International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

A Review On: Nano-Suspension

Nikita Avchar
Dr. VedprakashPatil Pharmacy College, Aurangabad.

Submitted: 10-01-2023 Accepted: 21-01-2023

ABSTRACT:
Nanotechnology is that the science that deals with the method that happens at molecular level and of nano length scale size. Nano refers to the particle size vary of 1-1000 nm. Nanosuspensions are unit returning underneath engineering science. A pharmaceutical Nanosuspension is outlined as finely mixture, biphasic, spread solid drug particles in associate liquid vehicle, size between 10-50 nm stabilized by surfactants and polymers and ready by appropriate ways for drug delivery applications. It provides economical delivery of hydrophobic medicine and will increase the bioavailability. Nanosuspension is a good and promising technology to enhance poor solubility and bioavailability of the medicine. High pressure homogenization, Precipitation media milling Melt emulsification are commercial methods for preparation of nanosuspensions. Nanosuspension consists of a submicron colloidal dispersion of pharmaceutically active ingredient particles in the liquid phase, which is stabilized by surfactant. Poor water solubility is a major problem for the manufacturing of formulation. The drug particle reduces leads to enhance the surface area as well as bioavailability. Nanosuspension prepared by way of a number of methods. Techniques such as media milling, high-pressure homogenization have been used commercially for producing Nanosuspension. Recently engineering of nanosuspension employs emulsion and microemulsion as a templet.

Key words: drug delivery, nanosuspension, solubility, bioavailability, colloidal dispersion,

I. INTRODUCTION:

A range of parameters like solubility, stability at room temperature, compatibility with solvent, excipient, and photostability play a critical role in the successful formulation of drugs. Till date, more than 40% of the new chemical entities being generated through drug discovery programs are lipophilic or poorly water-soluble compounds. [1,2] Many formulation approaches are available to solve the problems of low solubility and low bioavailability of drugs. The conventional approaches include micronization, use of fatty solutions, use of penetration enhancer or cosolvents, surfactant dispersion method, salt formation, precipitation, etc., but still, these techniques having limited utility in solubility enhancement for poorly soluble drugs. Additional approaches are vesicular system like liposomes, dispersion of solids, emulsion and microemulsion methods, and inclusion complexes with cyclodextrins, which show beneficial effect as drug delivery system but major problems of these techniques are lack of universal applicability to all drugs.[3] Over the last decades, nanoparticle engineering has been developed and reported for pharmaceutical applications.[4] Nanotechnology can be used to solve the problems associated with various approaches described earlier. Nanotechnology is defined as the science and engineering carried out in the nanoscale that is 10−9 m. The drug microparticles/micronized drug powder is transferred to drug nanoparticles by techniques like Bottom-Up Technology and Top-Down Technology.[5] Nanosuspensions are submicron colloidal dispersions of nanosized drug particles stabilized by surfactants.[6] Nanosuspensions consist of the poorly water-soluble drug without any matrix material suspended in dispersion.[7] These can be used to enhance the solubility of drugs that are poorly soluble in water as well as lipid media. As a result of increased solubility, the rate of flooding of the active compound increases and the maximum plasma level is reached faster. This approach is useful for molecules with poor solubility, poor permeability, or both, which poses a significant challenge for the formulators. The reduced particle size renders the possibility of intravenous administration of poorly soluble drugs without any blockade of the blood capillaries. The suspensions can also be lyophilized and into a solid matrix. Apart from these advantages, it also has the advantages of liquid formulations over others.[8] In the present review, we are mainly focusing on the different methods of preparation associated merits, demerits, and its pharmaceutical application as drug delivery system.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

ADVANTAGES OF NANOSUSPENSION[3]

1. Its general applicability to the utmost drugs and its simplicity.
2. It can be useful for poorly water-soluble drugs.
3. It can be given by any route.
4. Reduced tissue irritation in the case of subcutaneous/intramuscular administration.
5. Rapid dissolution and tissue targeting can be reached by the IV route of administration.
6. Oral administration of nanosuspensions provides fast onset, reduced fed/fasted ratio and improved bioavailability.
7. The absorption from the absorption window of the drugs can be increased due to a reduction in the particle size.
8. In case of ocular administration and inhalation delivery, higher bioavailability and more consistent dosing
9. Drugs with high log P-value can be formulated as nanosuspensions to raise the bioavailability of such drugs.
10. Enhancement in biological performance due to high dissolution rate and saturation solubility of the drug.
11. Ease of manufacture and little batch-to batch variation.
12. Long term physical stability.
13. Nanosuspensions can be incorporated in tablets, pellets, hydrogel, and suppositories are suitable for various routes of administration.
14. Increasing the amorphous portion in the particles, most important to a potential change in the crystalline structure and higher solubility.
15. The opportunity of surface-modification of nanosuspension for site-specific delivery.
16. Possibility of significant production, the pre-requisite for the introduction of a delivery system to the market.

DISADVANTAGE OF NANOSUSPENSION[6-8]

1. Physical stability may be a challenge in formulation.
2. Sedimentation & compaction will cause issues.
3. It is large ample care should be taken throughout handling & transport.
4. Improper dose.
5. The care should be taken throughout handling & transport, as a result of the preparation can be bulk.
6. Dose fixation can be tough.
7. Uniform & correct dose cannot be achieved

FORMULATION OF NANOSUSPENSION9-[11]1.

Stabilizer

Stabilizer plays a very important role within the formulation of nanosuspensions. within the absence of an acceptable stabilizer, the high surface energy of nano-sized particles will induce agglomeration or aggregation of the drug crystals. the most functions of a stabilizer square measure to wet the drug particles totally. The type and quantity of stabilizer includes a pronounced impact on the physical stability and in-vivo behaviour of nanosuspensions. In some cases, a mix of stabilizers is needed to get a stable Nanosuspension.

Organic solvents

Organic solvents is also needed within the formulation of nanosuspensions if they're to be ready mistreatment AN emulsion or microemulsion as a templet. As these techniques square measure still in their infancy, elaborate info on formulation concerns isn't obtainable. The satisfactoriness of the organic solvents within the pharmaceutical space, their toxicity potential and also the easy their removal from the formulation have to be compelled to be thought-about once formulating a nano suspensions mistreatment emulsions or microemulsions as templates.

Co-surfactants

The choice of co-surfactant is important once mistreatment microemulsions formulate nanosuspensions. Since co-surfactant scan greatly influence section behaviour, the impact of co-surfactant on uptake of the inner section for elect microemulsions composition and on drug loading ought to be investigated. though the literature describes the employment of gall salts and dipotassiumglycerrhizinate as co-surfactants, numerous solubilizers, like Transcutol, glycofurol, plant product and isopropyl alcohol, is safely used as co-surfactants within the formulation of microemulsions20,21

Different additives

Formulation concerns Nanosuspensions could contain additives like buffers, salts, polyols, cryoprotectant, reckoning on either the route of administration or the properties of the drug moiety

Amino acid-based stabilizers

Leucine copolymers have been incontestable to with success manufacture stable drug nanosuspensions in liquid medium. phospholipid is pre-ferried as helpful agent for sterile, steam heating sterilizable duct nanosuspensions. albumen has been utilized as a surface stabilization and drug targeting at various

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

concentrations as low as zero.003% up to five in nano-suspension . alternative pharmaceutically acceptable amino acid co-polymers used for the physical stability of nano-crystals were essential amino acid, proline, and beta globulin.

polysaccharide based mostly derivatives

HPMC, hydroxypropyl cellulose (HPC), hydroxyethyl polysaccharide (HEC) have been widely used as helpful agent in nanosuspensions. The underlying mechanism of steric stabilization provided by these polymers is due to surface adsorbable hydrophobic groups.

PROPERTIES OF NANOSUSPENSION

1. **Long-Term Physical Stability:**

Ostwald ripening is accountable for crystal growth and subsequently, formation of microparticles. Ostwald ripening was brought on through the variations in dissolution pressure/saturation solubility between small and large particles. Molecules diffuse from the higher concentrated area around small particles (higher saturation solubility) to areas around larger particles possessing lower drug attention. This leads to the formation of a supersaturated solution around the large particles and, therefore, to drug crystallization and increase of the large particles. The diffusion process of the drug from the small particles to the large particles leaves a location around the small particles that are now not saturated any more, for this reason leading to the dissolution of the drug from the small particles and eventually completes the disappearance of the small particles [8].

2. Internal Structure of Nanosuspension:

The high-energy input during the disintegration process causes structural adjustments inside the drug particles. When the drug particles are uncovered to high-pressure homogenization, particles are transformed from a crystalline state to an amorphous state. When the drug particles are exposed to high-pressure homogenization, particles are converted from a crystalline state to amorphous state. The exchange in the state relies upon the hardness of the drug, number of homogenization cycles, chemical nature of the drug, and power density applied by means of the homogenizer [8].

3. Adhesiveness:

There is a distinct increase in the adhesiveness of ultra-fine powders compared to coarse powders. This adhesiveness of small drug nanoparticles can be exploited for expanded oral delivery of poorly soluble drugs. A considerably excellent report is that of the enlarge in bioavailability for danazol from 5% (as micro suspension) to 82% (as nanosuspension) [5]

4. Crystalline State and Morphology:

A potential change in the crystalline structure of nanosuspensions, saying increasing the amorphous fraction in the particle or even creating clearly amorphous particles is an attribute of consideration. The application of high pressures at some point of the production of nanosuspensions used to be found to promote the amorphous state [5].

5. Increase in Saturation Solubility and Velocity of Drug:

The dissolution of the drug is increased due to an increase in the surface area of the drug particles from micrometres to the nanometer size. According to the Noyes-Whitney equation, dissolution velocity increases due to an increase in the surface area from micron size to particles of nanometer size.

$dx/dt = [(D \times A)/ h] [Cs-X/V]$ -----Equation (1)

Where; D is the diffusion coefficient, dx/dt is the dissolution velocity, A is the surface region of the particle, h is the thickness of the diffusion layer, V is the volume of the dissolution medium, and X is the concentration in the surrounding liquid [9] .

6. Nanosuspension Provide Versatility:

The flexibility provided in the modification of surface properties and particle size and ease of postproduction processing of nanosuspensions enable them to be integrated into various dosage forms, such as tablets, pellets, suppositories, and hydrogels, for various routes of administration, as a result proving their versatility.

7. Nanosuspension Enhance Bioavailability:

Drug with poor solubility, poor permeability or poor solubility in the gastrointestinal tract will lead to poor oral bioavailability. Nanosuspension resolves the trouble of poor bioavailability by solving the trouble of poor solubility, and poor permeability throughout the membrane.

PREPARATION OF NANOSUSPENSION

For the preparation of nanosuspensions, mostly two methods namely “Bottom up technology” and “Top down technology” are used[10] Bottom up technology is an assembling

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

method to form nanoparticles like precipitation, microemulsion, melt emulsification method and top down technology involves the disintegration of larger particles into nanoparticles, examples of which are high-pressure homogenization and milling methods. The principles of these methods are described in detail and their merits and demerits. [11,12]

Precipitation Method

Precipitation method is a general method used to prepare submicron particles of poorly soluble drugs.[13-15] In this method, drug is dissolved in solvent and then solution is mixed with solvent to which drug is insoluble in the presence of surfactant. Rapid addition of solution to such solvent (generally water) leads to rapid supersaturation of drug in the solution, and formation of ultrafine amorphous or crystalline drug. This method involves nuclei formation and crystal growth which are mainly dependent on temperature. High nucleation rate and low crystal growth rate are primary requirements for preparing a stable suspension with minimum particle size.[16]

High-Pressure Homogenization

This technique involve the following three steps: First, drug powders are dispersed in a stabilizer solution to form presuspension; after that, presuspension is homogenized by high pressure homogenizer at a low pressure sometimes for premilling; and finally homogenized at a high pressure for 10 to 25 cycles until the nanosuspensions are formed with desired size.[9]

Homogenization in Aqueous Media (Dissocubes)

Dissocubes technology was developed by Muller in 1999. The instrument can be operated at pressure varying from 100 to 1 500 bars (2 800 – 21 300 psi) and up to 2 000 bars with volume capacity of 40 ml (for laboratory scale). For preparation of nanosuspension, it is essential to prepare a presuspension of the micronized drug in a surfactant solution using high-speed stirrer. According to Bernoulli's Law, the flow volume of liquid in a closed system per cross section is constant. The reduction in diameter from 3 cm to 25 μm leads to increase in dynamic pressure and decrease of static pressure below the boiling point of water at room temperature. Due to this, water starts boiling at room temperature and forms gas bubbles, which implode when the suspension leaves the gap (called cavitation) and normal air pressure is reached. The size of the drug nanocrystals that can be achieved mainly depends on factors like temperature, number of homogenization cycles, and power density of homogenizer and homogenization pressure. Preprocessing like micronization of drug and high-cost instruments increases the overall cost of dosage form. Various drugs like Amphotericin B, Ordinon, Thiomerasol, Fenofibrate, Melarsoprol, Buparvaquone, Prednisolone, Carbamazepine And Dexamethasone were prepared as nanosuspensions using this method.[5]

Homogenization in Nonaqueous Media (Nanopure)

Nanopure is suspension homogenized in water-free medium. It is "deep-freeze" homogenization where the drug suspensions in nonaqueous medium are homogenized at 0o C or sometimes below the freezing point. Because of very high boiling point and low vapor pressure of water, oils, and fatty acids, the drop of static pressure is not enough to begin cavitation in nanopure technology.[17]

Milling Techniques

Media milling

Liversidge et al. had a patent on nanocrystal technology.[19] In this technique, drugs are subjected to media milling for nanoparticle production. Effect of impaction between the milling media and drugs gives essential energy for disintegration of the microparticulate system into nanoparticles. In this process, the chamber of milling is charged with the milling media involving drug, stabilizer, and water or suitable buffer, which is rotated at a very high shear rate to generate suspension. Residues left behind in the finished product is a major problem of this method.[20]

Dry cogrinding

Since many years, nanosuspensions are prepared through wet grinding processes by using pearl ball mill. Nowadays, nanosuspensions can be prepared by dry milling methods. Stable nanosuspensions are prepared by using dry grinding of poorly soluble drug with soluble polymers and copolymers after dispersing in liquid medium. Itoh et al. have described the colloidal particles formation of many poorly water-soluble drugs like nifedipine, griseofulvin, and glibenclamide with sodium dodecyl sulfate and polyvinylpyrrolidone as stabilizer.[21-23]

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

Lipid emulsion/microemulsion template

Nanosuspensions are also obtained by just diluting the emulsion, formed by using a partially water-miscible solvent as the dispersed phase. The emulsion technique is applicable for drugs which are either partially water miscible or soluble in volatile organic solvents. Additionally, microemulsion templates can also produce nanosuspensions. Microemulsions are dispersions of two immiscible liquids like water and oil and stabilized thermodynamically by surfactant or cosurfactant. The drug is either loaded into preformed or internal phase of microemulsion and can be saturated by intimate mixing of drugs.[20] Griseofulvin nanosuspension is prepared by the microemulsion technique by using water, butyl lactate, lecithin, and the sodium salt of taurodeoxycholate.[24]

Microprecipitation – High-pressure homogenization (Nanoedge)

Nanoedge is a combination of microprecipitation and highpressure homogenization techniques. Method includes precipitation of friable materials followed by fragmentation under high shear and/or thermal energy.[25,26]

Melt emulsification method

Solid lipid nanoparticles are mainly prepared by melt emulsification method. Kipp and co workers firstly prepare nanosuspensions of ibuprofen by using melt emulsification method. It is a four-step procedure. Drug is first added to aqueous solution having stabilizer. The solution is heated at temperature higher than the melting point of the drug and then homogenized by high-speed homogenizer for the formation of emulsion. The temperature is maintained above the melting point of the drug during overall process. Finally, the emulsion is cooled to precipitate the particles. The particle size of nanosuspension mainly depends on parameters like drug concentration, concentration and type of stabilizers used, cooling temperature, and homogenization process.[28]

Nanojet technology

This technique is also called opposite stream technology, uses a chamber where a stream of suspension is divided into two or more parts. Both streams are colloid with each other at high pressure. The high shear force produced during the process results in particle size reduction. Dearns had prepared nanosuspensions of atovaquone using the microfluidization process. The major disadvantage of this technique is the high number of passes through the microfluidizer and that the product obtained contains a relatively larger fraction of microparticles.[29]

Supercritical fluid methods

Various methods like rapid expansion of supercritical solution (RESS) process, supercritical antisolvent process, and precipitation with compressed antisolvent (PCA) process are used to produce nanoparticles. In RESS technique, drug solution is expanded through a nozzle into supercritical fluid, resulting in precipitation of the drug as fine particles by loss of solvent power of the supercritical fluid. By using RESS method, Young et al. prepared cyclosporine nanoparticles having diameter of 400 to 700 nm. In the PCA method, the drug solution is atomized into the CO2 compressed chamber. As the removal of solvent occurs, the solution gets supersaturated andfinally precipitation occurs. In supercritical antisolvent process, drug solution is injected into the supercritical fluid and the solvent gets extracted as well as the drug solution becomes supersaturated.[30]

EVALUATION OF NANOSPONGES:

Nanosuspensions are characterized for appearance, colour, odour, assay, related impurities, particle size, zeta potential, crystalline status, dissolution studies, and in-vivo studies.

In-vitro Evaluation:

1. Mean Particle Size and Size Distribution:

Various parameters of nanosuspensions like saturation solubility, dissolution velocity, physical stability, dissolution velocity, physical stability, and biological performance depend on the mean particle size and particle size distribution. Mean particle size and particle width (poly-dispersity index) can be decided through Photon Correlation Spectroscopy (PCS), laser diffraction, and colter current multi-sizer. The Poly-dispersity index (PI) be low for the long-term stability of the nanosuspensions. PI value of 0.1–0.25 shows a narrow size distribution, whereas a PI value larger than 0.5 suggests a very broad distribution. Due to the low measuring range (3nm to 3 μm) of PCS, the determination of the contamination of the nanosuspension (by drugs having a particle size greater than 3 μm) is difficult. So, to observe and quantify the microparticles that may have been generated in the course of the production process,

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

laser diffractometry (LD) analysis should be carried out in addition to PCS analysis. Particles ranging from 0.05–80 μm and in certain units, particle sizes up to 2000 μm can be measured via using LD. Particle size analysis via the Coulter counter method is vital (in addition to PCS and LD) for nanosuspensions that are meant for intravenous administration. Coulter counter is a more efficient and appropriate method than LD analysis as it gives the absolute number of particles per volume unit for the different size classes. It quantifies the contamination of nanosuspensions through microparticulate drugs [1] .

2. Particle Charge (Zeta Potential):

Zeta potential determines the stability of the nanosuspension. Both the stabilizer and the drug govern the zeta potential of a nanosuspension. Zeta potential of minimal ±30mV is required for electrostatically stabilized nanosuspension, and ±20mV is required in case of electrostatic and steric stabilization.

3. Crystalline State and Particle Morphology:

It is necessary to know the crystal morphology of the drug in the nanosuspension. Polymorphic or morphological modifications in a drug that appears during nano-sizing can be determined via the information of crystalline state and particle morphology. The amorphous state of the drug formed during the preparation of nanosuspension is determined via X-ray diffraction analysis. It gives information about the adjustments in the physical state of the drug particles as well as the extent of the amorphous fraction. Differential scanning calorimetry can be used additionally. Scanning electron microscopy is additionally used to get exact information about particle morphology. The effect of high-pressure homogenization on the crystalline structure of the drug is estimated via X-ray diffraction analysis in aggregate with differential scanning calorimetry. 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.

4. Saturation Solubility and Dissolution Velocity:

The dissolution velocity and the saturation solubility are enhanced through the formula of nanosuspensions. Reduction in particle size results from the increased dissolution pressure and hence the solubility. Change in surface tension takes place as the solubility will increase (due to particle size reduction), which leads to increased saturation solubility. Different physiological solutions at different pH and different temperatures are used to carry out the determination of the saturation solubility and dissolution velocity according to the techniques suggested in the pharmacopeia. In-vivo overall performance (blood profiles, plasma peaks, and bioavailability) of the formulation is assessed by using these parameters. An increase in saturation solubility can be explained by using the Ostwald Freundlich equation 19. Determination of the dissolution velocity of nanosuspensions gives information about the advantages of nanosuspension over conventional formulations, especially in sustained-release dosage forms

The Ostwald-Freundlich equation is:

$C(r) = C(\infty) \exp (2\gamma M / r\rho RT)$ ------Equation (1)

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 [18] .

5. Stability:

Nanosuspensions Stability depends on the particle size of the suspended particles. The reduction in the particle size to the nano range will increase the surface energy of the particles, and the tendency of the particles to agglomerate increases. Therefore the stabilizers are used to reduce the chances of Ostwald ripening and to improve the stability of the suspension by means of providing a steric or ionic barrier. Stabilizers like cellulosic, Poloxamers, Polysorbates, lecithin, polyoleate, and Povidones are generally used in the nanosuspensions. Lecithin is desired in the improvement of parental nanosuspensions. Nanosuspensions can be stored at different stress conditions like distinctive temperatures (15, 25, 35 45°C), thermal cycling, and mechanical shaking and alternate in their mean particle size can be accompanied for three months. Different concentrations of small molecule surfactants (like sodium lauryl sulfate (SLS) and do fax 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 [19] .

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

6. pH:

The pH of the nanosuspension can be easily measured by means of the use of a pH meter [20].

7. Osmolarity:

Practically, the Osmolarity of nanosuspension can be measured by way of using Osmometer[20].

8. Drug Content:

The drug content material of nanosuspension formulation can be carried out with the aid of extracting the nanosuspension in the appropriate solvent mixture, like Methanol: THF (1:1) mixture, shaken well and then centrifuged. The supernatants can be separated and diluted with the same solvent combination, and the absorbance can be measured at appropriate λ-max. The drug content then can be calculated the usage of the calibration curve [20] .

In-vivo Evaluation:

Particular drug and route of administration require the specific in-vivo evaluation of the nanosuspensions. Generally, the formulations are administered with the aid of the required route, and the plasma drug concentrations are decided via HPLC-UV visible spectro-photometry. Surface hydrophilicity/hydrophobicity (which determines interaction with cells prior to phagocytosis), adhesion properties, and the interaction with body proteins are normally evaluated via in-vivo parameters. The monitoring of the in-vivo overall performance of the Nanosuspensions and the establishment of the relationship between in-vitro release and in-vivo absorption are required in order to prepare a successful preparation. Irrespective of the route of the administration and the delivery systems. The rate of dissolution influences the in-vivo biological overall performance of oral nanosuspensions. The size of nanoparticle and surface properties of the particles determines the organ distribution for intravenously injected nanosuspensions. The invivo organ distribution conduct of the nano-suspension is affected by means of hydrophilicity/ hydrophobicity and interactions of particles with plasma proteins. Surface hydrophobicity is determined with the aid of hydrophobic interaction chromatography, and absorption of protein is determined by 2-D PAGE quantitatively and qualitatively after intravenous injection of nanosuspensions of the drug in animals.

Applications

Applications of nanosuspensions had land marking history and therefore the applications given area unit few .

1. Oral drug delivery

The oral route is that the most popular route for drug delivery owing to its various well-known blessings. .Orally administered antibiotics like atovaquone and bupravaquone mirror this downside alright. Nanosizing of such medicine will result in a dramatic increase in their oralabsorption and bioavailability.Nanosuspension can lead to increased mucoadhesion which can increase gastrointestinal transittime and lead to increased bioavailability. The enhancement in oral bioavailability can be attributed to increased surface area, saturation solubility and the adhesiveness of the drug Nanosuspension. Taste masking of particulate system is also easily possible.

2. Channel drug delivery

One of the vital applications of nanosuspension technology is that the formulationof intravenously administered product. IV administration leads to many blessings,such as administration of poorly soluble medicine while not employing a higher concentration of toxicco-solvents, improving the therapeutic result of the drug accessible as typical oralformulations and targeting the drug to macrophages nanosuspensions of poorly soluble drugtarazepide are ready to beat the restricted success achieved victimisation typical solubilizationtechniques, like use of surfactants, cyclodextrins, etc., to boost bioavailability[25]

3. Respiratory organ drug delivery

Nanosuspensions might persuade be a perfect approach for delivering medicine that exhibitpoor solubility in respiratory organ secretions. liquid nanosuspensions will benebulized victimisation mechanical or supersonic nebulizers for respiratory organ delivery. as a result of oftheir tiny size, it's possible that in every aerosol drop a minimum of one drug particle iscontained, resulting in a additional uniform distribution of the drug in lungs[26]. The nanoparticulate nature of the drug permits the speedy diffusion and dissolution of the drug at the location of action.

4. Ocular drug delivery

Nanosuspensions will persuade be a boon for medicine that exhibit poor solubility inlachrymal fluids. Nanosuspensions, by their

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

inherent ability to boost the saturationsolubility of the drug, represent a perfect approach for ocular delivery of hydrophobic medicine and Nanoparticulate nature of the drug permits its prolonged residence within the culdesac, giving sustained unleash of the drug.

5. Targeted drug delivery

Nanosuspensions will be used for targeted delivery as their surface properties and in-vivobehavior will simply be altered by dynamic either the stabilizer or the surroundings. The engineering of stealing nanosuspensions (analogous to stealing liposomes) by victimisation numerous surface coatings for active or passive targeting of the required website is that the way forward for targeted drug delivery systems.

6. Mucoadhesion of the nanoprticles

Nanoparticles orally administered within the kind of a suspension diffuse into the liquidmedia and chop-chop encounter the membrane surface. The direct contact of the particles with the enteric cells through a bioadhesive part is that the commencement before particle absorption.

7.Bioavailability enhancement

The poor oral bioavailability of the drug could also be because of poor solubility, poor porousness,or poor stability within the alimentary canal (GIT). Nanosuspensions resolve the matter of poor bioavailability by finding the dual issues of poor solubility and poor porousness across the membrane. Bioavailability of poorly soluble oleanolic acid, a hepatoprotective agent, was improved employing a nanosuspension formulation. The therapeutic result was considerably increased, that indicates higher bioavailability. This was because of the quicker dissolution (90% in twenty min) of the freeze-dried nanosuspension powder when put next with the dissolution from a rough powder (15% in twenty min) .

Marketed Preparations

Sr no.	Product Drug	Compound	Company
1.	RAPAMUNE	Sirolimus	Wyeth
2.	EMEND R	Aprepitant	Merck
3.	TriCor®	Fenofibrate	Abbott
4.	MEGACE©ES	Megestrol Acetate	PAR Pharmaceutical
5.	Avinza R	Morphine Sulphate	King Pharmaceutical
6.	Focalin R	XR Dexmethylphenidate Hydrochloride	Novartis
7.	Ritalin	Methylphenidate Hydrochloride	Novartis
8.	LA.ZanaflexCapsulesTM	Tizanidine Hydrochloride	Acorda

II. CONCLUSION

This review presents the recent progress in therapeutic nanosuspensions produced by various techniques such as high pressure homogenisation, media milling, and emulsification. However, in early stages, several in vivo studies clearly demonstrate the potential of these drug delivery vehicles in parenteral, oral, ocular, and pulmonary administration, where not only a controlled release but also an appropriate bioadhesion is required. The research on drug nanosuspensions is in its infancy.

However, these systems carry flexibility and opportunity for further tailoring particles, surface properties to optimise in vivo responses, and generation of new clinical approaches for treating a number of diseases (heart, cancer, diabetes, Parkinson's, Alzheimer's, etc.) are required. Considering that nanoparticle uptake is size dependent, working on the size optimization of drug nanosuspension can help us prepare an appropriate nanosuspension formulation with better diffusion through the mucus gel layer. In addition,

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 847-856 www.ijprajournal.com ISSN: 2249-7781

incorporation of polymers on the particle surface and size reduction can be regarded as the future step in nanosuspension research.

REFERENCE:

[1]. Dhiman, Dharmila S and Thakur, GS: Nanosuspension: A recent approach for nano drug delivery system. Int J Curr Pharm Res 2017; 3(4).

[2]. Purkayastha HD and Hossian SKI: Review Article on nanosuspension: a modern technology used in drug delivery system. International Journal of Current Pharmaceutical Research 2019; 11(3).

[3]. Date AA, Kulkarni RM and Patravale VB: Nanosuspensions: A promising drug delivery. Journal of Pharmacy & Pharmacology 2018; 56: 827-40

[4]. Elaine M, Liversidge, Gary G and Liversidge M: Drug nanoparticles formulating poorly water soluble compounds. Toxicologic Pathology 2019; 36: 4348.

[5]. Jagdale DM, Kamble VA and Kadam VJ: Nanosuspension a novel drug delivery system. International Journal of Pharma and Bio Sciences 2017; 1(4): 352-60.

[6]. Yadav M, Dhole S and Chavan P: Nanosuspension: a novel techniqus in drug delivery system. 2017; 3(12) 410- 33.

[7]. Geetha G, Poojitha U and Khan KAA: Various Techniques for Preparation of Nanosuspension. International Journal of Pharma Research & Review 2018; 3(9): 30-37.

[8]. Yadav GV and Singh SR: Nanosuspension: a promising drug delivery system pharmacophore. (An International Research Journal) Pharmacophore 2018; 3(5): 217-43.

[9]. Singh K and Chandra D: Nanosuspension: way to enhance the bioavailibility of poorly soluble. International Journal of Current Trends in Pharmaceutical Research 2017: 1(4): 277-87.

[10]. Keck C and Muller R: Drug nanocrystals of poorly soluble drugs produced by high pressure homogenization. European Journal of Pharmaceutics and Biopharmaceutics 2018; 62(1): 3-16. 11. Nash RA: Suspensions. In: Swarbrick J, Boylan J.C (Ed). Encyclopedia of pharmaceutical technology. Second edition vol. 3. New York, Marcel Dekker 2017; 2045- 3032.

[11]. Dalith M, Maheswari U, Reddy AK and Venkatesha T: Nanosuspensions: Ideal approach for the drug delivery of poorly water soluble drugs. Der Pharmacia Lettre 2016: 3(2): 203-13.

[12]. Giddam PAK: Nanosuspension technology, a review. International Journal of Pharmaceutics 2019: 2(4): 35-40.

[13]. Malakar, Basu A and Ghosh A: Nanosuspension: A nanoheterogeneous carrier for drug delivery system. International Journal of Pharmaceutical and Biological Archives 2017; 3(1): 4-13.

[14]. Keck C and Muller R: Drug nanocrystals of poorly soluble drugs produced by high pressure homogenization. European Journal of Pharmaceutics and Biopharmaceutics 2016; 62(1): 3-16.

[15]. Shilpa CP, Shrenik KC, Ritesh AM, Sachin J and Mukesh RP: Nanosuspension -A Novel Approaches in Drug Delivery System. International Journal of Pharma Research & Review 2016; 2(12): 30-39.

[16]. Chingunpituk J: A review on nanosuspension technology for drug delivery. Walailak J Sci& Tech 2017; 4(2): 139- 53.

[17]. Kawakami K: Modification of physicochemical characteristics of active pharmaceutical ingredients & application of supersaturable dosage forms for improving bioavailability of poorly improving of poorly absorbed drugs. Advanced Drug Delivery Reviews, 2017.

[18]. Burgess DJ, Gokhale R, Kumar S and Verma S: Physical stability of nanosuspensions: Investigation of the role of stabilizers on Ostwald ripening. International Journal of Pharmaceutics 2016; 406(1-2): 145-52.

[19]. Patel M, Shah A and Patel KR: Nanosuspension: A novel approach for drug delivery system. JPSBR 2018; 1(1): 1- 10,

[20]. Peters K, Leitzke S, Diederichs JE, Borner K, Hahn H and Moller RH: Preparation of clofazimine nanosuspensions for intravenous use and evaluation of its therapeutic efficacy in murine Mycobacterium avium infection. J AntimicrobeChemother 2017; 45: 77-83.

[21]. Jacobs C, Kayder O and Muller RH: Nanosuspension as a new approach for the formulation of poorly soluble drug tarazepide. Int J Pharma 2018; 196: 161-64.
[22]. Ponchel G, Montisci MJ, Dembri A, Durrer C and Duchkne D: Mucoadhesion of colloidal particulate systems in the gastrointestinal tract. Eur J Pharm Biopharm 2017: 44: 25-31.
[23]. Thattil JG, Kumar KK and Kumar BD: Nanosuspension technology in pharmaceuticals. J Bio Innov 2018; 7(2): 660-77.
[24]. Chen Y, Liu J, Yang X, Zhao X and Xu H: Oleanolic acid suspension: preparation, in-vitro characterization and enhanced hepato-protective effect. J Pharma Pharmacol 2017; 57: 259-26.
[25]. Arunkumar N, Deecaraman M and Rini C: Nanosuspension technology and its applications in drug delivery. Asian J Journal of Pharmaceutics 2019; 3: 168-73.
[26]. Pu X, Sun J, Li M and He Z: Formulation of nanosuspensions as a new approach for the delivery of poorly soluble drugs. Current Nanoscience 2016; 5: 417- 27.
[27]. Torchilin V: Hand Book of Nano biomedical Research, 2017; 3: 180
[28]. Dearns R. Atovaquone pharmaceutical compositions. US Patent US 6018080, 2000.
[29]. Young TJ, Mawson S, Johnston KP, Henriska IB, Pace GW, MishraAK. Rapid expansion from supercritical to aqueous solution to produce submicron suspension of water insoluble drugs. BiotechnolProg 2000;16:402-7.
[30]. Kumar AN, Deecaraman M, Rani C. Nanosuspension technology and its applications in drug delivery. Asian J Pharma 2009;3:168-73.
[31]. Chen Y, Liu, J, Yang X, Zhao X, Xu H. Oleanolic acid nanosuspensions: Preparation, in-vitro characterization and enhanced hepatoprotective effect. J Pharm Pharmacol 2005;57:259-64.
[32]. Higgins JP. Spectroscopic approach for on-line monitoring of particle size during the processing of pharmaceutical nanoparticles. Anal Chem 2003;75:1777-85.
[33]. Setler P. Identifying new oral technologies to meet your drug delivery needs for the delivery of peptides and proteins and poorly soluble molecules. London: IIR Limited Drug delivery system; 1999.
[34]. Muller RH, Jacobs C. Production and characterization of a budesonide nanosuspension for pulmonary administration. Pharm Res 2002;19:189-94.
[35]. Yang JZ, Young AL, Chiang PC, Thurston A, Pretzer DK. Fluticasone and budesonide nanosuspensions for pulmonary delivery: Preparation, characterization, and pharmacokinetic studies. J Pharm Sci 2008;97:4869-78.
[36]. Liang YC, Binner JG. Effect of triblock copolymer non-ionic surfactants on the rheology of 3 mol% yttria stabilised zirconia nanosuspensions. Ceram Int 2008;34:293-7.
[37]. Muller RH, Grau MJ. Increase of dissolution rate and solubility of poorly water soluble drugs as nanosuspension. Proceedings. World Meeting APGI/APV, Paris. 1998;2:62-624.