International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 579-598 www.ijprajournal.com ISSN: 2249-7781

Nanosuspensions

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Submitted: 09-01-2023 Accepted: 19-01-2023

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 varyof 1-1000 nm. Nanosuspensions area unit returning underneath engineering science. A pharmaceutical Nanosuspension is outlined as terribly finely mixture, biphasic, spread solid drug particles in associate liquid vehicle, size below one one stable by surfactants and polymers ready by appropriate ways for drug delivery applications. It provides economical delivery of hydrophobic medicine and will increase the bioavailability. Nanosuspension is a pretty and promising technology to enhance poor solubility and bioavailability of the medicine. This review describes the ways of preparation, and applications of nanosuspensions within the field of pharmaceutical sciences.

KEYWORDS: Nanosuspensions, polymers, drugs. Saturation solubility, Dissolution rate

I. INTRODUCTION:

Nanosuspensions are unit mixture dispersions associated biphasic system consisting of drug particles spread in an liquid vehicle during which the diameter of the suspended particle is a smaller amount is a smaller amount in size.

Reduction of drug particles to nanometre vary ends up in associate increased dissolution rate because of multiplied extent and saturation solubility.Nanosuspensions have disclosed their potential to tackle the issues related to the delivery of poorly soluble and poorly water-and lipid-soluble medicine, and area unit distinctive due to their simplicity and also the blessings they confer over different methods. This review focuses on the assorted aspects of nanosuspensions and their potentials as promising strategy in drug delivery. engineering science is outlined because the science and engineering meted out within the nanoscale that's 10-9 meters.Nanotechnology is associate applicable facet of a broader space of nano science that is one in every of the future and extremely difficult yet as rewardful key analysis space within the fashionable scientific discovered. it's the science of tiny particle having distinctive properties, that amendment on neutering the scale of the particle. In recent years,a lot of attention has been targeted on engineering science for delivering formulations, that is being applied to reinforce the solubility & bioavailability of hydrophobic medicine. The formulation of nanosized particles are often enforced to any or all drug compounds happiness to biopharmaceutical system (BCS) categories II and IV to extend their solubility and thence partition into epithelial duct barrier. There area unit several standard ways for increasing the solubility of poorly soluble medicine, that embrace micronization, solubilization exploitation cosolvents, salt form,surfactant dispersions, precipitation technique, and oily answer.

NEED FOR NANOSUSPENSIONS:

Preparing nanosuspensions is most well-liked for the compounds that square measure insoluble in water (but square measure soluble in oil) with high log P worth.Conventionally the medicine that square measure insoluble in water however soluble in oil part system square measure developed in cyst, emulsion systems however these lipidic formulation approaches aren't applicable to all or any medicine. In these cases nanosuspensions square measure most well-liked. In case of medication that square measure insoluble in each water and in organic media rather than mistreatment lipidic systems Nanosuspensions square measure used as a formulation approach.Nanosuspension formulation approach is most fitted for the compounds with high log P worth, high temperature and high dose.When to travel for Nano Suspensions Approach Preparing nano suspensions is most well-liked for the compounds that square measure insoluble in water (but square measure soluble in oil) with high log P worth. Conventionally the medicine that square measure insoluble in water however soluble in oil part system square measure developed in cyst, emulsion systems however these lipidic just in case ofmedication that square measure insoluble in each water and in organic media rather than mistreatment lipidic systems Nanosuspensions square measure used as a formulation approach. Nanosuspension formulation approach is most

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fitted for the compounds with high log P worth, high temperature and high dose

CRITERIA FOR CHOICE OF DRUG FOR NANOSUSPENSIONS-

Nanosuspension are often ready for the API that's having either of the followingcharacteristics

1.)Water insoluble however that square measure soluble in oil (high logP) or API square measure insoluble in each water and oils.

2.)Drugs with reduced tendency of the crystal to dissolve, despite the solvent.3.) API with massive dose.

NANOSUSPENSIONS:

A pharmaceutical nanosuspension is outlined as a awfully finely mixture, biphasic, dispersed, solid drug particles in binary compound vehicle, size below 1μm, with none matrix material, stabilized by surfactants & polymers, ready by appropriate ways for drug delivery applications, through numerous routes of administration like oral, topical, parenteral, ocular & pulmonic routes.

Nanosuspensions is dispersions of nanosized drug particles stable by surfactants. they will even be outlined as a biphasic system consisting of pure drug particles distributed in an binary compound vehicle within which the diameter of the suspended particle is a smaller amount is a smaller amount insize.

Nano may be a Greek word, which suggests 'dwarf'. Nano suggests that it's the issue of 10-9 or one billionth. The Nanosuspensions may be preserved or spray dried and also the nanoparticles of a Nanosuspension may be incorporated in an exceedingly solid matrix.A nanosuspension not solely solves the downside of poor solubility & bioavailability however conjointly alters the materia medica of drug, that improves safety & effectivity. Nanosuspension formulation approach is most fitted for the compounds with high log P price, high melting purpose & dose. Nanosuspension has been according to reinforce sorption & bioavailability it should facilitate to scale back the dose of the convectional oral dose forms. Drug particle size reduction results in a rise in extent & consequently within the rate ofdissolution as delineate by Nernst-Brunner &Levich modification of the Noyes-Whitney equation.Nanosuspensions is accustomed enhance the solubility of medicine that square measure poorly soluble in binary compound likewise as lipide media. As a result, the speed of flooding of the active compound will increase and also the most plasma level is reached quicker (e.g., oral or endovenous administration of the nanosuspension). this is often one in every of the distinctive blessings that it's over different approaches for enhancing solubility.

ADVANTAGES OF NANOSUSPENSION:

Improved biological performance Ease of manufacture and scale-up Long-term physical stability Versatility

Increase within the oral absorption Improved dose proportion.

Its general relevancy to most medicine & simplicity

It is applied for poorly water soluble medicine.

It is given by any route.

Reduced tissue irritation just in case of subcutaneous(SC)/intramuscular(IM) administration.

Increase within the dissolution speed and saturation solubility of the drug.

DISADVANTAGE OF NANOSUSPENSION:

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 thepreparation can be bulk.

6.) Dose fixation can be tough.

7.)Uniform & correct dose can not be achieved.

FORMULATION OF NANOSUSPENSION-

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 behavior of nanosuspensions. In some cases, a mix of stabilizers is needed to get a stable Nanosuspension.
2. **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

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Volume 8, Issue 1 Jan-Feb 2023, pp: 579-598 www.ijprajournal.com ISSN: 2249-7781

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.

3. Co-surfactants-

The choice of co-surfactant is important once mistreatment microemulsions formulate nanosuspensions. Since co-surfactant scan greatly influence section behavior, 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

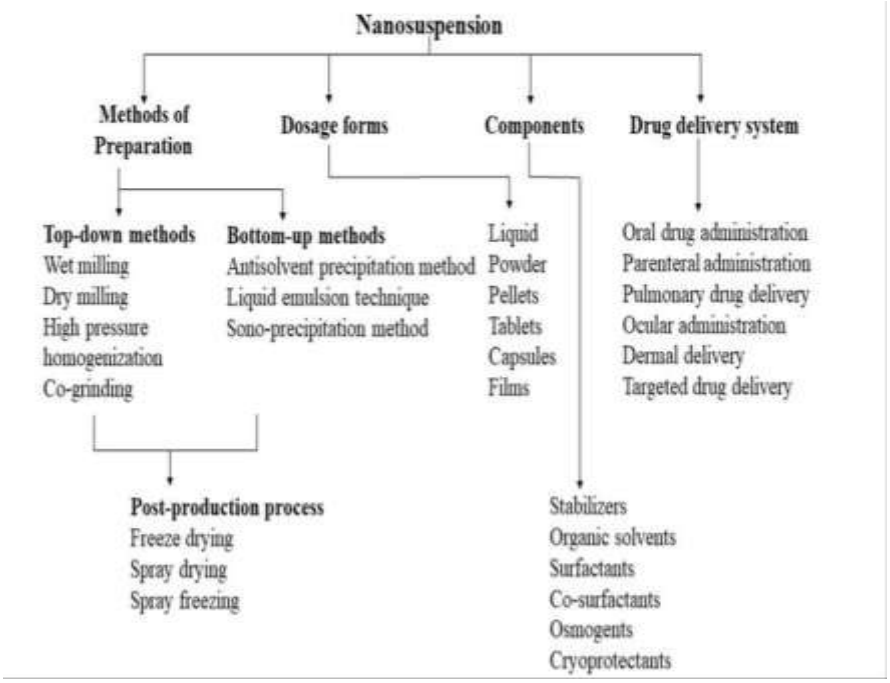
4. different additives -Formulation concerns Nanosuspensions could contain additives like buffers, salts, polyols, osmogentand cryoprotectant, reckoning on either the route of administration or the properties of the drug moiety

5. Amino acid-based stabilizers

Leucine copolymers havebeen demonstrated to successfully produce stable drugnanocrystals in aqueous medium. Lecithin is pre-ferred as stabilizing agent for sterile, steam heat sterilizable parenteral nanosuspensions. Albumin has been employed as a surface stabilization and drug targeting atvvarious concentrations as low as 0.003% up to 5% in nano-suspension . Other pharmaceutically acceptable aminoacid co-polymers used for the physical stability of nano-crystalswere arginine, proline, and transferrin.

6. Cellulose based derivatives -

HPMC, hydroxypropyl cel-lulose (HPC), hydroxyethyl cellulose (HEC) have beenwidely used as stabilizing agent in nanosuspensions. Theunderlying mechanism of steric stabilization provided by these polymers is due to surface adsorbed hydrophobic groups



1.) bottom-up technology:

1.Precipitation technique.-

Precipitation has been applied for years to organize submicron particles at intervals the last decade, particularly for the poorly soluble medicine. Typically, the drug is first off dissolved in solvent. Then this resolution is with a compatible antisolvent within the presence of surfactants. speedy addition of a drug resolution to the antisolvent (usually water) results in fast supersaturation of drug within the mixed resolution and generation of ultrafine crystalline or

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amorphous drug solids. This method involves 2 phases nuclei formation and crystal growth. once getting ready a stable suspension with the minimum particle size, a high nucleation rate however low rate of growth is critical.
.Advantage :1) Use of simplest and customary strategies.

3) Higher saturation solubility is one amongst the advantage for precipitation compared to alternative technique of preparation.
Disadvantages :

1) Drug solubility is that the main criteria.
2) The solvent miscibility with a minimum of one non-solvent is to be needed.
3) Complete removal of solvent residues is another one amongst the difficult step,therefore increasing production prices.
4) The preservation of particle character is no bit troublesome (i.e. size, just in case of amorphous fraction). It are often done by mistreatment spray appliance as a second step method for the particle size preservation.

Nanosuspensions square measure made by mistreatment high-shear media mills or pearl mills. The mill consists of a edge chamber, edge shaft and a recirculationchamber. associate binary compound suspension of the drug is then fed into the mill containing tiny grinding balls/pearls. As these balls rotate at a awfully high shear rate beneath controlled temperature, they fly through the grinding jar interior and impact against the sample on the alternative grinding jar wall. The combined forces of friction and impact turn out a high degree of particle size reduction. The edge media or balls square measure fabricated from ceramic- sintered aluminum oxide or zirconia or extremely cross-linked styrene organic compound with high abrasion resistance. A planetary ball mill (PM100 andPM200; Retsch GmbH and Co., KG, Haan, Germany) is one example of kit that may be wont to come through a grind size below zero.1 µm. A Nanosuspension of Zn- Insulin with a mean particle size of a hundred and fifty nm was ready mistreatment the wet edge technique.

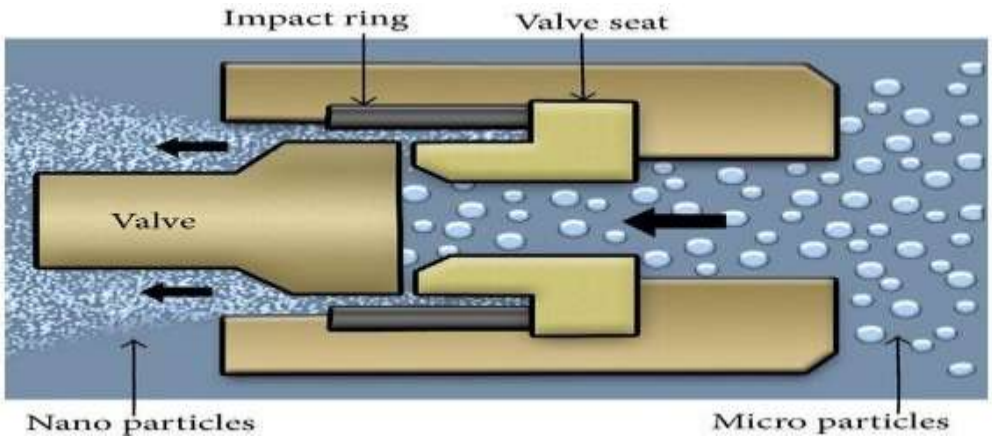
Advantages

1. easy technology
2. cheap method concerning the edge itself
3. Large-scale production doable to some extent (batch process).

Disadvantages

1. Potential erosion from the edge material resulting in product contamination
2. length of the method not being terribly production friendly.
3. Potential growth of germs within the water section once edge for an extendedtime.
4. Time and prices related to the separation procedure of the edge material from the drug nanoparticle suspension, particularly once manufacturing channel sterileproduct.

2) High Pressure Homogenization –



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a) Dissocubes:

In this case, the suspension of the drug is formed to go through atiny low passage that end in a discount of the static pressure below the boiling pressure of water, that results in boiling of water and formation of gas bubbles. once the suspension leaves the gap and traditional gas pressure is reached once more, the bubbles collapse and also the close half containing the drug particles rushes to the middle and within the method colloids, inflicting a discount within the particle size. Most of the cases need multiple passes or cycles through the homogenizer, that depends on the hardness of drug, {the desired|the specified|the needed} mean particle size and also the required homogeneity. to supply a Nanosuspension with the next Concentration of solids, it's most popular to begin blend with terribly fine drug particles, which might be accomplished by pre-milling. the main advantage of high- pressure blend over media edge is that it are often used for each diluted further as targeted suspensions and additionally permits antiseptic production.

b) Nanopure:

Nanopure is suspensions homogenized in water-free media or water mixtures. within the Dissocubes technology,the cavitation is that the determinative issue of the method. But, in distinction to water, oils and oily fatty acids have terribly low vapor pressure and a high boiling purpose. Hence,the drop of static pressure won't be enough enough to initiate cavitation. Patents covering disintegration of chemical compound material by high- pressure blend mention that higher temperatures of concerning 800C promoted disintegration, that can not be used for unstable compounds. In nanopure technology, the drug suspensions within the non- binary compound media were homogenized at 00C or perhaps below the temperature and thence square measure referred to as "deep-freeze" blend.

c) Nanoedge:

The basic principles of Nanoedge square measure constant as that of precipitation and blend. a mixture of those techniques leads to smaller particle size and higher stability in an exceedingly shorter time. the main disadvantage of the precipitation technique, like crystal growth and long run stability, are often resolved mistreatment the Nanoedge technology. during this technique, the precipitated suspension is more homogenized; resulting in reduction in particle size and avoiding crystal growth. Precipitation is performed in water mistreatment water-miscible solvents like wood spirit, alcohol and isopropyl alcohol. it's fascinating to get rid of those solvents fully, though they will be tolerated to a definite extent within the formulation. For an efficient production of Nanosuspensions mistreatment the Nanoedge technology, associate evaporation step are often enclosed to supply a solvent-free changed beginning material followed by hard-hitting blend

3) Melt emulsification technique :

In this technique drug is spread within the solution of stabilizer associated heated on top of the melting purpose of the drug and homogenized to administer an emulsion. throughout this method, the sample holder was enwrapped with a heating tape fitted with temperature controller and also the temperature of emulsion was maintained on top of the melting purpose of the drug. The emulsion was then cooled down either slowly to temperature or on associate icebath. soften emulsification technique relative to the solvent diffusion technique is total dodging of organic solvents throughout the assembly method.

4) Dry Co-Grinding :

Recently, Nanosuspensions are often obtained by dry edge techniques. productive add getting ready stable Nanosuspensions mistreatment dry-grinding of poorly soluble medicine with soluble polymers and copolymers when dispersing in an exceedingly liquid media has been according. several soluble polymers and co-polymers like PVP, synthetic resin glycol (PEG), hydroxypropyl alkyl group polysaccharide .

5.)Micro emulsion template:

This technique follows associate organic solvent or mixture solvent loaded with the drug spread in associate binary compound section containing appropriate surfactants to make associate emulsion. The organic section is then gaseous beneath reduced pressure to form drug particles precipitate outright to make the Nanosuspension that is stabilised by surfactants. Another technique makes use of part water-miscible solvents like radical nurse, radical alcohol and triacetin because the form rather than dangerous solvents.

Advantages

Use of specialised instrumentation isn't necessary.
Particle size will simply be controlled by dominant

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the dimensions of the emulsiondrop.
Ease of scale-up if formulation is optimized properly.

Disadvantages
Drugs that square measure poorly soluble in each binary compound and organic media can not be developed by this method.
Need for diultrafiltration for purification of the drug Nanosuspension, which can render the method pricey.
High quantity of surfactant/stabilizer is needed as compared to the assembly techniques delineated earlier.

Post-production process
Post-production process of nanosuspensions becomes essential once the drugcandidate is very at risk ofvhydrolytic cleavage or chemical degradation.
Processing may also be needed once the simplest potential stabilizer is not able to stabilize the nanosuspension for a extended period of your time or there square measure acceptableness restrictions with respect to the required route.
Considering these aspects,techniques like lyophillization or spray drying could beemployed to provide a dry powder of nano-sized drug particles. Rational choice must be created in these unit operations considering the drug properties and economic aspects. Generally, spray drying is additional economical and convenient than lyophillization.

Technique	Merits	Demerits
Precipitation	Simple process Stable products Low need of energy Low cost of equipment Ease of scale up	Growing of drug crystals needs to be limit by surfactant addition Drug must be soluble at least in one solvent Narrowly applying space, wide size distribution and potential toxicity of nonaqueous solvents
High-pressure homogenization	Simple technique General applicability to most drugs Useful for formation of very dilute as well as highly concentrate nanosuspension Aseptic production possible Low risk of product Contamination ease of scale-up	High number of homogenization cycles Pretreatment of micronized drug particles and presuspending materials before subjecting it to homogenization Possible contamination of product could occur from metal ions coming through wall of the homogenizer
Media milling	High flexibility in handling Very few batch to batch variation in particle size High flexibility in handling large quantities of drugs Ease of scale up	Possible erosion of material from the milling pearls Require milling process for hours to days Prolonged miling may induce the formation of amorphous lead to instability
Dry cogrinding	Easy process Require short grinding time No organic solvent	Generation of residue of milling media
Liquid emulsion/microemulsion template	Simple process Small size particles Stable products Low need of energy High drug solubilization Uniform particle distribution Ease of manufacture	Use of high amount of surfactant and stabilizers Use of hazardous solvent
Melt emulsification	Avoidance of organic solvents compared to the solvent diffusion	Formation of large particles Solvent diffusion

Characterization of Nanosuspension
1.)Particle size distribution -
The most acceptable characterization parameter for the nanosuspension area unit the mean particle size and breadth of particle size distribution that verify thechemistry properties like saturation solubility, dissolution rate, physical stability and even biological performance.[18] A amendment in particle size changes saturated solubility and dissolution rate. Smaller the particle size additional are going to be the saturated solubility and dissolution.

2. Zeta potential -
Zeta potential determines the physical stability of nanosuspension.Zeta potential is associate degree indirect mensuration of the thickness of the diffusion layer, i.e.will be wont to predict future stability. so as to get a nanosuspension exhibiting sensible stability, for associate degree electro statically stabilised

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nanosuspension a minimum letter of the alphabet potential of ± 30mv is needed whereas within the case of a combined static and steric stabilization, a minimum letter of the alphabet potential of ±20mV is fascinating.

3. Crystal morphology

X-ray optical phenomenon analysis together with Differential scanning measuring device and scanning microscopy is employed to see the polymorphic changes because of impact of air mass blending within the crystalline structure of the drug. Nanosuspension will endure a amendment within the crystalline structure, which can be to associate degree amorphous kind or to alternative polymorphic forms owing to air mass blending. associate degree multiplied quantity of amorphous drug fraction might induce higher saturation solubility.

4.)Saturation solubility and dissolution velocity-

Nanosuspension will increase the dissolution rate and saturation solubility. Size reduction ends up in increase within the dissolution pressure.An increase in solubility that happens with comparatively low particle size reduction could also be primarily because of a amendment in physical phenomenon resulting in multiplied saturation solubility.

5) Density

Specific gravity or density of the formulation is a very important parameter. A decrease in density typically indicates the presence of entrapped air inside the structure of the formulation. Density measurements at agiven temperature ought to be created victimisation well mixed,uniform formulation; exactness measuring system facilitate such measurements.

6) pH Value

The hydrogen ion concentration price of liquid formulation ought to be taken at a given temperature and solely once subsiding equilibrium has been reached, to reduce "pH drift" and conductor surface coating with suspended particles. solution mustn't be supplemental to the external part of theformulation to stabilised the hydrogen ion concentration.

7) Droplet Size

The drop size distribution of small emulsion vesicles will be determined by eitherlight-weight scattering technique or microscopy. Dynamic light-weight scattering photometer that uses a argonon optical maser of wavelength 632 nm.

2.In-Vivo Biological Performance

The institution of associate degree in-vitro/in-vivo correlation and therefore the watching of the in-vivo performance of the drug is an important a part of the study, regardless of the route and therefore the delivery system utilized. it's of the foremost importance within the case of intravenously injected.

Nanosuspensions since the in-vivo behavior of the drug depends on the organ distribution, that successively depends on its surface properties, like surface property and interactions with plasma proteins. In fact, the qualitative and quantitative composition of the supermolecule absorption pattern determined once the shot of nanoparticles is recognized because the essential lfactor for organ distribution. Hence, appropriate techniques have to be compelled to be employed in order to judge the surface properties and supermolecule interactions to urge an inspiration of in-vivo behavior. Techniques like hydrophobic interaction natural action will be wont to verify surface property, whereas 2-D PAGE will be utilized for the quantitative and qualitative mensuration of supermolecule surface assimilation once shot of drug nanosuspensions in animals.

Applications

Applications of nanosuspensions had land marking history and therefore theapplications 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.

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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 bioavailability25

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 lungs26. 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 solubilityinlachrymal fluids. Nanosuspensions, by their 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 drug24

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 systems27

6. Mucoadhesion of the nanoprticles

Nanoparticles orally administered within the kind of a suspension diffuse into theliquidmedia 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 twentymin) .

Nanosuspensions based on their route of administration

Route	Drugs	Therapeuticclass	Company/author
Oral route	Carbamazepine	Psycholytic	D.Douroumis
	Megestrolacetate	Steroidhormone	ParPharmaceuticals
	Paliperidonepalmitate	Antischizophrenia	Johnson andJohnson
	Insulin	Diabetes	BioSante
	Ketoprofen	Analgesic	RemonJ.P.
	Azithromycin	Antimicrobial	DianruiZhang
	Albendazole	Anthelminticdrug	MittapalliP.K.

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	Tarazepide	**SelectiveCCKa-antagonist**	**C.Jacobs**
	Griseofulvin	**Antifungal**	**BorisY.Shekunov**
	Mitotane	**AdrenalCortexHormones**	**MicheleTrotta**
	Cilostazol	**cagent**	**Jun-ichiJinno**
	Aphidicolin	**Antileishmanial**	**O.Kayser**
	Buparvaquone	**Antibiotic**	**MüllerR.H.**
	Fenofibrate	**Lipidlowering**	**SkyePharma**
	Cytokineinhibitor	**Crohn'sdisease**	**ElanNanosystems**
	Emend	**Anti-emetic**	**ElanNanosystems**
	Rapamune	**Immunosuppressant**	**ElanNanosystems**
	Probucol	**Lipidlowering**	**JyutaroShudo**
	Danazol	**Hormone**	**RogersT.L.**
Parental	**Naproxen**	**Anti-inflammatory**	**AnchaleeAin-Ai**
Intravenous	**Loviride**	**Antivirotic**	**B.VanEerdenbrugh**
	Clofazimine	**Antimycobacterials**	**K.Peters**
	Oridonin	**Anticancer**	**LeiGao**
	Ascorbylpalmitate	**Antioxidant**	**VeerawatT.**
	Dihydroartemisinin	**Antimalarial**	**JirapornC.**
	Omeprazole	**Protonpumpinhibitor**	**JanMöschwitzer**
	Thymectacin	**Anticancer**	**ElanNanosystems**
	Paclitaxel	**Anticancer**	**AmericanBioscience**
Ophthalmic	**Hydrocortisone**	**Glucocorticoid**	**M.A.Kassem**

The New Drug Application Based on Nanosuspensions Technique Reportedand Marketed by Now:

Drugs	**Indication**	**Author orCompany**	**Route**	**Status**
Paclitaxel	Anticancer	American Bioscience	Intravenous	Marketed

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Danazol	Hormone	Rogers T.L.	Oral	Reported
Naproxen	Anti-inflammatory	AnchaleeAin-Ai	Oral/parenteral	Reported
Probucol	Lipid lowering	JyutaroShudo	Oral	Reported
Rapamune	Immunosuppressant	ElanNanosystems	Oral	Marketed
Emend	Anti-emetic	ElanNanosystems	Oral	Marketed
Cytokine inhibitor	Crohn‟s disease	ElanNanosystems	Oral	Phase II
Fenofibrate	Lipid lowering	SkyePharma	Oral	Marketed
Megestrol acetate	Steroid hormone	Par Pharmaceuticals	Oral	Marketed
Paliperidone pal-mitate	Anti-schizophrenia	Johnson andJohnson	Oral	Phase III
Loviride	Antivirotic	B. Van Eerdenbrugh	Intravenous	Reported
Busulfan	Anticancer	Skye Pharma	Intrathecal	Undisclosed
Budesonide	Asthma	Jerry Z. Yang	Pulmonary	Reported

Fluticasone	Asthma	Jerry Z. Yang	Pulmonary	Reported
Insulin	Diabetes	BioSante	Oral	Undisclosed
Clofazimine	Antimycobacterials	K. Peters	Intravenous	Reported
Buparvaquone	Antibiotic	Müller R. H.	Oral	Reported
Oridonin	Anticancer	Lei Gao	Intravenous	Reported
AZ68	Anticancer	Kalle S.	Oral/I.V.	Reported
Ascorbylpalmitate	Ascorbylpalmitate	Veerawat T.	Intravenous	Reported
Hydrocortisone	Glucocorticoid	M.A. Kassem	Ophthalmic	Reported
Prednisolone	Glucocorticoid	M.A. Kassem	Ophthalmic	Reported
Hexadecadrol	Glucocorticoid	M.A. Kassem	Ophthalmic	Reported
Aphidicolin	Antileishmanial	O. Kayser	Oral	Reported
Dihydroartemisin in	Antimalarial	Jiraporn C.	Intravenous	Reported

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Cilostazol	Antiplatelet agent	Jun-ichiJinno	Oral	Reported
Carbamazepine	Psychotolytic	D. Douroumis	Oral	Reported
Omeprazol	Proton pump inhibitor	Jan Möschwitzer	Intravenous	Reported
Thymectacin	Anticancer	Elan Nanosystems	Intravenous	Undisclosed
Silver	Eczema	NUCRYST	Topical	Phase III
Mitotane	Adrenal Cortex Hormones	Michele Trotta	Oral	Reported
Griseofulvin	Antifungal	Boris Y. Shekunov	Oral	Reported
Tarazepide	Selective CCKa-antagonist	C. Jacobs	Oral	Reported
Albendazole	Anthelmintic drug	Mittapalli P. K.	Oral	Reported
Azithromycin	Antimicrobial	Dianrui Zhang	Oral	Reported
Ketoprofen	Analgesic	Remon J.P.	Oral	Reported

Current Marketed Pharmaceutical Products Based on Nanosuapensions

Sr no.	**Product Drug**	**Compound**	**Company**
1.	RAPAMUNE	Sirolimus	Wyeth
2.	EMEND®	Aprepitant	Merck
3.	TriCor®	Fenofibrate	Abbott
4.	MEGACE®ES	Megestrol Acetate	PAR Pharmaceutical
5.	Avinza®	Morphine Sulphate	King Pharmaceutical
6.	Focalin®	XR Dexmethylphenidate Hydrochloride	Novartis

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 579-598 www.ijprajournal.com ISSN: 2249-7781

7.	Ritalin®	Methylphenidate Hydrochloride	Novartis
8.	LA.ZanaflexCapsulesTM	Tizanidine Hydrochloride	Acorda
9.	TriglideTM	Fenofibrate	First Horizon Pharmaceutical

Summery of drug Nanosuspensions.

Drug	Drug deliveryroute	Manufacturing method	Indication
Silybin	Oral, IV	IV HPH	Human prostate cancer
All-trans retinoic acid(ATRA)	IV, oral, and skin	Modified precipitation method	Antiproliferate drug against tumor
Mitotane	Oral	Emulsion astemplate	Symptomatic treatmentof advanced adrenocortical carcinoma (ACC)
Clofazimine	Intravenous	High-pressure homogenization	Murine Mycobacterium aviuminfection

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Volume 8, Issue 1 Jan-Feb 2023, pp: 579-598 www.ijprajournal.com ISSN: 2249-7781

Cyclosporin A	Inhalation	Antisolvent precipitation	In Immunosuppression
Amphotericin B	Ocular	Solvent displacement process	Management of ophthalmic fungalinfections
Olmesartan medoxomil	Oral	Media milling	Antihypertensive agent

Simvastatin	Oral	Nanoprecipitation	Lipid-lowering agent
Azithromycin	Oral	Dry cogrinding	Treatment of vasculardiseases
Nifedipine	Oral	Dry cogrinding	Treatment of vasculardiseases
Salbutamolsulfate	Pulmonary inhalation	HPH	Antiasthmatic
Diclofenac	Transdermal	Emulsification	NSAID
Oridonin	IV	HPH	Antitumor
Albendazole	Oral	HPH	Lipophilic anthelminticdrug
Loviride	IV	Milling	Antivirotic

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Naproxen	I.P	Precipitation	Analgesic activity
Paclitaxel	IV	HPH	Anticancer
Ibuprofen	Ocular	Emulsion solvent diffusion method	Ocular anti-inflammatory activity

RECENT PATENTS ON NANOSUSPENSION TECHNOLOGY

In the past decades, nanosuspensions are investigated for their potent applications in drug delivery systems and it's been determined that nanosuspensions possess the potential to boost the bioavailability and effectiveness of drug candidates. varied patents are granted over nanosuspension technology.

Patent/ Application Number	**Publication/ Application Date & Year**	**Patent Description**
WO2016135753Al	Sept. 1, 2016	This patented work involves the development of a methodology for topically utilized nanosuspension through the process of milling.
WO2016081593Al	May 26, 2016	The patented invention describes the nanosuspension fabricated with a therapeutically active moiety. Such moiety is an active nutraceutical having poor

		solubility profile.
US20160317534A1	Nov. 3, 2016	This patent gives information about a nanosuspension prepared with the lyophilized drug. Such nanosuspension possessed sufficient stability during long-term storage.
US20160206577	Jul. 21, 2016	This patented study reflects the method of fabrication of nanosuspension of an antibacterial moiety that improves the stability and reduced toxicity of the drug.
US20150238446A1	Aug. 27, 2015	The researchers reported the development of stable hexaflumuron nanosuspension that can be injected into fishes for controlling sea lice.
CN105708844A	June 29, 2016	This patented work describes the development method of ophthalmic nanosuspension of tobramycin & dexamethasone. The process was found to

		be reproducible, effective, stable and convenient.
CN105315249A	Feb. 2, 2016	This patent is related to the development method of simvastatin nanosuspension to
		enhance the efficiency of drug delivery systems.
CN105534947A	Feb. 16, 2016	The patented work involves a method of developing a celecoxib nanosuspension capsule which can be converted into solidified powder through freeze drying.
CN104814926	Aug. 5, 2015	This invention stated that the nanosuspension of lurasidone was fabricated through the combination of nano-precipitation and high-pressure homogenization method.
US9023886B2	May 5, 2015	The patented invention demonstrates the formation of nanosuspension of poor water soluble drug through microfludization

		technique.

II. CONCLUSION:

The formulation of poorly soluble medicine has forever been a difficult downside featured by pharmaceutical scientists. during this case, nanosuspension formulations are often thought of as a promising candidate. varied techniques delineated during this review alone or together are often with success accustomed solve the poor bioavailability downside of hydrophobic medicine and medicines that square measure poorly soluble in binary compound and organic solutions. Nanosuspensions are often administered through oral, parenteral, ophthalmic, pulmonary, and topical routes. It will play a awfully necessary role for human betterment because the technology is straightforward, needs less excipients, and will increase dissolution speed and saturation solubility.

Nanosuspension solved poor bioavailability downside of hydrophobic medicine and medicines that square measure poorly soluble in binary compound and organic solutions. Productions techniques like media edge and high homogenizer square measure used for big scale production of Nanosuspensions.

Nanosuspensions are often administered through oral, parenteral, pulmonary, ocular and topical routes. Nanosuspension formulations square measure promising candidates for enhancing the solubility of poorly water soluble medicine. Nanosuspension technology are often combined with ancient dose forms: tablets, capsules, pellets, and may be used for canal merchandise. The dissolution issues of poorly water soluble medicine are for the most part solved to boost drug absorption & bioavailability. to require advanateg of nanosuspension drug delivery, easy formulation technologies & selection applications, nanosuspensions can still be interest as oral formulations & non-oral administration develop within the future.

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