CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://zenodo.org/records/12578716

https://www.iajps.com/volumes/volume11-june-2024/24-issue-06-june-24/

Available online at: http://www.iajps.com *Review Article*

REVIEW ON NANOSUSPENSION TECHNOLOGY

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Article Received: April 2024 **Accepted: May 2024** **Published: June 2024**

Abstract:

Solubility is a essential factor for developing drug delivery system for poorly water soluble drugs. Most of the recently discovered drugs are insoluble in water and hence poorly absorb with reduced bioavailability that leads to more production efforts.Nanosuspension is a simple and more beneficial than other approaches. Technique like high pressure homogenization, wet milling, bottom up technology and top down technology have been applicable for manufacturing of Nano suspension. They are delivered by various routes such as parenteral, oral, ocular and pulmonary route.

Keywords- *Nano suspension, Solubility, Surfactants, Poor soluble drug, Manufacturing, Application, Bioavailability.*

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Please cite this article in press Puja Aher et al **Review On Nanosuspension Technology .,*Indo Am. J. P. Sci, 2024; 11 (6).***

1. INTRODUCTION:

A Nano suspension is a submicron colloidal dispersion of Nano sized drug particles stabilized by surfactants. [7] It is a very finely colloid, biphasic, dispersed, solid drug particles in aqueous vehicle, having size below 1µm, without any matrix material, prepared by suitable methods for drug delivery applications.[1] A Nano suspension is solves the problem of poor solubility & bioavailability as well as alters the pharmacokinetics of drug & that improves safety & efficacy. Nano suspension has been reported to enhance adsorption & bioavailability it may help to reduce the dose of the convectional oral dosage forms. Drug particle size reduction leads to an increase in surface area & so in the rate of dissolution as described by Nernst-Brunner & Lavish modification of the Noyes- Whitney equation.[2] Over the last decades, nanoparticle engineering has been develop and reported for pharmaceutical applications.[8] Depending on the production technique applied changes in crystalline structure of the drug particles may also occur. An increasing amount of amorphous drug fraction could induce higher saturation solubility. The absence of particle with large differences in their size in Nano suspensions prevents the existence of different saturation solubility's and concentration gradients, so preventing the Oswald ripening effect. 9] Higher saturation solubility may be caused by rising amount of amorphous drug fraction. [10] In Nano suspension technology, the drug is maintained in the crystalline state with reduced particle size, leading to increase dissolution rate & therefore improved bioavailability. Nana suspensions can successfully formulate the brick dust molecules for improved dissolution & good absorption [1, 2]

Advantages of Nano suspension-[12]

1) Enhance the solubility and bioavailability of drugs.
2) Suitable for hydrophilic drugs.
3) Long-term physical stability
4) Increase in the oral absorption
5) Improved dose proportionality.
6) It can be applied for poorly water soluble drugs.

Disadvantages for Nano suspension Drug delivery system [14]

1) Physical stability, sedimentation & compaction can cause problems.
2) It is bulky sufficient care must be taken during handling & transport.
3) Improper dose.
4) Uniform & accurate dose cannot be achieved
5) The solvent needs to be miscible with at least one non- solvent.

Method of Preparation of Nanosuspensuions: [1, 2]

Mainly there are two methods for preparation of Nanosuspensions:-

1) Bottom-up technology (Hydrosols) 2) Top-down technology

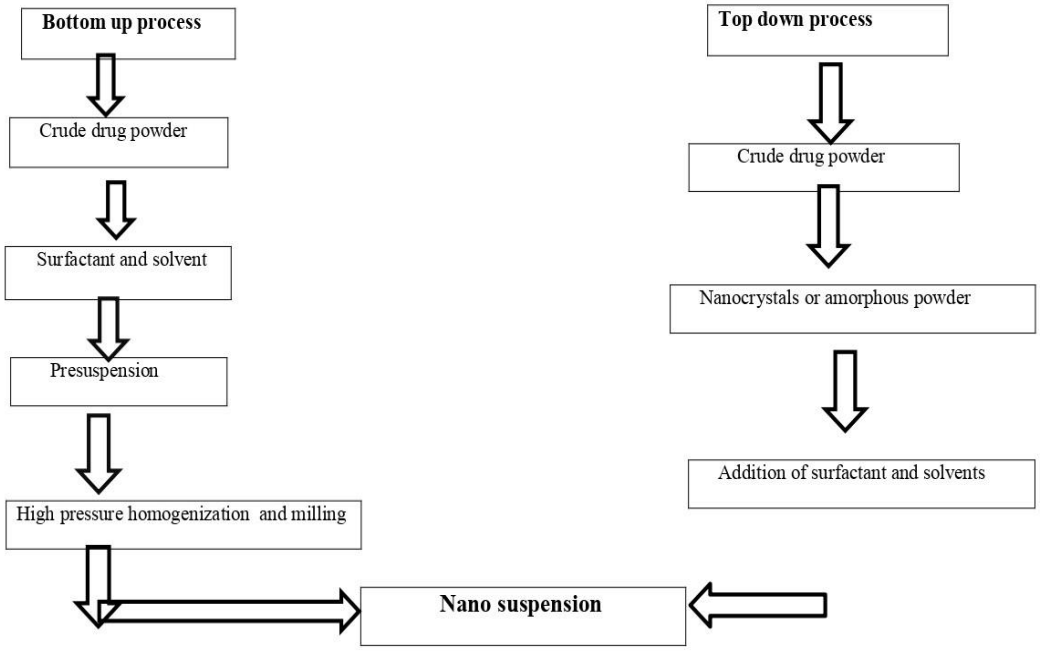

Fig.1 Approaches for preparation of nanosuspension [27]

2) **Bottom-up technology** [3,4]
1) The term "Bottom-up technology" means that one starts from the molecular level, and goes via molecular association to the formation of a solid particle. It means that we are discussing classical

Advantage: [11]
1) Use of simple and low cost equipment.
2) Higher saturation solubility is the advantage for precipitation compared to other methods of Nano suspension preparation.

Disadvantages:
1) The drug need to soluble in at least one solvent and solvent needs to be miscible with non-solvent.
2) It is not applicabe to the drugs, which are poorly soluble in both aqueous and non-aqueous media.
3) Solvent residues need to be removed, thus increasing production costs.
4) It is an Iittle bit tricky to preserve the particle character (i.e. size, especially the amorphous fraction). In general, it is recommended that a second consecutive process has to be performed for particle preservation that is spraydrying or lyophilisation.

2) Top-Down Technology
The top down technologies include -
a) Media milling
b) High pressure homogenization

a) Media Milling (Nano Crystals) [5]
Nano suspensions are produced by using high-shear media mills or pearl mills. The mill consists of a milling chamber, milling shaft and a recirculation chamber. An aqueous suspension of the drug is then fed into the mill containing small grinding balls/pearls. As these balls rotate at a very high shear rate under controlled temperature, they fly through the grinding jar interior and impact against the precipitation techniques by reducing the solvent quality.
For example-By pouring the solvent into a no solvent or changing the temperature or a combination of both. Precipitation is a classical technique in pharmaceutical chemistry and technology.
sample on the opposite grinding jar wall. The combined forces of friction and impact produce a high degree of particle size reduction. The milling media or balls are made of ceramic-sintered aluminium oxide or zirconium oxide or highly cross-linked polystyrene resin with high abrasion resistance.

Principle-
The high energy and shear forces generated as a result of the impaction of milling media with the drug provide the energy input to break micro particulate drug into Nano-sized particles. The milling medium is composed of glass, zirconium oxide or highly cross-linked polystyrene resin. [6]

Advantages-
1) Simple technology
2) Low-cost process regarding the milling itself
3) Large-scale production possible to some extent (batch process).

Disadvantages-
1. Potential erosion from the milling material leading to product contamination
2. Duration of the process not being very production friendly.
3. Potential growth of germs in the water phase when milling for a long time.
4. Time and costs associated with the separation procedure of the milling material from the drug nanoparticle suspension, especially when producing parenteral sterile products.

b) High Pressure Homogenization-

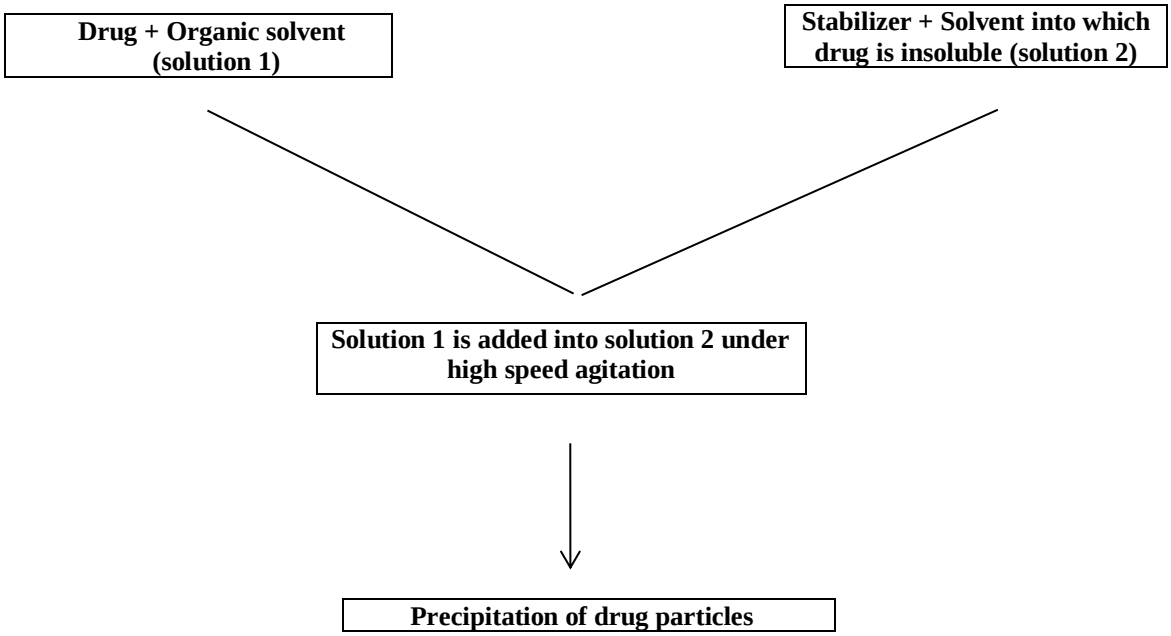

Fig: - 2 Method for preparation of nanoedge.

Homogenization is the process of emulsifying liquids of two liquids (i.e.liquids that are not soluble in one another)or uniformly dispersing solid particles through a liquids. [28]

Dissocubes

In Disso cubes, the suspension of the drug is made to pass through a small orifice that result in a reduction of the static pressure below the boiling pressure of water, which leads to boiling of water and formation of gas bubbles. It is crystalline nanopartical of active substances obtained by a liquid state high energy process using a high pressure piston gap homogenizer to reduce the drug particle size in the presence of surface modifiers that associate the freshly generated drug interface.[7,8]

Nanopure

Nanopure is suspensions homogenized in water-free media or water mixtures. In the Dissocubes technology,the cavitation is the determining factor of the process.But, in contrast to water, oils and oily fatty acids have very low vapour pressure and a high boiling point. In nanopure technology, the drug suspensions in the non- aqueous media were homogenized at 00C or even below the freezing point and hence are called "deep-freeze" homogenization [7,8]

Nanoedge

The basic principles of Nanoedge are the same as that of precipitation and homogenization. A combination of these techniques results in smaller particle size and better stability in a shorter time. The major drawback of the precipitation [9]

3. Formulation consideration:

3.1 Stabilizer

The main function of a stabilizer is to prevent ostwald's ripening and agglomeration of Nanosuspensions in order to yield a physically stable formulation by providing steric or ionic barrier. The type and amount of stabilize has a pronounced effect on the physical stability and in vivo behavior of Nanosuspension.

Stabilizers that have been used so far are poloxomers, polysorbate, cellulosics, povidones, and lecithins.Lecithin is the stabilizer of choice if one intends to develop a parentally acceptable and autoclavable nanosuspension[3,10,15].

3.2 Organic Solvent

Organic solvents are used in the formulation of Nanosuspension if emulsions or micro emulsions are used as a template.[18] The pharmaceutically acceptable less hazardous water miscible solvent, such as methanol,ethanol, chloroform, ispropanol, and partially water miscible solvents ethyl acetate, ethyl formate, butyl lactate, triacetin, propylene carbonate, benzyl alcohol,are preferent in the formulation over the conventional hazardous solvents, such as dichloromezthane.

3.3 Co-Surfactants

When using microemulsions to formulate Nanosuspensions,the option of cosurfactant is important.As a cosurfactants can greatly influence

phase behaviour, the effect of co-surfactant on uptake of the internal phase for selected micro emulsion composition and on drug loading should be investigated. [17]Although the literature describes the use of bile salts and dipotassium glycerrhizinate as surfactants, various solubilizes, such as Transcutol, glycofurol, ethanol and isopropanol, can be safely used as co-surfactants in the formulation of microemulsions.

3.4 Other additives

Nanosuspensions may contain additives such as buffers, polyols,salts, osmogent and cryoprotectant.[16]

4. Post-production processing

Post-production processing of Nanosuspensions becomes essential when the drug candidate is highly susceptible to hydrolytic cleavage or chemical degradation. Processing may also be required when the best possible stabilizer is not able to stabilize the Nanosuspension for a longer period of time or there are acceptability restrictions with respect to the desired route. Considering these aspects,techniques such as lyophilization or spray drying may be employed to produce a dry

Powder of nano-sized drug particles. Rational selection has to be made in these unit operations considering the drug properties and economic aspects. Generally, spray drying is more economical and convenient than lyophilization. [3, 10]

4.1 Characterization of Nano suspension:

Nano suspensions are characterized for appearance, color, odor, assay, related impurities, particle size, zeta potential, crystalline status, dissolution studies and in vivo studies.[3,10]

The most important characterization techniques are as follows-

1) In-vitro evaluations-

2) In-Vivo evaluation-

1) In-Vitro evaluation-

Various parameters of Nano suspension like saturation solubility, dissolution velocity, physical stability, and biological performance depends on the mean of particle size distribution.[13]

2) **In-Vivo evaluation-**

Particular drug and route of administration requires the specific in vivo evaluation of the

Nano suspension .Generally formulations are administer by required route and the plasma drug concentration

Are determine by HPLC -UV visible spectrophotometry.

Applications of Nano suspension-

(1) Orally :-

Nanosuspesion should fix the matter because, attributed to increased area and increased adhesiveness; it aids to improve the dissolution rate and subsequent absorption.**[**18] Increase mucoadhesion,which can increase transit time via GIT with raised bioavailability, may be induced by Nano suspension .Additionally ,taste hiding is easy to perform.[19]

(2) Pulmonic:-

In Nano suspension are also useful for the delivery of drug that show low solubility within pulmonary fluids.

For Ex- Aerosols, Inhalers of dry powder, etc. [20]

Different types of nebulizer are available for the administration of liquid formulations. Some of the drugs successfully tried with pulmonary route are budesonide, ketotifen, ibuprofen, indomethacin, nefedifin, intraconazole, interleukin-2, p53 gene, leuprolide, doxorubicin, etc.[21]

(3) Parentally:-

Nano suspension do not turn poorly soluble non-injectable drugs into and intravenous formulations. It is useful as injectable formulations throughout this technology. [22]

Nano suspension are administred through various paranteral routes such as intraarticular , intraperitonial ,intravenous, etc . Additionally nanosuspensions increase the efficacy of parentrally adminstered drug .[23]

4) Targeted Drug Distribution:-

Nanosuspension for sutaible for targeting perticular organs because of there surface properties.The drug will be taken up by mononucleur phagocytic system which allows regions specific delivery.

Foe EX- Antifungal, antimicobacterial, or antineishmanial drugs.[24]

5) Ophthalmic :-

Intrensic ability to increase the solubility of saturation of medication, Nano suspension represent a great approach to ocular delivery of hydrophobic medicine.[25]

Thus, nanosuspension formulation offers a promising way of improving the shelf-life bioavailability of drug after ophthalmic application.[26]

CONCLUSION:

The dissolution problems of poorly water soluble drugs have been largely solved to improve drug absorption and bioavailability. Nanosuspension technology can be combined with traditional dosage form:-Tablets, Capsules, Pellets and can be used for parentral products. For large scale production of nanosuspensions , media milling and high pressure

homogenization technology have been successfully used.The application of nanosuspension are oral and parental routes have been very well established. However,delivery through nasal, buccal and topical delivery is done.

REFERENCES:

[1] Xiaohui P, Jin S, Mo L, Zhonggui H, Formulation of Nanosuspensions as a New Approach for the Delivery of Poorly Soluble Drugs, Current Nanoscience 2009; 5: 417-427

[2] Wagh KS, Patil SK, Akarte AK, Baviskar DT, Nano suspension - A New Approach of Bioavailability Enhancement, International Journal of Pharmaceutical Sciences Review and Research, 2011; 8: 61-65.

[3]Patil SA, Rane BR, Bakliwal SR, Pawar SP, Nano suspension: At A Glance, International Journal of Pharmaceutical Science, 2011; 3(1): 947-960.

[4] Bansal.S, Bansal M, Kumria R, Nanocrystals: Current Strategies and Trends, International Journal of Research in Pharmaceutical and Biomedical Sciences, 2012; 3 (1): 406- 419

[5] Pandey S, Nano suspension: Formulation, Charcterization and Evaluation, International Journal of Pharma and Bio Sciences, 2010; 1(2): 1-10.

[6] Date, AA; Kulkarni , RM and Patravale , VB(2004), "Nanosuspensions: A promising drug delivery",Journal of Pharmacy and Pharmacology, 56:827-840.

[7]Barret ER.Nanosuspension in drug delivery Nat Rev.2004;3:785-96.

[8]Vermaa S,Lan Y,Gokhale R,Burgessa DJ.Quality by design approach to understand process of nanosuspension preparation.Int J Pharm.2009;377:185-98.

[9]VB Patravale,AA Date and RM Kulkarni.Nanosuspension:a promising drug delivery strategy.J.Pharm.Phamacol.2004;56,827-40.

[10]Mitrovic JR,Divovic B,Knutson DE,Dokovic JB,Vulic PJ,Randjelovic DV,et al.Nanocrystal dispersion of DK-I-56-1,a poorly soluble pyrazoloquinolinone positive modulator of α6 GABAA receptors:Formulation approach towards improve in in vivo performance.European Journal of Pharmaceutical Sciences.2020;152(2020):1-12

[11]Tehrani AA,Omranpoor MM,Vatanara A,Seyedabadi M, Ramezani V. Formation of nanosuspentions in bottom-up approach : theories and optimization.DARU Journal of Pharmaceutical Sciences.2019;27(2019):451-73.

[12]Liversidage GG,Cundy KC. Particle size reduction for improvement of oral bioavailability of hydrophiobic drugs: Absolute oral bioavailability of nanocrystalline danazol in beagle dogs.Int J Pharm. 1995; 125:91-7.

[13]Venkatesh T, Nanosuspensions: Ideal Approach for the Drug Delivery of Poorly Water Soluble Drugs, Der Pharmacia Lettre, 2011; 3(2): 203-213. [16]1

[14]Prasanta D,Nanotechnology for the delivery of poorly solublr drugs,The Global Journal of Pharmaceutical Research,1(3),2012,225-250.

[15] Oktay AN,IIbasmis-Tamer S,Karakucuk A,Celebi N.Screening of Stabilizing agent to optimize flurbiprofen nanosuspensions using experimental design.Journal of Drug Delivery Science Technology.2020;57(2020):1-12.

[16] Mathew A,Jacob S,Shyma M.Nanosuspension Loaded Oral Films:A Breakthrough Approach.Journal of Pharmaceutical Science and Research. 2020;12(8)1012-7.

[17] Nayak BS, Mohanty B, Roy H,Patnaik A.Nanosuspension:Bioavailability enhancing novel approach.International journal of pharmacy and biological sciences.2018;8(2):540-54.

[18] Khandbahale SV. A Review-Nanosuspension Technology in Drug Delivery System .Asian Journal of Pharmaceutical Research.2019;9(2):130-8.

[19] Li G, Lu Y, Fan Y, Ning Q, Li W.Enhance oral bioavailability of magnolol via mixed micelles and nano suspensions based on soluplus ®-Poloxamer 188.Drug Delivery.2020;27[1]:1010-7.

[20]Xing Y, Lu P,Xue Z, Liang C,Zhang B, Kebebe D, et al.Nano-Strategies for Improving the Bioavalibility of Inhaled Pharmaceutical Formulation.Mini reviews in medicinal chemistry.2020;20(13):1258-71.

[21]Heidi MM, Yun-Seok R, Xiao W.Nanomedicine in pulmonary delivery. Int J Nanomed.2009;4:299-399

[22]Ahire E Thakkar S Darshanwad M,Misra M. Prenteral nanosuspensions : a brief review from solubility enhancement more novel and specific application. Acta Pharamacetica Sinica B.2018;8(5):733-55.

[23]Liversidge EM ,Liversidge GG,Cooper ER, Nanosizing : A formulation approach for poorly -water-soluble compounds.Eur J Pharm Sci.2003;18:113-20.

[24] Kayser O,Lemke A, Hernandz-Trejo N. The impact of Nanobiotechnology on the development of new drug delivery system. Curr Pharm Biotech.2005;6:3-5.

[25]Bhumaekar P,Mishra R, Dubey B. Development chitosan grafted nanosuspension for ocular delivery of ciprfloxacin. International journal of pharmacy practice and pharmaceutical sciences2019;1[2]79-85.

[26] Liang YC, Binner JG. Effect of triblock copolymer non-ionic surfactant on the rheology of 3

mol % yttria stabilised zirconia nanosuspensions . Ceram Int.2008; 34:293-7.
[27] Grau MJ, Kayser O,Muller RH. Nanosuspensions of poorly soluble drugs reproducibility of small-scale production.Int J Pharm.2000;196:155-7.
[28]Hintz RJ, Johnson KC. The effect of paetical size distribution on dissolution rate and oral absorption.Int J Pharm .1989;51:9-17.
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