NANOSUSPENSION: AN INNOVATIVE APPROACH TO ENHANCE BIOAVAILABILITY

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ABSTRACT

In order to address issues like poor bioavailability that are connected to the administration of hydrophobic medications, particularly those that are poorly soluble in aqueous as well as organic media, nanosuspensions appear to be a novel and yet commercially viable strategy. The successful development and commercialization of new medicinal treatments is severely hampered by solubility. Since 40% of the active compounds discovered using the new high-throughput screening paradigm are lipophilic. Thus, it loses a great deal of potential as a novel medication candidate. Many pharmacologically active compounds have been prevented from entering the market as a result of this restriction. Therefore, due to their adaptable qualities and distinctive advantages, nanosuspensions have become a viable method for the effective administration of hydrophobic drugs.

KEYWORDS: Nanosuspension, homogenization, Quasi- emulsion solvent technique

DEFINITION [1, 2]

"Very finely dispersed solid drug particles in an aqueous vehicle, stabilised by surfactants, for either oral and topical use or parenteral and pulmonary administration, with reduced particle size, leading to increased dissolution rate and therefore improved bioavailability," is the definition of a pharmaceutical nanosuspension. The suspended particle has a diameter of less than 1 m. (i.e. 0.1nm-1000 nm). The average particle size ranges between 200 and 600 nm, and the particle size distribution of the solid particles in nanosuspensions is typically smaller than one micron. An increase in the surface area and, consequently, the dissolution velocity, is connected to an increase in the dissolving rate of micronized particles (particle size 10 m). Due to the vapour pressure effect, nanosized particles can accelerate dissolution and improve saturation solubility.

NEED OF NANOSUSPENSION [3-5]

More than 40% of medications have trouble being formulated into standard dose forms because they are not water soluble. The issue is more complicated for class II medicines since they have poor solubility in both aqueous and organic environments. 6 For such molecules with high log P values that are soluble in oil but insoluble in water, nanosuspension preparation is preferred. There are many ways to deal with issues of low solubility and low bioavailability, including micronization, co-solvency, oily solution, salt creation, solid dispersion, ß-cyclodextrin inclusion complex, and other strategies. However, many of these methods do not work with all medications, in which case nanosuspensions are preferable. In place of lipidic systems, nanosuspensions are employed as a formulation strategy for medications that are insoluble in both

water and inorganic media. The compounds with a high log P value, high melting point, and high dosage are the best candidates. Drugs that are poorly soluble in aqueous and lipid media may be made more soluble using nanosuspensions. As a result, the active ingredient floods the body more quickly, reaching the maximal plasma level sooner. This is one of its distinctive advantages over other methods of improving solubility. It is helpful for compounds that have poor solubility, poor permeability, or both. Formulators face a lot of challenges because of these properties.

Major issues associated with poorly water-soluble compounds

- ✓ Poor bioavailability.
- ✓ Inability to optimize lead compound selection based on efficacy and safety
- ✓ Fed/fasted variation in bioavailability
- ✓ Lack of dose-response proportionality
- ✓ Suboptimal dosing
- ✓ Use of harsh excipients, i.e., excessive use of co-solvents and other excipients
- ✓ Use of extreme basic or acidic conditions to enhance solubilization

PREPARATION OF NANOSUSPENSION [6-12]

There are two methods for preparation of nanosuspension. They are 'Bottom up technology' and 'Top down technology'. In Bottom up technique, the drug is dissolved in a solvent for the synthesis of nanoparticles, and the solvent is then introduced to a non-solvent to precipitate the small drug particles.

Precipitation was used to create nanosuspensions of all-trans retinoic acid. The advantage of the precipitation process over other techniques for creating nanosuspension is the use of straightforward, inexpensive equipment as well as the benefit of enhanced saturation solubility. Drugs that are poorly soluble in both aqueous and non-aqueous media cannot be precipitated. The medicine must be soluble in at least one solvent that is miscible with nonsolvent in order to use this method. The main difficulty is preventing crystal formation brought on by Ostwald ripening, which is brought on by various saturation solubilities near variously sized particles.

The top-down technologies include:

(a) media milling

(b) high pressure homogenization

(c) emulsion diffusion method

(d) supercritical fluid method and these are preferred over the precipitation methods.

A. Media milling (Nanocrystals or Nanosystems)

The technique was initially created by liversidge et al.) In this technique, pearl mills or high-shear media mills are used to create nanosuspensions. A milling chamber, a milling shaft, and a recirculation chamber make up the media mill. Glass, zirconium oxide, or strongly cross-linked polystyrene resin serve as the frames for the milling media. The milling medium, also known as pearls, are rotated at a very high shear rate after being charged with water, medication, and stabiliser in the milling chamber.

The milling procedure is carried out in a temperature-controlled environment. The energy input required to break down the microparticulate drug into nanoparticles is provided by the high energy and shear forces

produced as a result of the impaction of the milling media with the drug. A time profile of 30 to 60 minutes is needed to accommodate the unimodal distribution profile and mean diameter of 200. Both micronized and non-micronized drug crystals can be processed effectively using the media milling technique. Once the technique and formulation are improved, very little batch-to-batch fluctuation in the dispersion's quality is seen. Using the pearl milling technique, a nanosuspension of naproxen with a mean particle size of 300–600 nm was created.

B. Homogenization Dissocubes

When homogenising, the suspension is forced through a valve with a small aperture while under pressure. The APV micron LAB 40 (APV Deutschland Gmb) homogenizer is the one that is most frequently used to prepare nanosuspension. However, Stansted and other piston-gap homogenizers can also be utilised. In some instruments, a maximum pressure of 2000 bars can be obtained. The instrument can be operated at pressures ranging from 100 to 1500 bars. Depending on the drug's hardness, the preferred mean particle size, and the needed homogeneity, the majority of situations necessitate many passes or cycles through the homogenizer. There are many high-pressure homogenizers with capacities ranging from 40 ml to a few thousand litres. Before putting the drug through the homogenization process, it's important to create a suspension of the micronized drug in a surfactant solution using high-speed stirrers. Bernoulli's equation predicts that during the homogenization process, the dynamic pressure of the fluid will rise while the static pressure will fall below the boiling point of water at room temperature. As a result, gas will be produced. The drug microparticles can disintegrate into nanoparticles due to the high implosion forces. Additionally, the high-speed collision of the particles contributes to the drug's nanosizing. The implosion forces are sufficiently high to break down the drug microparticles into nanoparticles. Additionally, the collision of the particles at high speed helps to achieve the nano-sizing of the drug.

- ✓ **Effect of homogenization pressure**

Particle size reduces as pressure rises. The studies showed that the homogenization pressure and particle size had an inverse relationship.

- ✓ **Number of homogenization cycles**

It is anticipated that the particle size will decrease as the number of homogenization cycles rises. The requisite particle size cannot be obtained in a single homogenization cycle. Usually, several cycles are needed. The number of cycles depends on the drug's hardness, the level of homogeneity needed, and the preferred mean particle size. Using this method, an omeprazole nanosuspension was created.

- ✓ **Nanoedge**

The precipitation and homogenization procedures use the same basic premise as Nanoedge. This method has the benefit of achieving more stability and smaller particle size in a shorter amount of time. In this method, the precipitated suspension is further homogenised to achieve smaller particle size and prevent crystal formation. Water miscible solvents, such as methanol, ethanol, and isopropanol, are used to precipitate in water. By including an evaporation phase to produce modified starting material that is solvent free, followed by high pressure homogenization, it is intended to entirely eliminate the solvent.

- ✓ **Nanojet technology**

Because of the enormous shear forces created during the procedure, nanojet technology is also known as contrary stream technology. In this method, a stream of suspension in two or more separated sections was passed with high pressure and made to colloid with each other.

C. Emulsion-based solvent diffusion

They can be utilised as templates to create nanosuspension in addition to being employed as a medication delivery system. For pharmaceuticals that are soluble in either a volatile organic solvent or a partly water-miscible solvent, emulsions can be used as templates. Such solvents can be utilised in the emulsion's dispersed phase. To create an emulsion, an organic solvent or combination of solvents containing the medication is distributed in an aqueous phase containing the appropriate surfactants while being stirred. High pressure homogenization was used to further homogenise the resulting emulsion. The emulsion was diluted with water and homogenised using a homogenizer after homogenization cycles in order to disperse the organic solvent and turn the droplets into solid particles. Since one particle develops in each emulsion droplet, it is feasible to regulate the size of the emulsion in order to regulate the particle size of the nanosuspension. Increasing the organic phase intake and, ultimately, the drug loading in the emulsion by surfactant composition optimization. Initially, organic solvents such as methanol, ethanol, ethyl acetate, and chloroform were used. However, their application in standard manufacturing processes has been constrained due to environmental risks and worries about residual solvents endangering people. This approach was used to create nanosuspensions of ibuprofen, diclofenac, and acyclovir.

D. Melt emulsification method

In this procedure, the medication is mixed with an aqueous solution of the stabiliser, heated above the drug's melting point, and homogenised to produce an emulsion. The sample holder was wrapped in a heating tape with a temperature controller during this procedure, and the temperature of the emulsion was kept above the drug's melting point. The emulsion was then carefully cooled to room temperature or placed in an ice bath. The fundamental benefit of using the melt emulsification approach over the solvent diffusion method is that no organic solvents are ever used in the manufacturing process. This method46 was used to create an ibuprofen nanosuspension. The solubility rate of ibuprofen nanosuspension made using the melt emulsification approach is higher than that made using the solvent diffusion method.

E. Supercritical fluid method

The organic solvents used to prepare traditional techniques including solvent extraction and evaporation, solvent diffusion, and organic phase separation techniques are harmful to the environment and the body's physiological systems. Supercritical fluid technology has been looked at for the preparation of biodegradable micro and nanoparticles to address the issue that was caused by the conventional method because supercritical fluids are safe for the environment. Supercritical anti-solvent (SAS), precipitation with compressed anti-solvent process (PCS), and fast expansion of supercritical solution are the most popular methods for employing supercritical fluids (RESS). The solute to be micronized is dissolved using the SAS process using a liquid solvent, such as methanol, that is completely miscible with the supercritical fluid (SC CO2); under the process conditions, however, the solute is insoluble in the supercritical fluid, so

the extraction of the liquid solvent by supercritical fluid results in the instantaneous precipitation of the solute, which produces nanoparticles. The SAS approach was used to create nanoparticles of griseofulvin50 and the medication dexamethasone49 phosphate (for microencapsulation). RESS differs from the SAS process in that its solute is dissolved in a supercritical fluid (such as supercritical methanol) and then the solution is rapidly expanded through a small nozzle into a region lower pressure, thus the solvent power of supercritical fluid dramatically decreases and solute eventually precipitates. This method is used for the production of polymeric nanoparticles.

FORMULATION CONSIDERATIONS [13-19]

- **Stabilizer**

The stabilising agent is crucial in the creation of nanosuspensions. The high surface energy of nanosized particles can cause the drug crystals to aggregate or clump together in the absence of a suitable stabiliser.

By supplying steric or ionic barriers, stabilisers serve the primary purposes of thoroughly wetting the drug particles, preventing Ostwald's ripening and agglomeration of nanosuspensions to produce a physically stable formulation. The type and quantity of the stabiliser significantly affects the in vivo behaviour and physical stability of nanosuspensions. In certain circumstances, a combination of stabilisers is necessary to produce a stable nanosuspension. The formulation's drug-to-stabilizer ratio, which might range from 1:20 to 20:1, needs to be looked into for a given situation. Lecithins, povidones, poloxamers, polysorbates, and cellulosics are some of the stabilisers that have been researched so far. If one wants to create a parenterally acceptable and autoclavable nanosuspension, lecithin is the stabiliser of choice.

- **Organic solvents**

If nanosuspensions are to be created utilising an emulsion or microemulsion as a template, organic solvents may be needed in the formulation. Due to the nascent nature of these procedures, detailed information on formulation considerations is not yet available. When creating nanosuspensions utilising emulsions or microemulsions as templates, it is important to take into account the organic solvents' acceptance in the pharmaceutical industry, their potential for toxicity, and how simple it will be 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. Additionally, when the nanosuspensions are created using a microemulsion as a template, partially water-miscible organic solvents can be employed as the internal phase of the microemulsion.

- **Co-surfactants**

When creating nanosuspensions using microemulsions, the co-surfactant selection is crucial. Co-surfactants can have a significant impact on phase behaviour, thus it is important to look at how they affect drug loading and internal phase uptake for a particular microemulsion composition. Although the literature describes the use of bile salts and dipotassium glycerrhizinate as co-surfactants, various solubilizers, such as Transcutol, glycofurol, ethanol and isopropanol, can be safely used as co-surfactants in the formulation of microemulsions.

❖ **Other additives**

Nanosuspensions may contain additives such as buffers, salts, polyols, osmogent and cryoprotectant, depending on either the route of administration or the properties of the drug moiety.

In Vitro Evaluation [20-27]

❖ **Mean particle size and size distribution**

Numerous characteristics of nanosuspensions, including saturation solubility, dissolving velocity, physical stability, and biological performance, are dependent on mean particle size and particle size distribution. Laser diffraction, coulter current multi-sizer, and photon correlation spectroscopy (PCS) can all be used to calculate the average particle size and particle width (poly-dispersity index). The nanosuspensions' long-term stability depends on a low polydispersity index (PI). A PI score between 0.01 and 0.25 indicates small size spectrum A PI value larger than 0.5 denotes a relatively broad distribution, in contrast. It is challenging to determine whether a nanosuspension is contaminated by medicines with particle sizes larger than 3 m due to the PCS's limited measuring range (3 nm to 3 m). Laser diffractometry (LD) analysis should therefore be performed in addition to PCS analysis in order to identify and quantify any microparticles that may have been produced during the production process. LD can be used to measure particles with diameters ranging from 0.05 to 80 micrometres, and in some equipment, up to 2000 micrometres. In addition to PCS and LD, Coulter counter particle size analysis is crucial for nanosuspensions meant for intravenous delivery. As it provides the absolute number of particles per volume unit for the various size classes, the Coulter counter is a more effective and appropriate technique than LD analysis. It measures the degree to which tiny drug particles contaminate nanosuspensions.

❖ **Particle charge (Zeta Potential)**

The stability of the nanosuspension is determined by the zeta potential. The zeta potential of a nanosuspension is governed by both the stabiliser and the medication. For electrostatically stabilised nanosuspension, a zeta potential of at least 30mV is necessary, while 20mV is needed in the case of electrostatic and steric stabilisation.

❖ **Crystalline state and particle morphology**

The drug's crystal shape in the nanosuspension must be understood. The crystalline state and particle morphology can be used to identify polymorphic or morphological changes in drugs that take place during nano-sizing. By using X-ray diffraction analysis, the amorphous state of the drug created during the creation of the nanosuspension is identified. It provides details on the physical state changes in the drug particles as well as the volume of the amorphous fraction. Additionally, differential scanning calorimetry can be employed. Obtaining precise data on particle morphology is also done via scanning electron microscopy. X-ray diffraction analysis in conjunction with differential scanning calorimetry is used to determine the impact of high pressure homogenization on the drug's crystalline structure. Techniques like scanning electron microscopy (SEM), atomic force microscopy (AFM) or transmission electron microscopy (TEM) are preferred for determining the exact size and morphology of nanoparticles in suspension.

❖ **Saturation solubility and dissolution velocity**

By creating nanosuspensions, the dissolving velocity and saturation solubility are improved. Reduced particle size leads to higher solubility and dissolving pressure. As the solubility rises (due to a reduction in particle size), the surface tension changes, increasing the saturation solubility. According to the procedures described in the pharmacopoeia, different physiological solutions are employed to determine the saturation solubility and dissolution velocity at various pH levels and temperatures. These measures are used to evaluate the in vivo performance (blood profiles, plasma peaks, and bioavailability) of formulations. The Ostwald- Freundlich equation16 can be used to explain an increase in saturation solubility. The information about the benefits of nanosuspension over conventional formulations, particularly at SR doses, is provided by the determination of the dissolution velocity of nanosuspensions.

The Ostwald-Freundlich equation is:

$$C(r) = C(\infty) \exp (2\gamma M / r\rho RT)$$

Where C(r) and C(∞) are the solubilities of a particle of radius r and of infinite size. γ, M, and ρ are interfacial tension at the particle surface, the molecular weight of the solute, and the density of the particle, respectively.

❖ **Stability**

Nanosuspensions The size of the suspended particles affects stability. The surface energy of the particles increases as their size decreases to the nano range, and their propensity to clump together also increases. Because they act as a steric or ionic barrier, stabilisers are employed to lessen the likelihood of Ostwald ripening and to increase the stability of the suspension. Stabilizers such as lecithin, polyoleate, polysorbates, poloxamers, and povidones in nanosuspensions use . The creation of parentral nanosuspensions is preferable with lecithin. 1 The mean particle size of nanosuspensions can be monitored for three months while they are held under various stress conditions, such as varied temperatures (15, 25, 35, and 45°C), thermal cycling, and mechanical shaking. Different concentrations of small molecule surfactants (like sodium lauryl sulfate (SLS) and dowfax 2A1 (DF)) and polymeric stabilizer (like Hydroxypropyl methylcellulose (HPMC)) can be evaluated to determine the effect of stabilizer type and micellar solubilized drug on Ostwald ripening.

❖ **pH**

The pH of the nanosuspension can be easily measured by using pH meter.

❖ **Osmolarity**

Practically, Osmolarity of nanosuspension can be measured by using Osmometer.

❖ **Drug content**

The drug content of a nanosuspension formulation can be determined by centrifuging the nanosuspension after extracting it in a suitable solvent mixture, such as a Methanol: THF (1:1) mixture. It is possible to separate the supernatants, dilute them with the same solvent mixture, and then measure the absorbance at an appropriate maximum. Using the calibration curve, the drug content can then be determined.

❖ **In Vivo Evaluation**

The in vivo evaluation of the nanosuspensions must be tailored to the drug and method of delivery. In general, the formulations are supplied by the necessary route, and HPLC-UV visible spectrophotometry is used to measure the plasma drug concentrations. In vivo measures are typically used to assess surface hydrophilicity/hydrophobicity (which impacts interaction with cells prior to phagocytosis), adhesion qualities, and interaction with body proteins. No matter the route of administration or the delivery mechanism, monitoring the in-vivo performance of the Nanosuspensions and establishing a link between in-vitro release and in-vivo absorption are necessary for the production of a successful preparation. Oral nanosuspensions' in-vivo biological performance is influenced by the rate of dissolution. The organ distribution for intravenously injected nanosuspensions is determined by the nanoparticle size and surface characteristics of the particles. The hydrophilicity/hydrophobicity and interactions of the nanoparticles with plasma proteins have an impact on the nanosuspension's in vivo organ distribution behaviour. After intravenous injection of drug nanosuspensions in animals, surface hydrophobicity is assessed using hydrophobic interaction chromatography, and protein absorption is assessed qualitatively and quantitatively using 2-D PAGE.

Evaluation of the Surface Modified of Particles [28-32]

❖ **Surface Hydrophilicity**

Additional factors that affect the in vivo fate of the drug nanoparticles in intravenously injected nanosuspensions must be identified. One of the crucial factors influencing the in vivo organ distribution following intravenous injection is surface hydrophilicity or hydrophobicity. The interaction with cells prior to phagocytosis is determined by the surface hydrophobicity. In addition, it is an important parameter for the adsorption of plasma proteins, which is a crucial component of organ distribution. The surface hydrophobicity must be assessed in the drug nanoparticles' original habitat, which is an aqueous dispersion media, in order to prevent artefacts. Hydrophobic interaction chromatography (HIC), which was previously used to assess the hydrophobicity of bacteria's surfaces before being applied to the assessment of nanoparticulate drug carriers, is an appropriate technology.

❖ **Adhesion properties**

Male Wistar rats may be employed in an in vivo bioadhesive investigation. Each animal is typically given a single oral dose of 1ml of an aqueous slurry containing 10 mg of the drug-loaded nanoparticles (or around 45 mg of particles per kg of body weight). At one and three hours after administration, the animal is killed via cervical dislocation. The stomach, small intestine, and other organs are visible through the abdominal cavity, Cecum is removed, the mesentery is opened lengthwise, and phosphate saline buffer is washed (pH 7.4). Additionally, the stomach, small intestine, and cecum are divided into segments measuring 2 cm in length and digested for 24 hours in an appropriate alkali. By adding 2 ml of methanol and vortexing the samples for one minute, the drug is recovered from the digested samples. To determine the percentage of attached nanoparticles to the mucosa, a sample (1 ml) of the supernatants will be spectrofluorimetrically tested for the presence of the medication. Standard curves for the medication may also be produced for calculations.

❖ **Interaction with body proteins**

By incubating mucin and nanoparticles (1:4 weight ratio) in an acidic or neutral media, the in vitro interaction between nanoparticles and mucin can be examined. At a temperature of 37°C, stirring is used during the incubation process. After centrifuging the dispersions, 150 l of each supernatant is poured into a test plate. The plate and the Micro BCA Protein Assay Reagent Kit (150 l) are then combined, and the mixture is incubated at 37 °C for 2 hours. This approach states that colorimetry can be used to determine mucin absorbance at the drug's maximum concentration. By measuring the difference between the mucin's original concentration and the concentration found in the dispersion during incubation and centrifugation, the amount of mucin adsorbed to the nanoparticles may be calculated. The calculations can be made on the basis of mucin standard curves.

APPLICATION OF NANOSUSPENSIONS [33-45]

❖ **Bioavailability enhancement**

Low oral bioavailability of a drug is caused by poor solubility, permeability, or solubility in the gastrointestinal tract. The issue of poor bioavailability is fixed by nanosuspension by addressing the issues of poor solubility and poor permeability across membranes. When diclofenac was created in a nanosuspension form, the rate of dissolution increased. After 60 minutes in SGF and (2O), diclofenac 1 nanosuspension dissolves at a rate of 25% and 10% compared to coarse suspension, while diclofenac dissolves at a rate of 50% and 35% compared to coarse suspension. Celecoxib, a COX2 inhibitor that is poorly soluble, had its bioavailability increased by utilising a nanosuspension formulation. When compared to micronized tablets, the breakdown rate and extent of the crystalline nano-sized celecoxib alone or in tablet form increased dramatically54. Budesonide and spirolactone are poorly soluble medications. In comparison to saturated solution form, the flow through the monolayer of the coca-2 cell is increased in the nanosuspension generated with varied surfactant concentrations. The increased bioavailability of the nanosuspension formulation is a result of the higher flux. Compared to solutions of micronized fenofibrate, poorly soluble fenofibrate after oral administration had a higher bioavailability.

❖ **Ocular administration**

Ointments and suspensions are suggested for the delivery of drugs that are poorly soluble in cul-de-sacs. The benefits of suspensions include a longer residual period in cul-de-sacs and the avoidance of more tonicity from water-soluble medicines. The pace at which a suspension dissolves in lachrymal fluid determines how readily it is absorbed by the eye. The pace at which the medication dissolves, however, varies depending on the entrance and outflow of lacrimal fluid. In the lachrymal fluid, nanosuspension reaches saturation solubility, making it the best method for delivering hydrophobic medications to the eyes. The drug was released continuously from the nanosized drug particles due to their longer residual period in the cul-de-sac. The incorporation of nanosuspension in hydrogel bases, mucoadhesive bases, or ocular inserts can result in the sustained release of medication for a predetermined period of time. By adding the nanosuspension to the polymers, the sustained release in the cul-de-sac can also be accomplished. The shelf life and bioavailability of a diclofenac-loaded bipolymeric nanosuspension for ocular use were both increased. It has been demonstrated that administering hydrocortisone nanosuspension intravenously

improves drug absorption and lengthens therapeutic action. Ibuprofen eudragit RS100 nanosuspension had more ocular anti-inflammatory efficacy than ibuprofen lysate. Acyclovir's cumulative percent drug release after 24 hours ranged from 79.28 to 95%, demonstrating the effectiveness of the controlled release capability of the ophthalmic nanosuspension. The goals of enhanced contact duration, longer release, and decreased frequency of administration have been met with acyclovir-loaded nanoparticles.

- **Intravenous administration**

Parenteral administration is an invasive method. Despite all of these drawbacks, the parenteral route continues to be valuable because to its unique benefits, including immediate action in an emergency situation, a lower medication dose, and the capacity to effectively focus the medicine to the intended site of action, particularly in the event of severe infections. When a medicine is either not absorbed through the gastrointestinal system or goes through considerable first-pass metabolism, the parenteral route is frequently used as a replacement. In vivo research using a mouse model of sarcoma 180 solid tumour showed that oridonin nanosuspension significantly inhibited tumour growth more than ordonin solution at the same dosage.

- **Pulmonary administration**

For lung distribution, aqueous nanosuspension can be nebulized using a mechanical or ultrasonic nebulizer. Because the medicine is nanoparticulate, it can quickly diffuse and dissolve at the site of action. The increased adhesiveness of the drug to mucosal surfaces also allows for a longer drug residence duration at the absorption site. The ability of nanosuspensions to provide an initial rapid beginning of action and then a controlled release of the active moiety is extremely advantageous and is required by the majority of lung illnesses. Additionally, because nanosuspensions typically include a very small percentage of microparticulate medication, they avoid unintentional particle deposition in the mouth and pharynx, which reduces the drug's local and systemic side effects. Fluticasone showed deep lung deposition and rapid lung absorption in pharmacokinetic experiments following intratracheal injection of nanosuspensions, with solubility having a crucial role in lung retention and duration of action66. Budenoside drug nanoparticles were nebulized using an ultrasonic nebulizer, and the pharmacokinetics were similar to those of pulmicort respules in terms of AUC, Cmax, and Tmax.

- **Targeted drug deliver**

Targeted medication distribution can also be done using nanosuspensions. The mononuclear phagocytic system can be used to create a targeted drug delivery system. Anti-mycobacterial, anti-fungal, or anti-leishmanial medicines can be delivered specifically to macrophages if the infectious pathogen is still present intracellularly. Using different surface coatings for active or passive targeting is the next step in the strategy for a tailored medication delivery system. Peter created a clofazimine nanosuspension that enables passive targeting to the reticuloendothelial system. For the majority of Mycobacterium avium strains, nanocrystalline drug concentration of clofazimine in liver, spleen, and lungs achieved comparable high concentrations to liposomal formulation. Similar to this, pulmonary nanosuspensions of acceptable medication candidates, such as amphotericin B, rather than stealth liposomes27, can effectively treat disorders such pulmonary aspergillosis. Atovaquone nanosuspension concentration has been demonstrated

by Scholer to be high in the brain, lungs, serum, and liver and to have increased therapeutic efficacy against toxoplasma encephalitis in mouse mice infected with toxoplasma gonidii.

- **Mucoadhesion of the nanoparticles**

Due of their small size, nanoparticles can cling to the surface of the mucosa. Prior to particle absorption, the particles must first adhere to one another. Nanosuspensions are created with hydrogels derived from mucoadhesive polymers, such as various kinds of carbopol and chitosan, to further extend the adhesive duration. The nanosuspension's adhesiveness not only aids in increasing bioavailability but also enhances targeting of parasites that are still present in the G)T, such as Cryptosporidium parvum. It has been noted that bupravaquone mucoadhesive nanosuspensions offer a benefit to TRC alpha-deficient mice infected with Cryptosporidium parvum oocytes.

- **Topical formulations**

Additionally, water-free ointments and creams with greater saturation solubility and improved drug absorption into the skin might contain drug nanoparticles.

CONCLUSION

Hydrophobic pharmaceuticals and medications that are poorly soluble in aqueous and organic solutions have poor bioavailability issues that have been resolved by nanosuspension. For the mass manufacture of nanosuspensions, production methods such media milling and high pressure homogenizer are employed. The administration of nanosuspensions can be done orally, parenterally, pulmonary, ocularly, or topically. Since nanotechnology is straightforward, there are less excipient requirements, higher dissolve rates, and greater solubility, many medications with low bioavailability are produced in nanosuspension form.

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