JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

REVIEW ON NANOSUSPENSION DRUG DELIVERY SYSTEM

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ABSTRACT

Solubility proves to be a hurdle for the successful development and commercialization of new drug products. Since 40% of the active substances being identified through the new paradigm in high – through put screening are lipophilic. So,its viability as a potential drug candidate reduces manifold. Because of this, many pharmacologically active molecules have failed to reach in to the market. Therefore, Nanosuspensions have emerged as a promising strategy for the efficient delivery of hydrophobic drugs. Techniques such as media milling and high-pressure homogenization have been used commercially for producing nanosuspensions. Recently, the engineering of nanosuspensions employing emulsions and microemulsions as template has been addressed in the literature[1]. The unique features of nanosuspensions have enabled their use in various types of dosage forms, including specialized delivery systems such as mucoadhesive hydrogels. Rapid strides have made in the delivery of nanosuspensions by parenteral, per-oral, ocular and pulmonary route. The following work deals with the special factors of nanosuspensions, the preparation methods, advantages, characterization of nanosuspensions, patents, marketed products and their applications[2].

Nanosuspension

Nanosuspensionis a sub- micron colloidal dispersion of drug particles which are stabilized by surfactants, polymers or mixture of both. They can also define as the biphasic system consisting of pure drug particle dispersed in an aqueous vehicle in which the diameter of the suspended particle is less than 1 um in size.

The particle size distribution of the solid particle in nanosuspension is usually less than 1micron with an average particle size ranging from 200 and 600 nm.

Need of Nanosuspension

BCS Classdrugs are poorly water soluble and their pharmacokinetic studies shows low oral bioavailability.To solve these problems, techniques like dissolution in aqueous mixtures with an organic solvent, formation of beta cyclodextrin complexes, solid dispersions, drug in salt form and micronization, has been developed to increase drug dissolution rate.

A pharmaceutical nanosuspension is an as very fine dispersion of soliddrug particles in an aqueous vehicle stabilized by surfactant[3]. In nanosuspensiontechnology, the drug is maintained in the required crystalline state with reduced particle size, leading to an increased dissolution rate and therefore improved bioavailability.

KEYWORDS: Nanosuspension, Nanosuspension Techniques, Applications, Marketed products and Patents.

ADVANTAGES OF NANOSUSPENSION DRUG DELIVERY SYSTEM

- Can be applied for poorly water-soluble drugs
- Can be given by any route.
- Oral administration provides rapid onset, reduced fed/fasted ratio and improved bioavailability.
- Ocular administration and inhalation delivery provides higher bioavailability and more consistent dosing.
- Due to reduced particle size of nanosuspension,the absorption form and absorption window can be enhanced.
- Improvement in biological performance due to high dissolution rate and saturation solubility of drugs.
- Long term physical stability.
- Nanosuspensions can be incorporated in tablets, pellets, hydrogel are suitable for various routes of administration.
- Surface – modification of nanosuspension possible, for site specific delivery.
- Provides a passive drug targeting.
- Dose reduction is possible.
- Higher drug loading can be achieved.
- Enhance the solubility and bioavailability of drug[4].

DISADVANTAGES OF NANOSUSPENSION DRUG DELIVERY SYSTEM

- Physical stability of the drug and compaction can cause problems.
- It is bulky sufficient.
- Special care must be taken during the handling and transport.
- Improper dose[5].

SELECTION OF DRUG FOR NANOSUSPENSIONS:

Nanosuspension can be prepared for the Active Pharmaceutical ingredient that is having following characteristics:

- Water insoluble but which are soluble in oil (high logP) or API are insoluble in both water and oils[6].
- API with very large dose.

FORMULATION CONSIDERATIONS:

1. **Stabilizers:** The main function of stabilizer is to wet the drug particles thoroughly and to prevent Ostwald's ripening and agglomeration of nanosuspension in order to yield a physically stable formulation by providing steric or ionic barriers. The drug –to-stabilizer ratio in the formulation may vary from 1:20 to 20.1 stabilizers that have been used so far are poloxamers, polysorbate, cellulosic, povidones and lecithin's. Lecithin is the stabilizer of choice to develop a parentally acceptable and autoclavableNanosuspensions[7].
2. **Surfactants:** Surfactants are incorporated to improve the dispersion by reducing the interfacial tension. They act as deflocculating agents.
   Eg: Tweens and spans – widely used surfactants.
3. **Co-Surfactants:** The selection of co- surfactant is important when using microemulsion to formulate.
   Eg: Bile salts, DipotassiumGlycerrhizinate, Transcutol, Glycofurol, Ethanol and Isopropanol.

4. **Organic solvent**: Nanosuspensions, when prepared by using emulsion or microemulsion template, then organic solvents are used in formulation pharmaceutically acceptable less hazardous solvents ared used for the preparation of formulation.Eg: Methanol, Ethanol, Chloroform, Isopropanol, Ethyl acetate, Ethyl fumarate, Butyl lactate, Triacetin, Propylene carbonate, Benzyl alcohol.
5. **Other additives**: Selected according to the requirement of the route of administration or the properties of the drug moiety. Eg: Buffers, Salts, Polyols, Osmogens and Cryoprotectant[8].

METHOD OF PREPARATION:

Methods of preparation of nanosuspensions:

- **Bottom-Up process –form**

Nanoparticles from precipitation, microemulsion, melt emulsification method.

- **Top-down process**

Nanoparticles obtained by high-pressure homogenization and milling methods.

Bottom-UpTechnology:

The methods of precipitation i,e Hydrosols are called Bottom Up technology. Precipitation method is used to prepare submicron particles of poorly soluble drugs. In this method, thedrug is dissolved in solvent and solution is mixed with solvent in which drug is insoluble in the presence of surfactant[9]. Rapid addition of solution to such solvent (generally water) leads to rapid super saturation of drug in the solution, and formation of ultrafine amorphous or crystalline drug. High nucleation rate and low crystal growth are primary requirements for preparation of a stable suspension with maximum particle size. The limitation of this precipitation technique is that the drug needs to be soluble in at least one solvent needs to be miscible with nonsolvent.

Examples includes

- Solvent- Antisolvent method
- Super critical fluid process
- Emulsification –Solvent evaporation technique
- Lipid emulsion /Micro emulsion template

Precipitation Method:

Precipitation has been applied to prepare submicron particles, especially for the poorly soluble drugs. The drug is dissolved in a solvent, next this solution is mixed with a miscible antisolvent in the presence of thesurfactants. Rapid addition of a drug solution to the antisolvent leads to super saturation of drug and formation of ultrafine crystalline drug solids. Precipitation method involves two phases - nuclei formation and crystal growth[10]. When preparing a stable suspension with the minimum particle size, a high nucleation rate and but low growth rate is necessary. Both the rates are depending on temperature. In this method the drug needs to be soluble in at least one solvent which is miscible with non-solvent.

Advantages: Simple process, Ease of scale up and Economical production**.**

Disadvantages: Growing of crystals needs to be limit by surfactant addition.

Supercritical fluid process:

This technique utilizes solubilization andnanosizing technologies. Super Critical fluids (SCF) are non-condensable dense fluids whose temperature and pressure are greater than its critical temperature (TC) and critical pressure (Tp). This process allows the micronization of drug particles to submicron level. The low solubility of poorly water-soluble drugs and surfactants in supercritical CO2 and the high pressure required for these processes restrict the utility of this technology in the pharmaceutical industry.

Solvent evaporation:

Here the solutionsof polymer are prepared in volatile solvents and emulsions. The emulsion is converted into a nanoparticle suspension on evaporation of the solvent for the polymer, which is allowed to diffuse through the continuous phase of the emulsion. Conventionally, two main strategies are being used for the formation of emulsions, the preparation of single-emulsions, e.g., oil-in water (o/w) or double –emulsions, e.g., (water –in –oil)-in –water, (w/o)/w. These methods require high –speed homogenization or Ultrasonication, followed by evaporation of the solvent, by continuous magnetic stirring at room temperature or under reduced pressure. The solidified nanoparticles are collected and washed with distilled water to remove the additives[11].

Lipid emulsion/microemulsion template:

This method applicable for drugs they are soluble in either volatile organic solvents or partially water miscible solvents. Here the drug was dissolved in suitable organic solvent and it is emulsified in aqueous phase using suitable surfactants. Then the organic solvent was slowly evaporated under reduced pressure to form drug particles precipitating in the aqueous suspension of the drug in the required particle size. The suspension formed can be suitably diluted to get nanosuspensions. Microemulsions as templates can produce Nanosuspensions. Microemulsions are thermodynamically stable and clear dispersions of two immiscible liquids such as oil and water stabilized by interfacial film of the surfactant and co-surfactant.

Advantages: High drug solubilization, long shelf life and easy to manufacture.

Disadvantages:

- Use of hazardous solvent
- Use of high amount of surfactant and stabilizers.

Melt emulsification method:

In this technique, The drug is dispersed in aqueous solution of the stabilizer and heated above the melting point of the drug and then homogenized to give an emulsion. During this process,the sample holder was enwrapped with a heating tape filled with temperature controller and the temperature controller and the temperature of emulsion was maintained above the melting point of the drug emulsion was then cooled down either slowly to room temperature or on an ice-bath.

Advantages: Melt emulsification technique relative to the solvent evaporation method is total avoidance of organic solvents during the production process.

Disadvantages: Formation of larger particles and few complaint objects than solvent evaporation.

Top-down process:

The Top-down process involves the disintegration from large particles, microparticles to nanosized particles. The techniques used area's follows:

- High pressure homogenization
- Nanoedge
- Nanopure
- Media milling
- Dry –co-grinding

High pressure homogenization:

This method is most widely used for preparing nanosuspensions of many poorly aqueous soluble drugs. The process involves three steps:

- Drug powders are dispersed in stabilizer solution to form presuspension .
- The presuspension is homogenized in high pressure homogenizer at a low pressure for premilling.

Different methods are developed based on the preparations of Nanosuspensions are:

- **Homogenization in aqueous media (Disso cubes):**

In this technique, the suspension contains a drug and surfactant is forced under pressure through a nanosized aperture valve of a high-pressurehomogenizer[12].

Principle:

This method is based on cavitation principle. The dispersion present in 3cm diameter cylinder is suddenly passed through a very narrow gap of 25um. It leads to increase in dynamic pressure and decrease of static pressure below the boiling point of water at room temperature due to reduction in diameter from 3cm to 25um. Then water starts boiling at room temperature and also forms gas bubbles, that implode when the suspension leaves the gap.

Advantages:

1. This does not cause the erosion of the processed materials.
2. It is applicable to the drugs that are poorly soluble in both aqueous and organic media.

Disadvantage:

1. Pre-processing like micronization of drug is required.

- **Homogenization in nonaqueous media (Nanopure):**

Nanopure is suspensions homogenized in water-free media or water mixtures like PEG 400, PEG1000. Temperature will be room temperature, 0 degree or even at freezing point .So it is known as deep freeze homogenization. It is the best method for the thermolabile substances at milder conditions. In this technology the nanocrystals of the drug dispersed in liquid polyethylene glycol (PEG) or various oils can be directly filled as drug suspensions into HPMC capsules or gelatin[13].

- **Nano edge:**

The principle involved in Nano edge technology is the combination of both precipitation and homogenization.

Principle:

In this technique drug is dissolved in an organic solvent and this solution is mixed with the miscible anti-solvent for precipitation. Drug precipitates due to low solubility in the water solvent mixture. Precipitation is coupled with high shear processing, which is accomplished by combination of rapid precipitation and high-pressure homogenization.

- **Nano jet:**

This method is also called as opposite stream technology,it uses a chamber where a stream of suspension whichis subdivided into two or moreother parts, which colloid with each other at high pressure. The high shear faces produced in this process leads to reduction in particle size.

Limitation:

- High numbers of passes (nearly about 75) are required through the microfluidizer, and the product obtained contains a relatively large fraction of micro particles.
- This process requires large production time.

Milling techniques:

- **Media milling:**

This method was first developed by Liversidge (1992). The Nanosuspensions in this technique areprepared by high shear media mill.The milling chamber was charged with the milling media, water, drug and stabilizer and rotated at a high shear rate under controlled temperature at least 2-6 days. The high shear forces are formed as a result of impaction of milling media with the drug which results in breaking of drug particles to nanosized particles.

Principle:

In this technique, the milling medium is composed of glass, zirconium oxide and polystyrene resin. The process can be performed in either batch or recirculation mode. In batch mode, the time required to obtain dispersions with unimodal distribution profiles and mean diameter <200nm is 30-60 min.

Advantages:

- Very dilute as well as highly concentrated nanosuspensions can be prepared by handling 1 mg/ml to 400mg/ml drug quantity.
- Nanosized distribution of final nanosizedproduct.
- Ease of scale-up and little batch –to-batch variation.

Disadvantages:

- Generation of residues of milling media, which may be introduced in the final product as a result of erosion
- The media milling techniques is time consuming.
- Scale up is not easy due to moil size and weight.

- **Dry-Co-grinding:**

Recent technique, dry-co-grinding can be carried out easily and economically and can be conducted without organic solvents.

Advantages:

- Easy process and no organic solvent required.
- Require short grinding time.

CHARACTERIZATION OF NANOSUSPENSIONS:

Nanosuspensions are characterized for appearance, color, odor, assay, related impurities, particle size, zeta potential, crystalline morphology status, dissolution studies and in vivo studies. Among these the essential characterization techniques are[14]:

- **Mean particle size and particle size distribution:**
  The mean particle size and particle size distribution affect the saturation solubility, dissolutionrate, physicalstability, even in vivo behavior of nanosuspensions. The particle size distribution can be determined by photon correlation spectroscopy (PCS), laser diffraction (LD) and Coulter counter multisizer. PCS can also be used for identifying the width of particle size distribution (polydispersity index, PI). A PI value of 0.1 -0.25 indicates a fairly narrow size distribution, if PI value greater than 0.5 indicates a very broad distribution. The coulter counter gives the absolute number of the particles per volume for the different size classes and it is more efficient and appropriate technique[15].

- **Surface charge (zeta potential):**
  Zeta potential gives information about the surface charge properties and the long-term physical stability of the nanosuspensions. For a stable suspension stabilized only by elrectrostatic repulsion, a minimum zeta potential of _+30 mV is essential , where as in case of a combined electrostatic and steric stabilizer , a zeta potential of _+20 mV would be sufficient.

- **Crystalline state and particle morphology :**
  The evaluation of the crystalline state and particle morphology helps in understanding the polymorphic or morphological changes that a drug may undergo when subjects to nanosizing . Because of High pressure homogenization nanosuspensions can undergo a change in the crystalline structure, which may be to an amorphous form or to other polymorphic forms.
- **Saturation solubility and Dissolution velocity:**
  The saturation solubility of the drug in different physiological buffers as well as at different temperatures should be assessed using methods described in the literature. The investigation of the dissolution velocity of nanosuspensions reflect the advantage that can be achieved overconventional formulations, especially when designing the sustained release dosage forms based on nanoparticulate drugs. The evaluation of saturation solubility and dissolution velocity helps in determining the invitro behavior of the formulation[16].
- **Stability:**
  Stability of nanosuspensions depends on the particle size of the suspended particles. Decrease in the particle size to the nano range increases the surface energy of the particles, and the tendency of the particles to agglomerate increases. Therefore the
  Stabilizers are used to decrease the chances of Ostwald ripening and to improve the stability of the suspension by providing a steric or ionic barrier, stabilizers like cellulosic,poloxamers, Polysorbates, lecithin,polyoleate and povidones are generally used in the nanosuspensions. Nanosuspensions can be stored at different stress conditions like different temperature (15^0C,25^0C,35^0C,45^0C), thermal cycling, and mechanical shaking and change in their mean particle size can be followed for three months. 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 prepared Nanosuspension was taken in 10ml beaker and pH was measured by using pH meter.

- **Osmolarity:**
  The Osmolarity of Nanosuspensionsis measured by using Osmometer.
- **Drug content:**
  Drug content of nanosuspension formulation was carried out by taking lyophilized power (weigh equivalent to 5mg of drug) appropriate solvent mixture like methanol: THF (1:1) mixture, shake well centrifuge. The supernatants are separated and diluted with same solvent mixture and absorbance is measured at suitable ƛmax . The drug content is calculated using the calibration curve.
  Total volume of nanosuspension = total volume of nanosuspension × amount of drug in aliquot/volume of aliquot.

APPLICATIONS OF NANOSUSPENSIONS:

Nanosuspensions have various pharmaceutical and biopharmaceutical applications:

- Formulating the drug as nanosuspensions increases the saturableconcentration ,dissolution rate as well as bioavailability of the drug[17].
- These nanosuspensions are having application in different routes of administrations like oral, parenteral, topical, ophthalmic, mucoadhesive, pulmonary and targeted drug delivery.

Oral Drug Delivery:

Oral route is the most preferable route for many of the drugs especially in the case of orally administering antibiotics such as atovaquone and buparvaquone. Nanosizing of drugs can lead to a dramatic increase in their oral absorption and subsequent bioavailability can be explained by the adhesiveness of drug nanoparticles to the mucosa. The oral administration of naproxen nanoparticles leads to an area under the curve (AUC) (0-24h) of 97.5 mgh/I compared with naproxen nanosuspensions and naproxen tablets. In case of danazole (gonadotrophin inhibitor) nanosuspensions has absolute bioavailability of 82.3 and the conventional dispersion only 5.2%. Amphotericin B is an anti-parasitic drug with poor solubility whose intravenous injection and infusion can be related with considerable fluctuation of drug concentrations in the blood. Oral administration of Amphotericin B nanosuspension, produced by high pressure homogenization potentially reduced parasite numbers by maintaining constant blood levels in the plasma. In addition, nanosuspension showed good stability and good shelf-life characteristics. Milk thistle plant (Silybummarianum) isolate-silybin, used as a therapeutic agent for human colon cancer and prostate cancer. The effectiveness of Silybin as antitumor drug was limited due to its poor water solubility and low bioavailability after oral administration[18]. Nanosizing the drug particle to a size ranging from 100 to 1000nm could improve the solubility and bioavailability. The study of Silybinnanosuspension for its antitumor activity against human prostatic carcinoma PC-3 cell line (in vitro model) indicated that Silybinnanosuspension could be a potential source of medicine for the treatment of human prostate cancer.

- **Parenteral Drug Delivery:**

Nimodipine is used in patients with subarachnoid hemorrhage related vasospasm. Oral administration of nimodipine showed low bioavailability due to high first-pass metabolism in the liver. Intravenous administration is an alternative to oral administration which could give better bioavailability. Nimodipinenanosuspension prepared by high pressure homogenization, showed less local irritation and phlebitis risks which indicated that

nimodipinenanosuspension is a promising new drug formulation for intravenous therapy of subarachnoid hemorrhage related vasospasm. The drug clofazimine is given as iv, the concentration in the liver, spleen and lungs reached a high level i,e.; greater than minimum inhibitory concentration , for most of the mycobacterium avium strains.

Pulmonary Drug Delivery:

Drugs that are inadequately dissolvable in pulmonary secretions may be formulated with the help of the nanosuspensions. These medications are conveyed as suspensions aerosols or as dry powders by method for dry powder inhalers. Nebulization is generally achieved with the use of ultrasonics or mechanical nebulizer.

Advantages of nanosuspension over conventional pulmonary formulations:

- Increase in diffusion and dissolution rate at the site of action leading to increase in bioavailability of the drug.
- Drug has affinity to mucosal surfaces.
- Drug gets evenly distributed in the lungs as all the droplets of aerosols contains nanoparticles as compared to the macro particulate form of the drug.

Here we are using nano-preparations for the drugs which have poor solubility in pulmonary secretions. For the lung delivery mechanical or ultrasonic nebulizer nebulizes it. Eg: budesonide.

Ocular Drug Delivery:

Nanosuspensions plays a vital role for drugs that exhibit poor solubility in lachrymal fluids. The nano-size drug particles showed higher solubility, higher dissolution rate, higher bio adhesion, corneal penetration and increases the residence time in a culde-sac and avoidance of high tonicity created by water-soluble drugs. It indicated that diameter of the particles size less than 10µm will reduce particle irritation to the eye, diminish tearing and therefore increase the efficacy of an ocular treatment[19].

Eg: The nanosuspensions of hydrocortisone, prednisolone and dexamethasone was developed using high pressure homogenizer showed enhanced rate and extent of ophthalmic drug absorption as well as the intensity of drug action.

- **Targeted Drug Delivery:**

Nanosuspensions can be used for targeted delivery as their surface properties and in vivo behavior can easily be altered by changing the stabilizer. Their versatility and ease of scale up enable the development of commercially viable nanosuspensions for targeted delivery especially in the brain targeting. The engineering of stealth nanosuspensions by using various surface coatings for active or passive targeting of the desired site is the future of targeted drug delivery systems.

Eg: Targeting of Cryptosporidium parvum, the organism responsible for cryptosporidiosis was achieved by using surface modified mucoadhesivenanosuspensions.

- **Bioavailability enhancement:**

Nanosuspensionssolve the problem of poor bioavailability by twin problems of poor solubility and poor permeability across the membrane. Bioavailabilityof thepoorly soluble oleanolic acid was improved using a Nanosuspensions formulation. The therapeutic effect was significantly enhanced due to the faster dissolution

(90% in 20min) of the Lyophilized Nanosuspensions powder when compared with the dissolution from a coarse powder (15% in 20min) and thus bioavailability[20].

Topical formulations:

Incorporating the nanocrystalline form of drug into creams and water-free ointments leads to an increased saturation solubility of the drug in the topical dosage form , thus enhancing the diffusion of the drug into the skin.

Mucoadhesive of the nanoparticles:

Nanoparticles that are orally administered in the form of a suspension are diffuse into the liquid media andthen rapidly encounter the mucosal surface. After this, concentrated suspension acts as a reservoir of particles and an adsorption process takes place very rapidly. The direct contact of the particles with the intestinal cells through a bio adhesive phase is the first step before absorption[21]. The adhesiveness of the nanosuspensions helps to improve bioavailability and targeting of the parasites persisting in the GIT.

ADVANTAGES OF NANOSUSPENSION OVER CONVENTIONAL FORMULATION[22]

Route of administration	Disadvantages of conventional formulations	Benefits of Nanosuspensions
Oral	Slow onset of action/poor absorption	Rapid onset of action/improved solubility so improved bioavailability
Ocular	Lacrimal wash off /low bioavailability	Higher bioavailability /dose consistency
Intravenous	Poor dissolution / nonspecific action	Rapid dissolution /tissue targeting
Intramuscular	Low patient compliance due to pain	Reduced tissue irritation
Inhalations	Low bioavailability due to low solubility	Rapid dissolution / high bioavailability

RESEARCH WORKS ON NANOSUSPENSIONS:

JOURNAL	YEAR OF PUBLICATION	TITLE OF AUTHOR	MATERIAL AND RESULT	CONCLUSION
Scholars Academic Journal of Pharmacy(SAJP)	2016	Nanosuspension in Drug Delivery-A Review	Keywords- Nanotechnology, Nanosuspensions, polymers, drugs.	Nanosuspension formulation have been largely solved the solubility as well as dissolution problems to improve drug absorption. It has therapeutic advantages, such as simple method of preparation, less requirement of excipients, increased saturation solubility[23].

Journal of Advanced Pharmaceutical Technology and Research	2011	Nanosuspension: An Approach to enhancethe solubility of drugs	Keywords: Bioavailability, colloidal dispersion, drug delivery, nanosuspension, solubility.	Nanosuspensions are distinctive and commercially feasible approach to solve the problems of hydrophobic drug such as poor solubility and bioavailability. For large scale production of nanosuspensions, media milling and high-pressure homogenization technology have been successfully used.
International Journal of Pharmaceutical Sciences and Research	2020	Nanosuspension: A Promising drug delivery system for poorly water-soluble drug and Enhanced bioavailability	Keywords: Nanosuspension, solubility, bioavailability,	The advances in production methodologies the usage of emulsions or microemulsions as templates have been provided still essential. Attractivefeatures, such as increased dissolution velocity, improvedbio adhesive.
European Journal of Pharmaceutical Sciences	2023	Nanosuspensions technology as a Master key for nature products drug deliverysystem and in vivo fate	PEG, glycerol, oil, gelatin capsules,	This provides an overview of rece3nt development in the efficiency of nanosuspensions technique for the nature products drug delivery, including nanosuspensions preparation approaches, typically nature products nanosuspensionformulated, the guidelines for stabilizer screening, the effect of stabilizer and particle size on in vivo fate of intravenously administered nanosuspensions.
Asian Journal of Reserch in Pharmaceutical Sciences	2018	Different Techniques for preparation of Nanosuspension with Reference to its characterization and various Application-A Review	Keywords: Nanosuspension, nanotechnology, techniques for preparation, particle size, pharmaceutical applications.	The smart nanosuspensions as the new generation offer much more flexibility in drug loading, modulation of release and improved performance in producing final dosage forms such as creams, tablets, capsules .The aim has been to developed therapeutic nanotechnology under taking, particularly for targeted drug therapy.

PATENTS ON NANOSUSPENSIONS:

Because of such a versatile technology of nanosizing, there are many Patents on this technology[24]

Nanocrystal	Company	Patent/Patent application examples
Hydrosol	Novartis (Prev.Sandoz)	GB 22 69 536
Nanomorph	Soligs/Abbott	D 1963 7517
Nanocrystal	Elan Nanosystems	US 5,145,684
Dissocubes	SkypePharma	US 5 858,410
Nanopure	PharmaSol	PCT/EP00/0635
Nanoedge	Baxter	US6884436

Current Marketed Nanosuspension formulations

Product	**Drug**	**Indication**	**Company**
Triglide	Fenofibrate	Treatment of hypercholesterolemia	First horizon pharmaceutica
Tricor	Fenofibrate	Treatment of hypercholesterolemia	Abbott
Megace	Megestrolaceyate	Appetite stimulant	PARPharmaceutical
Rapamune	Sirolimus	Immunosuppresant	Wyeth
Emend	Aprepitant	Antiemetic	Merck
Sporanox	Itraconazole	Antifungal	Janssen pharma
Invegasustenna	Paliperidone palmitate	Antipsychotic	Janssen pharma

CONCLUSION:

Nanosuspension appear to be a unique and yet commercially viable approach to combating problems such as poor bioavailability that are associated with the delivery of hydrophobic drugs, including those that are poorly soluble in aqueous and organic media. Production methods such as Media milling and also High-pressure Homogenization have been successfully employed for the large-scale production of Nanosuspensions[25]. The advances in production methodologies using emulsions or microemulsions as templates have provided still simpler approaches for production but with limitations. Further investigation in this regard is still essential. Some features, such as increased dissolution velocity, increased saturation solubility, improved bio adhesivity, have widened the applications of Nanosuspensions in parenteral and oral routes have been realized. Moreover, their applications in buccal,nasal and topical delivery are still awaiting exploration. The development of the stealth Nanosuspensions laced with the functionalized surface coatings that are capable of eliciting passive or active targeting as per the requirements can be regarded as the future step in the Nanosuspension research.

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