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NANOSUSPENSIONS: AN UPDATED REVIEW FOR SOLUBILITY ENHANCEMENT OF POORLY SOLUBLE DRUGS

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Abstract

Solubility plays and important role in development of dosage forms. The large number of newely discovered drugs is insoluble in water and other solvents. For such type of drugs Nano- suspension plays an important role during their development. These problems mainly arise mainly BCS class II type of drugs which are classified by Biopharmaceutical classification system. Nanosupension dosage form consist of poorly soluble drugs in which drug is suspended into dispersion. Preparation method of this type of dosage form is simple and this method is applicable for all type drugs having poor aqueous solubility. Nanosupension not only solve the solubility related problem on the contrary it increases the stability, safety, efficacy, and bioavailability. The present review describes its preparation methods, different features, needs, formulation, evaluation, characterization, applications, and current marketed formulations.

Keywords: Solubility enhancement**,** Nanosuspension, Dispersion, Stability, Parenteral.

Introduction

One of the key factors in achieving the optimum drug concentration in the systemic circulation for the desired (expected) pharmacological response is solubility, the phenomenon of solute dissolving in solvent to produce a homogeneous system. The main issue in developing formulations for new chemical entities as well as for generic development is low water solubility. Over 40% of the NCEs (new chemical entities) created by the pharmaceutical sector are essentially water insoluble. A significant difficulty for formulation scientists is solubility. (Kale et al., 2020) Any medicine that is to be absorbed must be present in solution at the absorption site. Particle size reduction, crystal engineering, salt creation, solid dispersion, use of surfactants, complexation, and other techniques are used to increase the solubility of poorly soluble pharmaceuticals. These techniques include physical and chemical drug changes as well as additional approaches. The choice of a solubility-improving technique depends on the drug's properties, the site of absorption, and the requirements for the dosage form. (Patel et al., 2015)

According to IUPAC, solubility is the analytical make-up of a saturated solution represented as a percentage of a specific solute in a specific solvent. Units of concentration, molality, mole fraction, mole ratio, and other units may be used to express solubility. (Chalk et al., 2019)

The development of nanosuspension technology makes it a promising contender for the effective delivery of hydrophobic medications. Drugs that are poorly soluble and insoluble in both water and oils are treated with this method. A pharmaceutical nanosupension is a biphasic system made up of nanoscale drug particles stabilised by surfactants for parenteral and pulmonary delivery as well as oral and topical application. (Swarbrick et al., 2002) The solid particles in nanosupension typically have a particle size distribution less than one micron, with an average particle size between 200 and 600 nm. Precipitation technique, media milling, high-pressure homogenization in water, high-pressure homogenization in non-aqueous medium, and a combination of Precipitation and high-Pressure homogenization are some of the different techniques used to prepare nanosupension. (Patravale et al., 2004)

Nanosupension drug delivery

Nanosupension is defined as a very finely divided solid drug particles in an aqueous or organic solvent which can either be used as oral or topical or pulmonary route of administration is called as Nanosupension. Particle size of nanosupension is less than 1 micron having average particle size range between 200 to 600 nm. (Kovalchuk et al., 2019)

Features of Nanosuspension (Kirichenko et al., 2020**)**

- **Particle Size:** 300 to 10 microns
- **Doses:** 10 to 20µg/ml
- **Routes of administration:** IV, IM, ID Injection, Oral, Topical, Respiratory.

Need Of Nanosuspension Drug Delivery

The preparation of nanosuspension is preferred for compounds with high log P values that are insoluble in water. When drugs are insoluble in both organic media and water, nanosuspension is used as a formulation approach rather than a lipidic system because it is more suitable for drugs with high log P values, high melting points, and high doses. (Pawar et al., 2017)

Poor bioavailability of drugs

Poor water solubility, a slower rate of dissolution, poor stability of the dissolved drug at physiological pH, poor penetration through biological membranes, and significant first pass metabolism are indications of a drug with low bioavailability. When taken orally, medicines that are poorly water soluble require substantial dosages to reach therapeutic plasma concentrations. The main issue in developing novel medication formulations is low water solubility. Any medicine that is to be absorbed must be present at the absorption site in the form of an aqueous solution. (Khan et al., 2016)

Lack of Dose response priority

Drugs are crucial to maintaining human health and selecting the best medication and dosage for each patient is a constant problem for clinicians. In the past, pharmacies and pharmacists frequently employed compounding to individualise prescriptions and deliver medication in various formulations and doses that weren't publicly accessible. Lesko et al., 2012)

Enhance the solubility drugs

For the absorption through the nose, the drug's solubility in the powder form is a key factor. It is a significant determinant in the drug's ability to pass through biomembranes and be absorbed. The drug is known to be absorbed when it is in solution form. (Hosey et al., 2017)

METHOD OF PREPRATION OF NANO SUSPENSION

Bottom up technology

Precipitation of supersaturated liquids is the foundation of the bottom-up strategy. It is commonly used to create nanosuspension in both bulk solutions and individual droplets. The solvent-anti-solvent approach, supercritical fluid processing, spray drying, and emulsion-solvent evaporation are a few pharmaceutical techniques that utilise this methodology. It is noteworthy that the process of producing nanoparticles involves numerous processes, including supersaturation, nucleation, diffusion of the solute molecules, and nanoparticle development.

The bottom-up approach has a number of benefits, including the ability to produce monodisperse particles, or particles with a narrow size distribution, the use of low energy and low processing temperatures for drugs that are thermolabile, the lack of sophisticated equipment requirements, and the fact that the process is generally cost-effective. This approach has recently been used to manufacture and commercialise various medicinal drugs, including Griseofulvin and Nabilone. Additionally, research has shown that the nanosuspension of the sold Danazol (a gonadotropin inhibitor) has higher improvement than the micro-suspension. Fascinatingly, combination techniques were used to create fenoibrate and Nitrendipine nanosuspensions. (Ahmadi Tehrani et al., 2019)

However, rapid growth can lead to the production of a variety of unstable polymorphs, hydrates, and solvates, including needle-shaped particles. Additionally, the use of anti-solvents or non-solvents is not recommended because even small amounts of residual medium might cause physicochemical instability. Therefore, non-solvents are eliminated either by supercritical fluid (SCF), which requires high pressure pump, temperature, and precision nozzle designing, or by evaporative precipitation into aqueous solution (EPAS). (Liu et al., 2016)

Top-down Technology

Top-down methods depend on milling, high pressure homogenization, and pulsed laser fragmentation to size-reduce and break down big materials into nanometer-sized particles. A spinning tool is used to mill materials, which produces smaller crystals or amorphous particles as a result of the constant mixing of particles with milling pearls.

High speed rotation, however, can produce a lot of heat, which degrades materials that are susceptible to heat. Additionally, milling can activate a drug particle's surface, which can change a number of physiochemical aspects of the particle, including its capacity to flow. To produce nanocrystals, high-pressure homogenization (HPH) is also used. The piston-gap homogenizer and the microfluidizer are two popular homogenizer designs that are regularly used to reduce particle size. (Ahmadi Tehrani et al., 2019)

Antisolvent Precipitation method

In this method water was used as an antisolvent precipitation of nanosuspension. The drug was dissolved in an ethanol solution that is water miscible, and the solution was then quickly added to water that contains a growth inhibitor or stabiliser. This is simple process having equipment coast is lower. This method has limitation, it requires at least one solvent is miscible with nonsolvent and it has chances of crystal growth in formulation. (Kuk et al., 2019)

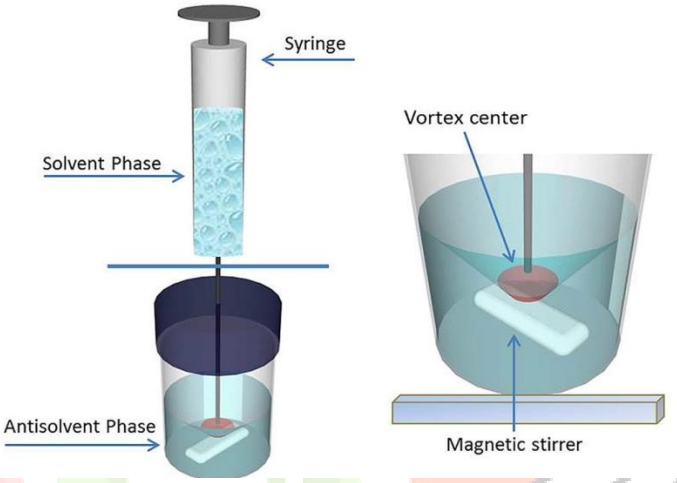

Figure 1.Prepration of nanosuspension by antisolvent precipitation method (Shariare et al., 2018**)**

Microemulsion template

This method involves dispersing a drug-loaded organic solvent or mixture of solvents into an aqueous phase with the appropriate surfactants to create an emulsion. Under lower pressure, the organic phase evaporates, causing the drug particles to rapidly precipitate and form nanosupension, which surfactants stabilise. (Jassim et al., 2018) Drugs that are either partially water soluble or soluble in the volatile organic solvents can be used in emulsion formulations. Additionally, nanosuspensions can be created using Microemulsion templates. Dispersions of two immiscible liquids, such as water and oil, are thermodynamically stabilised by a surfactant or cosurfactant are known as microemulsions. The drug can be saturated by close drug mixing and is either loaded into the internal or prepared phase of the microemulsion. Water, butyl lactate, lecithin, and the sodium salt of taurodeoxycholate are used to create a gliseofulvin nanosuspension using the microemulsion process. (Trotta et al., 2002)

Emulsification diffusion method

This process uses butyl lactate, benzyl alcohol, triacetin, and ethyl acetate as the dispersion phase, which are somewhat water-miscible and volatile organic solvents. The drug-loaded solvent mixture or organic solvent is dispersed to create the emulsion, which is then combined with water using high pressure homogenization or other methods. When droplets become solid particles due to dilution, the internal phase diffuses into the external phase, resulting in the production of nanosuspensions. The particle size is determined by the size of the emulsion droplets. Due to potential environmental risks and difficulties with human safety, the use of organic solvents including ethyl acetate, ethanol, methanol, and chloroform as well as the existence of residual solvents in the final products are significant downsides of this method. Emulsion diffusion has been used to create acyclovir nanosuspensions. (Yadollahi et al., 2015)

Media milling method

Milling is characterised as a "top-down" method for producing fine particles since it uses mechanical energy to physically transform coarse particles into finer ones. In medication formulations intended for parenteral, respiratory, and transdermal application, fine drug particles are particularly sought. For two to seven days, the milling chamber is changed with new milling media, water, medication, and stabiliser. The rotational speed is extremely high Glass zirconium oxide or polystyrene resin with a high degree of cross-linking make up the milling media. (Medarević et al., 2018) The drug impaction of the milling media with the drug results in the shattering of micro particulate drug to nano size particles, which generates the high energy shear forces. The biggest issue with this approach is that if any milling material is left in the end product, it may be difficult to administer. This method is applicable for those drugs which are poorly soluble in aqueous or organic media. This method has disadvantage during manufacturing because materials are eroded by balls which is problematic during storing or it is time consuming process. (Sawant et al., 2016)

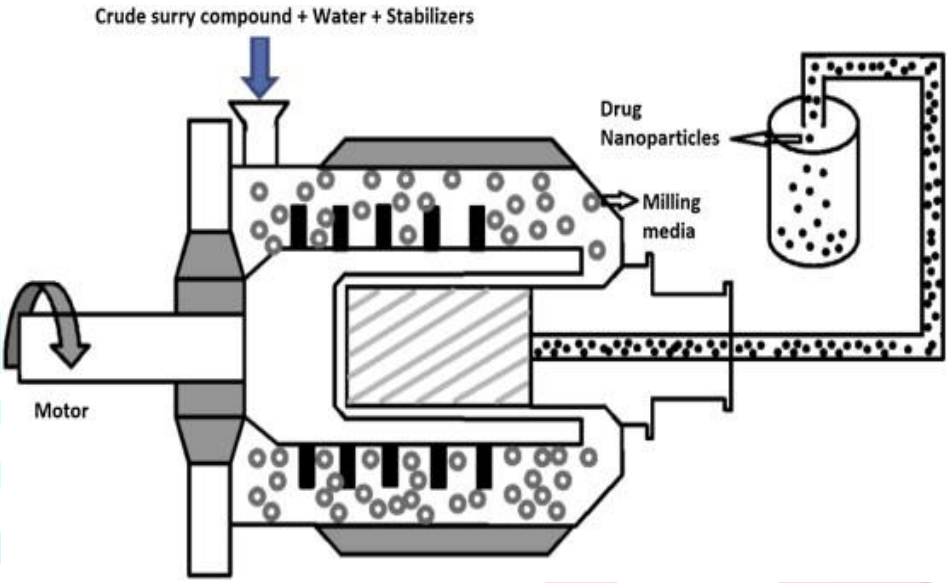

Figure 2.Media milling method of Nanosuspension

High pressure homogenization

It is the most popular technique for creating nanosuspensions of multiple medicines with low water solubility. There are three steps in formulation to create pre-suspensions, medication powders are first dissolved in stabiliser solution. In order to premill, the pre-suspension is secondly homogenised in a high pressure homogenizer at a moderate pressure. Once the nano-suspensions of the correct size are created, the mixture is finally homogenised at high pressure for 10 to 25 cycles. In method has advantage over media milling method because there are no chances of contamination. Parentral nanosupension are mostly prepared by this method. (Gora et al., 2016)

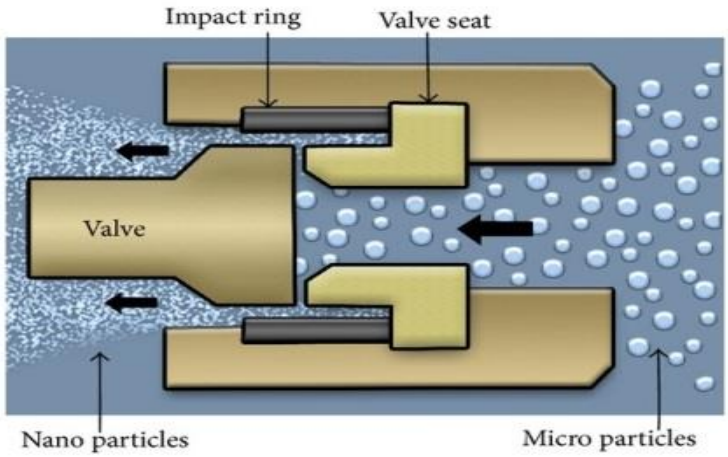

Figure 3. Schematic representation high pressure homogenization

Homogenization in aqueous media

Suspension is force under pressure via a valve with a small opening. It is most popular technique for creating nanosuspensions of numerous medications that are not easily soluble in water. This equipment may be operated at pressures ranging from 100 to 1500 bars (2800 to 21300 psi).Dissocubes are created utilising high pressure homogenizers with piston-gap design. The APV Micron LAB 40 homogenizer is a popular model for this.

A high-pressure plunger pump and a relief valve make up a high-pressure homogenizer (homogenizing valve).The plunger pump's job is to supply the energy needed for the relief. A fixed valve seat and an adjustable valve make up the relief valve. Together, they create a radial precision gap that is movable. As result the force operating on the valve, the gap conditions, resistance, and consequently the homogenising pressure change. (Khandbahale et al., 2019)

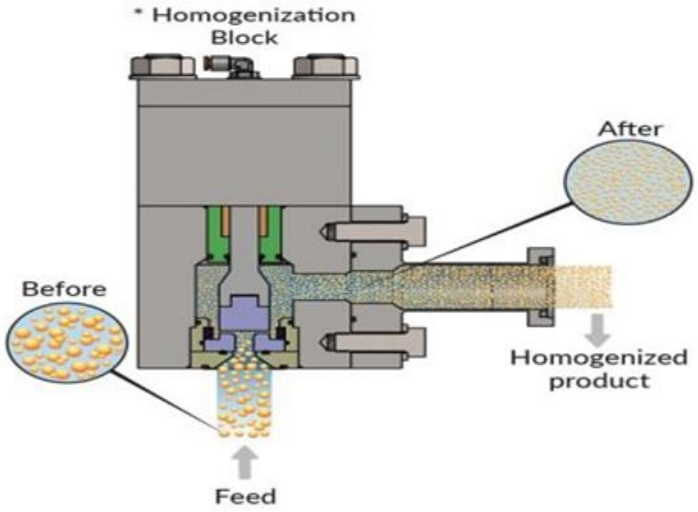

Figure 4. Homogenization in aqueous media

Principle of Dissocubes:

The cavitation mechanism underlies the particle size reduction in piston gap homogenizers. High shear forces and particle collisions result in a reduction of particles as well. The dispersion inside a cylinder with a 3 cm diameter suddenly flows through a 25 m-wide opening. The flow volume of liquid in a closed system per cross section is constant, according to Bernoulli's Law. The drop in diameter from 3 cm to 25 um results in a rise in dynamic pressure and a fall in static pressure below the water's ambient temperature boiling point. Due to this, water begins to boil at room temperature and produces gas bubbles that explode when cavitations, or the suspension leaving the gap, and normal air pressure are attained. Temperature, the number of homogenization cycles, the power density of the homogenizer, and homogenization pressure are the key determinants of the size of the drug nanocrystals that can be produced. (Patel et al., 2016)

Nanojet Technology

This process, also known as opposite stream or nanojet technology, makes use of a chamber in which a stream of suspension is split into two or more components that collide under high pressure. Particle size reduction is a result of the process's strong shear force. The M110L and M1105 microfluidizers are examples of equipment that utilise this technique (Microfluidics). (Chinthaginjala et al., 2020)

Nanoedge Technology

It combines the homogenization and precipitation techniques. The medication is dissolved in an organic solvent, and the resulting solution is then precipitated by adding a miscible antisolvent. It homogenises the suspension of the precipitated particles. The drug nanoparticles that precipitate have a propensity to continue growing crystals until they reach the size of microcrystals. It is necessary to process those using high-energy forces (Homogenisation). They can be totally crystalline, slightly amorphous, or completely amorphous, which causes issues with long-term stability and bioavailability. As a result, the precipitated particle suspension is then homogenised to maintain the particle size that was achieved during the precipitation process. The drawbacks of precipitation technique long term stability problem can be solved by Nanoedge technology. (Vedaga et al., 2019)

Supercritical Fluid Method

Drug solutions can be utilised to create nanoparticles using supercritical fluid technology. Three different approaches have been tried: precipitation with compressed anti-solvent process, supercritical anti-solvent process, and rapid expansion of supercritical solution (RESS) (PCA). The RESS involves expanding the drug solution in supercritical fluid through a nozzle, which causes the supercritical fluid to lose solvent power and cause the drug to precipitate as tiny particles. This method produced cyclosporine nanoparticles with sizes between 400 and 700 nm. In the PCA procedure, a chamber containing compressed CO_2 is used to atomize the medication solution.

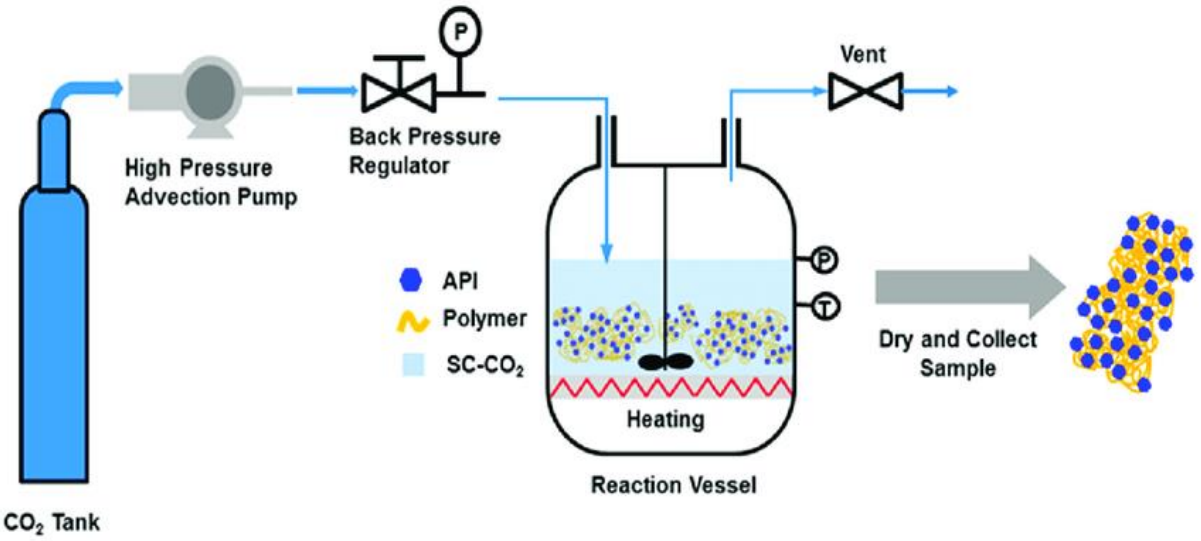

Figure 5.Nanosuspension prepared using Supercritical fluid technology

The solution becomes supersaturated as the solvent is withdrawn, which causes it to precipitate as tiny crystals. A drug that is poorly soluble in a supercritical fluid is used in the supercritical anti-solvent procedure along with a drug solvent that is also miscible with the supercritical fluid. When the drug solution is injected into the supercritical fluid, the solvent is removed and the drug solution becomes supersaturated as a result. After that, the medication precipitates as tiny crystals. This drawback of this method is it requires high pressure CO_2 and it is difficult to maintain. (Kulkarni et al., 2015)

Solvent evaporation method

The polymer solutions are made in emulsions and volatile solvents for the solvent evaporation process. On evaporation of the solvent, the emulsion transforms into a suspension of nanoparticles. The polymer's solvent, which is permitted to diffuse through the emulsion's continuous phase. The polymer concentration, stabiliser concentration, and homogenizer speed all had an impact on particle size. The manufacture of single emulsions, such as oil-in-water (o/w) or double-emulsions, such as (water-in-oil)-in-water, (w/o)/w, are the two primary ways for creating emulsions in conventional procedures. In order to evaporate the solvent using one of these techniques, high-speed homogenization or ultrasonication must first be performed. This solvent must then be continuously stirred magnetically at ambient temperature or under reduced pressure. The obtained solidified nanoparticles from ultracentrifugation were lyophilized after being rinsed with distilled water to eliminate any additions like surfactants. Oil-in-water (o/w) and (water-in-oil)-in-water (w/o)/w are examples of single-emulsions. (Sinha et al., 2015)

FORMULATION OF NANO SUSPENSION

Stabilizer

Acid inhibitors (amines, epoxides, phenols, pyridines, trimethylamine, alcohols, alkyl halides, and azo-aromatic compounds), metals, antioxidants, and light inhibitors are some of the chemicals added to formulations to improve their performance and longevity.

Polymers including polyvinyl pyrrolidone (PVP), hydroxypropyl methyl cellulose (HPMCs), and hydroxypropyl cellulose (HPCs), as well as ionic and nonionic surfactants such Tweens and Poloxamers and polyoxyethylene, are stabilisers frequently employed to stabilise nanosuspensions. (Kulkarni et al., 2015)

Organic solvents

When formulating nanosuspensions using emulsions or microemulsions as templates, it is important to take into account the acceptance of organic solvents in the pharmaceutical industry, their potential for toxicity, and how simple it is to remove them from the formulation. The formulation is preferred over the traditional hazardous solvents, such as dichloromethane, by using the pharmaceutically acceptable and less hazardous water miscible solvents, such as ethanol and isopropanol, and partially water-miscible solvents, such as ethyl acetate, ethyl formate, butyl lactate, triacetin, propylene carbonate, and benzyl alcohol.
(Gigliobianco et al., 2018)

Surfactants

A popular alternative for the dissolving of poorly soluble drugs is micellar solubilization. The methods of pH modification, cosolvency, micellization, and complexation are commonly used. The stabilisation and creation of nanosuspensions have been effectively accomplished using a variety of surfactants, including Tweens, sodium dodecyl sulphate, and co-surfactants, including bile salts, transcutol, glycofurol, ethyl alcohol, and isopropyl alcohol. (Jacob et al., 2020)

Co-surfactants

Drugs are made more soluble by cosurfactants, which work by lowering interfacial tension. Ionic or nonionic cosurfactant that aid in system stabilisation by forming dynamic micelles lowers interfacial tension in formulation. (Rawal et al., 2018) Transcutol, glycofurol and ethanol is mainly used co-surfactants in nanosuspension.

Other additives

The other additives in formulation of nanosuspension include buffers (maintained pH environment), osmoagents (maintained tonicity in case of parentral nanosuspension) and cryoprotectants (antifreeze agents). (Pawar et al., 2017)

EVALUATION AND CHARECTERIZATION NANOSUSPENSIONS

Mean Particle Size and Size Distribution

Due to their control over other features including saturation solubility, dissolving rate, physical stability, and in vivo performances, particle size and size of distribution are important characteristics. Most frequently, photon correlation spectroscopy or dynamic light scattering are used to determine the average particle size. (Sinha et al., 2015)

Zeta potential

The stability of the suspension is indicated by the zeta potential. A minimum zeta potential of 30 mV is necessary for a stable suspension stabilised exclusively by electrostatic repulsion, although a zeta potential of 20 mV would be sufficient in the case of an electrostatic and steric stabiliser working together. (Li et al., 2007)

Shape and Morphology

The most popular methods for analysing the morphology and form of dispersed nanoparticulates are transmission electron microscopy (TEM) and scanning electron microscopy (SEM). SEM is a crucial technique for observing changes in particle size (similar to agglomeration during solvent evaporation) before and after water removal when NSs are processed into dried powder form (e.g., by spray drying or lyophilization). Cryoprotectants are typically used during freeze drying to prevent this aggregation occurrence. (Ahuja et al., 2015)

Crystalline state and particle morphology

By examining the crystalline state and particle morphology, can be determined by whether nanosized particles have undergone polymorphic or morphological changes. As high-pressure homogenization is necessary for nanosuspension, during formulations crystalline structure changes and may be changed to amorphous or other polymorphic forms. X-ray diffraction analysis and differential scanning calorimetry are used to determine how the drug particle's in solid state has changed and how much it is amorphous. (Zawar et al., 2018)

STABILITY OF NANOSUSPENSION

The aggregation of the drug crystals is caused by the high surface energy of nanoscale particles. The stabilizer's key role is to thoroughly saturate the drug particles in order to prevent Ostwald ripening and Nanosuspension agglomeration and to provide a physically stable formulation by acting as a steric or ionic barrier. Stabilizers such cellulosics, poloxamer, polysorbates, lecithin, polyoleate, and povidones are frequently utilised in nanosuspensions. When creating parenteral Nanosuspensions, lecithin may be preferred. (Guan et al., 2022) The following table shows the relationship between Zeta potential and emulsion stability.

Table1: Relationship between Zeta potential and emulsion stability. (Ghaseminezhad et al., 2016)

Stability Characteristics	Avg. Zeta Potential in millivolts
Maximum agglomeration and pre	0 to +3
Range of strong agglomeration and precipitation	+5 to -5
Threshold of agglomeration	-10 to -15
Threshold of delicate dispersion	-16 to -30
Moderate stability	-31 to -40
Fairly good stability	-41 to -60
Very good stability	-61to -80
Extremely good stability	-81 to -100

PHARMACEUTICAL APPLICATION OF NANOSUPENSIONS

Oral drug delivery system

Oral suspension provides for liquid medication, which is recommended in the geriatric and paediatric age groups while ensuring chemical stability. Other benefits include disguising the bitterness of medications, increasing the time they take to work, boosting the aqueous solubility of drugs that aren't very water soluble, and improving drug dissolution and bioavailability. Additionally, suspension is the preferred option if the medicine is insoluble in water and other solvents are prohibited. (Jacob et al., 2020)

Oleanolic acid has a wide range of uses, including hepatoprotective, antitumor, antibacterial, anti-inflammatory, and antiulcer properties. However, due to its low aqueous solubility, it exhibits unpredictable pharmacokinetics when taken orally. When oleanolic acid is applied as a nanosuspension, the dissolution rate rises to nearly 90% in the first 20 minutes as opposed to barely 15% for medication powder that has been micronized. The rate of drug dissolution is accelerated when drug particle size is decreased to the nanoscale, and drug particle adherence to the mucosa may also be improved. Drug intestinal absorption is increased by increased blood-to-GIT concentration gradient and improved interaction with intestinal cells (bioadhesive phase). Low intersubject variability, dosage proportionality, and better oral absorption are some benefits of the nanosuspension. Drug nanosuspensions can be easily included into a variety of dosage forms, such as tablets, capsules, and rapid melts, by employing normal manufacturing procedures. (Jacob et al., 2020)

Parentral drug delivery system

It is uncommon to provide intravenous and intraspinal preparations in a form other than aqueous solutions. The use of alternative forms by intravenous administration is discouraged by the risk of capillary obstruction, particularly in the brain. Even though complete parenteral nutrition has used microemulsions, the particle size of the dispersed phase is strictly controlled below 5 m. Parenteral products can be administered intramuscularly, subcutaneously, or topically as solutions, suspensions, or emulsions. (Jacob et al., 2020)

Various parental routes, including intraarticular, intraperitoneal, intravenous, etc., are used to give nanosuspensions. Additionally, parenterally given medications work better because to nano suspensions. According to reports, paclitaxel nanosuspension is superior in lowering the average tumour burden. In female mice infected with Mycobacterium avium, clofazimine nanosuspension performed better than liposomal clofazimine in terms of stability and efficacy. (Pawar et al., 2017)

Ophthalmic drug delivery system

For a sustained release of the medications, nanosuspensions are used. Using Eudragit, Liang and colleagues created cloricromene nanosuspension for ocular administration. An experiment revealed that the rabbit eye's aqueous humour has higher drug availability. Therefore, nanosuspension formulation offers a potentially effective technique to increase the drug's bioavailability and shelf life following ophthalmic application. (Pignatello et al., 2002)

Pulmonary drug delivery system

Drugs with poor pulmonary secretion solubility may be delivered most effectively by nanosuspensions. These medications are now administered using dry powder inhalers or suspension aerosols. (Patravale et al., 2004) Drugs used in dry powder inhalers and suspension aerosols frequently undergo jet milling and have micron-sized particle sizes, because the medication moiety in suspension aerosols and dry powder inhalers is microparticulate and has a wide particle size distribution. (Malamatari et al., 2016)

Targeted drug delivery system

Because of surface characteristics and the behaviour of the stabiliser may be easily changed in vivo, nanosuspensions can also be employed for targeting. (Pawar et al., 2017) The mononuclear phagocytic system can uptake the medication to enable localised administration. If the infectious pathogen is still present inside the cells, this can be utilised to direct anti-mycobacterial, anti-fungal, or anti-leishmanial medications toward the macrophages. In order to increase medication targeting against leishmania-infected macrophages, Kayser created a nanosuspension of Aphidicolin. (Patel et al., 2020)

MARKETED NANOSUSPENSIONS

Table2: Currently marketed Nanosuspensions (Jacob et al., 2020)

Trade Name/Company	Drug	Dosage form and its route of administration	Nanosuspension method	Indication
Abraxane®/Abraxia Biosciences	Paclitaxel	Freeze-dried powder for injection/ Parenteral	nab™	Metastatic breast cancer
Cesamet®/Lilly	Nabilone	Capsule/Oral	Coprecipitation	Antiemetic
Emend®/Merck	Aprepiant	Capsule/Oral	Nanocrystal*Elan Nanosystems	Antiemetic
Giris-PEG*/Novartis	Griseofulvin	Tablet /Oral	Coprecipittation	antifungal
Invega Sustenna®/ Johnson & Johnson	Palperidone palmitate	Liquid nanosuspension/ Parenteral	High pressure homogenization	Schizophrenia
Megace ES*/Par Pharmaceutical Companies	Megestrol-acetate	Liquid nanosuspension/ Oral	Nanocrystal*Elan Nanosystems Media milling	Anti-anorexic
Triglide®/First Horizon Pharma	Fenofibate	Tablet /Oral	IDD-P® Skyepharma	Hypercholesterolemia
Avinza®/King Pharmaceuticals	Morphine sulphate	Tablet /Oral	Nanocrystal*Elan Nanosystems	Psychostimulant
Ritalin®/Novartis	Methyl Phenidate HCl	Tablet /Oral	Nanocrystal*Elan Nanosystems	Muscle Relaxant
Zanaflex™/Acorda	Tizanidine HCl	Capsule/Oral	Nanocrystal*Elan Nanosystems	Muscle Relaxant
Focalin®XR/Novart	Dexmethylpheni	Tablet /Oral	Nanocrystal*El	CNS

is	date hydrochloride		an Nanosystems	Stimulant
Ostim*/Heraseus Kulzer	Hydroxyapatite	Paste/Injection	-	Bone substitute
EquivaBone®/Zimmer Biomet	Hydroxyapatite	Paste/Injection	-	Bone substitute
Vitoss*/Stryker	Calcium phosphate	Foam packs, Foam strips/Injection	-	Bone substitute
Ryanodex®/Eagle Pharmaceuticals	Dantrolene sodium	Freeze-dried powder for injection/intravenous	-	Malignant hypothermia

CONCLUSION

Nanosuspension shows high level bioavailability for poorly soluble drugs. In order to increase issues with hydrophobic drug delivery, such as poor bioavailability and lower absorption, nanosuspensions provides an novel and commercial approach for solutions. For the bulk production of nanosuspensions, particularly those that are poorly soluble in both aqueous and organic media, manufacturing techniques such media milling and high-pressure homogenizer are mainly used. Nanosuspension type of drug delivery involves various types of drug administration such as oral, ophthalmic, parentral, pulmonary and targeted. Hence the above review shows the nanosupension is beneficial drug delivery system for poorly soluble drugs, and it has universal formulation approach for increasing therapeutic performance of such type of drugs.

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