# A Breif Review On Nanosuspension Technology For Solubility Enhancement

Dr. Kiran C. Mahajan<sup>1\*</sup>, Miss.Mohini S. Deore<sup>2</sup>, Mr. Sushant S. Gaikwad<sup>3</sup>,

# Dr.Ganesh Y. Dama<sup>4</sup>

 <sup>1,2,3</sup>Department of Pharmaceutics, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist.- Pune, 410504.
<sup>4</sup>Department of Pharmacognosy, SGMSPM's Sharadchandra Pawar College of Pharmacy, Dumbarwadi (Otur), Tal- Junnar, Dist.- Pune, 410504.

# ABSTRACT

significance The of the newly developed and auspicious future of "nanosuspensions," a novel dosage form, is mentioned in the current article. Reducing the size of particles, especially through nanonization, is a general and non-specific method to improve the pharmacokinetic of irresolvable medications. The significance of the planning, assessment, and ongoing research ondifferent medications and their suitable applications is emphasized in the

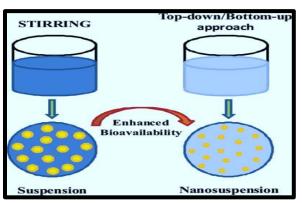
essay.Extremely low bioavailability is a key issue with poorly soluble medicine s. To addressthese issues, formulation as nanosuspension presents a compelli ng and optimistic substitute.The pure, poorly watersoluble medication in nan osuspension is suspended in a dispersi on of nomatrix material.Making a nano suspension is easy and works with any medication that is insoluble in water.A nanosuspension not only addresses th e issues of low solubility and bioavaila bility, but it also modifies the drug's ph armacokinetics, enhancing its safety an d effectiveness. The preparation techni ques, characterization, and uses of the nanosuspension are covered in this rev iew paper.

**KEYWORDS** Nanosuspension, Bio availability, Solubility, Preparation & characterisation ,Bottom up technology, Top down technology.

# INTRODUCTION

The adequate preparation of medicine depends upon a number of factors, influencing solubility, strength at noromal environment, similar solvents, excipients, & photostability. Lipophilic or poorly water-soluble compounds make up more than 40% of the novel chemical entities discovered so far through drug development programs. Drugs with limited solubility and low bioavailability can be solved using a variety of formulation techniques. Conventional methods such as micronization, fatty solution application, penetration enhancer or cosolvent application, surfactant

dispersion method, salt creation, limited precipitation, etc. have effectiveness in increase the resolvable of irresolvablemedication. Other strategies include inclusion complexes with cyclodextrins, dispersion of solids, emulsion and microemulsion techniques, and vesicular systems like liposomes, which have positive effects as be applied to improve the solubility of medications that have low solubility in lipid and water-based mediums. Increased solubility causes the active ingredient to flood at a faster pace, reaching the maximum plasma level more quickly. This method works well for compounds that are difficult for formulators to work with because they have poor permeability, poor solubility, or both. Because of the smaller particle irresolvabletreatment size, couldbeconduct circulatory within vital fluid obstructing vessels. Additionally, the suspensions can be lyophilized to form a solid matrix. It also has the benefits of liquid formulations over other formulations, in addition to these advantages. The main topic until review exists various preparation techniques linked with merits. drawbacks, along with their use in medicine is medication delivery device.



# fig1. flow diagram for manufacturing process for nanosuspension

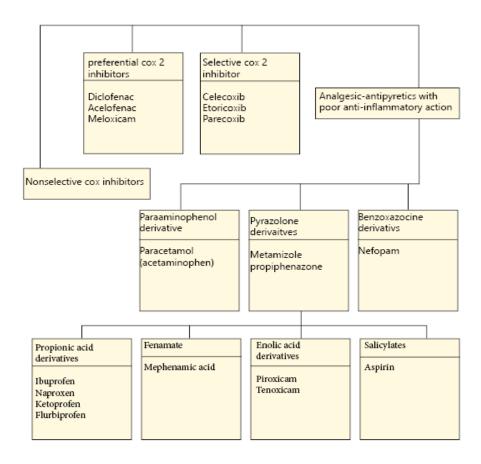
A group of medicament is called NSAIDs is prescribed to treat fever, pain, and other inflammatory conditions. The FDA has approved a family of medications known as (NSAIDs)

(ibuprofen, mefanicacid, diclofanac

melosicam,)for use as analgesics, antipyretics, and anti-inflammatory drugs. NSAIDs can be given to handle myalgia, menstrual pain, rheumatic condition, fever, galactosemia, migraines, near, in some cases of acute trauma, they can be used to replace opioids.NSAIDs typically derived into growth based on their chemical structure and selectivity.

1831

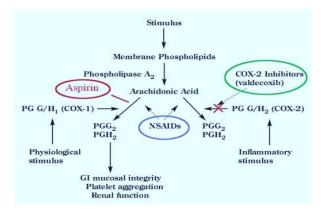
# Nonsteroidal Antiinflammatory Drugs/Antipyretic-Analgesics



1832

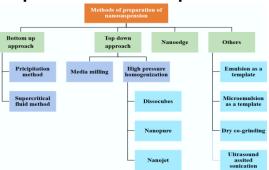
#### **Mechanism Of Action**

An inhibitory effect of NSAIDs is mostly seen on the enzyme cyclooxygenase. Arachidonate cannot transform thromboxanes, be to dinoprostonewithoutphospholipid. The absence of these eicosanoids is for acrosseprospctive answerable nearcurative advantage of NSAIDs. In prostaglandins particular, induce vasodilation, raise the hypothalamic temperature set-point, and contribute anti-nociception, while to thromboxanes are involved in platelet adhesion.



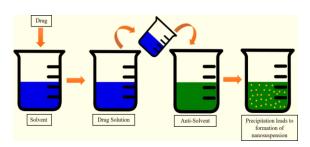
**fig3. mechanism of action of nsaids** There are COX1 and COX2 two isoenzy mes of cyclooxygenase.In addition to it s role in maintaining renal function, pla telet aggregation,the membrane pacak ing the alimentary tract,COX1 such con stitutively produced in the body.Induci ble expression of COX2 occurs during an inflammatory reaction, rather than c onstitutively in the body.Because they block both COX1 and COX2 the majori ty of NSAIDs are nonselective.But beca use they only target COX2 COX2 select ive NSAIDslike celecoxibhave a differen t profile of adverse effects.COX2 selecti ve NSAIDs are important because they should reduce inflammation without h arming the gastric mucosa because CO X1 is the primary mediator for maintai ning gastric mucosal integrity while CO X2 is primarily involved in inflammatio n.

# **Preparation Of Nanosuspension**



# fig4.different approaches for the preparation of nanosuspension

As seen Figure Bottom of technology and Top down technology are the two main technices used to prepare nanosuspension. Тор down technolohyinvoles breaking down digger particals in to nanoparticals; exmapales of this process include high-presseurehomoginization and of milling technices. Bottom technology involes assembly ways to make nanoparticles, such as precipitation, microemulsion, and melt emulsification process.



# fig5.formulation of nanosuspension by the solvent antisolventmethod

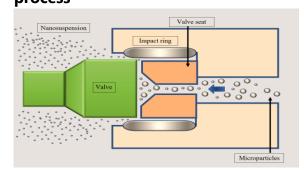
# **Method Of Precipitation**

A common technique for creating submicron particles of poorly soluble medications is precipitation. This involves approach dissolving the medicament in aagueous, mixing the solution with a solvent that contains a surfactant, making the drug insoluble. Quick addition of the medicamentwithin solution to such a solvent (usually water), causing the drug quickly become to supersaturated and form amorphous drug particles. These method include the creation of centeralong with development of crystals, both of which temperature-dependent. are The preparation of constant interruption with the smallest possible grain size primarily need nucleation process of bottomcrystal development increase.

#### **High Pressure Adsorption**

The three phases involved in this technique are as follows: To create presuspension, drug powders are first spread in a stabilizing mixture. Suspension is also homogenized using a maximum poweredsonicatorat littleforce occasionally such premilling.Ultimately, maximum poweredultrasonication is performed comparable10 to 25 round to create nanosuspensions of the wanted rate.

fig6.Schematicrepresentation of the high pressure homogenization process



# Methods Of Milling Milling Media

A patent for nanocrystal technology was held by Liversidge et al. This method produces nanoparticles by media milling pharmaceuticals. The medications' impaction with the milling media provides the necessary energy for the microparticulate system to break down into nanoparticles. In order to create suspension, the medication, stabilizer, water, or appropriate buffer are added to the milling media inside the chamber, inside of then twist alongexcessive strain rate. One of the main issues with this process exists such residues so that left withsuch final product.

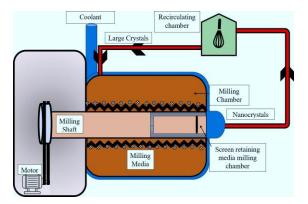


fig7.Media milling process: schematic representation

# **Arid Cogrinding**

For many years, pearl ball mills have been used in wet grinding procedures to prepare nanosuspensions. Currently, nanodispersions can be ready using techniques for dry milling. After dispersing in a liquid medium, poorly soluble drugs are dry ground with soluble polymers and copolymers to create stable nanosuspensions. Many water-soluble medications, weakly including glibenclamide, griseofulvin, and nifedipine, have been shown to form colloidal particles when stabilized with sodium dodecyl sulfate and polyvinylpyrrolidone by Itoh et al.

# **Method Of Melt Emulsification**

The primary technique for creating solid lipid nanoparticles is melt emulsification. Kipp and colleagues initially use the melt emulsification approach to generate ibuprofen nanosuspensions. Here's the four-step process.Previouse,near medication with added to a balance-containing aqueous mixture. Until create an emulsion, near mixture is intense to aenvironment greater than close drug's flash pointalong with also sonication using ultrasonication. Throughout near entire procedure, close condition is kept overnear drug's flash point. The emulsion is then chilled to the particles to precipitate. The concentration comparable drug, close kind along withintentness like stabilizers employed, near cooling and close temperature, homogenization process the are primary agentinfluencing near size parallel particles with close nanosuspension.

# **Supercritical Fluid Techniques**

Many techniques, equivalentsame as near supercritical increase such as the low temperature method, Nanoparticles are produced using the compressed antisolvent (PCA) technique also disintegrative method. The process include developing a drug mixture through a nozzle into a supercritical fluid, which causes the supercritical liquid dissolving agent charge to evaporate close precipitate near medicamentsame as small tiny piece. Young et al. synthesized 400-700 nm diameter cyclosporine

nanoparticles by employing the RESS technique.

Nearmedicamentmixtureexistsdisintegr ated the CO2 compressed compartment innear PCA procedure. The mixture becomes glutted as the dissolving agent with discard, leading to precipitation with near end. The medicament mixture is injected inside low temperature during low temperature antisolvent procedure, which remove a mixture and causes nearmedicament mixture to becomeglutted.

# ImplementationOf Nanosuspensions 1.Oral Administration:

This is the recommended method of administration. However, some medications have restricted absorption solubility, which and limits their bioavailability and decreases their effectiveness. When this happens, nanosuspensions can help by increasing surface area and adhesiveness, which improves the absorption and dissolution rate. By mucoadhesion, improving nanosuspensions can also lengthen the time that food travels through the gastrointestinal tract, which increases bioavailability. Increases in the nanosuspension's adhesiveness. saturation solubility, and surface area are thought to be responsible for the improved oral bioavailability. Moreover, nanosuspensions make it simple to hide the flavor of particulate matter.

### 2.Parenteral Administration:

Using nanosuspensions, non-injectable medications with poor solubility must transformed into formulations be suitable for intravenous delivery. Making nanosuspensions for parenteral use is crucial, and recent advancements inquire within ground occupy showed such near use of Nanosuspen for injectable formulations effective. is Today's nanosuspension highly regulated technologies allow for the production of homogeneous tiny piece superior manage the largest grain size. Several investigation publications highlight the value of nanosuspensions for parenteral administration.

# **3.Ocular Delivery:**

Nanosuspensions are a possible way to medications with limited provide lachrymal fluid solubility. They are the ideal method for administering medications to the eyes because they make hydrophobic medicines more soluble at saturation. Effective nanosuspension delivery systems have been developed by researchers for certain medications, such as glucocorticoids.

# 4.Delivery Through The Lungs:

Nanosuspensions may be advantageous for the delivery of medications with low solubility in the lungs. The restrictions on Present-day

pulmonary administration methods, like aerosols and dry powder inhalers, have a short residence time and restricted diffusion to the target location. Nanosuspensions provide a way around these limitations. The effective formulation of fluticasone and budesonide as nanosuspensions for pulmonary delivery are two examples.

#### **5.Topical Administration:**

Medications in nanocrystalline form can improve saturation solubility, which raises the drug's penetration. Nanocrystals are a good choice for cutaneous application due to their enhanced permeability, adhesiveness, and increased membrane penetration.

#### 6.Targeted Delivery:

The drug's absorption rate is affected incidentally dimension area its nanoparticles. Targeted delivery is achieved by modifying each in-vitro way of acting of nanoparticles by near modification analogous their surface properties. Targeted medication delivery systems can be developed by methods such as developing intelligent crystals or covert nanocrystals of less than 100 nm in particle size. Making nanosuspensions is an economically viable method for targeted distribution because of its ease of use. The surface characteristics of the particles, including their nonpolar, price, along

with concentration or attending of opretionalorganization, particular distribution of influence the the particles inside the body. The successful use of proguanil crystline particlepolishedalongpolysorbate 80 for effective parasite eradication in the brain during toxoplasmosis treatment is evidence of the potential of polysorbate80-polishedcrystline particlesuchmind tormenting.

#### Conclusion

This review study highlights the latest developments in therapeutic nanosuspensions made possible by a number of methods, including Bottom up approach,Top down approach emulsification, media milling, and high pressure homogenization.But early on, a number of in vivo investigations make it abundantly evident that these drug delivery methods have applications in parenteral, oral, ophthalmic, topical and pulmonary administration.These systems do. however, offer flexibility and the chance to further customize particles, surface characteristics to maximize in vivo responses, and the creation of narrativemedicinal way such near comparable with various therapy Working size illnesses. on the optimization of medication

#### References

- Nugrahani I, Auli WN. Diclofenacproline nano-co-crystal development, characterization, in vitro dissolution and diffusion study. Heliyon. 2020 Sep 1;6(9).
- Patel VR, Agrawal YK. Nanosuspension: An approach to enhance solubility of drugs. Journal of advanced pharmaceutical technology & research. 2011 Apr;2(2):81.
- 3) Kawabata Y, Wada K, Nakatani M, Yamada S, Onoue S. Formulation design for poorly water-soluble drugs based on biopharmaceutics classification system: basic practical and approaches applications. International journal of pharmaceutics. 2011 Nov 25;420(1):1-0.
- Hedaya M, Bandarkar F, Nada A. In vitro and in vivo evaluation of ibuprofen nanosuspensions for enhanced oral bioavailability. Medical Principles and Practice. 2021 Aug 11;30(4):361-8.
- 5) Katara R, Sachdeva S, Majumdar DK. Design, characterization, and evaluation of aceclofenac-loaded Eudragit RS 100 nanoparticulate system for ocular delivery. Pharmaceutical Development and Technology. 2019 Mar 16;24(3):368-79.
- Alshehri S, Shakeel F, Ibrahim M, Elzayat E, Altamimi M, Shazly G, Mohsin K, Alkholief M, Alsulays B,

Alshetaili A, Alshahrani A. Influence of the microwave technology on solid dispersions of mefenamic acid and flufenamic acid. PloS one. 2017 Jul 31;12(7):e0182011.

- 7) Prasanna G. Formulation Development and Evaluation of Cilnidipine Nanosuspension for the treatment of Hypertension using Anti-Solvent Precipitation and Ultrasonication Method (Doctoral dissertation, College of Pharmacy, Madras Medical College, Chennai).
- 8) Alekhya A, Sailaja AK. Formulation Evaluation of Letrozole and Nanosuspension By Probe Sonication Method using Boxbehnken Design. Current Nanomaterials. 2023 Sep 1;8(3):266-79.
- 9) Ahire E, Thakkar S, Darshanwad M, Misra M. Parenteral nanosuspensions: a brief review from solubility enhancement to more novel and specific applications. Acta Pharmaceutica Sinica B. 2018 Sep 1;8(5):733-55.
- Batlouni M. Nonsteroidal antiinflammatory drugs: cardiovascular, cerebrovascular and renal effects. Arquivosbrasileiros de cardiologia. 2010;94:556-63.
- **11**) Chin WW, Parmentier J, Widzinski M, Tan EH, Gokhale R. A brief literature and patent review of nanosuspensions to a final drug product. Journal of Pharmaceutical

Sciences. 2014 Oct 1;103(10):2980-99.

- 12) Boyd BJ, Bergström CA, Vinarov Z, Kuentz M, Brouwers J, Augustijns P, Brandl M, Bernkop-Schnürch A, Shrestha N, Préat V, Müllertz A. Successful oral delivery of poorly water-soluble drugs both depends on the intraluminal behavior of drugs and of appropriate advanced drug delivery systems. European Journal of Pharmaceutical Sciences. 2019 Sep 1;137:104967.
- 13) Junghanns JU, Müller RH. Nanocrystal technology, drug delivery and clinical applications. International journal of nanomedicine. 2008 Dec 1;3(3):295-310.
- 14) Sievens-Figueroa L, Bhakay Α, Jerez-Rozo JI, Pandya N, Romañach RJ, Michniak-Kohn B, Igbal Z, Bilgili Davé RN. Preparation E, and characterization of hydroxypropyl methyl cellulose films containing stable BCS Class drug nanoparticles for pharmaceutical applications. International journal 2012 Feb of pharmaceutics. 28;423(2):496-508.
- **15)** Ran Q, Wang M, Kuang W, Ouyang J, Han D, Gao Z, Gong J. Advances of combinative nanocrystal preparation technology for improving the insoluble drug

solubility and bioavailability. Crystals. 2022 Aug 25;12(9):1200.

- 16) Chang TL, Zhan H, Liang D, Liang JF. Nanocrystal technology for drug formulation and delivery. Frontiers of Chemical Science and Engineering. 2015 Mar;9:1-4.
- 17) Kalimuthu S, Yadav AV. Nanobased Drug Delivery System: A Review. Research Journal of Pharmacy and Technology. 2009;2(1):21-7.
- 18) Keck CM, Müller RH. Drug of poorly nanocrystals soluble drugs produced by high pressure homogenisation. European journal of pharmaceutics and biopharmaceutics. 2006 Jan 1;62(1):3-16.
- 19) Morakul Β, Suksiriworapong J, Langguth P, Chomnawang MT, Junyaprasert VB. Dissolution enhancement and in vitro performance of clarithromycin nanocrystals produced by precipitation-lyophilizationhomogenization method. European

Journal of Pharmaceutics and Biopharmaceutics. 2014 Nov 1;88(3):886-96.