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REVIEW ON NANOSUSPENSION TECHNOLOGY

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ABSTRACT

Solubility is an essential factor for drug effectiveness, independent of the route of administration. Poorly soluble drugs are often a challenging task for formulators in the industry. Large proportions of newly discovered drugs are water insoluble, and therefore poorly bioavailable contributing to deserted development effort. Nanosuspension technology solved the problem of drugs which are poorly aqueous soluble and less bioavailability. Stability and bioavailability of the drugs can be improved by the Nanosuspension technology. Preparation of Nanosuspension is Simple and applicable to all drugs which are insoluble in water. Nanosuspensions are prepared by using wet mill, high pressure homogenizer, emulsion-solvent evaporation, melt emulsification method and super critical fluid techniques. Nanosuspensions can be delivered by oral, Parenteral, pulmonary and ocular routes. Nanosuspensions can also be used for targeted drug delivery when incorporated in the ocular inserts and mucoadhesive hydro gels.

Keywords: Nanosuspension, Solubility enhancement, Bioavailability.

INTRODUCTION

Nanosuspensions are colloidal dispersions of nanosized drug particles stabilized by surfactants. They can also be defined as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle in which the diameter of the suspended particle is less than 1μm in size. Reduction of drug particles to nanometer range leads to an enhanced dissolution rate not only because of increased surface area but also because of saturation solubility. The increase in the saturation solubility and solution velocity of Nanoparticle is due to increase of vapour pressure of the particles [1].

Preparation of nanosuspension

Preparation of Nanosuspensions were reported to be a more cost effective and technically more simpler alternative than liposomes and other conventional colloidal drug carriers, particularly for poorly soluble drugs and yield a physically more stable product.

Types of Nanosuspension Methods:

1. Precipitation:

The most common method of precipitation used is anti solvent addition method in which the drug is dissolved in an organic solvent and this solution is mixed with a miscible antisolvent. Mixing processes vary considerably. Precipitation has also been coupled with high shear processing [2].

2. Lipid Emulsion/Micro emulsion Template:

Lipid emulsions as templates are applicable for drugs that are soluble in either volatile organic solvents or partially water miscible solvents. In this method the drug will be dissolved in the suitable organic solvent and then emulsified in aqueous phase using suitable surfactants. Then the organic solvent will be slowly evaporated under reduced pressure to form drug particles precipitating in the aqueous phase forming the aqueous suspension of the drug in the required particle size [3].

3. High Pressure Homogenization:

It is the most widely used method for the preparation of the Nanosuspensions of many poorly water soluble drugs .The principle of this method is based on cavitation in the aqueous phase. The particles cavitations forces are sufficiently high to convert the drug micro particles into Nanoparticles. The concern with this method is the need for small sample particles before loading and the fact that many cycles of homogenization are required [4].

4. Milling Techniques:

a. Media milling:

In this technique, the Nanosuspensions are produced using high-shear media mills or pearl mills. The media mill consists of a milling chamber, a milling shaft and a recirculation chamber.

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The drug Nanoparticles are obtained by subjecting the drug to media milling. High energy and shear forces generated as a result of impaction of the milling media with the drug provide the necessary energy input to disintegrate the micro particulate drug into nanosized particles. The milling medium is usually composed of glass, zirconium oxide or highly cross-linked polystyrene resin [5].

b. Dry grinding:

Since many years, Nanosuspensions are prepared through wet grinding processes by using pearl ball mill. Nowadays, Nanosuspensions can be prepared by dry milling methods. Stable Nanosuspensions are prepared by using dry grinding of poorly soluble drug with soluble polymers and copolymers after dispersing in liquid medium. Itoh et al. have described the colloidal particles formation of many poorly water-soluble drugs like nifedipine, griseofulvin, and Glibenclamide with sodium dodecyl sulfate and Polyvinylpyrrolidone as stabilizer [6, 7].

5. Lipid emulsion/micro emulsion template:

Nanosuspensions are also obtained by just diluting the emulsion, formed by using a partially water-miscible solvent as the dispersed phase. The emulsion technique is applicable for drugs which are either partially water miscible or soluble in volatile organic solvents. Additionally, micro emulsion templates can also produce Nanosuspensions. Micro emulsions are dispersions of two immiscible liquids like water and oil and stabilized thermodynamically by surfactant or co surfactant. The drug is either loaded into preformed or internal phase of micro emulsion and can be saturated by intimate mixing of drugs. Griseofulvin nanosuspension is prepared by the micro emulsion technique by using water, butyl lactate, lecithin, and the sodium salt of taurodeoxycholate [8, 9].

6. Micro precipitation – High-pressure homogenization (Nanoedge):

Nanoedge is a combination of micro precipitation and high-pressure homogenization techniques. Method includes precipitation of friable materials followed by fragmentation under high shear and/or thermal energy [10].

7. Melt emulsification method:

Solid lipid Nanoparticles are mainly prepared by melt emulsification method. Kipp and co workers firstly prepare Nanosuspensions of ibuprofen by using melt emulsification method. It is a four-step procedure. Drug is first added to aqueous solution having stabilizer. The solution is heated at temperature higher than the melting point of the drug and then homogenized by high-speed homogenizer for the formation of emulsion.

The temperature is maintained above the melting point of the drug during overall process. Finally, the emulsion is cooled to precipitate the particles. The particle size of nanosuspension mainly depends on parameters like drug concentration, concentration and type of stabilizers used, cooling temperature, and homogenization process [11].

8. Nanojet technology:

This technique is also called opposite stream technology, uses a chamber where a stream of suspension is divided into two or more parts. Both streams are colloid with each other at high pressure. The high shear force produced during the process results in particle size reduction. Dearns had prepared Nanosuspensions of atovaquone using the micro fluidization process. The major disadvantage of this technique is the high number of passes through the micro fluidizer and that the product obtained contains a relatively larger fraction of micro particles [12].

9. Supercritical fluid methods:

Various methods like rapid expansion of supercritical solution (RESS) process, supercritical antisolvent process, and precipitation with compressed antisolvent (PCA) process are used to produce Nanoparticles. In RESS technique, drug solution is expanded through a nozzle into supercritical fluid, resulting in precipitation of the drug as fine particles by loss of solvent power of the supercritical fluid. By using RESS method, Young et al. prepared cyclosporine Nanoparticles having diameter of 400 to 700 nm. In the PCA method, the drug solution is atomized into the CO2 compressed chamber. As the removal of solvent occurs, the solution gets supersaturated and finally precipitation occurs. In supercritical antisolvent process, drug solution is injected into the supercritical fluid and the solvent gets extracted as well as the drug solution becomes supersaturated [13, 14].

EVALUATION OF NANOSUSPENSIONS:

In-Vitro Evaluations:

a. Particle size and size distribution:

It is the most important parameter in the evaluation of the suspensions as it is having the direct effect on the solubility and dissolution rate and the physical stability of the formulation. The mean particle size and the width of particle size can be determined by Photon Correlation Spectroscopy (PCS), laser diffraction and coulter current multisizer [15].

b. Particle charge (Zeta Potential):

The particle charge is of importance in the study of the stability of the suspensions. Usually the zeta potential of more than ±40mV will be considered to be required for the stabilization of the dispersions. For electro statically stabilized nanosuspension a minimum zeta potential of ±30mV is required and in case of combined steric and electrostatic stabilization it should be a minimum of ±20mV of zeta potential is required [16].

c. Crystalline Sate and Particle Morphology:

It is of importance as there are chances of the polymorphism during the storage of the Nanosuspensions.

Hence it is necessary to study the crystal morphology of the drug in suspension. Differential Scanning Calorimetry (DSC) is most commonly used for such studies [17].

d. Saturation solubility and Dissolution Velocity:

The main advantage associated with the Nanosuspensions is improved saturation solubility as well as dissolution velocity. These are studied in different physiological solutions at different pH. Kelvin equation and the Ostwald-Freundlich's equations can explain increase in saturation solubility. Determination of these parameters is useful to assess in vivo performance of the formulation [18].

e. Stability of Nanosuspensions:

Stability of the suspensions is dependent on the particle size. As the particle size reduces to the nanosize the surface energy of the particles will be increased and they tend to agglomerate. So stabilizers are used which will decrease the chances of Ostwald ripening and improving the stability of the suspension by providing a steric or ionic barrier [19, 20].

APPLICATION OF NANOSUSPENSIONS

Bioavailability enhancement:

Bioavailability enhancement Drug with poor solubility, poor permeability or poor solubility in gastrointestinal tract will leads to poor oral bioavailability. Nanosuspension resolves the problem of poor bioavailability by solving the problem of poor solubility, and poor permeability across the membranes [21].

Ocular administration:

For delivery of poorly soluble drug in cul-de-sac suspensions and ointments are recommended. Suspensions have advantages of prolonged residual time in cul-de-sac and avoidance of higher tonicity produced by water soluble drugs. The ocular bioavailability of suspensions depends on the dissolution rate of the drug in lachrymal fluid [22].

Pulmonary administration:

Aqueous nanosuspension can be nebulized using mechanical or ultrasonic nebulizer for lung delivery. The nanoparticulate nature of the drug allows the rapid diffusion and dissolution of the drug at the site of action. At the same time, the increased adhesiveness of the drug to mucosal surfaces offers a prolonged residence time for the drug at the absorption site. This ability of Nanosuspensions to offer quick onset of action initially and then controlled release of the active moiety is highly beneficial and is required by most pulmonary diseases [23].

Targeted drug deliver:

Nanosuspensions can also be used as targeted drug delivery. The targeted drug delivery can be designed by incorporating the drug into the mononuclear phagocytic system. Targeted drug delivery can be used for the anti-mycobacterium, fungal or Leishmania drugs to macrophages if the infectious pathogen is persisting intracellular [24].

CONCLUSION

Nanosuspension solved poor bioavailability problem of hydrophobic drugs and drugs which are poorly soluble in aqueous and organic solutions. Productions techniques such as media milling and high pressure homogenizer are used for large scale production of Nanosuspensions. Nanosuspensions can be administered through oral, Parenteral, pulmonary, ocular and topical routes. Since nanotechnique is simple, less requirements of excipients, increased dissolution velocity and saturation solubility many poor bioavailability drugs are formulated in nanosuspension form.

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CONFLICT OF INTEREST:

The authors declare that they have no conflict of interest.

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