International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

Nanosuspension: A Strategy to Improve the Solubility of Medicines

Balram Singh[1], Dr. Prabhudutta Panda[2], Kanchan Mishra[3]
Institute of Technology and Management, Gida, Gorakhpur, UP, India

Submitted: 01-01-2023 Accepted: 08-01-2023

ABSTRACT
Low bioavailability is one of the main issues with poorly soluble medications. For medications like itraconazole, simvastatin, and carbamazepine, which are classed as BCS class II by the biopharmaceutical classification system and are poorly soluble in both aqueous and nonaqueous conditions, the issue is even more complicated. The use of formulation as a nanosuspension is an appealing and promising solution to these issues.Pure, insufficiently water-soluble medication is suspended in dispersion as a component of nanosuspension. All medications that are insoluble in water can be prepared as nanosuspension, which is a straightforward process. In addition to addressing the issues of poor solubility and bioavailability, a nanosuspension modifies the medication's pharmacokinetics, enhancing medicinal efficacy and safety. The preparation procedures, characterisation, and uses of the nanosuspension are covered in this review article.
Keywords: Pharmacokinetics,Nanosuspension, Itraconazole, Simvastatin, And Carbamazepine

I. INTRODUCTION

The formulation of pharmaceuticals successfully depends on a number of factors, including solubility, stability at ambient temperature, compatibility with solvent, excipient, and photostability. Over 40% of the novel chemical entities created to date by drug discovery programmes are lipophilic or have poor water solubility. [1,2]. There are numerous formulation strategies available to address the issues of low medication solubility and bioavailability. The traditional methods include micronization, the use of fatty solutions, the use of penetration enhancers or cosolvents, the surfactant dispersion method, salt formation, precipitation, etc. However, the effectiveness of these methods in improving solubility for poorly soluble drugs is still limited. Other methods include vesicular systems like liposomes, dispersion of solids, emulsion and microemulsion techniques, and inclusion complexes with cyclodextrins. These methods show promise as drug delivery systems, but their main drawback is that not all medications can be delivered using them. [3].Pharmaceutical uses for nanoparticle engineering have been developed and described throughout the previous few decades. [4] The issues with the various strategies mentioned before can be resolved using nanotechnology. Nanotechnology is the study of science and engineering at a size of 10-9 metres. Techniques like Bottom-Up Technology and Top-Down Technology are used to transform the drug microparticles/micronized drug powder into drug nanoparticles. [5]Nanosuspensions are colloidal dispersions of medication particles that are nanoscale in size and are stabilised by surfactants. [6] Nanosuspensions are made up of the insipidly water-soluble medication alone, suspended in dispersion. [7] These can be used to improve a drug's solubility if it is poorly soluble in lipid or water-based systems. A higher rate of flooding of the active chemical and a quicker ascent to the maximum plasma level are both effects of enhanced solubility.Molecules with weak solubility, poor permeability, or both can benefit from this strategy, which presents a considerable problem for formulators. Due to the smaller particle size, it is now possible to administer poorly soluble medications intravenously without worrying about blood capillary blockage. The suspensions can also be turned into a solid matrix by lyophilization. In addition to these benefits, liquid formulations have an advantage over others. [8] We are largely concentrating on the various preparation methods' benefits, demerits, and pharmaceutical applications as drug delivery systems in this review.

Design of Nanosuspention

As depicted in Figure 1, "Bottom up technology" and "Top down technology" are typically employed to prepare nanosuspensions. [10] Top down technology involves the decomposition of bigger particles into nanoparticles, examples of which include high-pressure homogenization and milling procedures.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

Bottom up technology is an assembly process to generate nanoparticles such precipitation, microemulsion, and melt emulsification method. In Table 1, the concepts of these techniques are shown in full, along with their benefits and drawbacks. [11,12].

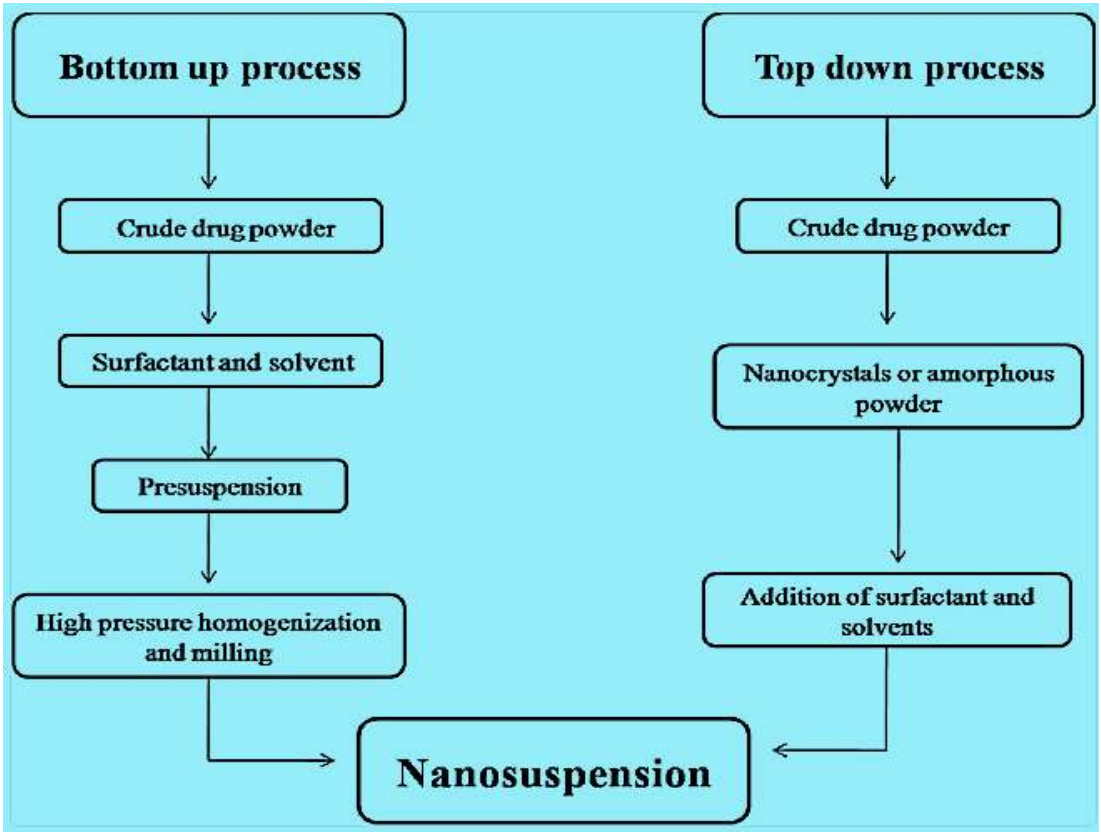

Fig1: Techniques for making nanosuspension

Method of Precipitation

A common technique for creating submicron drug particles that are poorly soluble is precipitation. [13–15] This procedure involves dissolving the drug in a solvent before adding the solution to the solvent, which the drug cannot dissolve in the presence of. Rapid addition of the solution to such a solvent (often water) causes the drug to quickly become supersaturated in the solution and forms an ultrafine amorphous or crystalline drug. This process involves crystal growth and nucleus production, both of which are largely temperature-dependent. To create a stable suspension with a small particle size, high nucleation rate and low crystal growth rate are essential. [16]

High-Pressure Homogenization

The following three phases are included in this technique: Presuspensions are created by first dispersing drug powders in a stabilising solution. Presuspensions are then homogenised by high pressure homogenizers at low pressure occasionally for premilling. Finally, presuspensions are homogenised at high pressure for 10 to 25 cycles until the nanosuspensions are formed with the desired size. [9]

Omogenization in Aqueous Media (Dissocubes)

Dissocubes technology was developed by Muller in 1999. The instrument can be operated at pressure varying from 100 to 1 500 bars (2 800 – 21 300 psi) and up to 2 000 bars with volume capacity of 40 ml (for laboratory scale). For preparation of nanosuspension, it is essential to prepare a presuspension of the micronized drug in a surfactant solution using high-speed stirrer. According to Bernoulli's Law, the flow volume of liquid in a closed system per cross section is constant. The reduction in diameter from 3 cm to

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

25 μm leads to increase in dynamic pressure and decrease of static pressure below the boiling point of water at room temperature. Due to this, water starts boiling at room temperature and forms gas bubbles, which implode when the suspension leaves the gap (called cavitation) and normal air pressure is reached. The size of the drug nanocrystals that can be achieved mainly depends on factors like temperature, number of homogenization cycles, and power density of homogenizer and homogenization pressure. Preprocessing like micronization of drug and high-cost instruments increases the overall cost of dosage form. Various drugs like Amphotericin B, Ordinon, Thiomerasol, Fenofibrate, Melarsoprol, Buparvaquone, Prednisolone, Carbamazepine And Dexamethasone were prepared as nanosuspensions using this method.[5]

Homogenization in Nonaqueous Media (Nanopure)

Nanopure is suspension homogenized in water-free medium. It is "deep-freeze" homogenization where the drug suspensions in nonaqueous medium are homogenized at 0°C or sometimes below the freezing point. Because of very high boiling point and low vapor pressure of water, oils, and fatty acids, the drop of static pressure is not enough to begin cavitation in nanopure technology.[17] Other homogenization technologies and patents on the homogenization processes are shown in Table 2.[18].

Milling Techniques

Media milling

Liversidge et al. had a patent on nanocrystal technology.[19] In this technique, drugs are subjected to media milling for nanoparticle production. Effect of impaction between the milling media and drugs gives essential energy for disintegration of the microparticulate system into nanoparticles. In this process, the chamber of milling is charged with the milling media involving drug, stabilizer, and water or suitable buffer, which is rotated at a very high shear rate to generate suspension. Residues left behind in the finished product is a major problem of this method.[20]

Dry cogrinding

Since many years, nanosuspensions are prepared through wet grinding processes by using pearl ball mill. Nowadays, nanosuspensions can be prepared by dry milling methods. Stable nanosuspensions are prepared by using dry grinding of poorly soluble drug with soluble polymers and copolymers after dispersing in liquid medium. Itoh et al. have described the colloidal particles formation of many poorly water-soluble drugs like nifedipine, griseofulvin, and glibenclamide with sodium dodecyl sulfate and polyvinylpyrrolidone as stabilizer.[21–23]

Lipid emulsion/microemulsion template

Nanosuspensions are also obtained by just diluting the emulsion, formed by using a partially water-miscible solvent as the dispersed phase. The emulsion technique is applicable for drugs which are either partially water miscible or soluble in volatile organic solvents. Additionally, microemulsion templates can also produce nanosuspensions. Microemulsions are dispersions of two immiscible liquids like water and oil and stabilized thermodynamically by surfactant or cosurfactant. The drug is either loaded into preformed or internal phase of microemulsion and can be saturated by intimate mixing of drugs.[20] Griseofulvin nanosuspension is prepared by the microemulsion technique by using water, butyl lactate, lecithin, and the sodium salt of taurodeoxycholate.[24]

Microprecipitation – High-pressure homogenization (Nanoedge)

Nanoedge is a combination of microprecipitation and high-pressure homogenization techniques. Method includes precipitation of friable materials followed by fragmentation under high shear and/or thermal energy.[25,26] The preparation method of nanoedge is shown in Figure 2.[27].

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

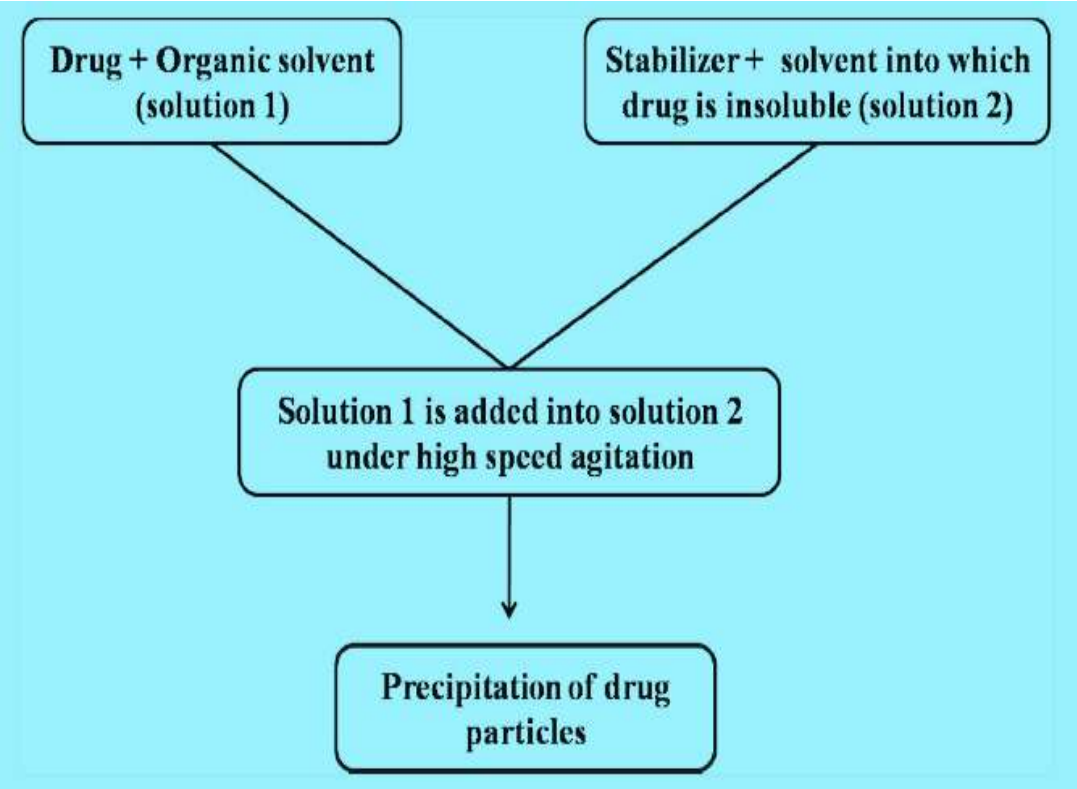

Figure 2: Technique for creating a nanoedge

Melt emulsification method

Solid lipid nanoparticles are mainly prepared by melt emulsification method. Kipp and co workers firstly prepare nanosuspensions of ibuprofen by using melt emulsification method. It is a four-step procedure. Drug is first added to aqueous solution having stabilizer. The solution is heated at temperature higher than the melting point of the drug and then homogenized by high-speed homogenizer for the formation of emulsion. The temperature is maintained above the melting point of the drug during overall process. Finally, the emulsion is cooled to precipitate the particles. The particle size of nanosuspension mainly depends on parameters like drug concentration, concentration and type of stabilizers used, cooling temperature, and homogenization process.[28]

Nanojet technology

This technique is also called opposite stream technology, uses a chamber where a stream of suspension is divided into two or more parts. Both streams are colloid with each other at high pressure. The high shear force produced during the process results in particle size reduction. Dearns had prepared nanosuspensions of atovaquone using the microfluidization process. The major disadvantage of this technique is the high number of passes through the microfluidizer and that the product obtained contains a relatively larger fraction of microparticles.[29]

Supercritical fluid methods

Various methods like rapid expansion of supercritical solution (RESS) process, supercritical antisolvent process, and precipitation with compressed antisolvent (PCA) process are used to produce nanoparticles. In RESS technique, drug solution is expanded through a nozzle into supercritical fluid, resulting in precipitation of the drug as fine particles by loss of solvent power of the supercritical fluid. By using RESS method, Young et al. prepared cyclosporine nanoparticles having diameter of 400 to 700 nm. In the PCA method, the drug solution is atomized into the CO2 compressed chamber. As the removal of solvent occurs, the solution gets supersaturated and finally precipitation occurs. In supercritical antisolvent process, drug solution is injected into the supercritical fluid and the solvent gets extracted as well as the drug solution becomes supersaturated.[30]

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

CHARACTERIZATION TECHNIQUES

The particle size, particle size distribution, and zeta potential affect the safety, efficacy, and stability of nanodrug delivery systems as well as dissolution performance is also altered by solid state of nanoparticles. Thus, characterization of nanoparticles plays a great role in forecasting in vitro and in vivo performance of nanodrug delivery systems. In vivo pharmacokinetic performance and biological function of nanosuspension strongly depends on its particle size and distribution, particle charge (zeta potential), crystalline state, and particle morphology.

Mean Particle Size and Particle Size Distribution

The mean particle size and particle size distribution affects saturation solubility, dissolution rate, physical stability, and in vivo performance of nanosuspensions.[9] The particle size distribution and its range named polydispersity index (PI) can be determined by laser diffraction (LD), photon correlation spectroscopy, microscope, and coulter counter.[31] PI gives the physical stability of nanosuspensions and should be as lower as possible for the long-time stability of nanosuspensions. A PI value of 0.1 to 0.25 shows a fairly narrow size distribution, and PI value more than 0.5 indicates a very broad distribution.[32] LD can detect and quantify the drug microparticles during the production process. It also gives a volume size distribution and can be used to measure particles ranging from 0.05 up to 2 000 μm.[33] The coulter counter gives the absolute number of particles per volume for the different size classes. It is more efficient and suitable than LD to quantify the contamination of nanosuspensions.[30]

Crystalline State and Particle Morphology

Polymorphic or morphological changes of nanosized particles can be checked by assessing the crystalline state and particle morphology.[30] As nanosuspension requires high-pressure homogenization, change in crystalline structure of formulation occurs which may be converted to either amorphous or other polymorphic forms.[31] Alteration in the solid state of the drug particles and the extent of the amorphous portion is determined by X-ray diffraction analysis[34] and supplemented by differential scanning calorimetry analysis.[30]

Surface Charge (Zeta Potential)

Surface charge properties of the nanosuspensions are studied through zeta potential. The value of particle surface charge indicates the stability of nanosuspensions at the macroscopic level. A minimum zeta potential of ±30 mV is required for electrostatically stabilized nanosuspensions[35,36] and a minimum of ±20 mV for steric stabilization.[37] The zeta potential values are commonly calculated by determining the particle's electrophoretic mobility and then converting the electrophoretic mobility to the zeta potential.[38] Electroacoustic technique is also used for the determination of the zeta potential in the areas of material sciences.[39].

Oral Drug Delivery

Poor solubility, incomplete dissolution, and insufficient efficacy are the major problem of oral drug administration. Due to smaller particle size and much larger surface to volume ratio, oral nanosuspensions are specially used to increase the absorption rate and bioavailability of poorly soluble drugs.[40] In case of azithromycin nanosuspensions, more than 65% drug was found to be dissolved in 5 hours as compared with 20% of micronized drugs.[41] The nanosuspension have advantages like improved oral absorption, dose proportionality, and low intersubject variability. By using standard manufacturing techniques, drug nanosuspensions can be simply incorporated into various dosage forms like tablets, capsules, and fast melts. The nanosuspension of Ketoprofen was successfully incorporated into pellets for the sustained release of drug over the period of 24 hours.[42]

Parental Drug Delivery

The present approaches for parental delivery include micellar solutions, salt formation, solubilization using cosolvents, cyclodextrin complexation, and more recently vesicular systems such as liposomes and niosomes. But these methods have limitations like solubilization capacity, parental acceptability, high manufacturing cost, etc. To solve the above problems, the nanosuspension technology is used. Nanosuspensions are administered through various parental routes such as intraarticular, intraperitoneal, intravenous, etc. Additionally, nanosuspensions increase the efficacy of parenterally administered drugs. Paclitaxel nanosuspension was reported to have their superiority in reducing the median tumor

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

burden.[43] Clofazimine nanosuspension showed an improvement in stability as well as efficacy above the liposomal clofazimine in Mycobacterium avium-infected female mice.[44] Rainbow et al. showed that intravenous nanosuspension of itraconazole enhanced efficacy of antifungal activity in rats relative to the solution formulation.[45]

Pulmonary Drug Delivery

For pulmonary delivery, nanosuspensions can be nebulized through mechanical or ultrasonic nebulizers. Due to the presence of many small particles, all aerosol droplets contain drug nanoparticles. Budesonide corticosteroid has been successfully prepared in the form of nanosuspension for pulmonary delivery.[46] Aqueous suspensions of the drug can be easily nebulized and given by pulmonary route as the particle size is very small. Different types of nebulizers are available for the administration of liquid formulations. Some of the drugs successfully tried with pulmonary route are budesonide, ketotifen, ibuprofen, indomethacin, nifedipine, itraconazole, interleukin-2, p53 gene, leuprolide, doxorubicin, etc.[47]

Ocular Drug Delivery

Nanosuspensions are used in ocular delivery of the drugs for sustained release. Liang and co-workers prepared cloricromene nanosuspension for ocular delivery using Eudragit. Experiment showed higher availability of drug in aqueous humor of rabbit eye. Thus, nanosuspension formulation offers a promising way of improving the shelf-life and bioavailability of drug after ophthalmic application.[37]

Targeted Drug Delivery

Nanosuspensions are suitable for targeting particular organs because of their surface properties. Along with this, it is easy to alter in vivo behavior by changing the stabilizer. The drug will be taken up by the mononuclear phagocytic system which allows region-specific delivery. This can be used for targeting antifungal, antimycobacterial, or antileishmanial drugs to macrophages if the pathogens persist intracellularly.[48] Kayser formulated an aphidicolin nanosuspension that improved the drug targeting to macrophages which were Leishmania infected. He stated that the drug in the form of nanosuspension had EC50 of 0.003 µg/ml, whereas the conventional form had 0.16 µg/ml.[49] Scholer et al. described an enhanced drug targeting to brain in the treatment of toxoplasmic encephalitis using an atovaquone nanosuspension.[50]

II. CONCLUSION

Nanosuspensions are distinctive and commercially feasible approach to solve the problems of hydrophobic drug such as poor solubility and poor bioavailability. For large-scale production of nanosuspensions, media milling and high-pressure homogenization technology have been successfully used. Striking characteristics, like improvement of dissolution velocity, increased saturation solubility, improved bioadhesivity, versatility in surface modification, and ease of postproduction processing, have widened the applications of nanosuspensions for various routes of administration. The applications of nanosuspensions in oral and parental routes have been very well established, although applications in pulmonary and ocular delivery have to be evaluated. However, their delivery through buccal, nasal, and topical delivery is yet to be done.

REFERENCES:

[1]. harma P, Denny WA, Garg S. Effect of wet milling process on the solid state of indomethacin and simvastatin. Int J Pharm. 2009;380:40–8.
[2]. Kakrana M, Sahooa NG, Judeh LZ, Wang Y, Chong K, Loh L. Fabrication of drug nanoparticles by evaporative precipitation of nanosuspension. Int J Pharm. 2010;383:285–92.
[3]. Lakshmi P, Ashwini KG. Nanosuspension technology: A review. Int J Pharm Sci. 2010;2:35–40.
[4]. Vermaa S, Lan Y, Gokhale R, Burgessa DJ. Quality by design approach to understand the process of nanosuspension preparation. Int J Pharm. 2009;377:185–98.
[5]. Nagaraju P, Krishnachaithanya K, Srinivas VD, Padma SV. Nanosuspensions: A promising drug delivery systems. Int J Pharm Sci Nano. 2010;2:679–84.
[6]. Barret ER. Nanosuspensions in drug delivery. Nat Rev. 2004;3:785–96.
[7]. Muller RH, Gohla S, Dingler A, Schneppe T. Wise D. Handbook of pharmaceutical controlled release technology. New York: Marcel Dekker; 2000. Large-scale

production of solid-lipid nanoparticles (SLN) and nanosuspension (Dissocubes) pp. 359–375.
[8]. Nanosuspension systems, Hamamatsu Nano technology. [cited 2011 Mar 5].
[9]. Liversidge GG, Cundy KC. Particle size reduction for improvement of oral bioavailability of hydrophobic drugs: Absolute oral bioavailability of nanocrystalline danazol in beagle dogs. Int J Pharm. 1995;125:91–7
[10]. Grau MJ, Kayser O, Muller RH. Nanosuspensions of poorly soluble drugs reproducibility of small-scale production. Int J Pharm. 2000;196:155–7.
[11]. Chingunpituk J. Nanosuspension technology for drug delivery. Walailak J Sci Tech. 2007;4:139–53.
[12]. Pu X, Sun J, Li M, He Z. Formulation of nanosuspensions as a new approach for the delivery of poorly soluble drugs. Curr Nanosci. 2009;5:417–27.
[13]. Matteucci ME, Brettmann BK, Rogers TL, Elder EJ, Williams RO, Johnston KP. Design of potent amorphous drug nanoparticles for rapid generation of highly supersaturated media. Mol Pharm. 2007;4:782–93.
[14]. Gassmann P, List M, Schweitzer A, Sucker H. Hydrosols-alternatives for the parenteral application of poorly watersoluble drugs. Eur J Pharm Biopharm. 1994;40:64–72.
[15]. Myerson AS, Ginde R. Butterworth-Heinemann. 2nd ed. Stoneham, MA: 1992. Handbook of Industrial Crystallization; pp. 45–6.
[16]. Bodmeier R, McGinity JM. Solvent selection in the preparation of poly (DL-lactide) microspheres prepared by solvent evaporation method. Int J Pharm. 1998;43:179–86.
[17]. Radtke M. Nanopure: Poure drug nanoparticles for the formulation of poorly soluble drugs. New Drugs. 2001;3:62–8.
[18]. Keck CM, Muller RH. Drug nanocrystals of poorly soluble drugs produced by high pressure homoginisation. Eur J Pharm Biopharm. 2006;62:3–16.
[19]. Liversidge GG, Cundy KC, Bishop JF, Czekai DA. Surface modified drug nanoparticles. US Patent. 1992;5:145–684.
[20]. Patravale VB, Date AA, Kulkarni RM. Nanosuspension: A promising drug delivery strategy. J Pharm Pharmacol. 2004;56:827–40.
[21]. Wongmekiat A, Tozuka Y, Oguchi T, Yamamoto K. Formation of fine drug particles by co-grinding with cyclodextrin: I: The use of β-cyclodextrin anhydrate and hydrate. Pharm Res. 2002;19:1867–72.
[22]. Itoh K, Pongpeerapat A, Tozuka Y, Oguchi T, Yamamoto K. Nanoparticle formation of poorly water soluble drugs from ternary ground mixtures with PVP and SDS. Chem Pharm Bull. 2003;51:171–4.
[23]. Mura P, Cirri M, Faucci MT, Gines-Dorado JM, Bettinetti GP. Investigation of the effects of grinding and co-grinding on physicochemical properties of glisentide. J Pharm Biomed Anal. 2002;30:227–37.
[24]. Trotta M, Gallarate M, Carlotti ME, Morel S. Preparation of griseofulvin nanoparticles from water-dilutable microemulsions. Int J Pharm. 2003;254:235–42.
[25]. Kipp JE, Wong J, Doty M, Werling J, Rebbeck C, Brynjelsen S. Method for preparing submicron particle suspensions. 2003 US Patent, 0031719 A1.
[26]. Noyes AA, Whitney WR. The rate of solution of solid substances in their own solutions. J Am Chem Soc. 1897;19:930–4.
[27]. Hintz RJ, Johnson KC. The effect of particle size distribution on dissolution rate and oral absorption. Int J Pharm. 1989;51:9–17. [Google Scholar]
[28]. Kipp JE, Wong J, Joseph CT, Doty M, Mark J, Rebbeck C, et al. Microprecipitation method for preparing submicron suspensions. 2003 US Patent, 6607784.
[29]. Dearns R. Atovaquone pharmaceutical compositions. 2000 US Patent US 6018080.
[30]. Young TJ, Mawson S, Johnston KP, Henriska IB, Pace GW, Mishra AK. Rapid expansion from supercritical to aqueous solution to produce submicron suspension of water insoluble drugs. Biotechnol Prog. 2000;16:402–7.
[31]. Kumar AN, Deecaraman M, Rani C. Nanosuspension technology and its

applications in drug delivery. Asian J Pharma. 2009;3:168–73.

[32]. Chen Y, Liu J, Yang X, Zhao X, Xu H. Oleanolic acid nanosuspensions: Preparation, in-vitro characterization and enhanced hepatoprotective effect. J Pharm Pharmacol. 2005;57:259–64.

[33]. Higgins JP. Spectroscopic approach for on-line monitoring of particle size during the processing of pharmaceutical nanoparticles. Anal Chem. 2003;75:1777–85.

[34]. Setler P. London: IIR Limited Drug delivery system; 1999. Identifying new oral technologies to meet your drug delivery needs for the delivery of peptides and proteins and poorly soluble molecules.

[35]. Muller RH, Jacobs C. Production and characterization of a budesonide nanosuspension for pulmonary administration. Pharm Res. 2002;19:189–94.

[36]. Yang JZ, Young AL, Chiang PC, Thurston A, Pretzer DK. Fluticasone and budesonide nanosuspensions for pulmonary delivery: Preparation, characterization, and pharmacokinetic studies. J Pharm Sci. 2008;97:4869–78.

[37]. Liang YC, Binner JG. Effect of triblock copolymer non-ionic surfactants on the rheology of 3 mol% yttria stabilised zirconia nanosuspensions. Ceram Int. 2008;34:293–7.

[38]. Muller RH, Grau MJ. Increase of dissolution rate and solubility of poorly water soluble drugs as nanosuspension.Proceedings. World Meeting APGI/APV, Paris. 1998;2:62–624.

[39]. Bond L, Allen S, Davies MC, Roberts CJ, Shivji AP, Tendler SJ, et al. Differential scanning calorimetry and scanning thermal microscopy analysis of pharmaceutical materials. Int J Pharm. 2002;243:71–82.

[40]. Boedeker BH, Lojeski EW, Kline MD, Haynes DH. Ultra-long duration local anesthesia produced by injection of lecithin-coated tetracaine microcrystals. J Clin Pharmacol. 1994;34:699–702.

[41]. Jia L, Wong H, Cerna C, Weitman SD. Effect of nanonization on absorption of 301029: Ex vivo and in vivo pharmacokinetic correlations determined by liquid chromatography/mass spectrometry. Pharm Res. 2002;19:1091–6.

[42]. Liversidge EM. Formulation and antitumor activity evaluation of nanocrystalline suspensions of poorly soluble anticancer drugs. Pharm Res. 1996;13:272–8.

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

[44]. Peters K, Leitzke S, Diederichs JE, Borner K, Hahn H, Muller RH, et al. Preparation of a clofazamine nanosuspension for intravenous use and evaluation of its therapeutic efficacy in murine Mycobacterium avium infection. J Antimicrob Chemother. 2000;45:77–83.

[45]. Rainbow B, Kipp J, Papadopoulos P, Wong J, Glosson J, Gass J, et al. Itraconazole IV nanosuspension enhances efficacy through altered pharmacokinetic in the rat. Int J Pharm. 2007;339:251–60.

[46]. Hernandez-Trejo N, Kayser O, Steckel H, Muller RH. Characterization of nebulized bupravaquone nanosuspensions-Effect of nebulization technology. J Drug Target. 2005;13:499–507.

[47]. Heidi MM, Yun-Seok R, Xiao W. Nanomedicine in pulmonary delivery. Int J Nanomed. 2009;4:299–319.]

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

[49]. Kayser O. Nanosuspensions for the formulation of aphidicolin to improve drug targeting effects against Leishmania infected macrophages. Int J Pharm. 2000;196:253–6.

[50]. Scholer N, Krause K, Kayser O, Moller RH, Borner K, Hahn H, et al. Atovaquone nanosuspensions show excellent therapeutic effect in a new murine model of reactivated toxoplamosis. Antimicrob Agents Chemother. 2001;45:1771–9.

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 1 Jan-Feb 2023, pp: 106-114 www.ijprajournal.com ISSN: 2249-7781

Table 1: Patents on homogenization procedures and homogenization technology

Technology	Company
Hydrosol	Novartis
Dissocubes	SkyePharma
Nanopure	PharmaSol
Nanoedge^{Tm}	Baxter
Nanocrystal^{Tm}	Elan Nanosystems
Nanomorph^{Tm}	Soligs

Table2: Available marketed drugs in the form of nanosuspension with their route of administration

Route	**Drugs**	**Therapeutic class**
Oral route	Tarazepide	SelectiveCCKa-antabonestic
	Insuline	Diabetes
	Ketoprofen	Anlgesic
Parental Intravenous	Naproxen	Anti-inflammatory
	Loviride	Antivirotic
	Omeparazole	Proton pump inhibitor
Opthalmic	Hydrocortisone	Glucocorticoid
Pulmonary	Budesonide	Asthma
Topical	Silver	Eczema