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NANOSUSPENSION: A COMPREHENSIVE REVIEW ON INTRODUCTION, METHODOLOGY, REQUIREMENT AND CHARACTERISATION

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ABSTRACT

Nanosuspensions are critical carriers in the development of new medication formulations. Because of their diverse properties and unique advantages, nanosuspensions have emerged as a viable technique for the proficient conveyance of hydrophobic medicines. Due to their cost adequacy and innovative effortlessness when contrasted with liposomes and other colloidal medication transporters, nanoscale frameworks stand out enough to be noticed as a way to tackle solubility difficulties. This review paper examines nanosuspension manufacturing methods, characterization techniques, applications, and patented goods to handle the issue of inadequately water-soluble medicines. There are two basic ways to make nanosuspension: 'bottom-up' and 'top-down' mechanisation. Stabilisers, organic solvents, cryoprotectants, pH adjusters, buffers, polyols, salts, and osmogent can be used to make nanosuspension, as can stirring speed, temperature, and additives such as stabilisers, organic solvents, cryoprotectants, pH adjusters, buffers, polyols, salts, and osmogent. Nowadays, nanosuspension is popular and used for targeted drug delivery systems.

KEYWORDS: Nanosuspension, Solubility, Bioavailability, Agglomeration, Nanoparticles, Mechanisation.

1. INTRODUCTION

A Novel Drug Delivery System (NDDS) is a novel and inventive approach whose services incorporates modern equipment artistic advancement, composition, updated gadgets and novel methodology for delivering various remedial substances throughout the anatomy to produce their desired pharmacological effects. It also incorporates scientific body site targeting, improved medication potency, control, and better drug release with a longer pharmacological impact. It necessitates creating newer, better, and safer medications with extended half-lives and high quantitative measurements of the relative safety of the medication. Recent advancements in this area of NDDS have opened up a slew of new research opportunities in nanotechnology and its derivatives. A pharmaceutical nanosuspension is an aqueous formulation containing very finely dispersed solid drug particles for oral, topical, parenteral and also pulmonary administration. Surfactants, polymers or a combination of both, as well as other excipients, stabilise a homogeneous therapeutic dissipation of sub-micron size in a nanosuspension. These are primarily intermittent systems that disseminate natural drug fragments in water-soluble medium. In nanosuspensions, solid fragments are typically smaller than 1 micron in dimensions, with standard particle dimensions of 400–700 nm. In a nanosuspension, the drug is made up of insoluble or poorly water-soluble particles. All medications that are water insoluble can be prepared as nanosuspensions.[1] Poor dissolution and absorption are addressed, and the pharmacokinetics of the drug are altered, enhancing medicinal potency and tolerability. The variety of particle sizes throughout the nanometer category can result in enhanced disintegrating pace and peak immersion for a nanosuspension, therefore frequently results in increased drug accessibility, in accordance with Noyes-Whitney and Ostwald-Freundlich tenets.[2] The smaller particle size also allows for the intravenous administration of poorly soluble medicines without capillary blockage. Lyophilization or mist draining of nanosuspensions allows the incorporation of the suspended nanoparticles into a rigid medium. The two most common approaches for making nanosuspensions are "bottom up" and "top down" engineering. Precipitation, micro emulsion, and melt emulsification processes are all examples of bottom up technologies for forming nanocrystals. Top-down nanotechnology uses processes like elevated homogenization and pounding to break up larger suspended particles into nanoparticles. Nanosuspensions are generally utilized for drugs that are very slightly soluble in water however freely soluble in oil.[3,4] Nanoparticles in a nanosuspension stick to the mucosal surface of the GI tract, extending the drug's contact duration and increasing its absorption. One of the major advantages of nanosuspension is that

it can be supervised via number of channels such as oral, intravenous, pulmonary, parenteral, cutaneous, and ophthalmic. Nanoparticles (NPs) in a nanosuspension enjoy a few upper hands over traditional dosage forms, including reduced dose, controlled drug release, prolonged therapeutic effect, reduced systemic toxicity, better medication absorption as the consequences of extended nanoparticle contact time on the mucosal layer, and increased drug concentrations in a diseased tissue. Nanoparticles may be an advantageous drug delivery technique for multiple routes of administration since they are excellent for very slightly soluble medicines and patients digest tiny particles quicker than heavier ones. Formulation consideration such as stirring speed, temperature, and additives like Stabilizers, organic solvents, cryoprotectants, pH adjusters, buffers, polyols, salts, and osmogent can be used to make nanosuspension.[5,6] When integrated into ocular inserts and mucoadhesive hydrogels, nanosuspension can be employed for ocular targeted medication administration also.

2. THE REQUIREMENT FOR NANOSUSPENSION TO INCREASE BIOAVAILABILITY

In this approach, the drug is conserved in the proper translucent condition with a smaller particle size, giving it a faster dissolving rate and therefore enhanced bioavailability. When the contact area (and hence the dissolving velocity) of micronized particles increases, the dissolution rate also increases. Nanoparticles can improve solution mobility and saturation solubility due to the influence of condensate stress. Moreover, the propagation distance between drug nanoparticles on their surfaces is reduced, resulting in a greater concentration gradient. When compared with microparticles, an increase in contact location and gradation of content results in a noticeably higher spike in dissolution velocity.[7]

3. ADVANCING NANOSUSPENSION[8,9]

- It is appropriate for medications that are poorly soluble or insoluble in water.
- Nanosuspension increases drug bioavailability and efficacy by addressing issues of poor solubility.
- Reduce tissue irritation, whether administered subcutaneously or intramuscularly.
- IV administration and mucoadhesive hydrogels can achieve rapid dissolution and tissue targeting.
- Nanosuspensions administered orally have a higher bioavailability and are more quickly absorbed.

- Enhanced bioavailability and tailored distribution of drugs, plus primarily uniform dosages, include all the benefits of ocular infusion and aerosol therapy.
- The presence of stabilisers and pH adjusters ensures material toughness over time.
- Nanosuspensions can be employed in tablet form, pellet form, hydrogel form, transdermal patches form, and suppositories form.

4. DEMERITS OF NANOSUSPENSION

- Problems with settling, steadiness of the material agglomeration, and compaction may occur.
- Since it is cumbersome, it must be handled and transported with extreme caution.
- If the suspension is not packed in unit dosage form, it may be difficult to achieve an accurate and uniform dose.

5. MANUFACTURING TECHNIQUES

Nanosuspension preparation is easier and less expensive than liposomes and other colloidal drug carriers on a technical level. It is especially useful for poorly soluble medicines, as it results in the production of a stable drug product. There is couple of strategies for making nanosuspensions i.e. "Top-down" and "Bottom-up" approach.[10]

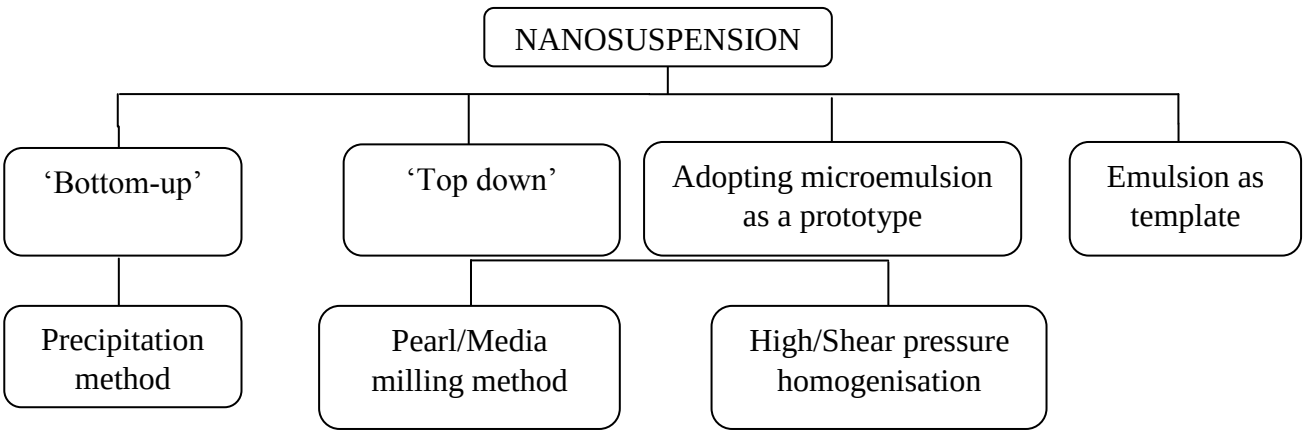

Figure 1: Methodology to generate a nanosuspension.

5.1 Upturned Technology

Bottom-up technology produces nano-sized particles by increasing particle size from the molecular to the nano-scale. 'Bottom-up' technique refers to the customary method of precipitation. Using this liquefication procedure, the drug is first dissolved in liquid substance before being mixed with any floppy anti-solvent.[11] Drug precipitation occurs due to the drug's poor solubility in the water-solvent mixture. To minimize agglomeration and the

creation of microparticles, the crystal development must be controlled by the use of a surfactant during the precipitation process.

Schematic Representation of Nanosuspension Formulation

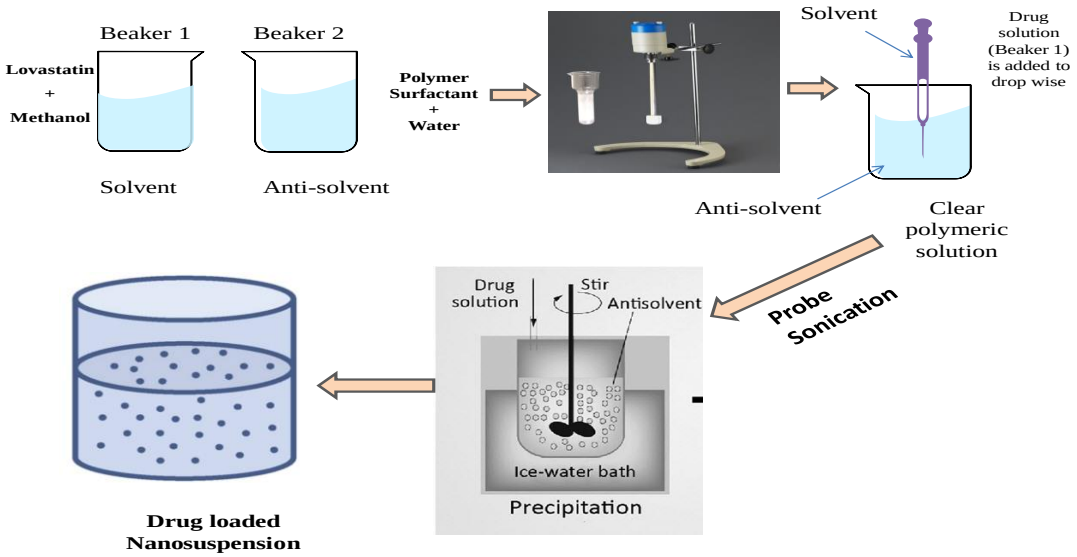

Figure 1 Formulation Method of Nanosuspension.

5.2 Controlled Technology

High/Shear-Pressure Homogenization

First, drug powder is breakdown in a solvent having stabilizer to generate pre-suspension; subsequently, this pre-suspension is homogenized an adequate preloading exertion and subsequently homogenized at an enormous amount force for 15-25 installments, until the desired nanosuspensions with 400-700 nm dimensions of particles are created.

5.2.1 Homogenization in an Aqueous/water media (Disso cubes)

The principle behind this procedure is cavitation, which entails imposing a suspension comprising a drug, polymers, and surfactant through a high-pressure homogenizer constituting a small opening, dropping the an inactive force just underneath the water's vapour level. A cylinder's dispersion around 3 cm diameter is abruptly passed via a 25µm wide gap.[12] This causes the water to boil and gas bubbles to develop. Particle size decrease occurs as a result of the encircling region supporting the drug particles rushing through the middle and collisions when a suspension escapes the space and usual airflow resumes. The cavitation force of the particles is sufficient to create drug nanoparticles from microparticles. It is often desirable to begin homogenization with relatively minute drug particles, which may

also be performed by pre-milling, for the creation of greater strength quantum suspensions of solid. High pressure homogenization has the advantage of being able to use it for both diluted and concentrated solutions, as well as allowing aseptic production.[13-15]

5.2.2 Milling Technique (nanocrystals or nanosystems)

This method is also known as the pearl milling technique, and it involves the use of high-shear mills create nanosuspensions. A chamber mill, a shaft mill or motor, and a recirculation compartment make up a media mill. Glass (yttrium-stabilized), zirconium oxide, ceramics, and polystyrene copolymers are generally used to frame the media mills. The slurry of drug, polymers, and stabilisers is supplied into the chamber mill, which is charged with media mills. The suspended materials are reduced in size in the media chamber, which is done at controlled temperatures. The microparticulate drug is converted into nanosized particles by severe mechanical attrition and impaction.[16]

5.2.3 Nanopure

Suspensions homogenised in non-aqueous or water-free medium are known as nanopure.[17] The drug suspension in non-aqueous fluid was homogenised in the nanopure technology at a low temperature, ideally at 0°C or even lower. According to literature on the disintegration of polymeric and drug components, high temperatures around 80°C promote disintegration by high pressure homogenization, which thermolabile molecules cannot employ, so this technology has an advantage over dissocubes because it can be used for thermolabile compounds. Deep-freeze method is another name for this method.[18,19]

5.2.4 Nanoedge

The nanoedge technology is a hybrid of homogenization and precipitation methods.[20] When both of these approaches are used, a suspension with lower particle size and greater stability is formed. A technique could alleviate the main limitations of hastiness approach, similarly crystal formation and agglomeration. Precipitation is carried out in solvents which are water miscible including ethanol, methanol and acetone, and the solvents are subsequently removed or evaporated from the media. Then the precipitation in suspension is homogenised further, resulting in particle size reduction and the avoidance of agglomeration.

5.2.5 Nanojet Technology

Nanojet is a technology that allows you to print with nanoscale precision. Nanosuspensions are made in a chamber where a suspension stream is split into at least two parts and then

colloided with every parts at high shear pressure. The reduction in particle size is beacause of the high shear impaction force created throughout the operation. In this methodology, the final product contains a high percentage of particles in micro range. For example, atovaquone nanosuspension by microfluidizer is an example of this approach known as opposite stream technology.[21]

5.3 Micro emulsion template

The medication is put into an organic solvent, then, dispersed in water-based phase with the required amount of emulsion-forming surfactants. Now, organic phase is removed causing the drug particles to precipitate fast, resulting in the Nanosuspension, which is then stabilised with surfactants. The procedure is expensive due to the high volume of surfactants and the necessity for ultrafiltration for purification.[22]

5.4 Emulsion as Template

To make nanosuspension, an emulsion is employed as a template. This technology can be used to make medications that are partially soluble in water. Organic solvents such as ethyl acetate, ethanol were used in the beginning. The resulting emulsion was homogenized further using high pressure homogenization. However, residual solvents' usage in ordinary manufacturing processes inspite of safeguarding along with the natural dangers, the operation remains constrained.[22]

5.5 Other Methods

5.5.1 Super Critical Fluid Method

Supercritical Fluid Technique has evolved as a significant solubilization technology, with increasing applications in particle size reduction. Supercritical liquid technology allows for the creation of nanoparticles concerning medication formulation. Diversification of the extreme remedy quickly is generally used to produce nanoparticles in which the super critical fluid and CO2 are initially delivered at the required pressure and temperature to the extraction chamber holding the solid substances. The supercritical solution expands rapidly in the precipitator, generating a pressure and temperature collapse that promotes the generation of droplets and particles.[23]

5.5.2 Dry-co grinding

Co-grinding is a method of preparing nanoparticles in which the medicine is processed with one or more excipients such as polyvinyl pyrrolidone(PVP) or polyethylene glycol (PEG),

resulting slightly diminished nanoparticle dimension. Among the benefits are: It's a simple method that doesn't require any organic solvents, requires little grinding time, enhance physicochemical properties and improves the dissolving of drugs that aren't very water soluble.[24]

6. REQUIREMENT FOR FORMULATION OF NANOSUSPENSION

6.1 Temperature

When making nano-suspensions, it's critical to keep the temperature at the right level. During the addition of drug containing solvent phase to the anti-solvent phase in the emulsion template method, homogenization is measured at a low temperature. Because of the volatile organic cleaners used in the formulation, maintaining a low temperature is a crucial consideration, since higher temperatures cause the formation of irregular particles owing to fast elimination. If a constant low temperature is kept throughout the process, the solvents are gradually removed from the process, resulting in the creation of circular and uniform nanoparticles.

6.2 Stabilizer

A stabilizer's primary job is of thoroughly wetting of the drug particles, inhibit clumping of drug particles, Ostwald's ripening, and maintain the constant consistency and desirable qualities of the nanosuspension until it is taken by the patient. In order to ensure stability, they also maintain an ionic or steric hinderance. The amount and kind of stabiliser has a significant impact on nanosuspension in vivo performance and stability. Poloxamers, polysorbate, tweens, HPMC, lecithins, and PEG 400 have all been utilised as stabilisers. If you want to make a nanosuspension of a poorly soluble medication, you should use poloxomers as a stabilizer.[25]

6.3 Organic Solvent

When microemulsions or emulsions or are employed as a template in the formation of nanosuspension, organic solvents are utilised. Methylene chloride, ethyl acetate, ethanol, methanol, and chloroform are common organic solvents. When a microemulsion is utilised as a template for the creation of nanosuspension, partially water-miscible organic volatile solvents such as glycols and ethyl acetate are commonly used.[25,26]

6.4 Co-surfactants

During creating nanosuspension employing tiny emulsion as a model, the choice of cosurfactant is crucial. Cosurfactants are utilized in addition to wetting agents or surfactants to increase product performance and stability. Surface tension can be reduced to almost nil with cosurfactants, and total viscosity can be reduced as well. The usage of bile salts and dipotassium glycyrrhizinate as cosurfactants has been documented in the literature. Other regularly used cosurfactants in the creation of nanoparticles include glycerol, sorbitol, butanol, and benzalkonium chloride.[27]

6.5 Stirring Speed

The speed at which the mixture is stirred is also an essential formulation parameter. High shear homogenization (HSH) can be used to homogenise nanosuspensions, resulting in an attrition force for particle size reduction. It has been discovered that raising the speed of stirring during HSH or the number of cycles during HPH tends to reduce particle size, which is not ideal, and that a normal speed must be maintained for the preparation. The ideal RPM for HSH is 20000 RPM, and the ideal cycle length for HSH is 5 to 6 cycles. This is due to the development of a lot of froth in the suspension as a result of the greater agitation speed, which causes the solid nanoparticles to separate early from the suspension medium. Therefore ineffective size reduction and divergence from the nano-sized range are possible outcomes.

6.6 Other Additives

The compatibility with the drug abuse, additionally nanosuspension may include components like buffering agent, minerals synthetic polyols and cryoprotectant. Cryoprotectants (DMSO, glycerol), buffers (acetate, phosphate), and osmogent (Mannitol-dextrose).

7. PROPERTIES OF NANOSUSPENSION[28-31]

7.1 Nanosuspension stability

It is also noteworthy that nanosuspension doesn't undergo Ostwald ripening, meaning they remain physically stable over time. The ripening process in Ostwald results in the growth of crystals and consequently the production of microparticles. The variations between tiny and bigger particles in dissolving pressure and saturation solubility cause Ostwald ripening.

7.2 Adhesiveness

The grip of extremely fine nanoparticles is much greater than that of ordinary materials. The direct delivery of barely dispersed medications could be improved by using the pharmaceutical nanostructures based on the extent.

7.3 Morphology and Crystalline state

One characteristic to examine is the possibility of changes in the crystalline lattice of nanosuspensions, such as more fractions of unformed particles or even the formation of totally amorphous particles. High pressures were used to make nanosuspensions, and it was discovered that this promoted the amorphous form. DSC or colorimetry studies and the scale of the unstructured proportion and any changes in the solidified aspect of the medicament molecules should have assessed using the X-ray diffraction examinations. SEM is favored for obtaining an accurate picture of lattice morphology of the particles.

7.4 Drug Saturation Solubility and Dissolution Velocity

Drugs dissolution velocity increases because of the increased particle dimensions from microns to nanometers, “according to the Noyes-Whitney equation”:

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

Here, D = coefficients of dissemination, A = particle extensive region, dx/dt = diluting speed, V = volume of the dissolving agent, h = diffusion layer thickness, and X = concentration in the encompassing fluids.

7.5 Intrinsic Arrangement

During the disintegration process, the rapid electric power produces structural lattice alterations throughout the drug molecule. Particles of the medication are changed from crystalline to amorphous states when exposed to high-pressure homogenization. Drug hardness, the total number of absorption cycles, the chemical composition of the drug, and the homogenizer speed are all factors influencing the change in state.

8. CHARACTERIZATION OF NANOSUSPENSION

Chemical, physical, and biological studies are commonly used to characterise nanosuspension. The nanosuspension's critical characterizations include crystalline lattice, DSC tests, mean particle size, particle size arrangement, particle shape, FT-IR, dissolving velocity, particle surface charge, saturation solubility, in-vivo biological studies, and stability

studies. Zeta potential (which determines particle charge), particle size, and particle size arrangement all have an impact on the stability, safety, and performance of nanodrug delivery systems. Particle size also affects dissolving performance in nanosuspension. As a result, the characterization of nanoparticles is critical in assessing the effectiveness of nanodrug delivery systems. The performance of nanosuspension in vivo and in vitro, as well as its pharmacological effect and biological function, is greatly influenced by nanoparticle shape, crystallised state, zeta prospective, diameter and dispersion of the fragments and energy.

8.1 Particle Size Distribution and Particle size of Nanosuspension

The breaking down rate, optimum concentration and stability of nanosuspension are all influenced by the particle size distribution (polydispersity index, Pl) and mean particle dimension on average. The physiochemical behaviour of a product, such as its dissolution, physical stability, and solubility, is determined by its particle size distribution. Zetasizer Nano ZS (Malvern instrument), the pattern of spread sizes may be determined using the coulter counter multisizer, laser diffraction (LD), along with distribution.[32] The P1 value of 0.1–0.25 implies a size arrangement that is nearly small, whereas a P range larger than 0.5 shows a distribution that is very wide. The Coulter multisizer provides the perfect quantity of particles as well as their size, and it is a more reliable and efficient technology than laser diffraction, which counts the size of particles in materials by measuring the angle of light scattered as a laser beam passes through them.[33]

8.2 Zeta Potential (electrokinetic potential)

The electrokinetic potential assesses and quantifies the thickness of the outer layer potential. Using the zeta potential, we can estimate the diffusion layer thickness, optimize the suspension, and speculate about durability. A minimal electrokinetic potential of 30 mV is necessary to create a nanosuspension with acceptable colloidal stability, whereas a minimal electrokinetic voltage of 20 mV is preferred for steric and electrostatic stabilization.[34]

8.3 pH

At a temperature of 251°C, the pH of nanosuspension is commonly determined with a digital pH metre. The pH metre electrode is dipped into the formulation and allowed to equilibrate for at least 1 minute. After that, the observations were recorded, and then the mean and standard were determined.

8.4 Crystal Morphology

Electron microscope for inspecting, electron microscope for transmission, and diffractions of X-rays analysis are used to examine the nanoparticle sample and alterations to the crystal arrangement known as polymorphism then extreme pressure causes homogenization, which results in medication dispersion. Because of the high-pressure homogenization and milling method, nanosuspension can change its crystalline shape, perhaps to an amorphous or other polymorphic state. As the percentage of amorphous drug fraction increases in a formulation, the saturation solubility can be enhanced.[35,36]

8.5 Stability of nanosuspensions

Nanoparticles with a high surface energy cause drug crystals to aggregate. The basic role of the stabiliser (such as poloxamer, tweens, etc.) is to moisten the drug particles, lower surface tension, inhibit agglomeration and Ostwald ripening of the nanosuspension, and construct a formulation that is physically stable by establishing an ionic or steric barrier, resulting in drug homogeneity. Lecithin, cellulosics, polysorbates, poloxamers, povidones, and polyoleates are examples of stabilisers commonly employed in nanosuspensions. In the formulation of parenteral nanosuspensions, lecithin may be preferred.[37,38]

8.6 Saturation solubility and dissolution velocity

Nanosuspension outperforms other approaches by increasing the dissolving velocity and saturation solubility, as well as the drug's bioavailability and pharmacological activity. The determination of saturation solubility and dissolution velocity provides insight into the formulation's in vitro and in vivo behaviour. According to Bohm et al., the dissolving pressure and velocity rise when the particle size is reduced to the nano range.[39] In the case of smaller particles, the dissolving pressure increases. The increase in solubility that happens as particle size decreases is mostly due to an alteration in interfacial tension, which leads to an increase in saturation solvability.

9. APPLICATIONS OF NANOSUSPENSIONS

9.1 Enhancement of Bioavailability

The explanation for the poor oral bioavailability of the drug may lie in its poor solubility, which further produces poor permeability and, as a result, poor pharmacological impact. To address these difficulties, poorly soluble medicines are nanosuspended to enhance bioavailability.[40] Surfactants and stabilisers are used in a nanosuspension to resolve the issue of poor bioavailability. The limited solubility of oleanic acid is overcome by using a

nanosuspension formulation. When compared to the dissolution of traditional dosage forms, the therapeutic impact of the lyophilized nanosuspensions powder was dramatically boosted (90% in 20 min).[41]

9.2 Targeted Drug Delivery

It is possible to customise the distinctive features of the outer layer and into the body performance of nanosuspensions by adding either stabilisers or excipients to change combined into the body and superficial characterstics. Therefore, it is possible to develop focus conveyance with an economically feasible nanosuspension due to their adaptability and ease of scaling up. Over the past few years, buparvaquone and amphotericin B nanosuspensions were made by enhancing the surface properties of these nanosuspensions for mobile or submissive targeting of the target site.[42]

9.3 Parenteral Drug Delivery

To reduce side effects and target the drug to a specific portion of the body, parenteral aqueous nanosuspensions are manufactured in aseptic circumstances. Nanosuspensions can also be sterilised via autoclaving, gamma radiation, or sterile filtration. Because omeprazole is totally metabolised in the liver, it is safe to inject omeprazole nanosuspension intravenously (IV) in order to prevent the chemical deterioration of it when taken orally.[43] Tissue focusing, rapid pharmacological impact, extended period of preservation in the bloodstream and lower toxicity are all potential advantages.

9.4 Pulmonary Drug Delivery

To treat COPD, the medication can be aerosolized or nebulized using nebulizers available on the market. The particle sizes of the aerosol droplets produced can be exploited to impact medication distribution in the lungs. The mucoadhesiveness of drug nanoparticles is increased, resulting in a longer contact period at the lungs squamous membrane. Hernandez-Trejo and colleagues created a physically stable buparvaquone nanosuspension for nebulization to target the lungs.[44]

9.5 Opthalmic Drug Administrations

For prolonged release, nanosuspensions are also used in ocular medication conveyance. These are mostly used for water-insoluble drugs. It lengthens the period that the eyes are in contact with each other. In comparison to the aqueous preparation, the anti-inflammatory action of ibuprofen is boosted when it is formed into a nanosuspension. Using Eudragit,

Liang and his colleagues created a nanosuspension filled with cloricromene for ocular application. As a result, nanosuspension formulation is a viable technique to improve the drug's pharmacological activity and bioavailability following ophthalmic application.[45]

9.6 Mucoadhesiveness of Nanoparticle

Orally administered nanoparticle suspensions diffuse fast into liquid media, enabling site-specific drug delivery to the epithelial aspect. The nanoparticles are immobilised at the intestinal epithelial aspect with the help of mucoadhesive polymers, a process known as "bioadhesion." The saturated suspension acts as a particle loch and the engrossment process happens quickly. Particles establish intimate touch with gastrointestinal cells prior to being absorbed. The mucoadhesiveness of the nanosuspension not only aids in drug absorption and bioavailability but also in tissue targeting, such as for parasites that remain in the GI tract, such as Cryptosporidium parvum.[46–48]

9.7 Topical Preparations

Incorporating the nano-crystalline form of the medication into creams, lotions and ointments increases drug saturation solubility in the topical dose form, which improves the drug's diffusion into the skin and hence its bioavailability and permeability. One of the main drawbacks of the transdermal method is the slow penetration of many medicines over the skin barrier. Penetration enhancers in topical formulations are used in these procedures to breach the epidermal barrier.[48]

10. CONCLUSION

The intake of hydrophobic medications, specifically those that are difficult to dissolve in both organic and aqueous solutions, is associated with poor bioavailability. Nanosuspensions offer a novel and economically feasible solution to this challenge. Nanosuspensions have been successfully produced on a wide scale using strategies including strong-shear stress homogenization and media grinding. Enhanced solubility, bioavailability, and mucoadhesion are all attractive qualities that have broadened the uses of nanosuspensions for diverse routes. Non-per oral and mouth administration have been extensively studied, and possibilities in bronchial and ophthalmic distribution have been discovered for nanosuspension. Poor solubility in water is quickly becoming a major roadblock for pharmaceutical research scientists working on oral medication delivery, necessitating the use of innovative formulation strategies. Drug nanocrystals are a universal formulation strategy for improving drug therapeutic efficacy in any mode of administration. As a result, nanosuspension

technology has the potential to deliver major advantages to patients as well as opportunities for research in the field of pharmacy.

Table 1: Patented Products on Nanosuspensions.

Application No. of Patent	Application Date and Year	Description of Patent
WO2020012044A1	2020-01-16	Creation of praziquantel and silicate in tiny structure, as well as its usage as an antiparasitic.[49]
US10729674B2	2020-08-04	Compositions of nanoparticle isoflavones, as well as techniques for producing and using them.[50]
EP2054036B1	2019-12-18	Ostwald withering in crystalline nanoparticle is lessened formulations of hydrophobic pharmaceuticals.[51]
US9616019B2	2017-04-11	A poorly soluble medication is nanosuspended via a microfluidization method.[52]
WO2016135753A1	2016-09-01	Advancement was involved in the copyrighted project of nanoparticulate topical composition.[53]
WO2016081593A1	2016 -05- 26	The claimed concept specified as preparation of nanosuspension.[54]
US20160317534A1	2016-11-03	A nanosuspension made using lyophilized medication is described in the patent.[55]
US20160206577A1	2016-07-21	This patented study provides a technique for producing a pharmaceutical aqueous nanosuspension including nanoparticulate like "4-(4-ethyl-5-fluoro-2-hydroxyphenoxy)-3-fluorobenzamide" and a stabilising agent.[56]
CN105708844A	2016-06-29	The invention of an ocular nanosuspension of tobramycin and dexamethasone is described in this patented work.[57]
CN105315249A	2016-02-02	The method of developing simvastatin nanosuspension to improve medication efficacy is described in this patent.[58]
CN105534947A	2016-02-16	The process for creating a celecoxib nanosuspension (solidified powder via freeze drying) capsule is described in the patented work.[59]
CN104814926A	2015-08-05	The synthesis of lurasidone nanosuspension using a blend of nano-precipitation and high-shear homogenization is demonstrated in this paper.[60]
US20150238446A1	2015-08-27	The researchers developed a stable aqueous nanosuspension of hexaflumuron that may be injected into fish to eliminate sea louse infestations.[61]

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