposomes and polymeric nanoparticles. This type of nanoparticles constitute solid lipid matrix with an average diameter below 1µm. Drug is normally incorporated in this matrix. These nanoparticles can also be produced by high pressure homogenization. Different surfactants are used to avoid aggregation and to stabilize the dispersion. These surfactants have an accepted GRAS (Generally Recognized as Safe) status.

6. Liposomes

Liposomes are lipid based vesicles that are extensively explored and most developed nanocarriers for novel and targeted drug delivery. Drugs that can deliver through liposomal delivery system are highlighted in. These vesicles are synthesized by hydration of dry phospholipids. Depending upon on their size and number of bilayers they are classified into three basic types:

• Multilamellar vesicles

These vesicles consist of several lipid bilayers separated from one another by aqueous spaces. These entities are heterogeneous in size, often ranging from a few hundreds to thousands of nanometers in diameter.

• Small unilamellar vesicles
Small unilamellar vesicles consist of a single bilayer surrounding the entrapped aqueous space having size range less than 100 nm.

• Large unilamellar vesicles
These vesicles consist of a single bilayer surrounding the entrapped aqueous space having diameters larger than 100 nm.

7. Polymeric Micelles
Polymeric micelles contains ampiphilic block copolymers assemble to form nanoscopic supramolecular core-shell structures called as 'polymeric micelles'. These micelles are formed in solution as aggregates in which the component molecules are generally arranged in a spheroidal structure with hydrophobic cores shielded from water by a mantle of hydrophilic groups. There are several examples of component molecule such as Amphiphilic AB-type or ABA-type block copolymers, where A and B are hydrophobic and Hydrophilic components, respectively. These polymeric micelles are usually <100 nm and are used for the systemic delivery of water-insoluble drugs. Their hydrophilic surface of these dynamic systems protects their nonspecifi c uptake by reticuloendothelial system.

Preparation of Nanoparticle and factor affecting nanoparticle
The selection of appropriate method for the preparation of nanoparticles depends on the physicochemical character of the polymer and the drug to be loaded. Nanoparticles can be prepared from a variety of materials such as proteins, polysaccharides and synthetic polymers. The selection of matrix materials is dependent on many factors including[2]

- Antigenicity of the final product.
- Biocompatibility and toxicity
- Degree of biodegradability
- Drug release profile desired
- Inherent properties of the drug (aqueous solubility and stability)
- Size of nanoparticles required
- Surface characteristics (charge and permeability)
- Nanoparticles have been usually prepared by three methods:
- Dispersion of preformed polymers
- Ionic gelation or coacervation of hydrophilic polymers
- Polymerization of monomers

Method for preparation of nanoparticles
1. Solvent Evaporation Method
2. Solvent Diffusion Method
3. Double Emulsion Method
4. Salting Out Method
5. Emulsion Diffusion Method
6. Solvent displacement Method
7. Coacervation method
8. Polymerization Method
9. Super critical Fluid Technique

1. Solvent Evaporation Method
Solvent evaporation method is one of the most frequently used methods for the preparation of nanoparticles. This method involves two steps (first is emulsification of the polymer solution into an aqueous phase and second is evaporation of polymer solvent, inducing polymer precipitation as nanospheres). This method is based on the solubility of polymer and hydrophobic drug since both polymer and hydrophobic drug are dissolved in an organic solvent (dichloromethane, chloroform or ethyl acetate) which is also used as the solvent for dissolving the. Mixture obtained from polymer and drug solution is then emulsified in an aqueous solution. This aqueous solution contains surfactant or emulsifying agent to form oil in water (o/w) emulsion. Once the stable emulsion forms, the organic solvent is evaporated either by continuous stirring or by reducing the pressure. Size range of nanoparticles was found to be influenced by the concentrations and type of stabilizer, polymer concentration and homogenizer speed[3].

2. Solvent Diffusion Method
This method is developed from solvent evaporation method in which the water miscible solvent along with a small amount of the organic solvent (water immiscible) is used as an oil phase. During the spontaneous diffusion of solvents between the two phases an interfacial turbulence is generated which may ultimately leads to the formation of small particles. Smaller particle size can be achieved by increasing the concentration of water miscible solvent increases. This method 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.

3. Double Emulsion method
Most of the emulsion and evaporation based methods suffer from the limitation of poor

entrapment of hydrophilic drugs. Therefore to encapsulate hydrophilic drug the double emulsion technique is employed, which involves the addition of aqueous drug solutions to organic polymer solution under vigorous stirring to form w/o emulsions. This w/o emulsion is added into second aqueous phase with continuous stirring to form the w/o/w emulsion. The emulsion then subjected to solvent removal by evaporation and nano particles can be isolated by centrifugation at high speed. The formed nanoparticles must be thoroughly washed before lyophilisation[5]. In this method the amount of hydrophilic drug to be incorporated, the concentration of stabilizer used, the polymer concentration, the volume of aqueous phase are the variables that affect the characterization of nanoparticles[5,6].

4. Salting Out Method

Method involves the separation of a water-miscible solvent from aqueous solution via a salting-out effect[7]. It's based on the on the separation of a water miscible solvent from aqueous solution via a salting-out effect. During the initial process polymer and drug are dissolved in a solvent which is subsequently emulsified into an aqueous gel containing the salting out agent and a colloidal stabilizer. Various types of salting out agents (electrolytes, such as magnesium chloride and calcium chloride, or non- electrolytes such as sucrose) and colloidal stabilizer (such as polyvinylpyrrolidone or hydroxyethylcellulose) have been used.

5. Emulsions-Diffusion Method

This is another widely used method to prepare nanoparticles. The encapsulating polymer is dissolved in a partially water-miscible solvent (such as propylene carbonate, benzyl alcohol), and saturated with water to ensure the initial thermodynamic equilibrium of both liquids. Subsequently, the polymer-water saturated solvent phase is emulsified in an aqueous solution containing stabilizer, leading to solvent diffusion to the external phase and the formation of nanospheres or nanocapsules, according to the oil-to-polymer ratio. Finally, the solvent is eliminated by evaporation or filtration, according to its boiling point. This technique presents several advantages, such as high encapsulation efficiencies (generally 70 %), no need for homogenization, high batch-to-batch reproducibility, ease of scale up, simplicity, and narrow size distribution.

6. Solvent Displacement/Precipitation Method

In this method preformed polymer is precipitated in an organic solution and organic solvent is diffused in the aqueous medium. Diffusion of organic solvent can be achieved in the presence or absence of surfactant. Semi polar water miscible solvent such as acetone or ethanol can be used to dissolve the polymers, drug, and or lipophilic surfactant. After their complete dissolution, solution is then poured or injected into an aqueous solution containing stabilizer under magnetic stirring. Nano particles are formed immediately by the rapid solvent diffusion. This step is followed by the removal of solvent from the suspensions under reduced pressure.[8]

7. Coacervation method

In this method two different aqueous phases are prepared for polymer [chitosan, a di-block co-polymer ethylene oxide or propylene oxide (PEO-PPO)] and the other is for polyanion sodium tripolyphosphate. This method is based on the strong electrostatic interaction between positively charged amino group of chitosan and negative charged tripolyphosphate to form coacervates with a size in the range of nanometer. Existence of strong electrostatic interaction between two aqueous phases leads to the formation of coacervates.[9]

8. Polymerization Method

This method involves polymerization of monomers to form nanoparticles in an aqueous solution. In polymerization drug is incorporated at two different stages (either by being dissolved in the polymerization medium or by adsorption onto the nanoparticles after polymerization completed)[10 , 11]. Ultracentrifugation can be used to purify nanoparticle suspension by removing various stabilizers and surfactants employed for polymerization, followed by the re-suspension of particles in an isotonic surfactant-free medium. This technique is reported for making poly (alkylcyanoacrylate) or polybutylcyanoacrylate nanoparticles. Desirable size of nanocapsule can be achieved by optimization of concentration of the surfactants and stabilizers[12].

9. Super Critical Fluid Method

In former process a liquid solvent (methanol) is selected on the basis of it's completely miscibility with the supercritical fluid (SC CO2). This is done to dissolve the solute to be

micronized at the process conditions. Since 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, results in the formation of nanoparticles.

Advantages

- Decreased patient-to-patient variability
- Enhanced solubility
- Increased oral bioavailability
- Increased rate of dissolution
- Increased surface area
- Less amount of dose required
- More rapid onset of therapeutic action

Disadvantages

- Small size & large surface area can lead to particle aggregation.
- Physical handling of nano particles is difficult in liquid and dry forms.
- Limited drug loading.
- Toxic metabolites may form.

Characterization of Nanoparticle[15-17]

1. Particle size
   Photon correlation spectrosc
   Laser diffractrometry
   Electron microscopy
2. Density
   Helium or air using a gas pycnometer
3. Molecular weight
   - Gel permeation chromatography using refractive index detector.
4. Structure and crystallinity
   - X-ray diffraction
5. Specific surface area
   - Sorptometer
6. Surface charge & electronic mobility
   - Surface charge of particle can be determined by measuring particle velocity in electrical field.
   - Laser Doppler Anemometry tech. for determination of Nanoparticles velocities.
   - Zeta potential can also be obtain by measuring the electronic mobility
7. Surface hydrophobicity
   - Hydrophobic interaction chromatography.
   - Two phase partition.
8. Invitro release
9. Nanoparticle yield
10. Drug entrapment efficiency

CONCLUSION

Nanoparticles are one of the novel drug delivery systems, which can be of potential use in controlling and targeting drug delivery as well as in cosmetics textiles and paints. Judging by the current interest and previous successes, nanoparticulate drug delivery systems seems to be a viable and promising strategy for the biopharmaceutical industry.

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