

Review Article

Nanosuspension in Drug Delivery-A Review

Rinku Jayaprakash, K. Krishnakumar, B. Dineshkumar, Rejin Jose, Smitha K Nair*

Dept. of Pharmaceutics, St James College of Pharmaceutical Sciences, Chalakudy, Thrissur, Kerala, India

***Corresponding author**

Smitha K Nair

Email: stjamespharmacyproject@gmail.com

Abstract: Nanotechnology is the science that deals with the process that occurs at molecular level and of nano length scale size. Nano refers to the particle size range of 1-1000 nm. Nanosuspensions are coming under nanotechnology. A pharmaceutical Nanosuspension is defined as very finely colloid, biphasic, dispersed solid drug particles in an aqueous vehicle, size below 1 μm stabilized by surfactants and polymers prepared by suitable methods for drug delivery applications. It provides efficient delivery of hydrophobic drugs and increases the bioavailability. Nanosuspension is an attractive and promising technology to improve poor solubility and bioavailability of the drugs. This review article describes the methods of preparation, and applications of nanosuspensions in the field of pharmaceutical sciences.

Keywords: Nanotechnology, Nanosuspensions, polymers, drugs.

NANOSUSPENSION

Nanotechnology is an emerging field in all areas of science, engineering and technology. It is a novel interdisciplinary area of comprehensive research that combines medicine and other life sciences. It offers a potential for unique and novel approaches with broad spectrum of application in cancer treatment including areas such as diagnostics, therapeutics and prognosis [1]. The main advantage of particles in the nano-metric range is its improved physical and chemical properties. The major parameters in drug delivery include particle size, surface area, hydrophobicity, crystallinity and surface charge [2]. More than 40% of new chemical entities being generated through drug discovery programmes are poorly water soluble. The formulation of poorly water soluble drugs has always been a challenging problems faced by pharmaceutical scientists [3]. There are many conventional methods such as micronization, solubilisation using co-solvents, surfactant dispersions and precipitation technique has been developed for improving solubility of poorly water soluble drugs [4]. But these techniques show limitations to the drugs which are not soluble in both aqueous and organic solvents. Nanosuspension technology can be used to solve the problems associated with various approaches described earlier. Nanosuspension is colloidal dispersion of nano-sized drug particles stabilized by surfactants. They can also define as a biphasic system consisting of pure drug particles dispersed in an aqueous vehicle. The diameter of suspended particle is less than 1 μm in size [5].

NEED OF NANOSUSPENSION FORBIOAVAILABILITY ENHANCEMENT:

Nevertheless, pharmacokinetic studies of BCS class-II drugs showed that they have a low oral bioavailability, which may be due to poor water solubility of drug. There are many classical pharmaceutical ways to improve drug dissolution rate such as dissolution in aqueous mixtures with an organic solvent, formation of β -cyclodextrin complexes, solid dispersions and drug salt form. During last 20 years a new technology, reducing drug particle size, has been developed to increase drug dissolution rate [6]. According to Noyes-Whitney equation, drugs with smaller particle size have enlarged surface areas which lead to increase dissolution velocity. Higher the dissolution rate together with the resulting higher concentration gradient between gastrointestinal lumen and systemic circulation could further increase oral bioavailability of drugs. A nanosuspension is a submicron colloidal dispersion of drug particles which are stabilized by surfactants [7]. A pharmaceutical nanosuspension is defined as very finely dispersed solid drug particles in an aqueous vehicle for oral, topical, parenteral or pulmonary administration. The particle size distribution of the solid particles in nanosuspensions is usually less than one micron with an average particle size ranging between 200 and 600 nm. In nanosuspension technology, the drug is maintained in the required crystalline state with reduced particle size, leading to an increased dissolution rate and therefore improved bioavailability [8].

CRITERIA FOR SELECTION OF DRUG FOR NANOSUSPENSIONS:

Nanosuspension can be prepared for the API that is having either of the following characteristics:

- Water insoluble but which are soluble in oil (high logP) or API are insoluble in both water and oils
- Drugs with reduced tendency of the crystal to dissolve, regardless of the solvent
- API with very large dose [9].

ADVANTAGES OF NANOSUSPENSION DRUG DELIVERY SYSTEM

1. It can be applied for poorly water soluble drugs.
2. Physically more stable than liposomes.
3. Most cost effective.
4. Reduction in tissue irritation.
5. Improved dose proportionality [10]

FORMULATION OF NANOSUSPENSION [11]

- **Stabilizers:** Wet the drug particles thoroughly; prevent Ostwald's ripening and agglomeration of nanosuspensions, providing steric or ionic barriers. eg: Lecithins, Poloxamers, Polysorbate, Cellulosics, Povidones.
- **Cosurfactants:** Influence phase behavior when micro emulsions are used to formulate nanosuspensions. eg: Bile salts, DipotassiumGlycerrhizinate, Transcutol, Glycofurol, Ethanol, Isopropanol.
- **Organicsolvent:** Pharmaceutically acceptable less hazardous solvent for preparation of formulation.eg: Methanol, Ethanol, Chloroform, Isopropanol, Ethyl acetate, Ethyl formate, Butyl lactate, Triacetin, Propylene carbonate, Benzyl alcohol.
- **Other additives:** According to the requirement of the route of administration or the properties of the drug moiety. eg: Buffers, Salts, Polyols, Osmogens, Cryoprotectan.

TECHNIQUES OF PREPARATION OF NANOSUSPENSION

Mainly there are two methods of preparation of nanosuspension. The conventional method of precipitation is called 'Bottom-up technology [12]. In bottom-up technology the drug is dissolved in a solvent, which is then added to a nonsolvent to precipitate the crystals. This technique is that during the precipitation procedure the growing of the drug crystals need to be controlled by addition of surfactant to avoid formation of microparticles. The 'Top- down' technologies are the disintegration methods and are preferred over the precipitation methods [13]. The top-down technologies include media milling, high pressure homogenization in water, high pressure homogenization in non- aqueous media and combination of precipitation and high pressure homogenization [14].

MEDIA MILLING [15]

Nanosuspensions are formulated by high shear media mills or pearl mills. It consists of milling chamber, recirculation chamber and milling shaft. Milling media consists of balls or pearls which are made up of ceramic sintered aluminium oxide or zirconium oxide. Milling chamber charged with milling media, water, drug, and stabilizer. Balls rotated at high shear rate under control temperature the balls have an impact on the sample. Due to the both forces of friction and impact particle size reduction occurs and nanosized particles will obtained.

HOMOGENIZATION

High pressure homogenization (dissocubes)

In this technique suspension is forced by a pressure plunger pump through a narrow valve under high pressure [16]. When the suspension is allowed to pass through the orifice the static pressure will be reduced below the boiling pressure of water which results in the boiling of water and formation of gas bubbles. When it leaves the orifice pressure will be normal and bubbles will implode. So surrounding particles will rush into the surface which causes the size reduction. This principle is employed in apvgaulin micron lab 40 homogenizer.

Homogenization in non-aqueous media (nano-pure)

It is homogenised in water free media or water mixture. Temperature will be 0 degree or even at freezing point. So it is known as deep freeze homogenisation. It is the best method for the thermolabile substances [17].

Nanoedge

This technique will be similar to homogenisation method or precipitation method. It is considered as the combination of these two methods which leads to the better stability and bioavailability. The suspension obtained by this method will be again homogenised to reduce the particle size and prevent crystal growth. In precipitation method there will be chances of crystal growth and long term stability problems. Nanotechnology will solve such problems. An evaporation technique is also included in the nano edge technology for the better production of nanosuspension which will result in the solvent free modified starting material.

PRECIPITATION TECHNIQUE (SOLVENT-ANTISOLVENT METHOD):

Precipitation method has been used for long years for the preparation of submicron particles. It is mainly used for the poorly soluble drugs. First drug is dissolved in a suitable solvent. This solution is then mixed with a miscible anti-solvent system in the presence of surfactants. Rapid addition of drug solution in to the anti-solvent leads to the sudden supersaturation of drug in the mixed solution forms ultrafine drug solids. Precipitation method involves two phases -

nuclei formation & crystal growth. When preparing a stable suspension with the minimum particle size, a high nucleation rate and but low growth rate is necessary. Both rates are depending on temperature. In this technique the drug needs to be soluble in at least one solvent which is miscible with non-solvent [18].

APPLICATIONS OF NANOSUSPENSION:

Oral Drug Delivery

Because of the numerous advantages oral route is the most preferable route for many of the drugs especially in the case of orally administering antibiotics such as atovaquone and bupravaquone. By making it in nanosize, its solubility and bioavailability will increase. The oral administration of naproxen nanoparticles leads to an area under the curve (AUC) (0-24 h) of 97.5 mg-h/l compared with naproxen nanosuspension and naproxen tablets. In the case of danazole (gonadotrophin inhibitor) nanosuspension has absolute bioavailability of 82.3 and the conventional dispersion only 5.2 % [19].

Parenteral Drug Delivery

The drug clofazimine is given as iv, the concentration in the liver, spleen and lungs reached a high level i.e.; greater than minimum inhibitory concentration, for most of the mycobacterium avium strains. Tarazepide is formulated as nanosuspension in order to overcome the use of surfactants and cyclodextrins to improve the bioavailability [20].

Pulmonary Drug Delivery

Here we are using nano-preparations for the drugs which have poor solubility in pulmonary secretions. For the lung delivery it is nebulised by mechanical or ultrasonic nebulizer. E. g: budesonide [21].

Ocular Drug Delivery

These mainly applied for hydrophobic drugs. It increases the residence time include sac. The best example of nanosuspension is ibuprofen. The anti-inflammatory activity of ibuprofen increased compared with the aqueous preparation [22].

CONCLUSION

Nanosuspension formulation have been largely solved the solubility as well as dissolution problems to improve drug absorption. It has therapeutic advantages, such as simple method of preparation, less requirement of excipients, increased saturation solubility and dissolution velocity of drug. Numbers of drug candidates are identified in drug discovery programs, but most of them are fairly poorly soluble. This challenges in pharma research to develop novel approaches to achieve a high solubility, stability and bioavailability of the drugs. Nanosuspension is commercially possible approach to solve the poor solubility as well as poor bioavailability problems of the drugs. For large-scale production of nanosuspension

formulation, high-pressure homogenization technology has been widely used. A nanosuspension formulation solves the poor solubility problems, but also improves drug efficacy.

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