International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Nanosuspension: A Novel Drug Delivery System

Siddheshwar Mitali Sanjay[1], Shile Vaishnavi Vyankati[2], Undhare Aradhana Santosh[3], Prof. Mr. Sole P P[4], Mr. Dr. Kolhe S. D[5]

[1,2,3]Student of Bachelor of Pharmacy, Anand Charitable Sanstha's College Of Pharmaceutical Science And Research, Ashti, India.
[4]Assistant Professor Anand Charitable Sanstha's College Of Pharmaceutical Science And Research, Ashti, India.
[5]Principal, Anand Charitable Sanstha's College Of Pharmaceutical Science And Research, Ashti, India .

Abstract:
It is over past two years ago. It has technology has been developed R& D pharmaceutical business. Nanotechnology is science is deals with the process that occurs at Molecular level and Nanolength scale size, Nano refer to the particle size range is 1- 1000 micrometre. Nano suspension can be used in oral, topical parenteral and pulmonary route of administration of drug delivery, Nano suspension is used in incorporated into ocular inserts and mucoadhesive hydrocele for targeted drug delivery. There are medication candidate is with very high effectiveness. Nanosuspension was prepared by using combination of high speed homogenization (HSH) and media milling (MM),Poligomer(stabilizer)ZIO2 heads (milling media). Reducing particle size in Nanosuspension is the primary cause of an increase in .Because of their specific qualities, nanosuspension can be used in a variety of dosage forms, including ones that require specialised delivery methods like mucoadhesive hydrogels.The Atomization of the drug discovery process through technologies like computer-aid drug design, combinatorial chemistry, an high-throughput screening is producing a large number of very effective therapeutic candidates. Regrettably, a lot of these potentiate medications are not very soluble in water. This review article describes the physicochemical properties of drug Nanosuspension, preparation methods and; it's potential clinical advantages.

Keywords: Nanosuspension, polymers, Bioavailability enhancement; surfactants; stabilizer.

Introduction:

The successful formulation of Pharmaceuticals depends in a number of factors, including solubility, stability at room temperature, compatibility with Solvent, excipient, and photostability[1]. A rapidly developing field in all branches of science, engineering, and technology is nanotechnology.[2] Pharmaceutical scientists have always faced the difficult task of formulating medications that are poorly soluble in water, and this challenge is predicted to get worse as more than 40% of newly created chemical entities from drug discovery programs are poorly soluble in water[3]. It presents the possibility of new and inventive methods with a wide range of applications in the treatment of cancer, encompassing fields like prognosis, therapies, and diagnostics. There are various methods for overcoming the problems caused by low solubility and bioavailability. It is concerned with changes in matter at the atomic or molecular scale, which usually occurs at a length of 1 to 100 nanometres[4]. Due to their limitations, these solubility enhancement techniques are not very useful for increasing solubility. Targeted medication delivery,

imaging, and molecular diagnostics are all made possible by nanotechnology, which contributes to successful therapies with fewer adverse effects. Nanotechnology is the study of science and engineering at the nanoscale, or 09–10 m[5]. Metricized medication microparticles Pharmaceutical powders are converted into nanoparticles by top-down and bottom-up approaches, as well as dissolution procedures[6]. The Greek term nano means "dwarf." The best candidates for the nanosuspension formulation strategy are those having large log P values, high melting points, and high doses.[7]

Nanosuspension:

Colloidal dispersions of nanoscale particles in a liquid media are known as nano-suspensions. These include mostly of less than 1µm-sized drug particles mixed with an antisolvent (probably water). The size of the particles in nano-suspensions typically ranges from 1 to 100 nanometres[8]. Because of their increased surface area and saturated solubility, drugs can dissolve more quickly when their particle size is reduced to such a small degree. It has been discovered that using Nanosuspension can effectively address the issues with traditional medication formulations[9]. These suspensions include distributed solid nanoparticles in a liquid phase, primarily water or a solution containing water. Drugs that have low solubility and bioavailability can be made safer and more effective by employing Nanosuspension. Nanosuspension technology makes it feasible to administer poorly soluble medications intravenously without running the danger of blood capillary blockage[10]. Nano-suspensions' special qualities and possible uses have drawn a lot of interest from a variety of industries[11]. Typical applications for nano-suspensions consist of:

1. Cosmetic Industry.
2. Food Industry.
3. Pharmaceutical industry.

Selection of drug to be formulated as Nanosuspension :

When an API exhibits one of the following traits, nanosuspension can be made for it:

- API are insoluble in both water and oils, or they are soluble in water but insoluble in oil (high logP).
- Medications with a decreased propensity for the crystal to dissolve in any kind of solution.
- API at really high dosage.
- Poor solubility.
- High Permeability.
- Target site.
- Stability[12].

Advantages of Nanosuspension :

1. nano-suspensions reduce particle size to the nanometre range, they can significantly increase the solubility of medications or chemicals that are weakly soluble.
2. Drugs that are not well soluble in water can use it.
3. Most cost effective.
4. Improved dose proportionality.
5. Targeted distribution of medications or active chemicals to particular cells, tissues, or organs is made easier by nano-suspensions[13].

Disadvantages of Nanosuspension :

1. Particle aggregation, also known as Ostwald ripening, can cause instability and an increase in particle size in nano-suspensions over time.
2. Complex procedures like high-pressure homogenization, wet milling, or precipitation techniques are used in the creation of Nanosuspension .
3. Physical stability, sedimentation and compaction cause problem.
4. It is bulky sufficient care must be taken during handling and transport.
5. Uniform and accurate dose cannot be achieved unless suspension[14].

Need of Nanosuspension for Bioavailability Enhancement :

However, pharmacokinetic analyses of BCS class-II medications revealed a low oral bioavailability, which could be brought on by the medication's weak water solubility. Over the past 20 years, a novel technique has been developed to enhance the rate of drug dissolution by decreasing the size of drug particles[15]. Oral bioavailability of medications may be further increased by higher dissolution rates and the consequent higher concentration gradient between the gastrointestinal lumen and systemic circulation. submicron colloidal dispersion of medicine particles stabilized by surfactants is called a nanosuspension. With an average particle size spanning between 200 and 600 nm, the solid particles in Nanosuspension typically have a particle size distribution of less than one micron.By maintaining the medication in the necessary crystalline state with smaller particles with nanosuspension technology, the bioavailability is enhanced as the rate of dissolving increases[16].

Formulation of Nanosuspension:

The ingredients that are necessary to create nanosuspension are:

Stabilizer: Stabilizers aid in the prevention of agglomeration formation in pharmaceutical formulations and stop particle aggregation, which gives the formulations physical stability.The kind and quantity of stabilizer utilized in the formulation of the Nanosuspension affects the nanosuspension' in-vivo performance Provide steric or ionic barriers to stop Ostwald's ripening and agglomeration of nanosuspension; fully wet the drug particles. For example: Lecithin's, Polysorbate, Poloxamers, Cellulosics, and Povidone [17].

Co-Surfactant: Surfactants are combined with co-surfactants to improve their properties when creating Nanosuspension-surfactants can be added to increase the surfactant's solubility, which will increase the stability of the nanosuspension. In nosuspensions, co-surfactants such polyethylene glycols, alcohols, and glycols are frequently utilized. When creating nanosuspension with micro emulsions, influence phase behavior. Such as potassium and bile saltsTranscutol, Glycofurol, Glycerrhizinate, Ethanol, and Isopropanol[18].

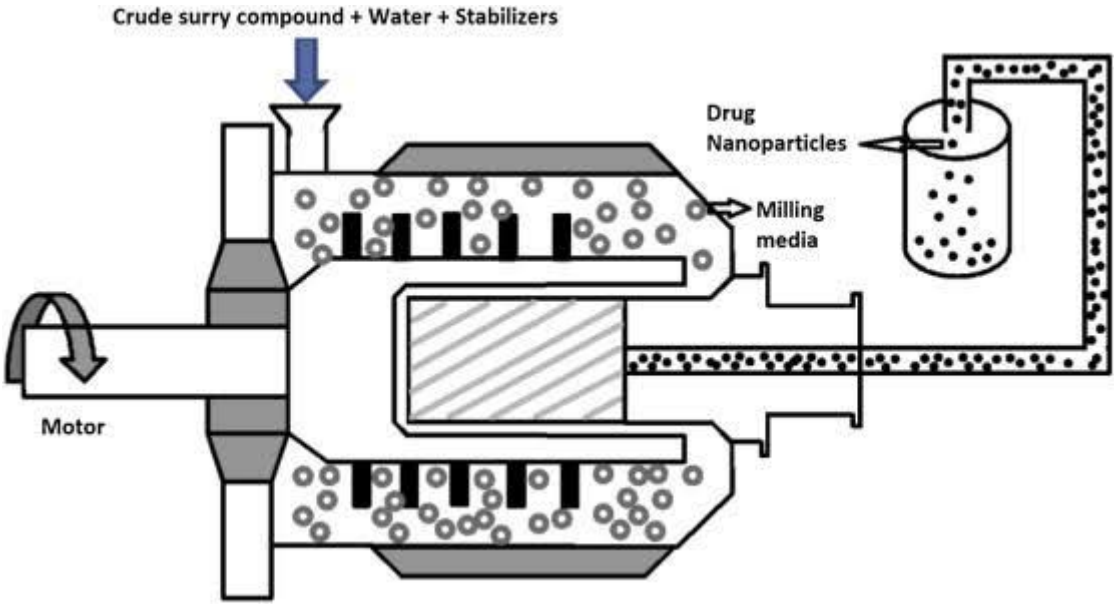
Organic solvent: Stable and non-hazardous organic solvent should be utilized in the formation of the nanosuspension. The majority of the time, when preparing a nosuspensions, volatile solvents like ethanol, methanol, chloroform, isopropanol, etc. utilized. Solvent for formulation preparation that is less toxic and appropriate for use in pharmaceuticals. Examples include butyl lactate, triacetin, propylene carbonate, benzyl alcohol, methanol, ethanol, chloroform, isopropanol, ethyl acetate, and ethyl formate[19].

Other additives: Salts, buffers, polyols, osmotic agents, and cryoprotectants are some other additives that are utilized in nanosuspension in addition to the components listed above. These additives are employed in accordance with the drug's physical and chemical characteristics as well as the method of administering

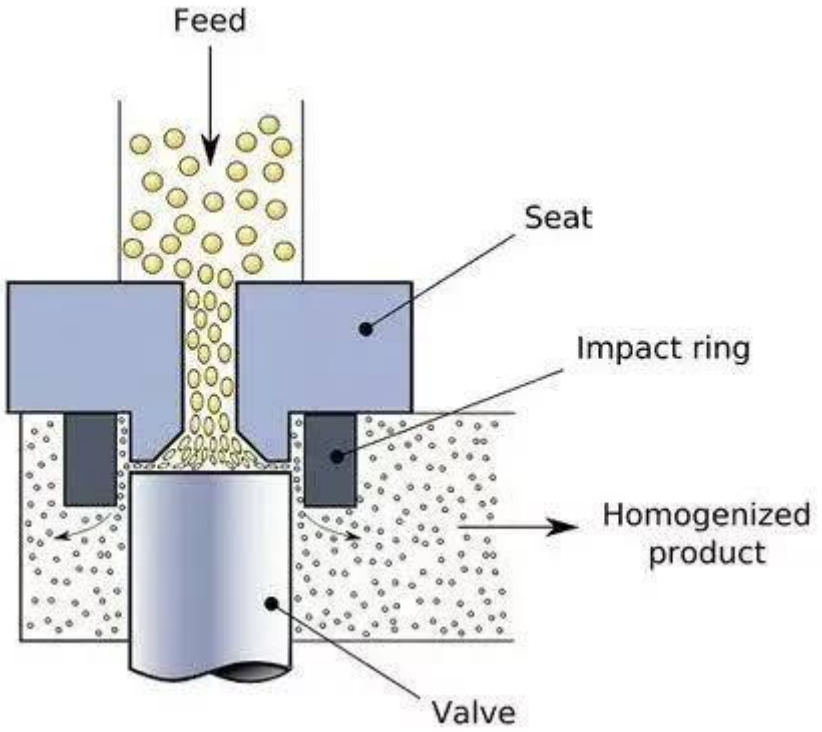
the nanosuspension. Based on the requirements of the drug's moiety's characteristics or the mode of administration. For example: Cryoprotectan, Osmogens, Polyols, Salts, and Buffers[20].

Method of preparation: There are primarily two ways to prepare nanosuspension. We refer to the traditional precipitation technique as "Bottom-up technology." The utilisation of inexpensive, basic equipment is the precipitation technique's main benefit[21]. The main difficulty with this method is that, in order to prevent the creation of microparticles, the growth of the drug crystals during the precipitation procedure must be regulated by adding surfactant. media milling, high pressure homogenization in water, high pressure homogenization in non-aqueous medium, and the combination of precipitation and high pressure homogenization are examples of top-down technologies[22].

Media Milling: Liverseys et al. (1992) developed it via a method that was patent-protected. Before being rebranded to announce that it had been acquired by Drug Distribution, the method was held by Nanosystems[23]. The components of it are the milling shaft, recirculation chamber, and milling chamber[24]. Ceramic sintered aluminium oxide or zirconium oxide balls, or pearls, make up the milling media. As a result, drug substance nanoparticles are created when micronized drug particles are reduced in size to nanosized particles. the milling media or pearls are rotated at a very high shear rate once the milling chamber is filled with the milling media, water, medication, and stabiliser. A high shear rate is used to spin the beads. The process of milling is finished at a controlled temperature.



High pressure Homogenizer: The disco cubes technique was created by R H Müller (Muller et al. 1998). Sky pharma plc currently owns the Disco Cubes patent, which was previously held by medication Delivery Services GmbH. Disco Cubes are made utilizing a high-pressure homogenizer of the piston-gap type. Commonly used homogenizers: APV Micron Lab 40. One fixed valve seat and one variable valve are used to make the release valve. These components produce a configurable radial precision differential. The force exerted on the valve modifies the gap's symmetry, resistance, and position. Using this technique, Kayser O et al. Created a nanosuspension containing amphotericin[25].



Nanoedge: This method combines two distinct processes—the homogenisation and precipitation techniques—that have comparable mechanics. Because nanoedge technology generates smaller particle sizes faster than other methods, it is regarded as superior. Precipitation approach has two key drawbacks: limited crystal formation and increased nanosuspension stability. In order to prevent crystal growth in the solution, a homogenisation process is used to produce particles of smaller sizes. First, a drug solution is prepared and quickly added to an anti-solvent solution, yielding information of supersaturated solution producing fine particles[26].

Applications of Nanosuspension: Nanosuspension applications are not just found in the pharmaceutical sector; they are also found in other industries. Below is a discussion of some of the main uses for nanosuspension.

Oral Drug Delivery: Lumefantrine nanosuspension was created by Shah Ripal Kumar et al. In 2021 for oral delivery. The study's goal was to increase the drug's solubility, which would then increase its oral bioavailability and antimalarial potency. Polysorbate 80 was the polymer utilized to create the nano suspension. In 2020, Liu Qiang et al. Created cilnidipine nanosuspension for oral use. Increasing the drug's oral bioavailability and rate of dissolution was the aim of the study. The nano suspension was prepared by wet milling, and the stabilizers PVP VA64 and SLS were used[27].

Parental Drug Delivery: When clofazimine is given intravenously, its concentration in the liver, spleen, and lungs reaches a high level, or greater than the lowest inhibitory concentration, for most strains of Mycobacterium avium. To improve its bioavailability, tripeptide is manufactured as a nanosuspension, which eliminates the requirement for surfactants and cyclodextrins[28].

Pulmonary Drug Delivery: Medication Administration to the Pulmonary System Here, we're using nano-preparations for drugs that don't dissolve well in pulmonary secretions. For lung delivery, it is nebulized using an ultrasonic or mechanical nebulizer. E. G: Budesonide[29].

Targeted Drug Delivery: Targeted medication administration The Nano suspension's stabilizers and surface properties may be readily altered in vivo, making them suitable for targeted distribution.

The development of commercially feasible nanotechnology systems for targeted medication distribution is made possible by the versatility and ease of large-scale and commercial production. Aphidicol was developed by Kaiser as a nano suspension for the creation of new drugs. At doses in the MG range, aphidicolin and action against Leishmania-infected macrophages were found to be highly active[30].

Mucoadhesive Drug Delivery

Buparvaquone mucoadhesive nanosuspension was produced and optimized by Muller R.H. et al. In 2001. The study's objective was to make buparvaquone more bioavailable. High pressure homogenization was the technique employed to create the nanosuspension[31].

Nasal Drug Delivery: Ivermectin intranasal nanosuspension spray was created by Aref Zaki F et al. In 2021 to treat COVID-19. The study's objective was to evaluate ivermectin's effectiveness in treating patients with moderate COVID-19 infections. The outcome demonstrates the effectiveness of the nanosuspension in treating COVID-19 patients[32].

Conclusion:

Regardless of the mode of administration, the use of drug nano solution is a universal formulation strategy for enhancing the therapeutic efficacy of these medications. When creating medications with low solubility and boosting their bioavailability, Nanosuspension are a useful option. This approach offers a number of formulations and therapeutic advantages, such as ease of preparation, fewer excipients, a faster rate of dissolution, saturation solubility, enhanced adhesion that results in lower bioavailability requiring fewer doses and faster-fed variability, and simplicity in scaling up. Such a nanosuspension can be produced for administration by oral, parenteral, ophthalmic, topical, or pulmonary routes. A commercially viable solution to the medications' issues with poor solubility and bioavailability is nanosuspension. High-pressure homogenization technology has been widely used for the large-scale manufacturing of nanosuspension formulations. Poor solubility issues are resolved by a nanosuspension formulation, which also increases therapeutic efficacy. Researchers are drawn to Nanosuspension because they can change a drug's pharmacokinetics, making it safer and more effective, in addition to improving solubility and bioavailability. Furthermore, nanosuspension technology can be applied to parenteral medicines and mixed with conventional oral dosage forms as tablets, capsules, and pellets.

Reference:

1. Lipinski C, Poor aqueous solubility – an industry wide Problem in drug discovery, American Pharm Rev, 5, 2002, 82 – 85.
2. Wagh KS, Patil SK, Akarte AK, Baviskar DT; Nanosuspension A new approach of Bioavailability enhancement,InternationalJournalOf Pharmaceutical Sciences Review and Research, 2011; 8: 60-62
3. Lakshmi P, Kumar GA; Nanosuspension Technology: a review; International Journal of Pharmacy and Pharmaceutical Sciences, 2010; 2: 35-40.
4. Zuccari G, Alfei S. Development of Phytochemical delivery systems by nanosuspension and nano-emulsion techniques. International Journal of Molecular Sciences. 2023 Jun 6;24(12):9824.
5. Kostas K, The emergence of Nanomedicine, 1, 2006, 1-3.
6. Chowdary KPR, Madhavi BLR, Novel drug delivery Technologies for insoluble drugs, Ind. Drugs, 42, 2005, 557 – 563.

7. Cornelia MK, Muller RH, Drug nanocrystals of poorly Soluble drugs produced by high – pressure Homogenisation, Eur. J. Pharm. Biopharm, 62, 2006,: 3–16.
8. Chinthaginjala H, Abdul H, Reddy AP, Kodi K, Manchikanti SP, Pasam D. Nanosuspension as Promising and Potential Drug Delivery: A Review. 2020. Int J Life Sci. Pharm Res. 2020;11(1):P59-66.
9. Kostas K , The emergence of Nanomedicine,1, 2006,1-3.
10. Sutradhar KB, Khatun S, Luna IP. Increasing possibilities of nanosuspension. Journal of nanotechnology. 2013 Jan 1;2013
11. Patel VR, Agrawal YK. Nanosuspension: An approach to enhance solubility of Drugs. Journal of advanced pharmaceutical Technology & research. 2011 Apr 1;2(2):81-7.
12. Shid RL, Dhole SN, Kulkarni N, Shid SL; Nanosuspension: A Review. Int J. Pharm. Sci. Rev. Res., 2013; 22(1): 98-106.
13. Muller RH, Jacobs C, Kayser O; Nanosuspension As particulate drug formulations in drug therapy. Rationale for development and what we can expect For the future. Adv Drug Delivery, 2001; 47(1): 3,19
14. Thattil JG, Kumar KK, and Kumar BD (2018). Nanosuspension technology in Pharmaceuticals. J Bio Innov 7: 660-677.
15. Soumya M, Gupta S, Jain R, Mazumder R; Solubility enhancement of poorly water soluble Drug by using nanosuspension technology. International Journal of Research and Development In Pharmacy and Life Sciences. 2013; 2: 642-649.
16. Arunkumar N, Deecarman M, Rani C; Nanosuspension technology and its application in Drug delivery. Asian Journal of Pharmaceutics .2009; 3:168-173.
17. Ghosh I, Bose S, Vippagunta R, Harmon F. Nanosuspension for improving the Bioavailability of a poorly soluble drug And screening of stabilizing agents to Inhibit crystal growth. International Journal of pharmaceutics. 2011 May 16;409(1-2):260-8.
18. Chinthaginjala H, Abdul H, Reddy AP, Kodi K, Manchikanti SP, Pasam D. Nanosuspension as Promising and Potential Drug Delivery: A Review. 2020. Int J Life Sci. Pharm Res. 2020;11(1):P59-66
19. Singare DS, Morella S, Gowthamrajan K, Kulkarni GT, Vooturi R, Rao PS. Optimization of formulation and process Variable of nanosuspension: An industrial Perspective. International journal of Pharmaceutics. 2010 Dec 15;402(1-2):213-20.
20. Godge GR, Garje MA, Dode AB, Tarkase KN. Nanosuspension Technology for Delivery of Poorly Soluble Drugs and Its Applications: A Review. International Journal of Pharmaceutical Sciences and Nanotechnology (IJPSN). 2020 Jul 11;13(4):4965-78.
21. Geetha, G., U. Poojitha, and K. Arshad Ahmed Khan. “Various techniques for Preparation of nanosuspension-a Review.” International Journal of Pharma Research & Review 3.9 (2014): 30-37.
22. Agarwal V, Bajpai M., “Preparation and Optimization of Esomeprazole Nanosuspension using Evaporative Precipitation– Ultra sonication”, Tropical Journal of Pharmaceutical Research, no (2014):497-503.
23. Patravale VB, Abhijit AD, and Kulkarni RM, Nanosuspension: a promising drug delivery strategy. J. Pharm. Pharmcol, 56, 2004, 827-840
24. Muller RH, Peters K, Nanosuspension for the Formulation of poorly soluble drugs I: Preparation by aSize – reduction technique, Int. J. Pharm, 160, 1998, 229–237.

25. Jahnke S, The theory of high – pressure Homogenization. In: Muller RH, Benita S, Bohm BHL, Emulsions and nano suspensions for the formulation of Poorly soluble drugs, Medpharm Scientific Publishers, Stuttgart, 1998, 177–200.
26. Nayak BS and Roy H (2018). Nanosuspension: Bioavailability Enhancing novel approach. Int J Pharm Biol Sci, 8: 540-554.
27. Shah R, Soni T, Shah U, Suhagia BN, Patel MN, Patel T, Gabr GA, Gorain B, Kesharwani P. Formulation development And characterization of lumefantrine Nanosuspension for enhanced antimalarial Activity. Journal of Biomaterials Science, Polymer Edition. 2021 May 3;32(7):833-57
28. Merisko L, Liversidge GG, et al. Formulation and antiTumor activity evaluation of nanocrystallineSuspensions of poorly soluble anti-cancer drugs, Pharm. Res, 13, 1996, 272– 278.
29. Muller RH, Jacobs C, Production and characterization Of a Budesonide nanosuspension for pulmonary Administration, Pharm. Res, 19, 2002, 189–194.
30. Kayser O, Nanosuspension for the formulation ofAphidicolin to improve drug targeting effects againstLeishmania infected macrophages, Int. J. Pharm.196, 2000, 253 – 256.
31. Müller RH, Jacobs C. Buparvaquone Mucoadhesive nanosuspension: Preparation, optimisation and long-term Stability. International journal of Pharmaceutics. 2002 Apr 26;237(1-2):151-61
32. Aref ZF, Bazeed SE, Hassan MH, Hassan AS, Rashad A, Hassan RG, Abdelmaksoud AA. Clinical, biochemical and molecular Evaluations of ivermectin mucoadhesive Nanosuspension nasal spray in reducing Upper respiratory symptoms of mild COVID-19. International journal of Nanomedicine. 2021 Jun 15:4063-72.