INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com
ISSN 2230 – 8407

Review Article

Nanosuspension Technology for Poorly Soluble Drugs: An Overview
Mohan Kumar A*, Selvamuthu Kumar R, Murali R, Srinivasan N
Department of Pharmacy, Annamalai University, Annamalai Nagar, Chidambaram, Tamil Nadu, India
*Corresponding Author Email: mohanams67@gmail.com

Article Received on: 28/12/19 Approved for publication: 06/02/20

DOI: 10.7897/2230-8407.110211

ABSTRACT

Solubility is the essential factor in the drug effectiveness, ability of the route of administration. Broad and proportion of freshly is discovered within the drug is water-insoluble and so poorly bioavailability contributing to desert development creation. Nanosuspension could be appeared as a promising strategy for the economical delivery of deliquescent drugs a result of them are versatile options and distinctive advantages. The down grading of the medication particles into a submicron go prompts a noteworthy increment in the disintegration rate; thus upgrades bioavailability of the nanosuspension and they contain sub microns and blend scattering of the pharmaceutically dynamic fixing particles. During a fluid part stable by wetter nanosuspension is conveyed by an oral channel respiratory organ and visual course of the organization during the investigation is focused on totally various methods for arrangement with benefits and negative mark portrayal properties application.

Keywords: Nanosuspension, bioavailability, ocular route, submicron, hepatoprotective.

INTRODUCTION

A nanosuspension may be a mixture dispersion of drug particles within the submicron range.1 A pharmaceutical nanosuspension is characterizing a really finely mixture, biphasic, dispersed, solid drug particles an binary compound vehicle, very of below 1 m with none matrix actual, stabilised by wetter and polymer, custom made by appropriate approach for drug delivery system functions through completely different routes of administration like oral and non-oral.2 The matter related to the delivery of poorly water-soluble and poorly water and lipid-soluble drugs. The matter of poor Solubility and poor bioavailability of nanosuspension however alters the pharmacokinetics of the drug and improves drug safety and efficaciousness.3 Nanosuspension establishment approach is most advisable for the compound with excellent log P value great melting point and dose. Nanosuspension has been reportable to be enhanced adsorption and bioavailability; it may help to reduce the dose of the route the conventional oral dosage form.4 Drug particles size contraction is result in an extent is increasing and consequently within the Nernst Brunner Levich modification of the Noyes Whitney equation is that the rate of dissolution as delineated. In Ostwald Freundlich equation is explained by particle size contraction because of the enhanced dissolution pressure. Nanosuspension is sterilisation from nanoparticles.3 Polymeric mixture carries of drugs are unremarkably nanoparticles. The developed the brick dust in solid lipid nanoparticles are lipid carriers of drugs. Nanosuspensions will fruitfully the establishment of brick dust molecules for developing dissolution and excellent absorption.5

Advantages of the Nanosuspension

● In developing the dissolution speed and congestion Solubility of drugs
● development within the oral absorption
● In physical stability very long time
● In oral absorption a rise
● It is implemented for poorly water-soluble drugs.
● Every route will provides it.4
● In weakened tissue inflammation just in case of hypodermic/intramuscular Administration.
● In biological performance is enhanced.
● In nanosuspension for site-specific delivery system.
● In nanosuspension is integrated in to tablets, pellets, hydrogel, and suppositories are appropriate for a unique route of administration.7

Disadvantages for Nanosuspension

● Uniform and exact value dose cannot be accomplished.
● Improper dose.
● Physical stability, sedimentation and compaction will cause complications.
● It is bulky sufficient care requisite be taken during handling and shipment.

Need of Nanosuspension

● Poor bioavailability
● Lack of dose response proportionality.5
● Use of harsh excipients, i.e. over the top utilization of co solvent and different excipients.
● Use of extraordinary essential or acidic conditions to upgrade solubilisation
● Use for inadequately water dissolvable just as inadequately natural solvent medications.

Features of Nanosuspension

● Small particle size: 300nm to 10 microns.6
Advantages
- Below volume doses 10-200 mg/ml.
- Safety increment in light of co-dissolvable end accordingly increment portion.
- Long-term dependability as long as 2 years at room temperature or 5°C.
- Route for measurement structure organization IV injection, IM injection, ID injection, oral, respiratory and different courses.
- Can be utilized for controlled and focused on conveyance of medications.

Disadvantages
- Cross-inked styrene resin. The high-energy shear forces are generated as a result of impaction of edge media with the drug leading to breaking the very small particulate drug to nano-sized particles. The first concern with the method is the residues of edge media remaining within the finished product can be problematic for administration. A Z-insulin with a mean particle size of 150 nm was ready using the wet milling technique.

Methods of Preparation of Nanosuspension

In nanosuspension preparation is most commonly two methods bottom up technology. And top down technology.

Bottom-up technology

The term bottom-up technology means that one starts from the molecular level and goes via molecular association to the development of a solid particle. Classical precipitation approach by reducing the solvent quality, for instance, by running the solvent into a non-solvent or ever-changing the temperature or a consolidation of both. Pharmaceutical chemistry and technology is precipitation may be a classical technique.

Advantages
- In most straightforward techniques and low-cost equipment.
- Higher saturation Solubility is the merits for precipitation related to the other and the approach of nanosuspension preparation.

Disadvantages
- The solvent demand to be miscible with at least one non-solvent.
- The drug demand to be soluble in at least one solvent (thus excluding all new drugs that are simultaneously poorly soluble in aqueous and organic media).

Top-Down technology

The top - down technologies
- Media milling
- High - pressure homogenization

Media milling

In high shear media mills or pear mills using by made in nanosuspension. In high shear media mill accustomed to ready nanosuspension. The edge chamber charged with milling media water drug and stabilizer that are turned the very high shear rate under and 2-3 days of controlled temperature. The glass of edge and media consists of composed of zirconium oxide or highly cross-inked styrene resin.

Advantages
- Simplest technology
- Below cost operation regarding the milling itself.
- Extensive scale production is, possible to some extent.

Disadvantages
- Period of the process not being very production-friendly.
- Potential erosion from the milling material leading to product development pollution. Potential erosion growth of germs in the water phase when milling for a long time.

High-pressure Homogenization
- Dissocubes
- Nanopure
- Nanoedge
- Nanojet

Dissocubes

For this situation, the suspension of the drug is made to go through a short opening that outcome in a decrease of the static pressure down the boiling pressure of Water which leads to boiling of water and arrangement of gas bubbles. In cylinder hole homogenizer particle size decrease is depends on the cavitation rule. Particles are additionally diminished by because of high shear power and a Collision of the particles against one another. The dispersion contained in 3 cm distance across chamber all sudden goes through a limited hole of 25 µm due to this water starts boiling at room temperature and structures gas bubbles which implode when the suspension leaves the whole and typical gaseous tension. The size of the drug nano crystals that can be accomplished for the most part relies upon factors like temperature number of homogenization cycles and power thickness of homogenizer and homogenization pressure.

Nanopure

In without water media or water blends suspensions homogenized in nanopure. A blends like PEG 400, PEG 1000 etc. Shallow vapour.

Pressure and high boiling point of water and oils and fatty acids. An In below freezing point of the homogenization can be done at room temperature and 00C is called as profound stop homogenization.

Nanoedge

The nanoedge technique is precipitation and homogenization is essential standards of nanoedge. The precipitation system such as crystal growth and long-standing stability can be resolved using the nanoedge technology is significant demerits. In particles of less size and excellent dependability in a short, time can be accomplished. In nanoedge method is trailed by high-pressure homogenization.
Nanojet

The nanojet is inverse stream innovation. In two or more pieces of the stream of suspension which colloid with some other high pressure due to high shear power created during the process particle size is produced.22

Emulsion diffusion method

In separated from the utilization of the emulsion as a drug conveyance vehicle they can likewise be utilized as layouts to create nanosuspension.22 The utilization of emulsion as layouts is pertinent for those drugs that are dissolvable in either unpredictable organic dissolvable or partially water-miscible dissolvable. In the dispersed phase of the emulsion dissolvable can be utilized. High-pressure homogenization is acquired emulsion was additionally homogenized. The emulsion was diluted with water to the cycle’s homogenization. To diffuse the organic dissolvable and convert the droplets into solid particle is homogenized by a homogenizer. In every emulsion droplet formed of one particle. In particles size of the nanosuspension by controlling the size of emulsion improved, the surfactant architecture expanded the admission of the organic phase and extreme the emulsion. In use of organic dissolvable is methanol, ethanol and ethyl acetate chloroform.23

Advantages

- In specialized equipment is used for not necessarily.
- Any of scale-up a formulation is optimized accurately.
- Particle size can freely be controlled by controlling the size of the emulsion droplet.

Disadvantages

- In demand for ultra-filtration for purification of the drug nanosuspension, which may render the process costly.
- Safety concerns because of the use of hazardous solvents in the process.
- High amounts of surfactant /stabilizer are required as compared to the production techniques described earlier.
- Drugs that are poorly soluble in both aqueous and inorganic media cannot be formulated by this technique.

Micro emulsion Templates

In organic dissolvable or blend dissolvable loaded with the drug scattered in an aqueous phase containing appropriate surfactants to form an emulsion is trailed by micro emulsion template methods; in the scattered of two immiscible liquid to stabilized by surfactant or co surfactant. The organic phase is then dissipated under decreased pressure to make drug particles precipitate instantaneously to form the nanosuspension, which is balanced out by surfactant also, another method makes utilize of partially water-miscible dissolvable for example, butyl lactate, benzyl alcohol, and triacetin as the dispersed phase instead of hazardous solvents.24

Advantages

- Uniform particle distribution.
- High drug solubilisation long shelf-life and any of the manufacturers.
- In specialized equipment is used is not necessary.
- Ease of scale-up a formulation is adequate optimized.

- Particle size can easily be controlled by controlling the size of the emulsion droplet.

Disadvantages

- Requires high amount of surfactant and stabilizers.
- In demand for di ultra-filtration for purification of the drug nanosuspension, which may the process costly.
- In each aqueous and organic media in the drug that are poorly soluble cannot be formulated by this technique.

Supercritical fluid method

In this process, micronization of drug particles inside a constrained scope of molecule size is done it structures particles size range 5-2000 nm in width. It produces nanoparticles from a drug solution. In two technique of the supercritical solution, processes are

- The Rapid expansion of supercritical solution process (RESS)
- Precipitation with a compressed anti solvent process (PCA)

(RESS) In includes the expansion of drug solution in Supercritical fluid through a nozzle which leads to loss of dissolvable intensity of supercritical fluid coming about. E.g., cyclosporine nanoparticles (400-700 nm).

(PCA) In this drug, solution is atomized into a chamber containing compacted CO2 as the solution is evacuated. Solution gets super saturation and along thus line precipitate accomplished crystal.25

Disadvantages

- In surfactant in supercritical Co2 and a high pressure require.
- Use of hazardous solvents and use of high proportion of surfactants and stabilizers as Compared with other techniques.

Melt emulsification method

In this method, drug and aqueous solutions having stabilizer is warmed this solution over the melting point of the drug to homogenized and by high-pressure homogenizer for the development of emulsion in emulsion cooled to the room temperature or ice shower in the hasten.26,27

Advantages

Avoidance of organic solvents

Disadvantages

Formation of large particles

Dry Co-grinding

In nanosuspension is additionally getting ready by dry milling strategy also in this technique, dry grinding of poorly water-soluble drugs with soluble polymers and copolymers are scattered in a liquid medium. Many polymers and copolymers are polyvinylpyrrolidone, hydroxypropyl methylcellulose, polyethylene glycol, cyclodextrin derivatives etc.27

Formulation considerations

- Stabilizer
● Organic solvent
● Surfactant
● Co-surfactant
● Other additive

Stabilizer

In stabilizer is to wet the drug particles in the fundamental capacity and counteract Ostwald ripening Agglomeration of nanosuspension. The amount of settling has a pronounced effect on the physical stability and vivo frame of mind of nanosuspension.28

E.g.: lecithin, Poly vinylalcohol, Sodium lauryl sulphate, poloxamers, polysorbate, cellulosic

Organic solvent

In the plan of nanosuspension is that organic dissolvable is utilized. In the event that emulsion or micro emulsion are utilized as a format. E.g. Water- miscible Solvent: ethanol and isopropanol.29

Partially water miscible: ethyl acetate, ethyl format, butyl lactate, propylene carbonate and benzyl alcohol.

Surfactant

E.g. Tween and spans, widely used surfactant

Co-surfactant

In Micro emulsion to formulate nanosuspension utilizing a Co-surfactant; in co-surfactant on take-up of the internal phase for chose for micro emulsion synthesis and on drug, loading should be researched. E.g. glycerol, ethanol, isopropanol, bile salts, dipotassium glycyrrhizinate etc.

Other additives

Nanosuspension may be added substance for example, buffers (acetate, phosphate) polyols, salts, cosogenic and cryoprotectant (sucrose as sugar).

Characterization of Nanosuspension

In-vitro evaluation

An orally administered formulation, these qualities are particularly significant. In various in a test, particularly of active constituents, changes in particle size, crystal habit and ensuing particle dissolution. Colour, odour, and taste in changing can likewise indicate chemical instability.

Particle size distribution

In the particle size appropriation can be dictated by photon correlation spectroscopy (PCS); also, laser diffractometry (LD) and Coulter counter method of analysis in particle size distribution. The mean particle size distribution and its range named poly dispersity index (PI) in PI given the physical stability API value 0.1-0.25 shows that narrow size distribution. The Coulter counter gives the most perfectly best number of particles per volume for the distinctive size. In the LD can identify and drug Micro especially and also give volume size distribution.

Zeta potential

In an indication of the stability of the suspension is utilized of Zeta potential. In a steady suspension stabilized by electrostatic resonance; zeta potential a minimum of +30 mV is required though the instance of a consolidated electrostatic and static stabilizer a Zeta potential of +20 mV would be adequate.

Drug entrapment efficiency

It is the percentage of drug that is successfully entrapped with in nanosuspension. Drug entrapment efficiency can be calculated using following equation,

\[
\text{Entrapment efficiency} \% = \frac{\text{INITIAL DRUG} - \text{FREE DRUG}}{\text{INITIAL DRUG}} \times 100
\]

Crystal morphology

To characterization the polymorphic changes because of the effect of high - pressure on homogenization in the crystalline structure of the drug. In X-ray diffraction analysis like a method in mix with differential scanning Calorimetry or differential thermal analysis can be utilized. In an adjustment in the crystalline structure can experience a nanosuspension, which might be to amorphous form or to other polymorphic forms because of high- pressure homogenization.

Droplet size

In micro emulsion can be dictated by light scattering technique. Furthermore electron microscopy is utilized. Dynamic light scattering spectrophotometer is utilization a neon laser of wavelength 632 nm.

Dissolution

It can expand the dissolution speed just as the immersion Solubility. The evaluation of immersion Solubility and dissolution speed help in deciding the in vitro behaviour of the formulation. An expansion in the dissolution pressures just as dissolution speed, which a decrease in the particle size to the nanometre range size decrease prompts an increment in the dissolution pressure. An expansion in Solubility that occurs with relatively low particle size decrease might be mainly due to changes in the surface tension leading to an expanded immersion Solubility.

Applications of Nanosuspension

● Oral drug delivery
● Parental drug delivery
● Ocular drug delivery
● Pulmonary drug delivery
● Target drug delivery

Oral drug delivery

Bioavailability enhancement

In poor bioavailability of nanosuspension by solving the twin inconvenience of poor Solubility and diminished penetrability over the Membrane. Oral administration of the gonad tropic inhibitor as Nan suspension prompts to total bioavailability of 82.3 and the conventional scattering. Just to 5.2 bioavailability of
poorly soluble oleamlic acid hepatoprotective agent was improved utilizing a nanosuspension.\textsuperscript{30,31}

**Parental drug delivery**

The drug particles are legitimately nano-sized; it turns out to be anything but difficult process almost all drugs for parenteral administration. And the absence of any dissolvable /co-solvent and, or any conceivably poisonous fixing in nanosuspension enable them to bypass the limits of parenteral administration attributed to conventional formulation strategies. And in nanosuspension enable a critical improvement in the parenteral tolerable dose of the drug leading to a decrease in the expense of the and also improved therapeutic execution.\textsuperscript{32,33}

**Ocular drug delivery**

In nanosuspension their inalienable capacity to better the immersion Solubility of the drug speak to a perfect methodology for visual conveyance of hydrophobic medications. Moreover in nanosuspension characteristic of the medication permits it’s drawn out living arrangement in the cul-de-sal is giving supported arrival of the medication.\textsuperscript{34} To accomplish economical arrival of the medication for a stipulated period, time nanosuspension can be joined in a reasonable hydrogel base or mucoadhesive base or even in visual augmentations.\textsuperscript{35}

**Pulmonary drug delivery**

In aqueous nanosuspension can be nebulised utilized an ultrasonic nebulizer or mechanical for lung conveyance. In their little size, all things considered in every aerosol droplet at least one drug particles are contained, prompting an increasing uniform distribution of the drug in the lung. The nanoparticles nature of the drug permits the quick dispersion and the dissolution of the drug at the site of action. E.g. budesonide a poorly water-soluble corticosteroid has been successfully formulated as a nanosuspension for pulmonary conveyance.\textsuperscript{36,37}

**Targeting drug delivery**

In the nanosuspension can be utilized for targeting as their surface properties and changing the stabilizer can rapidly after the \textit{in vivo} conduct. The drug will be take-up by the smononuclear phagocytic system to allow regional specific conveyance. This can be utilized for targeted anti mycobacteria, fungal or leishmanial drugs to the macrophages it the infection pathogen is persisting intra cellularly and in the kasyer formulated a nanosuspension of aphidicoline to improve drug targeting against leishmania contaminated macrophages.\textsuperscript{38}

**Mucoadhesion of the nanoparticles**

The particle is immobilized at the ventral surface by an adhesion mechanism referred to as bio adhesive from this moment on. The concentrated suspension as a reservoir of particles and an adsorption process takes place very rapidly. The adhesiveness of the nanosuspension not only helps to improve bioavailability but also improve targeting of the parasites persisting in the GIT e.g. cryptosporidium partum.

The bio adhesion can likewise be improved by improved a mucoadhesive polymer in the formulation.\textsuperscript{39}

**CONCLUSION**

Nanosuspension solved the unfortunate bioavailability problem of poorly water as well as organic soluble drugs. The media milling and high-pressure homogenizer are used for large scale production of nanosuspension. In nanosuspension can be administered through oral, parenteral, pulmonary and ocular, routes. Nanosuspension is simple fewer requirements of excipients, expanding dissolution rate and saturation Solubility

**REFERENCES**

2. Arunkumar N. Nanosuspensions A Novel Approach To Improve Solubility And Bioavailability Of Poorly Soluble Drugs; 2011.


Cite this article as:

Source of support: Nil, Conflict of interest: None Declared

Disclaimer: IRJP is solely owned by Moksha Publishing House - A non-profit publishing house, dedicated to publishing quality research, while every effort has been taken to verify the accuracy of the content published in our Journal. IRJP cannot accept any responsibility or liability for the site content and articles published. The views expressed in articles by our contributing authors are not necessarily those of IRJP editor or editorial board members.