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A REVIEW ON NANOSUSPENSIONS: A NOVEL APPROACH TO ENHANCE SOLUBILITY OF DRUGS

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ABSTRACT

One of the major problems associated with BCS (Biopharmaceutical classification system) class II and IV drugs is poor aqueous solubility of drugs such as Simvastatin, carbamazepine, nifedipine, phenytoin, itraconazole, furosemide, paclitaxel etc. Low aqueous solubility of drugs leads low bioavailability of drugs. Therefore, formulation of drug in form of nanosuspension is a good alternative to solve these problems and considered as promising strategy for efficient delivery of hydrophobic drugs. Nanosuspensions are prepared by using various technologies such as top down technology, bottom up technology, emulsion diffusion method, microemulsion template and supercritical fluid method. The reduction of particle size of drug into submicron level leads to increase in dissolution rate of drug, improves therapeutic efficacy, increases the bioavailability and reduce the toxicity of drug. Nanosuspensions can be delivered by various routes of administration such as oral drug delivery system, topical drug delivery system, mucoadhesive drug delivery system. This review describes the method of preparation, evaluation and applications of nanosuspensions.

KEYWORDS: Nanosuspension, poorly soluble drugs, bioavailability, solubility, homogenization.

INTRODUCTION

Nanosuspensions are defined as submicron colloidal dispersion of pharmaceutical active ingredient particles or nanosized drug particle in liquid phase, having size below 1µm,

without any matrix material which are stabilized by surfactants and polymers. Nanosuspensions are different from nanoparticles and solid lipid nanoparticles in such a way that nanoparticles are commonly colloidal carriers of the drugs where as solid lipid nanoparticles are lipid carriers of the drug, But in nanosuspension technology, the drug is maintained in required crystalline state with reduced particle size which leads to increase in dissolution rate and thus improves the bioavailability.[1] Nanosuspension technology can be implemented to all the drugs belonging to BCS class Ⅱ and Ⅳ drugs to increase their solubility as well as partition into gastrointestinal barrier. There are also many conventional methods for increasing in solubility of poorly soluble drugs which include micronation, solubilization using cosolvents, precipitation technique, surfactant dispersion and oily solution. Other techniques include liposomes, emulsions, microemulsion, solid dispersions etc but they are note applicable to all the drugs for solubility and bioavailability enhancement inorganic solvents. Drugs like clofazimine, nimesulide, neproxen, amphotericin B, Omeprazole, nifedipine all these hydrophobic in nature can be formulated as nanosuspensions.[2] These drugs are formulated using various types of excipients to increase the dissolution rate by increase in contact of surface area with dissolution medium. Some examples of excipients are.

- Wetting agents such as **sorbitan ester derivatives.**
- Disintegrants such as **croscarmellose sodium.**
- Cosolvents such as **PEG-400**.
- Cyclodextrins such as β- cyclodextrins.[3]

Need of Nanosuspension

- ❖ Now days, more than 40% of the drugs are poorly soluble in water, so they show difficulties in formulating them in conventional dosage forms. Same problem also arises with BCS Class Ⅱ drugs. The key modification from conventional formulation of suspension is the particle size distribution of solid particles in nanosuspensions which is usually less than 1µm, which increases surface area and saturation solubility, therefore overall bioavailability is improved.[4]
- ❖ The nanosuspension are preferred for the compound that are insoluble in water with high log P value and high melting point and high dose.[5]

Advantages Of Nanosuspension[6,7,8]

- ➢ Increase the dissolution rate and solubility of the drug.

- Improve the biological performance of drug.
- Nanosuspension technology can be given by any route of administration.
- Provide long term physical stability for the formulation.
- Rapid dissolution and tissue targeting can achieved by IV route of administration.
- Ease of manufacture and scaleup.
- Nanosuspension has low incidence of side effects by excipients.
- This type of formulation increase resistance to hydrolysis and oxidation.
- Nanosuspensions reduce volume of administration, essential for subcutaneous, intramuscular and Ophthalmic use.
- Nanosuspensions overcome delivery issues by maintaining the drug in preferred crystalline state of size sufficiently small for pharmaceutical acceptability.
- Nanosuspension can adhere to gastrointestinal mucosa which prolongs the contact time of the drug and thus enhances the absorption.
- Nanosuspensions can maintain the drug release over a prolong period of time and reduce systemic toxicity of drug.
- Nanosuspensions can be used for passive targeting.
- Nanosuspensions can reduce variation in fed/fasted conditions.

Disadvantages Of Nanosuspension[6]

- Bulky nature evokes problems during handling and transportation.
- Dose precision is note achieved.
- Sedimentation and compaction can cause problems.

Table 1: Advantages of Nanosuspension over conventional formulations.[9]

Route of administration	Disadvantages of conventional formulations	Benefits of nanosuspensions
Oral	Slow onset of action and Poor Absorption	Rapid onset of action and improved solubility therefore improved bioavailability
Ocular	Lacrimal wash off / low bioavailability	Dose consistency/ higher bioavailability
Intramuscular	Low patient compliance due to pain	Rapid tissue irritation
Inhalations	Low bioavailability due to low solubility	Rapid dissolution, high bioavailability, dose regulation
Intravenous	Poor dissolution and non-specific action	Rapid dissolution/ Tissue targeting.

Selection Of Drug for Nanosuspension[10]

- Drug which is water insoluble but soluble in oil.
- Drug with a reduced tendency for the crystal to dissolve, regardless of the solvent.

- Drug with high log P value along with high melting point.
- API with a very large dose.

Properties of Nanosuspensions

1. **Physical long-term stability:** The dispersed system shows physical instability due to Ostwald ripening which is responsible for crystal growth to form microparticles. Ostwald ripening is the phenomena observed in solid solutions or liquid solutions in which small crystals or solution particles dissolve and redeposit onto large crystals. It causes due to difference in dissolution velocity or saturation solubility of small and large particles. Molecules diffuses from the higher concentrated area around small particles to area around larger particles possessing lower concentration. This leads to formation of supersaturated solution around large particles. This diffusion process leaves an area around small particles that is not saturated anymore, which leads to the dissolution of the drug from small particles and finally completes the disappearance of the small particles.[10]
2. **Internal structure of nanosuspensions:** The high energy input during disintegration process causes structural changes inside the drug particles. When the drug particles are exposed to high pressure homogenization, the crystalline state of particles changes to amorphous state. The change in state depends upon hardness of the drug, power density applied by homogenizer, chemical nature of the drug and number of homogenization cycles.[11]
3. **Adhesiveness:** There is a distinct increase in adhesiveness of ultra fine powders as compared to coarse powders. The adhesiveness of small drug nanoparticles can be utilized for improved oral delivery of poorly soluble drugs. A Remarkable report is that of increase in bioavailability of Danazol from 5% as macro suspension to 82% as nanosuspension.[11]
4. **Crystalline state and Particle Morphology:** The assessment of crystalline state and particle morphology together helps in understanding the polymorphic or morphological changes in drug that may occur when subjected to nanosizing. Nanosuspension can change crystalline structure to amorphous form or other polymorphic forms by high pressure homogenization. The extent of the amorphous fraction can be determined by X-ray diffraction analysis, differential scanning calorimetry. For actual idea of particle morphology, scanning electron microscopy is preferred.[5]

5. **Passive targeting by nanosuspension:** Most of the drugs failed to give favorable outcomes because they don't have ability to reach the target site of action. Nanosuspension is an effective approach to overcome critical issues such as acting of drug on normal tissues which cause side effects and helps in development of targeted drug delivery system.[5]
6. **Increases in saturation solubility and dissolution velocity of drug:** Dissolution of drug is increased by increase in surface area of the drug particles from micrometers to nanometer.

According to Noyes- Whitney equation, dissolution velocity increases due to increase in surface area from micron size of particle to nanometer.

dx/dt = [(DxA)/h][Cs-X/V]

Where; D is diffusion coefficient

A is surface area of particle

dx/dt is dissolution velocity

V is volume of dissolution medium

h is the thickness of diffusion layer

X is the concentration in surrounding liquids.[5]

Methods Of Preparation of Nanosuspension

The preparation of nanosuspensions are simple alternative method than liposomes and other conventional colloidal drugs carriers but are cost effective. Preparation of nanosuspension is particularly for poorly soluble drugs and to achieve a more physically stable product. There are several methods for preparation of nanosuspension such as.

1. Top-down process technology
2. Bottom-up process technology[13]
3. Combined methods and newer methods.

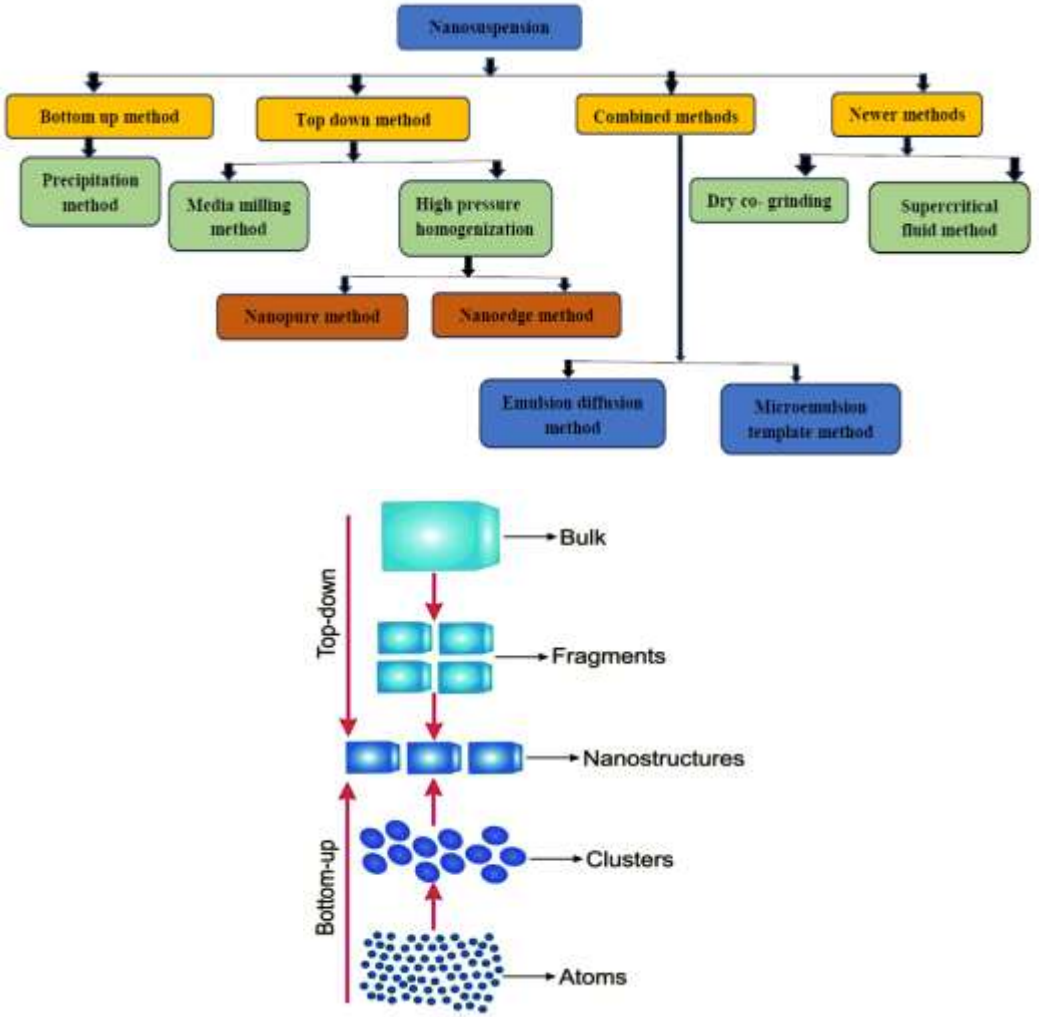

Figure 1: Schematic representation of top down and bottom-up approach.

(A). Bottom-up method

Bottom-up approach start from bottom i.e. from molecular level and goes to molecular association from the formulation of small solid particles. In this technique, the drug is entirely dissolved in a solvent and then this solvent solution is added to a non-solvent causing precipitation of drug. This method is used for manufacturing of nanosuspensions in bulk solutions as well as in single droplets[13]

- **Precipitation method[13,14]**

This method is also known as solvent- antisolvent precipitation method. In this method, drug is first dissolved in a solvent, then this solution is mixed with a miscible antisolvent in presence of surfactants. The rapid addition of drug solution to antisolvent leads to sudden super saturation of drug and form ultrafine crystalline or amorphous drug solids.

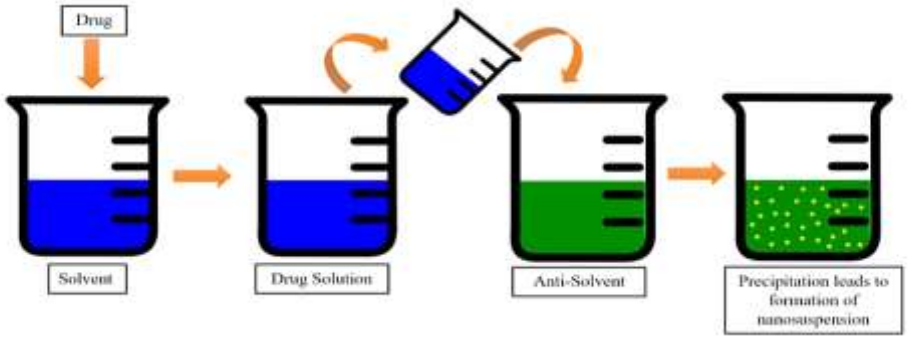

Figure 2: Formation of nanosuspension by solvent – antisolvent method.

Advantages

- It is a simple process.
- Ease of scale up and economical production.

Disadvantages

- Drug must soluble at least in one solvent.
- Growing of crystals needs to be limit by surfactant addition.
- Crystal growth need to be checked outside the nano-range with the help of an appropriate solvent.

(B) Top- Down Method

This method reduces large sized particles to nanosized particles. This includes media milling, high pressure homogenization[HPH]. HPH further includes nano edge method and nano pure method.[14]

➢ **Media milling[15]**

Media milling technique was developed by Liversidge et al. In this technique, high- shear media mills and pearl mills are used to produce nanosuspensions.[3] The media mill consists of a milling chamber, milling shaft and recirculation chamber. The chamber is charged with the milling media, water, drug and stabilizer. The media mill pearls are rotated at very high shear rate and this milling process is performed under controlled temperature. The crude slurry consist of water, drug and stabilizer is fed into the milling chamber and processed into nanocrystalline dispersion. The process can be performed in batch or in recirculation mode. In batch mode, 200nm sized dispersion can be obtained in 30-40min.

Principle

High shear forces are generated as a result of impaction of milling media with drug which provides energy input to break the micro particles drug into nano sized particles. Here the milling media is composed of zirconium oxide or highly cross-linked polystyrene resin and glass. Here very little batch to batch variation is observed in quality of the dispersions.

Advantages

- This method is applicable for the drugs that are poorly soluble in aqueous and organic media.
- This method can prepare highly concentrated nanosuspensions as well as very dilute nanosuspensions by handling drug quantity of 1mg/ml to 400mg/ml.

Disadvantages

- Scale up is note easy due to mill size and weight.
- This technique is time consuming.
- Nanosuspensions formed can be contaminated with material eroded from balls may be problematic when it is used for long therapy.
- Some fractions of particles are in micrometer range.

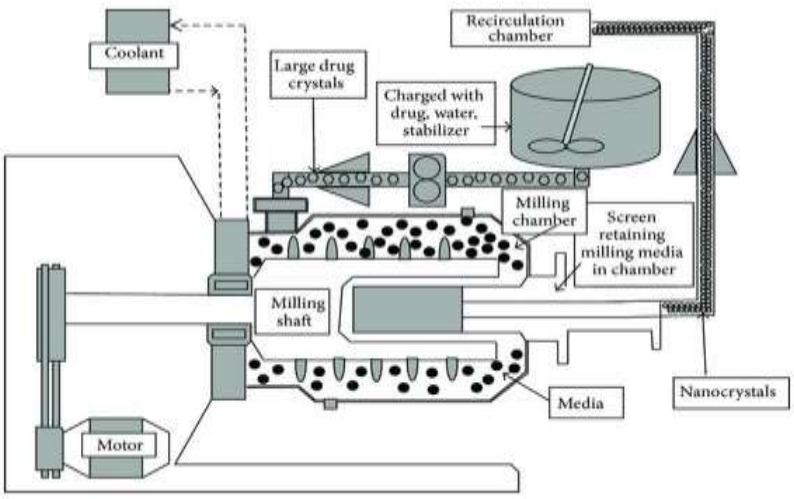

Figure 3: Schematic representation of media milling process.

➢ **High pressure homogenization**[11, 15, 16]

This method is most commonly used for preparation of nanosuspensions of drugs with very low aqueous solubility. Nanosuspensions are prepared by using high pressure piston gap homogenizers. Homogenization involves forcing of suspension under pressure through a

valve having narrow aperture. The instrument is operated at pressure varying from 100-1500 bars i.e. 2800-21300 psi and up to 2000 bars with volume capacity of 40ml for laboratory scale.

This method requires many cycles of homogenization and particle size need to be small before loading. A pre-suspension of micro sized drug particles is prepared in surfactant solution using high speed stirred. During homogenization, this drug suspension is pressed through the homogenization gap in order to achieve nanosuspensions of drug.

Principle

It is based on cavitation principle. Particles also reduced as a result of high shear forces particle collisions. A 25m wide hole allow the dispersion to flow through 3cm diameter cylinder.

According to Bernoulli's theorem, the flow volume of liquid in a closed system per cross section is constant. The static pressure can drop below the boiling point of water at ambient temperature while the dynamic and pressure rises due to the reduction in diameter from 3cm to 25m. As a result, when suspension exits the gap and normal air pressure are established, water begins to boil at room temperature and generates gas bubbles. The intense force is sufficient to break down micro sized particles into nanoparticles as well as collision of particles at high speed also help to achieve nanosized particles.

Advantages

- Drugs which are poorly soluble in both organic and aqueous media can easily be formulated into nanosuspensions.
- Flexibility in handling of drug quantity ranging from 1-400mg $mL\mu^{-1}$, thus this method can formulate very dilute as well as highly concentrated nanosuspensions.
- Litle Batch to batch variation with ease of scale up.
- Allows septic production of nanosuspensions for parenteral administration.

Disadvantages

- Costly machinery is required, which increase the cost of drug.
- Pre-processing is required, such as micronization of drug.

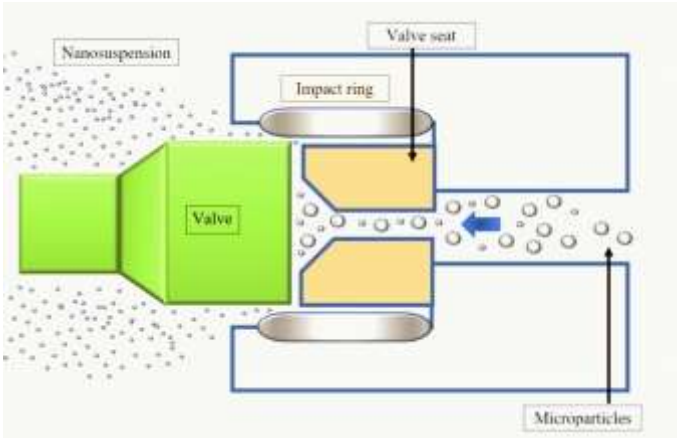

Figure 4: Schematic representation of high-pressure homogenization process.

1. **Nanopure method:** Nanopure is suspensions in water free media or water mixtures like PEG 400, PEG 1000. Temperature will be room temperature, 0 degree or even at freezing point. That why this method is also known as deep freeze homogenization.

In this method nanocrystals of drug are dispersed in liquid such as polyethylene glycol (PEG) or various oils can directly fill as drug suspensions into hydroxypropyl methylcellulose (HPMC) or gelatine. It is the best method for thermolabile substances at milder conditions.[17]

2. **Nano edge method:** This method is a combination of both precipitation and homogenization method. In this method, drug is dissolved in an organic solvent and this solution is mixed with miscible antisolvent for precipitation. Drug precipitates due to low solubility in water solvent mixture. Precipitation is coupled with high shear processing, which is accomplished by the combination of rapid precipitation and high-pressure homogenization.

The advantage of this method is that it overcomes the disadvantages of precipitation technique such as crystal growth and long-term stability by achieving particles of smaller size and better stability in a short time.[17]

(C) Combined methods

- **Emulsion diffusion method[18]**

In this method, emulsions are used as vehicle for drug delivery as well as template for generating nanosuspensions. This method is suitable only when the drug shows solubility in organic solvents (volatile) or solvents that shows partial solubility in water. The dispersed phase of emulsion contains these solvents, which carry the drug. This mixture of solvent is dispersed in an aqueous phase containing appropriate surfactants, leads to form emulsion.

The resulting emulsion is then stirred and high-pressure homogenization is employed to homogenised the emulsion. Then water is used to dilute the emulsion and further homogenised so that organic solvent gets diffused and droplet get converted into solid particles. Nanosuspensions particle size is adjusted accordingly by controlling the emulsion's size. Surfactants enhances the absorption of the organic phase. Solvents used in this process is ethanol, chloroform, ethyl acetate and methanol etc.

Advantages

- It is easy to regulate the particle size by adjusting the emulsion's droplet size.
- It doesn't require any specialised equipment.

Disadvantages

- Large amount of surfactants are needed as compared to another methods.
- Drugs whose solubility is limited in organic and aqueous media are not suitable for this method.
- Safety issues may arises due to use of hazardous solvents.

➢ **Microemulsion template method[19]**

Microemulsion are thermodynamically stable and isotopically clear dispersions of two immiscible liquids such as oil and water. This microemulsion is stabilized by an interfacial film of surfactant and co-surfactants. The drug can be either loaded into internal phase or pre-formed microemulsion can be saturated with the drug by intimate mixing. Suitable dilution yields the drug suspension.

Example, Griseofulvin nanosuspension is prepared by the microemulsion technique by using water, lecithin, butyl lactate and sodium salt of taurodeoxycholate.

(D) Newer methods

➢ **Dry Co- grinding[20]**

Dry co-grinding process is under the milling techniques where the dry-grinding of poorly soluble drugs with soluble polymers and co-polymers after dispersion in a liquid media are performed to produce stable nanosuspensions. In this technique, various polymers and copolymers are used such as polyethylene glycol(PEG), Polyvinyl pyrrolidone (PVP), Hydroxypropyl methyl cellulose (HPMC) And cyclodextrin derivatives. Dry co-grinding process enables to improve surface polarity and transform the crystalline form into

amorphous form. The amorphous form of drug candidate possesses better solubility than crystalline form in aqueous phase.

Examples, Nanosuspensions of drugs like Glisentide, Griseofulvin, Glibenclamide, clarithromycin, phenytoin, Naproxen, Nifedipine etc has been prepared by this method.

Advantages

- Require short grinding time.
- Easy process and no organic solvent required.

➢ **Supercritical fluid method**[12,14,21]

Supercritical fluid technology can be used to produce nanoparticles from drug solutions. The particle size reduction was achieved more by the solubilization and nanosizing technologies through supercritical fluid process. Supercritical fluids (SCF) are non-condensable dense fluids whose temperature and pressure are greater than its critical temperature (Tc) and critical pressure (Tp). This process allows micronization of drug particles to submicron level. In this method, the supercritical fluid comprising the API in a suitable solvent is expanded rapidly by flowing through the jet which causes evaporation of the solvent and leads to the precipitation of API as nanoparticles. In precipitation with compressed antisolvent method, carbon dioxide in supercritical form can be used for manufacturing of nanoparticles. This method involves injecting the drug solution into a chamber that contains compressed CO_2. Recent advances in SCF process are to create nanosuspensions of particle size 5-2000nm in diameter.

Example, nanoparticles of Griseofulvin are prepared by using this method.

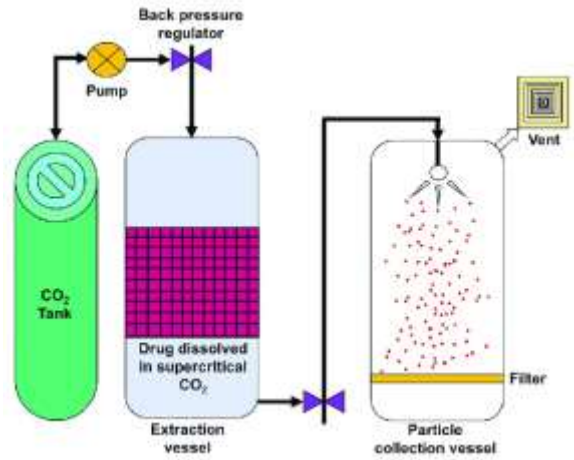

Figure 5: Simple setup of a supercritical fluid technology method.

Formulation Considerations

1. **Stabilizers:** The main function of stabilizers is to prevent Ostwald's ripening, to wet the drug particles thoroughly and agglomeration of nanosuspension in order to yield a physically stable formulation by providing ionic barriers. Various stabilizers used in nanosuspensions are polysorbate, poloxomers, povidones, lecithin, cellulosic etc. Lecithin is the stabilizer of choice to develop a parentally acceptable and autoclavable nanosuspension.[22]
2. **Organic Solvent:** Organic solvents are used when nanosuspensions are prepared by emulsion as template or microemulsion as a template method. Water miscible solvents like methanol, ethanol, isopropanol are used due to their low toxicity. Other solvents such as ethyl format, propylene carbonate, triacetin (partially miscible with water) are pharmaceutically accepted and preferred for nanosuspension formulation over traditional hazardous solvents such as dichloromethane.[23]
3. **Surfactants:** Surfactants are incorporated in nanosuspensions to reduce interfacial tension. They also act as wetting and deflocculating agents e.g. Tweens, spans are widely used surfactants.[11]
4. **Co-surfactants:** The choice of co-surfactant is critical when using microemulsion method to formulate nanosuspensions. Co-surfactants can influence phase behaviour and the effect of co-surfactant on uptake of internal phase for selected microemulsion composition and on drug loading should be investigated. Although the literature describes the use of bile salts and Dipotassium glycerrhizinate as co-surfactant and various solublizers like ethanol, isopropanol, glycofurol, transcutol can be safely used as co-surfactants in the formulation of microemulsions.[7]
5. **Other additives:** Nanosuspensions may also contain substances such as polyols, osmogent salts and cryoprotectants.[24]

Evaluation Of Nanosuspension

1. **Organoleptic properties:** Organoleptic properties needs to be considered in formulation that have to be given orally. Alterations in taste, aroma and colour indicates chemical instability in formulation. Changes in particle size, crystal habit indicates variation in taste for particular active compounds.[18]
2. **Particle size analysis:** The particle size of nanosuspension can be determined by using Motic digital microscope. The particle size of nanosuspension are determined in micrometre.[25]

3. **Entrapment efficiency:** To measure entrapment efficiency of nanosuspensions, 10ml of the freshly prepared nanosuspension are taken and centrifuged at 1000 rpm for 10min. The supernatant is removed and the amount of drug unincorporated was measured by taking the absorbance of supernatant solution at 275nm by using UV-Visible spectrophotometer.[25]
4. **Drug content:** 10mg of nanosuspensions are taken in 100ml of volumetric flask and diluted up to 100ml with methanol. The absorbance of resulting solution was measured at 234nm and drug content is calculated.[26]
5. **Particle charge (zeta potential):** The zeta potential of a nanosuspension gives an idea about potential of nanosuspension is control by both stabilizer and drug itself. For exhibiting good stability of nanosuspension and electrostatically stabilized nanosuspension, minimum zeta potential of 30mv is required whereas in the case of combined electrostatic and 20mv is desirable.[27]
6. **Crystal morphology:** Nanosuspension can undergoes an exchange in crystalline form to amorphous form because of high strain homogenization. To study the effect of high strain homogenization in crystal structure of drug, various techniques like X- ray diffraction analysis aggregated with differential scanning calorimetry can be applied.[28]
7. **Density:** Density is a vital parameter. It can be measured by hydrometer. A decrease in density often indicates the presence of entrapment of air in the structure of formulation.[28]
8. **pH and osmolarity:** The pH of nanosuspension is measured by pH meter and osmolarity is measured by using osmometer.[11]
9. **Dissolution velocity and saturation solubility:** Nanosuspension have an important advantage over other techniques that it can increase the dissolution velocity as well as saturation solubility. These two parameters can be determined by various physiological solutions. These two parameters help in determining the in-vitro behaviour of the formulation. Bohm *et al.* reported an increase in dissolution pressure as well as dissolution velocity with reduction in the particle size to nanometre range which leads to increase in dissolution pressure.[6]

Table 2: List of some marketed pharmaceutical nanosuspension products.[29,30,31]

Trade name/ company	Drug	Dosage form & route of administration	Nanosuspension method	Indication
Giris-PEG®/Novartis	Griseofulvin	Tablet/ oral	Coprecipitation	Antifungal
Invega Sustenna®/	Palperidone	Liquid nanosuspension/	High pressure	Schizophrenia

Johnson & Johnson	palmitate	parenteral	homogenization	
Ceasmet®/Lily	Nabilone	Capsule/ oral	Coprecipitation	Antiemetic
Tricor®/Abbott	Fenofibrate	Tablet/ oral	Nanocrystal®Elan nanosystems	Hypercholesterolemia
Sporanox®/ Janssen pharma	Itraconazole	Capsule/oral	Pearl milling technique	Antifungal
Rapamune®/ Wyeth	Sirolimus	Tablet/Oral	Nanocrystal technology	Immunosuppressant
Emend®/Merck	Aprepitant	Capsule/ nanocrystals	Elan drug delivery Nanocrystals®	Antiemetic
Megace®ES/ PAR pharmaceutical	Megestrol Acetate	Oral suspension	Elan drug delivery Nanocrystals®	Appetite stimulant

Applications Of Nanosuspension

1. Oral drug delivery

Oral route is the most preferable route for many of the drugs specially in case of orally administered antibiotics such as Atovaquone and buparvaquone. Their bioavailability and solubility increase by making in nanosized. In case of Danazole i.e. gonadotrophin inhibitor, nanosuspension have absolute bioavailability of 82.3% as compared to conventional dispersion which only has 5.2%.[32]

2. Pulmonary drug delivery

Nanosuspension prove to be an ideal approach for delivery of drug that have poor solubility in pulmonary secretions. Nanosuspension can be nebulized by using mechanical or ultrasonic nebulizers for lung delivery. Because of their small size, each aerosol particle contains at least one drug particle, which leads to more uniform distribution of the drug in lungs. The nanosized nature of drug allows rapid diffusion and dissolution of the drug at site of action.[5]

3. Targeted drug delivery

Nanosuspensions can be used for targeted drug delivery as their surface properties and in vivo behaviour can easily be changed. Their ease of scaleup and commercial product enable the development of commercially viable nanosuspensions for targeted delivery. They can be used for active and passive targeting of desired site.[31]

4. Ocular Drug delivery

This mainly applied for hydrophobic drugs. It increases the residence time in cull de sac. The example is Ibuprofen, its anti-inflammatory activity is increased as compared to aqueous preparation.[33]

5. Topical Drug delivery

Nanoparticles of drug can be incorporated in creams & water free ointments. The nanocrystalline form of drug leads to an increase in saturation solubility of drug in the topical dosage form. Thus, enhancing the diffusion of the drug into skin.[5]

6. Enhancement of Bioavailability

The poor oral bioavailability of the drug may be due to poor solubility and poor permeability or stability in GI tract. Nanosuspensions have the ability to solve both these problems and can enhance bioavailability. For example, Nanosuspension of Amphotericin B showed a significant improvement in its oral absorption as compared to conventional formulation.[34]

7. Mucoadhesion of the Nanoparticles

Nanoparticles orally administered in the form of a suspension diffuses into media and rapidly encounter the mucosal membrane. The particles are immobilized at intestinal surface by an adhesion mechanism called as “bio adhesion”. It is the first step before absorption. The adhesiveness of the nanosuspension not only help to improve bioavailability but also improves targeting of drug at site of action. Bio adhesion can be improved by including a mucoadhesive polymer in the formulation.[34]

CONCLUSION

Nanosuspension seems to be unique method to enhance bioavailability of hydrophobic drugs including those that are poorly soluble in organic media. The main goal of this review was to describe the various techniques for preparation of nanosuspension. Production techniques such as media milling, high pressure homogenization have been successfully employed for large scale production of nanosuspensions. Attractive properties such as increased dissolution velocity, increased saturation solubility, improved bioavailability has widened the application of nanosuspension for various routes. Nanosuspensions can be administered by different routes such as oral, parenteral, topical, pulmonary and ocular. Since nanosuspension technology is simple techniques with less requirements of excipients. Thus is a universal formulation approach to increase the therapeutic performance of poorly water soluble as well as organic soluble drugs in any route of administration.

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