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NANOPARTICLE FORMULATION - A NEW APPROACH TO ENHANCE DISSOLUTION & ORAL BIOAVAILABILITY OF POORLY SOLUBLE DRUGS

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Abstract: Main focus of this review study is that how nanoionization provides a new approach in pharmaceutical industry for dissolution and oral bioavailability of poorly soluble drugs by reducing drug particle size which ultimately increases surface area which leads fast dissolution and the bioavailability is enhances and drugs overdose and side effects are minimizes as small amount of drug is sufficient for better pharmacological activity.

Keywords: ***Nanoparticles, Dissolution, Bioavailability, Coacervation, polylactic acid***

INTRODUCTION

Nanoparticles are particles between 1 and 100 nanometres (nm) in size with a surrounding interfacial layer. The interfacial layer is an integral part of nanoscale matter, fundamentally affecting all of its properties. The interfacial layer typically consists of ions, inorganic and organic molecules. Organic molecules coating inorganic nanoparticles are known as stabilizers, capping and surface ligands. In nanotechnology, a particle is defined as a small object that behaves as a whole unit with respect to its transport and properties. 'Nano' is a prefix used to describe 'one billionth', or 10^{-9}, of something. The concept of nanotechnology was introduced by physics Nobel laureate Richard P Feynman. [1, 2, 3]

CLASSIFICATION OF NANOPARTICLES

There are various approaches for classification of nanomaterials. Nanoparticles are classified based on one, two and three dimension.

One dimension nanoparticles

One dimensional system, such as thin film or manufactured surfaces, has been used for decades in electronics, chemistry and engineering. Production of thin films (sizes1-100 nm) or monolayer is now common place in the field of solar cells or catalysis. These thin films are using in different technological applications, including information storage systems, chemical and biological sensors, fibre-optic systems, magneto-optic and optical device.

Two dimension nanoparticles

Carbon nanotubes (CNTs): Carbon nanotubes are hexagonal network of carbon atoms, 1 nm in diameter and 100 nm in length, as a layer of graphite rolled up into cylinder. CNTs are of two types,

- Single walled carbon nanotubes (SWCNTs)
- Multi-walled carbon nanotubes (MWCNTs)

Three dimension nanoparticles

Fullerenes (Carbon 60): Fullerenes are spherical cages containing from 28 to more than 100 carbon atoms, contain C60. This is a hollow ball composed of interconnected carbon pentagons and hexagons, resembling a soccer ball. [4]

PREPARATION OF NANOPARTICLES

Nanoparticles are 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:

(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

Nanoparticles preparation is most frequently by three methods:

(1) Dispersion of preformed polymers;

(2) Polymerization of monomers; and

(3) Ionic gelation or coacervation of hydrophilic polymers.

Methods like supercritical fluid technology also used now a days.

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).

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 ultrasonication may be employed.

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.

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 on to 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 (alkylcyanoacrylate) nanoparticles. [5]

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.

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), non toxicity, non flammability, and low price. The most common processing techniques involving supercritical fluids are supercritical anti solvent (SAS) and rapid expansion of critical solution (RESS). [6, 7]

EVALUATION OF NANOPARTICLES

✓ **Zeta potential**

The Zeta potential of a nanoparticle is commonly used to characterize 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.

✓ **Particle Shape**

SEM characterizes the nano suspension before going for evaluation; the nano suspension is lyophilized to form solid particles. The solid particles are coated with platinum alloy using a sputter coater.

✓ **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).

ADVANTAGES OF NANOPARTICLES

The advantages of using nanoparticles as a drug delivery system include the following:

- Particle size and surface characteristics of nanoparticles can be easily manipulated to achieve both passive and active drug targeting after parenteral administration.
- They control and sustain release of the drug during the transportation and at the site of localization, altering organ distribution of the drug and subsequent clearance of the drug so as to achieve increase in drug therapeutic efficacy and reduction in side effects.
- Site-specific targeting can be achieved by attaching targeting ligands to surface of particles or use of magnetic guidance.
- Controlled release and particle degradation characteristics can be readily modulated by the choice of matrix constituents. Drug loading is relatively high and drugs can be incorporated into the systems without any chemical reaction; this is an important factor for preserving the drug activity.

DISADVANTAGES OF NANOPARTICLES

- Small size and large surface area can lead to particle - particle aggregation, making physical handling of nanoparticles difficult in liquid and dry forms.
- In addition, small particles size and large surface area readily result in limited drug loading and burst release. These practical problems have to be overcome before nanoparticles can be used clinically or made commercially available.[1,2,8]

Nanoparticles Enhance Dissolution & Bioavailability of Poorly soluble drugs:

Nano technology in pharmaceutical industry is the latest technology which modifies physicochemical, micrometrics and biopharmaceutical properties of the poorly soluble drugs, thereby improving their solubility. Out of various techniques for solubility enhancement, physical modifications of drug products such as reducing the particle size and modifying crystal habit are common ways to increase drug solubility. Apart from conventional micronizing techniques, particle technology now deals with various particle and nanoparticle engineering processes as suitable methods of improving drug solubility. Poorly soluble drugs encounter biopharmaceutical delivery problems such as low bioavailability after oral administration, low penetration of the drug into the skin, large injection volume for intravenous (i.v.) administration and undesired side effects after i.v. injection when using traditional formulations. Drug nanoparticles possess outstanding features enabling to overcome the solubility problems including an increase in saturation solubility, an increase in dissolution velocity, and an increased adhesiveness to cell membrane. These features are resulted from transferring of particle size from macroparticle to nano dimension that changes their physicochemical properties on the basis of nanotechnology. [9, 10]

SUMMARY:

Nanoparticles are suitable for drugs that have poor solubility. Drug nanoparticles can be applied to all poorly soluble drugs to overcome their solubility and bioavailability problems. The decrease in particle size to nanometer range contributes to the increased particle surface, curvature, saturation solubility, dissolution velocity and further acceptable bioavailability. Many reports on drug nanoparticles within recent years exhibit excellent in vivo

performances of drug nanoparticles in different administration routes. In oral administration, drug nanoparticles offer great benefits of enhanced drug bioavailability allow the quickly absorption due to the fast dissolution that is suitable for the required fast onset drug. The increased solubility of drug nanoparticles also eliminates the food effect to drug absorption. Therefore, drug in nanoparticles formulations perform similar absorption in fed and fasted conditions. Another benefit of drug nanoparticles is that it can provide smaller dose administration to achieve moderate blood level and thus reduce the side effect from given larger dosage.

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