AN OVERVIEW OF NANOSUSPENSION PREPARATION, CHARACTERIZATION, AND EVALUATION AS A STRATEGY FOR POORLY SOLUBLE DRUGS

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Abstract- **The speed at which the drug development process is progressing is producing a number of novel drug candidates with good therapeutic efficacy but poor water solubility. Because of its unique physicochemical characteristics and submicron particle size, nanosuspension holds the potential to address numerous formulation and drug delivery challenges that are commonly linked to poorly soluble medicines in water and fat. To manufacture and scale-up nanosuspensions, conventional size reduction tools like media mills and high-pressure homogenizers as well as formulation strategies including solvent diffusion, emulsion-solvent evaporation, precipitation, and microemulsion procedures can be effectively used. For the successful manufacture and scaling-up of nanosuspensions, it is important to take into account two crucial factors: maintaining the stability in both the solid and solution states and resuspendability without aggregation. The versatility for surface modification and mucoadhesion for drug targeting, along with the notable improvement in bioavailability, have greatly broadened the application of this innovative formulation approach. Much research is now being done on the use of nanosuspensions in various drug delivery methods, including oral, ophthalmic, brain, topical, buccal, nasal, and transdermal routes. Receptor-mediated endocytosis in combination with oral drug delivery in nanosuspension has great promise for resolving most permeability-limited absorption and hepatic first-pass metabolism-related problems that negatively impact bioavailability. The development of enabling technologies, including nanosuspension, can address numerous formulation issues that currently plague protein and as well as peptide based formulation.**

Keywords: **Nanosuspension, novel drug delivery, solubility enhancement, Surfactant etc.**

INTRODUCTION:

The term "Nanosuspensions" refers to liquid phase submicron colloidal dispersions containing pharmaceutical active ingredient particles smaller than 1 μm in size, free of any matrix material and stabilized by surfactants and polymers.(1)

1. Solid lipid nanoparticles are lipid carriers of medications, whereas nanoparticles are polymeric colloidal carriers of drugs. This is how nanosuspensions differ from both types of nanoparticles. Many newly produced medications have low solubility, which makes it difficult to overcome established methods to address these solubility variables and can lead to issues with bioavailability. In many circumstances, medications are poorly soluble in both aqueous and organic environments. Making medication nanoparticles, or nanosuspensions, is a different and potentially effective strategy to solve these issues. Because of their many uses and distinct benefits, nanosuspensions have become a viable method for the effective administration of hydrophobic medications. Because of their distinct properties, nanosuspensions can now be used in a wide range of dosage forms, including ones that require specialized delivery methods like mucoadhesive hydrogels. The main benefits of this technique are its simplicity and broad application to the majority of medications.(2)
2. Nanosuspension preparation is easy and works with any medication that is water insoluble. Wet mills, high pressure homogenizers, melt emulsification, emulsion solvent evaporation, and supercritical fluid processes are used to prepare nanosuspensions. It is possible to administer nano-suspensions orally, parenterally, pulmonaryly, or intraocularly. Utilizing nanosuspensions in mucoadhesive hydrogels and ocular inserts allows for tailored drug delivery as well. At the moment, efforts are focused on expanding their use in medication administration that is site-

specific. The distribution of nanosuspensions via parenteral, preoral, ocular, and pulmonary routes has advanced quickly.[3]

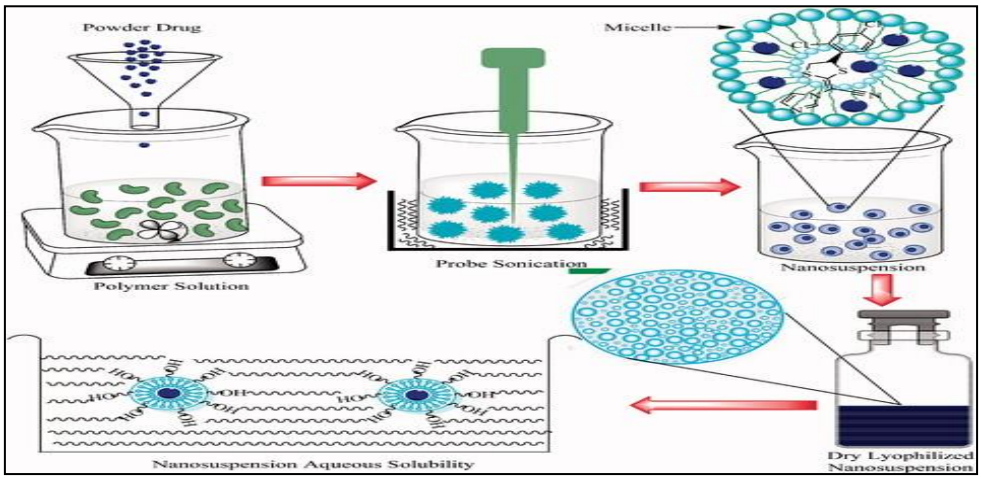

figure.1 general outline for nanosuspension preparation

- **WHEN TO GO FOR NANO SUSPENSIONS APPROACH**

Nano suspension preparation is the recommended method for compounds with high log P values that are soluble in oil but insoluble in water. Liposome and emulsion systems are typically used to develop medications that are soluble in oil phase systems but insoluble in water; however, these lipidic formulation techniques are not suitable for all pharmaceuticals. Nano suspensions are the favored method in these situations.[4] Rather than utilizing lipidic systems for the formulation of pharmaceuticals that are insoluble in both organic and water-based media, nanosuspensions are employed.For substances with high log P value, high melting point, and high dosage, the nanosuspension formulation technique is most appropriate.[5]

- **TECHNIQUES FOR PREPARATION OF NANOSUSPENSIONS**

Although technically easier to prepare than liposomes and other traditional colloidal drug carriers, nanosuspensions are said to be more economical. In particular, it is used to produce a physically more stable product and for pharmaceuticals that are poorly soluble. There are two opposite techniques for producing nanosuspensions: "Bottom-up process technology" and "Top-down process technology." The disintegration process from macroscopic particles, microparticles, to nanosized particles is followed via the top-down method.[6]

1. High pressure homogenization
2. Nanoedge
3. Nanopure
4. Media milling (Nanocrystals)

An assembly technique called "bottom-up" creates nanoparticles from molecules. Examples include the following:

1. supercritical fluid process.
2. emulsification solvent-evaporation technique.
3. Lipid emulsion/micro-emulsion template.
4. solvent evaporation process.
5. Melt emulsification method.

METHODS OF PREPARATION OF NANOSUSPENSION

1. HIGH PRESSURE HOMOGENIZATION:

This is the most popular technique for creating nanosuspensions of numerous medications that are poorly soluble in water. There are three steps to it. Presuspension is created by dispersing drug powders in stabilizer solution first. The presuspension is then homogenized in a high pressure homogenizer at a low pressure for premilling, and lastly homogenized at high pressure for 10 to 25 cycles, or until the appropriate size of nanosuspensions is achieved. This idea has led to the development of several techniques for creating nanosuspensions, including Disso cubes, Nanopure, Nanoedge, and Nanojet.[7]

2. HOMOGENIZATION IN AQUEOUS MEDIA (DISSO CUBES)

R.H. Muller invented the technique of homogenization in aqueous media in 1999, employing a high pressure homogenizer of the piston-gap type. Through the use of pressure, the medication and surfactant suspension is pushed through a high pressure homogenizer's nanoscale aperture valve.[8]

Principle: Cavitation, strong shear forces, and particle collisions cause the drug particles to shatter during homogenization. The drug suspension, housed in a cylinder with a diameter of approximately 3 mm, abruptly passes through a 25 μm homogenization gap, creating a high streaming velocity. According to Bernoulli's equation, below the room temperature boiling point of water, the fluid's dynamic pressure rises as the static pressure falls in the homogenization gap.[9] As a result, room-temperature water begins to boil, causing gas bubbles to form. These bubbles explode when the suspension exits the gap, a process known as cavitation, and regular air pressure is restored. It breaks down the drug microparticles into nanoparticles because the implosion forces are high enough. A further factor in the drug's nano-sizing is the high-speed particle collision. Viscosity enhancers can be used in some situations to increase the efficiency of nano-sizing because they increase the density of powder within the dispersion zone (homogenization gap) when viscosity is increased.[10]

The following process variables need to be looked into in order to get an optimum formulation.

3. EFFECT OF HOMOGENIZATION PRESSURE

To optimize the process parameters, it is important to examine the impact of the homogenization pressure on the particle size in each situation, given that the homogenizer has the capacity to handle pressures ranging from 100 to 1500 bars. It is anticipated that a smaller particle size will be obtained at higher homogenization pressures.[11]

4. NUMBER OF HOMOGENIZATION CYCLES

It is often not feasible to achieve the target particle size in a single homogenization cycle for a variety of medications. Usually, several cycles are needed. Therefore, homogenization can be completed in three, five, or ten cycles, depending on the drug's hardness, the needed homogeneity of the product, and the intended mean particle size. It is expected that a lower particle size will be obtained with more homogenization cycles. After each cycle of homogenization, the drug's particle size and polydispersity index can be analyzed to determine the ideal number of cycles.[12]

Merits:

- It is simple to synthesize medications into nanosuspensions, even if they are poorly soluble in organic or aqueous environments.
- Simple scaling up and minimal batch-to-batch differences.
- The end product contains a narrow size distribution of the drug nanoparticulate, and the aseptic manufacturing of nanosuspensions for parenteral administration is made possible.
- The ability to handle drug quantities with flexibility, ranging from 1 to 400 mg/mL, allowing for the production of both highly concentrated and very diluted nanosuspensions.

Demerits:

- It is necessary to get the medication particles micronized and to produce the suspension with high-speed mixers before homogenizing it.

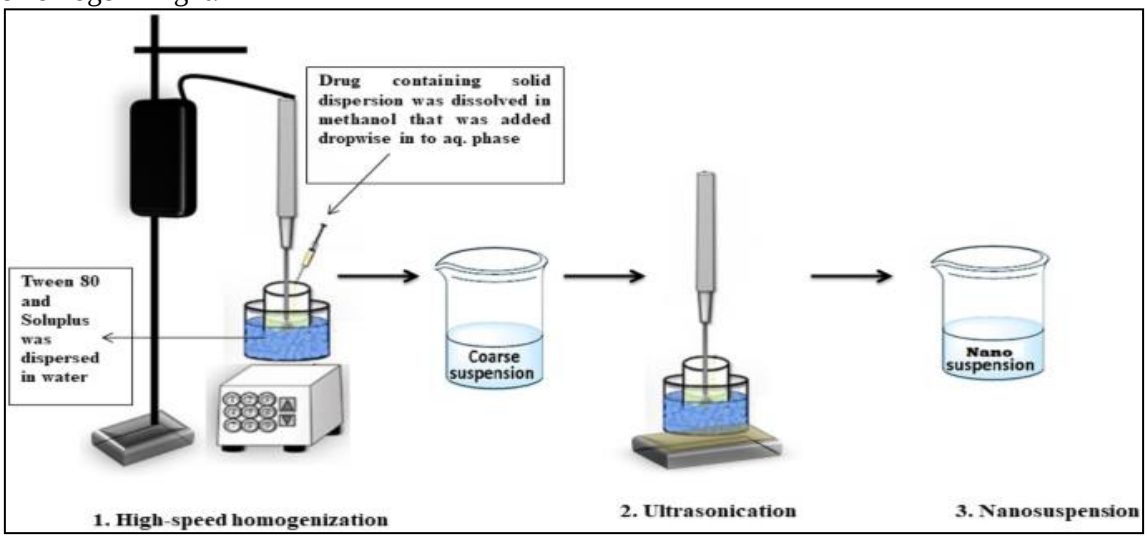

Figure.2 high pressure homogenization

5. MILLING METHOD

A. MEDIA MILLING

PRINICIPLE

The energy input needed to break the drug down into nanoparticulate form comes from the high energy and shear pressures produced when the drug is impounded into the milling media. Glass, zirconium oxide, or strongly cross-linked polystyrene resin make up the milling media. Either batch or recirculation mode can be used to carry out the procedure. It takes between thirty and sixty minutes in batch mode to achieve dispersions with unimodal distribution profiles and mean diameters less than 200 nm. Both micronized and non-micronized medication crystals can be processed effectively using the media milling method. There is virtually little batch-to-batch fluctuation in the dispersion quality after the formulation and the technique are tuned.(14)

Advantages :

- It is simple to construct medications into nanosuspensions even if they are poorly soluble in organic or aqueous media.
- Little fluctuation between batches and ease of scaling up.
- The finished nano-sized product has a narrow size dispersion. A comparison of naproxen crystal sizes prior to and following media milling.
- The ability to handle drug quantities with flexibility, ranging from 1 to 400 mg/ml, allowing for the production of both highly concentrated and very diluted nanosuspensions.

Disadvantages :-

- Time is required for the media milling process.
- Scale-up is difficult because of mill size and weight; some fractions of particles are in the micrometer range.

B. PRECIPITATION

Precipitation has been used to create submicron particles throughout the past ten years, particularly for medications that are poorly soluble. Before mixing the drug solution with a miscible antisolvent in the presence of surfactants, the drug is first dissolved in a solvent.

When a drug solution is added to the antisolvent, the drug suddenly becomes super saturated and ultrafine crystalline or amorphous drug solids are formed.(15)

Advantages

- Easy to scale up, affordable production, and a straightforward method.

Disadvantages :

- The inclusion of surfactants is necessary to control the growth of crystals.

C. DRY CO-GRINDING

A lot of nanosuspensions are now made using the dry milling method. Dry co-grinding is a simple, cost-effective process that doesn't require the use of organic solvents. Co-grinding improves the physical-chemical characteristics and solubility of pharmaceuticals that are poorly soluble in water by changing the drug's surface polarity and transforming it from a crystalline to an amorphous state.

Advantages :

- Simple to use and requires no organic solvent.
- Need little time for grinding.

Disadvantages :

- Production of milling media residue.
- Expensive equipment.

6. EMULSIFICATION-SOLVENT EVAPORATION TECHNIQUE

This method entails making a drug solution and then emulsifying it in a different liquid that acts as a nonsolvent for the medication. Precipitation of the medication results from solvent evaporation. With the use of a high-speed stirrer, large shear forces can be generated to regulate both crystal development and particle aggregation.

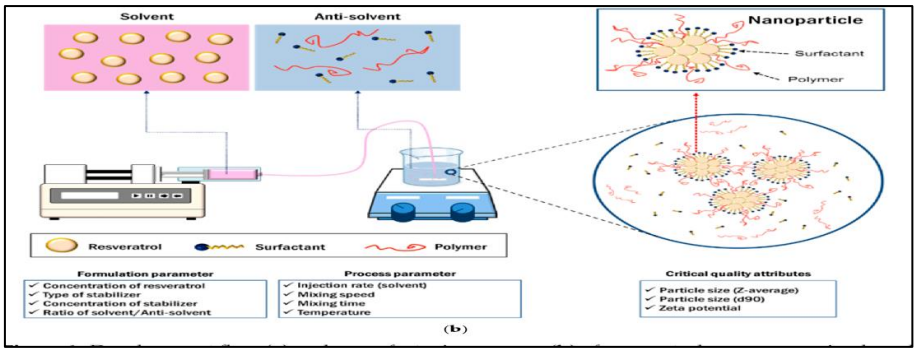

figure.3 emulsion solvent evaporation technique

7. SUPERCRITICAL FLUID PROCESS

By using the super critical fluid technique with solubilization and nanosizing technologies, a further reduction in particle size was attained. Noncondensable dense fluids with temperatures and pressures higher than their critical temperature (Tc) and critical pressure (Tp) are known as super critical fluids (SCF).Drug particles can be micronized to the submicron level thanks to this method. Recent developments in the SCF technique enable the creation of nanoparticulate suspensions with diameters ranging from 5 to 2000 nm. The low solubility of surfactants and medications that are weakly soluble in water in supercritical CO2 along with the high pressure needed for these operations limit the applications of this technology in the pharmaceutical sector.[16]

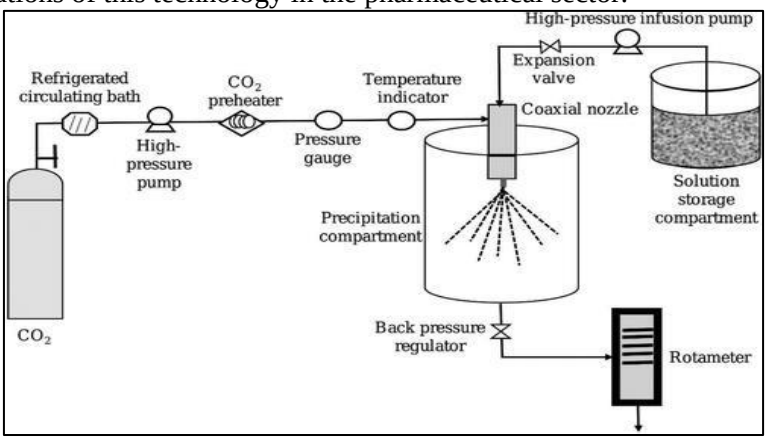

figure.4 supercritical fluid process

8. MELT EMULSIFICATION METHOD

This process involves dispersing the medication in the stabilizer's aqueous solution, heating it over the drug's melting point, and homogenizing it to create an emulsion. The temperature of the emulsion was kept above the drug's melting point throughout this procedure by wrapping the sample holder in a heating tape equipped with a temperature controller. After that, the emulsion was either allowed to gradually cool to room temperature or placed on an ice bath.

Advantages:-

- The complete avoidance of organic solvents during the production process is the advantage of the melt emulsification technology over the solvent evaporation method.

Disadvantages :-

- Smaller compliant objects and larger particles are formed compared to solvent evaporation.

9. HOMOGENIZATION IN NON-AQUEOUS MEDIA (NANOPURE)

Homogenized suspensions in water-free media or water mixes, such as PEG 400, PEG 1000, etc., are known as nanopure. The term "deep freeze" homogenization refers to the fact that the process can be carried out both at room temperature, or 0ºC, and below freezing point, or -20ºC.

10. NANOEDGE

Combining homogenization with precipitation results in nanoedge technology. The homogenization and precipitation core principles are the same. Using Nanoedge technology, it is possible to solve the main drawbacks of the precipitation process, such as crystal formation and long-term stability. It is possible to produce smaller-sized and more stable particles quickly.

11. NANOJET

It is also known as opposing stream technology, it works by splitting a suspension stream into two or more pieces. These parts then collide under high pressure, reducing the particle size as a result of the strong shear forces created in the process.[13]

12. LIPID EMULSION/MICROEMULSION TEMPLATE

Drugs that are soluble in volatile organic solvents or solvents that are slightly water miscible are the most suitable candidates for this approach. Using the appropriate surfactants, the medication was emulsified in an aqueous phase after being dissolved in an appropriate organic solvent. Subsequently, the organic solvent was gradually evaporated under lower pressure, causing drug particles to precipitate in the aqueous phase and create the necessary particle size aqueous suspension. After that, the suspension can be appropriately diluted to create nanosuspensions. Furthermore, nanosuspensions can be made using microemulsions as templates.Microemulsions are isotropically transparent, thermodynamically stable dispersions of two immiscible liquids, such water and oil, that are supported by a surfactant and co-surfactant interfacial coating. The medication can be intimately mixed into the pre-formed microemulsion to make it saturated, or it can be loaded into the internal phase. The medication nanosuspension is produced by appropriately diluting the microemulsion. Lipid emulsions are advantageous as templates for the generation of nanosuspensions because they are simple to make by regulating the emulsion droplet and simple to scale up. However, using organic solvents has an adverse effect on the environment, necessitating the use of significant volumes of stabilizer or surfactant.[17]

Advantages:-

- Long shelf life.
- Easy to manufacture.
- High drug solubility.

Disadvantages :-

- Use of very concentrated stabilizers and surfactants.
- Use of dangerous solvents.

13. SOLVENT EVAPORATION

The polymer solutions are made in volatile solvents and emulsions using the solvent evaporation method. However, in recent years, ethyl acetate, which has a superior toxicological profile, has taken the place of dichloromethane and chloroform, which were formerly used. When the solvent for the polymer evaporates and the emulsion is allowed to spread through its continuous phase, it transforms into a suspension of nanoparticles. Two primary approaches are utilized in traditional methods to generate emulsions: single-emulsions (such as oil-in-water, or o/w) and double-emulsions (such as water-in-oil, or w/o)/w). These techniques call for rapid homogenization or ultrasonication, then continuous magnetic stirring at ambient temperature or at low pressure to evaporate the solvent. The solidified nanoparticles are recovered by ultracentrifugation, and they are lyophilized after being cleaned of additives like surfactants using distilled water. The stabiliser, homogenizer speed, and polymer concentration all had an impact on the size of the particles. [18]

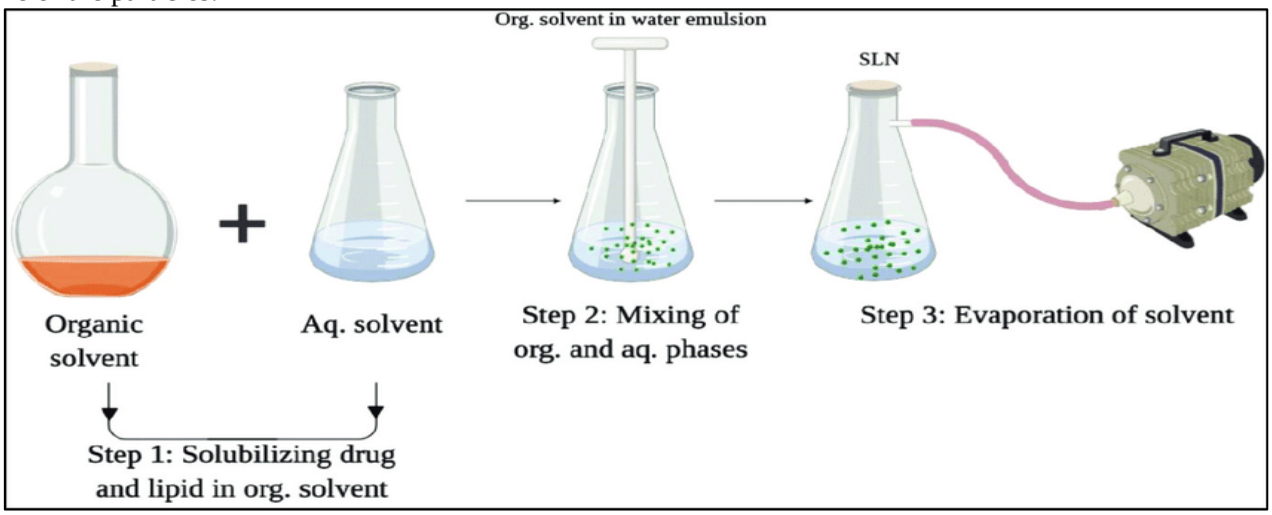

Figure.5 solvent evaporation method

IN-VITRO EVALUATION

1. Organoleptic properties

Formulations that must be administered orally must take these characteristics into account.Taste variations can be explained by changes in particle size, crystal habit, and subsequent particle disintegration, especially for active chemicals. Changes in flavor, scent, and color can all be signs of chemical instability.

2. Particle size distribution

Particle size affects physicochemical properties like physical stability, saturation solubility, and dissolving rate. The particle size distribution can be ascertained using a number of methods, such as photon correlation spectroscopy, laser diffraction (LD), and the Coulter counter multisizer. PCS can measure particles with a size range of 3 nm to 3 m, in contrast to LD, which has a measuring range of 0.05–80 m. Whereas LD provides a relative size distribution, the Coulter counter multisizer produces a predetermined quantity of particles. Given that the lowest capillary size is approximately 5–6 m, it is preferred for particles utilized for intravenous (IV) usage to be smaller than 5 m in order to prevent problems such capillary occlusion and embolism.[19]

3. Zeta potential

Zeta potential can be utilized to quantify the stability of the suspension. A zeta potential of at least 30 mV is required for a stable suspension that only relies on electrostatic attraction. Nonetheless, a zeta potential of 20 mV is thought to be sufficient when both steric and electrostatic stabilizing processes are operating.

4. Crystal morphology

The effects of high-pressure homogenization on the drug's crystalline structure can be investigated using methods such as differential scanning calorimetry or X-ray diffraction analysis in conjunction with differential thermal analysis. High-pressure homogenization in nanosuspensions can lead to changes in the crystalline structure, such as the appearance of amorphous or other polymorphic morphologies.

5. Dissolution velocity and saturation solubility

Nanosuspensions offer a substantial advantage over other techniques since they can raise the rate of dissolving and saturation solubility. In order to fully understand the formulation's behavior in vitro, these characteristics need to be investigated in a range of physiological solutions. Böhm et al. claim that increasing the particle size to the nanoscale area may accelerate and increase the dissolving pressure. It has been shown that the pressure of dissolution rises with decreasing size.

6. Density

The specific gravity, or density, of a formulation is an important consideration. Air trapped inside the formulation structure could be the source of the problem if the density drops. It is advised to determine density at a specific temperature using a homogeneous, thoroughly mixed mixture. Precision hydrometers are a useful tool for measuring density.

7. pH Value

To ensure equilibrium has been reached and to prevent "pH drift" and electrode surface coating caused by suspended particles, the pH value of an aqueous formulation must be evaluated at a specific temperature. It is advised against adding electrolytes to the formulation's outer phase in order to maintain pH stability.[20]

8. Droplet size

To determine the distribution of droplet sizes in microemulsion vesicles, electron microscopy can be employed. This can be done in a dynamic light scattering spectrophotometer using a neon laser with a wavelength of 632 nm.

9. Measurement of viscosity

The viscosity of lipid-based formulations with different compositions can be measured at different shear rates and temperatures using a Brookfield type rotational viscometer. The instrument's thermobath-controlled sample chamber, which must be maintained at 37°C, is where the measurement samples should be submerged.

10. Stability of nanosuspension

Drug crystals may assemble in nanosuspensions due to their high surface energies and small particle sizes. Stabilizers are necessary to completely moisten the drug particles, prevent agglomeration and Ostwald ripening, and form a physically stable formulation because they provide a steric or ionic barrier. Cellulosics, poloxamers, lecithin, polyoleate, and povidones are commonly used as stabilisers in nanosuspensions. Often times, lecithin is used as a component in parenteral nanosuspensions.[21]

IN-VIVO EVALUATION:

To track a drug's efficacy in the body, an in vitro/in vivo correlation must be established, regardless of the route and mode of delivery. This is important when discussing intravenously administered nanosuspensions since the drug's ability to distribute throughout the body depends on its surface characteristics, including its hydrophobicity and ability to interact with plasma proteins, both of which are influenced by the drug's in vivo behavior. It is widely acknowledged that the size and type of protein absorption pattern observed following intravenous injection of nanoparticles are important determinants impacting organ distribution. Using appropriate techniques to evaluate surface characteristics and protein interactions is essential to comprehending behavior in vivo.given via intravenous injection. Hydrophobic interaction chromatography is one technique for determining surface hydrophobicity, and 2-D PAGE is another technique for measuring and analyzing protein adsorption in animals following intravenous injection.[22]

Table 1 : Current marketed pharmaceutical products utilizing nanocrystaline formation

Product	Drug compound	Indication	Company	Nanoparticle technology
RAPAMUNE®	Sirolimus	Immunosuppressant	Wyeth	Elan Drug Delivery nanocrystals
EMEND®	Aprepitant	Antiemetic	Merck	Elan Drug Delivery nanocrystals
MEGACE® ES	Megestrol acetate	Appetite stimulant	PAR Pharmaceutical	Elan Drug Delivery Nanocrystals
TRICOR®	Fenofibrate	Treatment of hypercholesterolemia	Abbott	Elan Drug Delivery Nanocrystals
TRIGLIDE™	Triglide	Treatment of hypercholesterolemia	First Horizon Pharmaceutical	SkyePharma IDD®-P technology

APPLICATIONS OF NANOSUSPENSIONS

1.Oral drug delivery

The oral route is usually recommended because it has multiple well-known advantages.Some antibiotics that are used orally, such as atovaquone and Buparvaquone accurately reflects this issue. The nanosizing of such medications can result in a significant increase in oral absorption and, as a result, bioavailability. The area under the curve (AUC) (0-24 h) for naproxen nanoparticles was 97.5 mg-h/L, compared to 44.7 mg-h/L for naprosyn suspensions and 32.7 mg-h/L for anaprox tablets. The gonadotropin inhibitor Danazol has an absolute bioavailability of 82.3 when administered orally as a nanosuspension, but the traditional dispersion (Danocrine) has a bioavailability of only 5.2%. In comparison to the usual formulation, a nanosuspension of amphotericin B exhibited a considerable improvement in oral absorption.[23]

2. Pareneteral drug delivery

Nanosuspensions can be supplied by a variety of parenteral methods, including intra-articular, intraperitoneal, and intravenous injection. To administer via parenteral route, To minimise capillary occlusion, the drug must be solubilized or have particle/globule size less than 5 m. Furthermore, nanosuspensions have been shown to improve the efficacy of Drugs that are delivered intravenously. Paclitaxel nanosuspensions outperformed taxol in terms of lowering the median tumour burden. Similarly, when supplied as a nanosuspension, aphidicolin, a poorly water soluble novel anti parasite lead molecule, resulted in a lower EC50 when compared to DMSO-dissolved drug. Clofazimine nanosuspension, a poorly water-soluble antileprotic medication, demonstrated improved stability and efficacy in M. avium-infected female mice [35]. Rainbow and colleagues found that an intravenous itraconazole nanosuspension improved antifungal activity compared to a solution formulation in rats.[24]

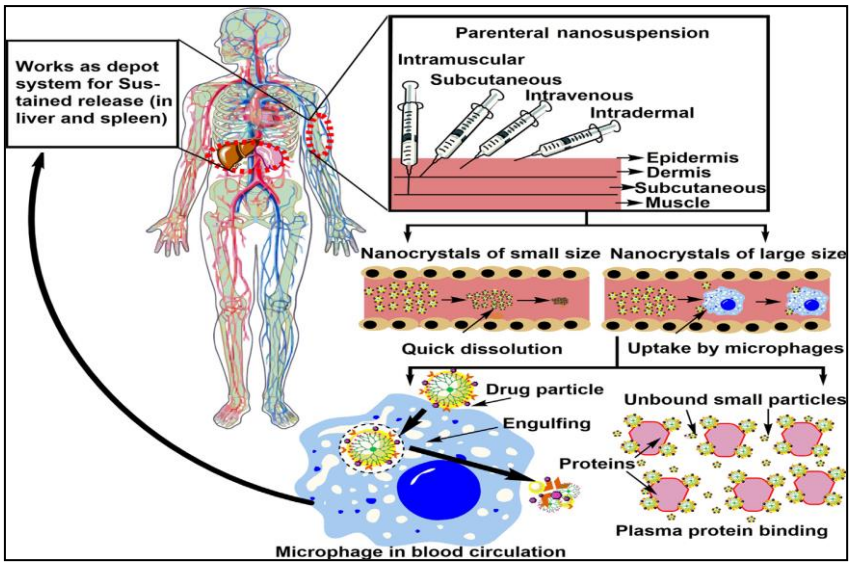

Figure 6. drug nanocrystals in vivo destiny after intravenous administration

3.Pulmonary drug delivery

Nanosuspensions could be an ideal method for delivering medications that are poorly soluble in pulmonary secretions. Mechanical or ultrasonic nebulization of aqueous nanosuspensions is possible. Nebulizers are used to administer medication to the lungs. Because of their small size, each aerosol droplet is expected to contain at least one drug particle, resulting in a more equal distribution of the drug in the lungs. The drug's nanoparticulate structure enables for fast diffusion and disintegration at the site of action. At the same time, the drug's improved adhesion to mucosal surfaces allows for a longer residence period at the absorption site. This feature of nanosuspensions provides a rapid onset of action, followed by controlled release of the active moiety, which is extremely advantageous and essential. By the majority of pulmonary illnesses. An ultrasonic nebulizer was used to successfully nebulize budesonide medicinal nanoparticles.[25]

4.Ocular drug delivery

Nanosuspensions can be beneficial for medications that are poorly soluble in lachrymal fluids. The eye's natural defences make medication administration challenging without causing tissue harm. Inadequate drug uptake and medication penetration into intraocular tissues impede drug administration. Nanoparticles and nanosuspensions are being developed for medicine delivery to intraocular tissues. Cross-linked polymer nanosuspensions of dexamethasone, for example, provide increased anti-inflammatory efficacy in a rabbit eye irritation model.

5.Targeted drug delivery

Because the surface characteristics and in vivo behaviour of nanosuspensions may be easily adjusted by altering either the stabiliser or the solvent, they can be employed for targeted distribution or the setting. The future of targeted drug delivery systems is the building of stealth nanosuspensions (similar to stealth liposomes) with varied surface coatings for active or passive targeting of the desired spot . Kayser created an aphidicolin nanosuspension to increase medication targeting against Leishmania-infected macrophages. He reported that the conventional version of the medicine had an effective concentration (EC 50) of 0.16 mcg/mL, whereas the the nanosuspension formulation demonstrated increased activity, with a (EC 50) of 0.003mcg/m.

6.Mucoadhesion of nanoparticle

Nanoparticles delivered orally in the form of a suspension diffuse into the liquid medium and quickly come into contact with the mucosal surface. The initial stage before particle absorption is direct particle interaction with intestinal cells via a bioadhesive phase. The adhesiveness of the nanosuspensions not only improves bioavailability but also improves targeting of parasites that persist in the GIT, such as cryptosporidium parvum. Because of their prolonged residence at the infection site, mucoadhesive Buparvaquone nanosuspensions reduced the infectivity score of cryptosporidiumparvumas by a factor of ten when compared to buparvaquone nanosuspensions without mucoadhesive polymers.[26]

CONCLUSION

The greatest formulation choice for rigid, hydrophobic medications restricted by high dosage, melting point, molecule weight, and log P. Nanosuspensions can be successfully prepared and scaled up by using conventional size reduction processes like wet milling and homogenization, as well as formulation strategies like precipitation, emulsion-solvent evaporation, solvent diffusion, and microemulsion procedures. This innovative formulation's usefulness has been greatly strengthened by significant improvements in bioavailability brought about by enhanced saturation and intrinsic

solubility, noticeable mucoadhesivity, and flexibility for surface modification in drug targeting. For formulation scientists, nanosuspension may prove to be an invaluable instrument in addressing numerous formulation and drug delivery obstacles related to diverse drug entities. The use of nanosuspensions in medication delivery systems for the mouth, eyes, and lungs has been the subject of much research in recent years. Furthermore, there is a lot of research being done on the use of nanosuspensions in various medication delivery methods, including topical, nasal, buccal, cerebral, and transdermal. Pharmaceutical experts have given nanosuspension a lot of thought, but more research is needed to determine the precise mechanisms underlying the stabilization, solidification, and redispersibility of dried nanosuspension.

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