International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 10(6): November-December 2020

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Review Article……!!!

Received: 07-04-2020; Revised: 31-10-2020; Accepted: 01-11-2020

SOLUBILITY ENHANCEMENT TECHNIQUES: AN UPDATED REVIEW

Latika S. Patil*, Archana P. Mahajan

TSPM's, Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India.

Keywords:

Solubility Enhancement, bioavailability, Dissolution, solid dispersion, inclusion complexes

For Correspondence:

Latika S. Patil

TSPM's, Trimurti Institute of Pharmacy, Jalgaon, Maharashtra, India

E-mail:

ijipls@gmail.com

ABSTRACT

Solubility, the phenomenon of dissolution of solute is solvent to give a homogeneous system, is one of the important parameters to achieve desired concentration of drug in systemic circulation for desired (anticipated) pharmacological response. Low aqueous solubility is the major problem encouraged with formulation development of new chemical entities as well as for the generic development. More than 40% NCES (new chemical entities) developed in pharmaceutical industry are Practically insoluble in water. Solubility is a major challenge for formulation scientist .Any drug to be absorbed must be present the form of solution at the site or absorption. Various techniques are used for the enhancement of solubility of poorly soluble drugs which include physical & chemical modification of drug and other method like particle size reduction, crystal engineering salt formation, solid dispersion, use of Surfactant Complexation and so forth, selection of solubility improving method depends on drug property, Side of absorption, and required dosage form characteristics.

1. INTRODUCTION

A number of methodologies can be adapted to improve solubilization of poor water soluble drug and further to improve its bioavailability . The techniques generally employed for solubilization of drug include micronization ,chemical modification, pH adjustment ,solid dipersion , complexatio, co-solvency , solubilization , hydrotropy etc.The concentration of solute is satursated solution is called as saturated concentration of the solution and beyond that is being to precipitate the excess amount of solute.Thebio -available of an orally administered drug depend primarily on its solubility in the GIT and its permeability across cell membrane. To transport across biological membrane, drug molecules are required to be present in dissolved form With present day drug discovery techniques, about 40% drugs coming in to the market are Lipophilic and fail to reach therapeutic range due to their poor aqueous solubility Poor aqueous solubility of drug not only limits biological application of drug but also challenge its pharmaceutical development. The solvent is generally a liquid, which can be a pure substance or a mixture of two liquids. One may also speak of solid solution, but rarely of solution in a gas.

Table 1: Solubility criteria as per I.P., 1985, B.P. 2010

Descriptive Term	Approximate volume of solvent in milliliters per gram of solute
Very soluble	Less than 1
Freely soluble	1 – 10
Soluble	10 – 30
Sparingly soluble	30 – 100
Slightly soluble	100 – 1000
Very slightly soluble	1000 - 10,000
Insoluble or Practically Insoluble	More than 10,000

Table 1.2: Solubility data interpretation (Chemical Sciences, 2001)

Solubility (µg/ml)	Classification	Comments
≤ 20	Low	Will have solubility problems
20–65	Moderate	May have solubility problems
≥ 65	High	No solubility problem

Table 1.3: Classification of Effective Permeability (Chemical Sciences, 2001)

Effective Permeability (cm/s)	Classification	Comments
≤ 0.1×10^{-6}	Low	Will have permeability problems
$0.1–1\times 10^{-6}$	Moderate	May have permeability problems
≥ 1×10^{-6}	High	No permeability problem

Table 1.4: BCS Classification (Dressman JB, 2004)

Sr. No.	Classes	Parameter
1.	Class I	High soluble and High permeability
2.	Class II	Low soluble and High permeability
3.	Class III	High soluble and Low permeability
4.	Class IV	Low soluble and Low permeability

2. IMPORTANCE OF SOLUBILITY

However, the major challenge with the design of oral dosage forms lies with their poor bioavailability. The oral bioavailability depends on several factors including aqueous solubility, drug permeability, dissolution rate, first-pass metabolism, presystemic metabolism, and susceptibility to efflux mechanisms. The most frequent causes of low oral bioavailability are attributed to poor solubility and low permeability.

The improvement of drug solubility thereby its oral bio- availability remains one of the most challenging aspects of drug development process especially for oral-drug delivery system. There are numerous approaches available and reported in literature to enhance the solubility of poorly water-soluble drugs. The techniques are chosen on the basis of certain aspects such as properties of drug under consideration, nature of excipients to be selected, and nature of intended dosageform.

TECHNIQUES FOR SOLUBILITY ENHANCEMENT

Solubility improvement techniques can be categorized in to physical modification, chemical modifications of the drug substance, and other techniques.

3.1.Physical Modifications: Particle size reduction like micron- ization and nanosuspension, modification of the crystal habit like polymorphs, amorphous form and cocrystallization, drug dispersion in carriers like eutectic mixtures,etc.

3.2. Chemical Modifications: Change of pH, use of buffer, derivatization, complexation, and salt formation.

3.3. Miscellaneous Methods: Supercritical fluid process, use of adjuvant like surfactant, solubilizers, cosolvency, hydrotro- phy, and novel excipients.

4. FACTORS AFFECTING THE SOLUBILITY

4.1. Temperature

Solubility affected by temperature. If the solution process absorbs energy then the solubility will increase with increasing temperature. If the solution process releases energy then the solubility will decrease with increasing temperature. It is the case for most of the solvents. The situation is though different for gases. With increase of the temperature they became less soluble in each other and in water, but more soluble in organicsolvents.

4.2. Particle size

The changes in the interfacial free energy that accompany the dissolution of particles ofvarying sizes cause the solubility of a substance to increase with decreasing particle size. The size of the solid particle influences the solubility because as a particle becomessmaller, the surface area tovolume ratio increases. The larger surface area allows agreater interaction with the solvent. For solids and liquid solutes, solubility not affectedby change in pressure but for gaseous solutes, solubility increases as pressure increasesand decrease as pressure decrease. The solubility depende nt bioavailability problem has become a major hurdle in drug development processes. Drug nanocrystals have been widely accepted by the pharmaceutical industry to improve thebioavailability of poorly water-soluble compounds. Top-down and bottom- up technologies are the two primary technical approaches of drug nanocrystal production. Though the top-down approach has been hugely successful on the commercial front, it has some inherent drawbacks that necessitate the emergence of alternateapproaches.

4.3. pH

If the pH of a solution of either a weakly acidic drug or a salt of such a drug is reduced then the proportion of unionized acid molecules in the solution increases. Precipitationmay occur therefore, because the solubility of the unionized species is less than that ofthe ionized form. Conversely, in the case of solutions of weakly basic drugs or their saltsprecipitation is favoured by an increase in pH. The relationship between pH and thesolubility and pKa value of acidic and basic drugs is given by Eqn,]1[Acidic drugs: pH= pKa + log s-s0/ s0 Basic drugs: pH = pKa + log s 0/ S- s0 Where pKa = dissociation constant of drug, s0 = solubility of unionised form, moles/litre, S=overall solubility ofdrug,moles/litre.

4.4. DielectricConstant

The solubility is a function of dielectric constant of polar and nonpolar medium. Mostoften, with hydrophobic drugs, the solubility decreases with increasing dielectric constant .

4.5. Molecular size

The larger the molecules of the solute are, the larger is their molecular weight and their size. It is more difficult it is for solvent molecules to surround bigger molecules. If all of the above mentioned factors ale excluded, a general rule can be found that larger particles are generally less soluble.

4.6. Polarity

In most cases solutes dissolve in solvents that have a similar polarity. Chemists use a popular aphorism to describe this feature of solutes and solvents: "Like dissolves like". Non-polar solutes do not dissolve in polar solvents and the other way round.

4.7. Physical Modification

Among various techniques for solubility enhancement, physical modifications ofdrug product such as reduction ofparticle size and modifying crystal habit are common approaches to increase drug solubility.

4.8. Modifications Chemical

Change of ph, use of buffer, derivatization, complexation, and salt formation. Miscellaneous Methods Supercritical fluid process, use of adjuvant like surfactant, solubilizers, cosolvency, hydrotrophy, and novel excipients.

4.9.Microniazation

Particle size reduction leads to increase in the effective surface area resulting in enhancement of solubilityand dissolution velocity of the drug. Micronization technique is used to improve dissolution rates of drugs into the biological environment, in order to improve the oral bioavailability. Particle size reduction methods include recrystallization of the solute particles from solutions using liquid antisolvents, along with labor intensive techniques like crushing, milling, grinding, freeze drying and spray-drying. The rapid expansion of supercritical solutions (RESS) is an alternative technique for the micronization of particles using supercritical carbon dioxide to quickly and naturally reduce the particle sizes of various drugs.

4.10.Nanosuspension :

Nanosuspension are sub micron colloidal dispersions of pure particles of drug which are stabilized by surfactants. Increased dissolution rate is due to larger surface area exposed, while absence of Ostwald ripening isdue tothe uniform and narrow particle sizerange obtained, which eliminates the concentration gradient.

Various particle technologies, from conventional size reduction methods to recent novel methods that can be used for formulating drugs with poor aqueous solubility as

4.11.Particle Size Reduction

The solubility of drug is often intrinsically related to drug particle size; as a particle becomes smaller, the surface area to volume ratio increases. The larger surface area allows greater interaction .

5. MATERIALS AND METHODS

5.1.Materials

TEL was provided by Unichem Laboratories, Mumbai, India as gift sample. Poloxamer 188 and 407 were a gift sample from Signet BASF, Mumbai, India. Talc, polyethylene glycol 6000, and polyvinylpyrrolidone K30 were procured locally from Otto Kemi, Mumbai, India. Acetonitrile, dichloromethane, chloroform, and N-methyl pyrrolidone were from Spectrochem Pvt. Ltd., Mumbai, India and were of analytical grade. Tocopheryl polyethylene glycolsuccinate 1000 was gifted by Isochem, France. Espheres neutral pellets (18–20#) were given as gift by Ideal Cures Pvt. Ltd., Mumbai

5.2. Methods

5.2.1. Determination of Solubility of TEL

The solubility of TEL in water and water miscible or partially water miscible organic solvents such as acetone, acetonitrile, dichloromethane, petroleum ether, chloroform, and N-methyl-2-pyrrolidone was determined by adding an excess of the drug in the solvents. Using a magnetic stirrer, the suspensions were stirred for 48 h at 37°C, filtered, and the drug content determined by HPLC. Each sample was analyzed in triplicate.

5.2.2. HPLC Analysis of TEL

The concentration of TEL was determined by RP-HPLC (Agilent Technologies 1120 series, Germany) using TC-C18 column (4.6 × 250 mm, 5 µm). Acetonitrile and 0.05 M potassium dihydrogen phosphate in a ratio 60:40 (adjusted to pH 3.0 with o-phosphoric acid) was used as the mobile phase at a flow rate of 1 ml/min. The eluent was analyzed at 271 nm by UV detector. The method was validated for accuracy, precision, and recovery.

5.2.3. Preparation of Nanosuspensions

TEL nanoparticles were prepared by evaporative antisolvent precipitation technique. Preliminary studies were carried out to investigate the solubility of TEL in various solvents like N-methyl pyrrolidone (NMP), acetonitrile, dichloromethane, and chloroform. The solvent in which TEL showed highest solubility was used for preparing the nanosuspensions. Required amount of TEL was dissolved in sufficient volume (10 ml) of selected solvent. The polymers/surfactants were dissolved in water (100 ml) separately and the resulting mixture was stirred at 4,000 rpm using a mechanical stirrer (Remi Motor RQT-124A). After formation of a homogenous solution, drug solution was added all at once using a micropipette with continuous stirring. After complete addition of the drug solution, stirring was continued for 2 h at 10,000 rpm. The suspension was kept for some time to allow the foam to dissipate. The different ratios by weight of polymer–surfactant combinations used for preparing nanosuspensions are listed in Table I. Control sample of suspension containing drug alone was prepared using similar conditions as above and subjected to particle size analysis.

5.2.4. Particle Size Measurement

The nanosuspensions were subjected to particle size analysis using Malvern Zetasizer (MAL 500999; Malvern Instruments, UK) based on dynamic light scattering. The measurements were made in triplicate and average particle size, polydispersity index, and zeta potential were determined in deionised and double-distilled water (Merck).

5.2.5. Ultracentrifugation

The nanosuspension which showed maximum decrease in particle size as compared to other nanosuspensions was subjected to ultracentrifugation using Beckmann Coulter

(Model: OptimaxXL100K with rotor: SW32Ti) operated at 20,000 rpm and 20°C for 45 min. The residue was subjected to freeze drying at −45°C to −51°C and pressure of 0.08 mbar using LABCONCO Freezone, 2.5, Kansas, USA. The supernatant and freeze-dried products were evaluated for drug content.

5.2.6. Surface Morphology

Morphology of the nanoparticles was investigated by a field emission scanning electron microscope (JSM 6303A, Joel, Tokyo, Japan). The drug particles were sputter coated with gold before observation.

5.2.7. Saturation Solubility

Saturation solubility of plain TEL and freeze-dried nanoparticles was determined by placing excess drug/product in 20 ml deionized water in a capped flask and stirring on an orbital shaker for 48 h. The suspension was double filtered using 0.1 µm filter and the filtrate after suitable dilution was injected into HPLC system and analyzed as previously described. The studies were also conducted in 0.1 N HCl, pH 6.8 buffer, and biorelevant media, i.e., FaSSIF and FeSSIF (12).

5.2.8. Fourier Transform Infrared Spectroscopy

The IR spectra was recorded using Fourier transform infrared spectrophotometer (450 plus, Jasco, Japan) with diffuse reflectance principle. The spectrum was scanned over a frequency range of 4,000–400 cm−1. The samples were ground with KBr and pressed into a disk shape for measurement.

5.2.9. Differential Scanning Calorimetry

The differential scanning calorimetry (DSC) thermograms were recorded using differential scanning calorimeter (DSC; 823e, Mettler Toledo, Japan). Approximately 2–5 mg of each sample was heated in a pierced aluminum pan from 30°C to 300°C at a heating rate of 10°C/min under a stream of nitrogen at flow rate of 50 ml/min. Thermal data analyses of the DSC thermograms were conducted using STARe software.

5.2.10. Powder X-ray Diffraction Studies

The powder X-ray diffraction studies (PXRD) spectra of samples were recorded using high power powder X-ray diffractometer (Ru-200B, Pune, India) with Cu as target filter having a voltage/current of 40 KV/40 mA at a scan speed of 4°/min. The samples were analyzed at 2θ angle range of 5–50°. Step time was 0.5 s and time of acquisition was 1 h.

5.2.11. Wettability

Tablets of plain TEL and nanoparticles of TEL were prepared using hydraulic press at pressure of 5 t (model: M-15, Technosearch Instruments, Mumbai) and contact angle between water and tablet surfaces was determined by static sessile drop method (13). It involved placing 10 µl of water on surface of tablet using micropipette. Photographs of the drop were taken after 10 s. It was carefully superimposed on tracing paper and contact angle was measured. Amaranth red was added to water to ensure proper visibility of the drop.

5.2.12. Specific Surface Area

Specific surface area of plain TEL and nanoparticles was measured using BET surface area analyser (model, SAA 2000; make, SP Consultants, Mumbai) using nitrogen as the adsorbate gas at 26°C. The instrument measures the quantity of adsorbate gas desorbed from a solid surface by sensing change in thermal conductivity of a flowing mixture of nitrogen (adsorbate 30%) and helium (inert carrier 70%) gas. The change in thermal conductivity brings about a proportional change in electrical conductivity of the mixture which is measured by the instrument and converted into volume of desorbed gas.

5.2.13. Solvent Residue and Metal Contamination

The freeze-dried product was analyzed by gas chromatography for residual solvent and atomic absorption spectroscopy for metal contamination. Shimadzu-GC-2014 system was used with helium as the carrier gas at a temperature range of 50–300°C and pressure of 20 kPa. RTX-Biodiesel TG was used as the column and the detector used was flame ionization detector.

6. ADVANTAGES & DISADVANTAGES

6.1. Advantages

1. Increase surface area –volume ratio improvement in solubility.

2. Molecular dispersion of the lipophilic drug within the hydrophilic carrier.

3. High drug stability and rapid release rate.

4. simple to formulate and analyses and simple to produce.

5. Effective methods of increasing solubility and dissolution rates of acids and basics drugs.

6. Increase chemical or metabolic stability higher water solubility.

7. Higher solubility in lipid membranes.

8. Improved oral or local absorption.

9. Enhanced brain penetration.

10. Reduced toxicity and local irradiation.

6.2. Disadvantages

1. Thermal stress may occur which harm thermosensitive or unstable active compounds

2. Selection of nontoxic hydrophilic solvent, carrier, coating materials, and their ratios

3. Risk for perception upon dilution with aqueous media varialabilty and toxicity with the use of extreme pH.

4. May accelerate hydrolysis or catalyze other degradation mechanism.

5. For Feasible For neutral compounds.

6. Prodruges cannot be feasible for all drug formulation.

7. Reconversion of salts into aggrades of their respective acid or base form.

8. Sometimes perception occurs.

9. Irritates the gastroinsentinal tract.

10. Not suitable For drugs having a high does number.

7. RESULTS AND DISCUSSION

Particle Size Analysis

TEL nanoparticles were prepared by bottom-up technology using evaporative antisolvent precipitation technique. As per the Ostwald–Mier theory (8), crystallization occurs when the solution reaches the appropriate degree of supersaturation which further leads to nucleation and crystal growth. Addition of saturated drug solution to the antisolvent generates a high degree of supersaturation resulting in the formation of large number of nuclei. Supersaturation is facilitated by rapid evaporation of the solvent. This reduces the tendency for crystal growth resulting in the formation of ultrafine crystals. The presence of stabilizers, which undergo preferential adsorption at the surface of particles further arrest the growth of crystals through steric or electrostatic stabilization (14). Additionally, the turbulence created due to high-speed stirring using a robust overhead mechanical stirrer also

ensures rapid nucleation and causes breakdown of the crystals thereby preventing them from growing to a larger size. Selection of the right solvent(s) and stabilizer(s) are critical for the nanoprecipitation process. The intention is not only to obtain nanocrystals but also sufficient yield to make the process cost effective. Various solvents that were screened include dichloromethane, chloroform, acetonitrile, and NMP and combinations thereof. Extensive literature was reviewed for selection of various stabilizers commonly used for nanoparticles and then screened for stabilizing TEL nanoparticles. The stabilizers selected included PEG 6000, TPGS, PVP K30, Poloxamer 188 and Poloxamer 407, singly and in combination.

Among the solvents, dichloromethane (DCM/€ = 8.93) was selected as the solvent for TEL due to its higher solubilization potential for TEL and low boiling point. These two are important parameters as rapid evaporation of the solvent is essential for higher supersaturation and rapid nucleation, all prerequisites for ultrafine crystal size. At the same time, too high a value of dielectric constant (€) will not be beneficial as the drug is highly lipophilic (log P = 7.7) and hence it will have limited solubility in the solvent. Though TEL was found to have maximum solubility in NMP its high boiling point (202°C) was a major deterrent as it could have led to problems of solvent residues in the final product. During manufacturing of nanosuspensions, there is an increase in particle surface area due to diminution of particle size and hence an increase in the solid–liquid contact area. This results in an increase in Gibbs free energy thus making the nanosuspensions thermodynamically unstable. An obvious outcome of this would be agglomeration of nanosized particles in an attempt to reduce interfacial area (15). Nanosuspensions were prepared using various polymeric or surfactant stabilizers, singly or in combination and were subjected to particle size analysis and measurement of zeta potential (Table II). It was found that when the stabilizers were used singly the particle size was higher as compared to when they were combined with TPGS (Fig. 2). The average particle size (Zav) of the plain drug suspension prepared under the same conditions was found to be ~2,500 nm. Nanosuspensions containing PVP K30 alone in a ratio of 1:1 showed Zav of 550.6 nm with a PDI of 1.0 whereas with PEG 6000 it was 778 nm with a PDI of 0.34. Nanosuspension containing Poloxamer 188 singly in a ratio of 1:1 with drug showed an average particle size of 523.4 nm. Combining TPGS with the above three polymers in a ratio of 1:1:1 showed a remarkable reduction in particle size thereby confirming the superior stabilizing ability of TPGS. The particle size for these batches ranged from 82.63 to 128.2 nm with the combination of PVPK30 and TPGS showing the least average particle size of 82.63 nm and PDI equivalent to 0.472. The d10%, d50%, and d90% were found to be 10.1, 16.2, and 41.3, respectively. Poloxamer 188, singly was not effective as a stabilizer, rather flocculation was observed. This could be due to its high hydrophilicity (HLB = 29) due to which it may not be undergoing preferential adsorption on the nanocrystal surface. However, in combination with TPGS, it worked synergistically to give a decreased particle size as TPGS has an intermediate HLB of 13. PEG 6000 alone produced nanoparticles with an average size of 778 nm and in combination with TPGS the particle size was found to be approximately 105 nm again alluding to the superior adsorption potential of TPGS and its ability to act synergistically with other surfactants or hydrophilic polymers for stabilizing a nanosystem. Greatest particle size reduction was observed with PVPK30 in combination with TPGS as PVPK 30 is reported

to be a protective colloid which is indicative of its greater adsorption potential for the nanoparticles (16). However with all three polymers, an increase in TPGS content led to an increase in particle size which could be attributed to an increase in viscosity due to TPGS (semisolid at room temperature) which precludes the adsorption of stabilizers onto the particles. The zeta potential of all the batches ranged between 6.54 and 10.8 mV. The low values are indicative of the shifting of the plane of shear, at which zeta potential is measured to a larger distance from the particle surface. This is expected as the stabilizers used for preparing the nanosuspensions are either hydrophilic polymers or non-ionic surfactants which stabilize the particles by steric stabilization. Any negative charge might be a result of ionization of surface functional groups present in the drug molecule/stabilizer or adsorption of solvent ions on the particles which gives rise to low zeta potential values.

References

1. Vandecruys R, Peeters J, Verreck G, Brewster M. Use of screening method to determine excipients which optimize the extent and stability of supersaturated drug solutions and application of this system to solid formulation design. Int J Pharm. 2007;342:168–175. doi: 10.1016/j.ijpharm.2007.05.006. [PubMed] [CrossRef] [Google Scholar]
2. Blagden N, de Matas M, Gavan PT, York P. Crystal engineering of active pharmaceutical ingredients to improve solubility and dissolution rates. Adv Drug Del Rev. 2007;59:617–630. doi: 10.1016/j.addr.2007.05.011. [PubMed] [CrossRef] [Google Scholar]
3. Kim C, Park J. Solubility enhancement for oral delivery: can chemical structure modification be avoided? Am J Drug Deliv. 2004;2:113–130. doi: 10.2165/00137696-200402020-00004. [CrossRef] [Google Scholar]
4. Merisko-Liversidge E, Liversidge G, Cooper E. Nanosizing: a formulation approach for poorly water soluble compounds. Eur J Pharm Sci. 2003;18:113–120. doi: 10.1016/S0928-0987(02)00251-8. [PubMed] [CrossRef] [Google Scholar]
5. Humberstone A, Charman W. Lipid-based vehicles for the oral delivery of poorly water soluble drugs. Adv Drug Del Rev. 1997;25:103–128. doi: 10.1016/S0169-409X(96)00494-2. [CrossRef] [Google Scholar]
6. Forster A, Rades T, Hempenstall J. Selection of suitable drug and excipient candidates to prepare glass solutions by melt extrusion for immediate release oral formulations. Pharm Tech Eur. 2002;14:27–37. [Google Scholar]
7. Davis ME, Brewster ME. Cyclodextrin-based pharmaceutics: past, present, future. Rev Drug Discov. 2004;3:1023–1035. doi: 10.1038/nrd1576. [PubMed] [CrossRef] [Google Scholar]
8. Keck C, Muller R. Drug nanoparticles of poorly soluble drugs produced by high pressure homogenization. Eur J Pharm Biopharm. 2006;62:3–16. doi: 10.1016/j.ejpb.2005.05.009. [PubMed] [CrossRef] [Google Scholar]
9. Timpe C. Oral drug solubilization strategies: applying nanoparticulate formulation and solid dispersion approaches in drug development. Featured Article in APV Drug Delivery Focus Group Newsletter. 2010:1.
10. Huang P, Wang X, Chen Z. Micronization of gemfibrozil by reactive precipitation process. Int J Pharm. 2008;360:58–64. doi: 10.1016/j.ijpharm.2008.04.026. [PubMed] [CrossRef] [Google Scholar]
11. Kocbeck P, Baumgartner S, Kristl J. Preparation and evaluation of nanosuspensions for enhancing the dissolution of poorly soluble drugs. Int J Pharm. 2006;312:179–186. doi: 10.1016/j.ijpharm.2006.01.008. [PubMed] [CrossRef] [Google Scholar]
12. Dressman J, Amidon GL, Reppas C, Shah V. Dissolution testing as a prognostic tool for oral drug. Absorption: immediate release dosage forms. Pharm Res. 1988;15:11–22. doi: 10.1023/A:1011984216775. [PubMed] [CrossRef] [Google Scholar]
13. http://en.wikipedia.org/wiki/Sessile_drop_technique. Accessed on 6 Dec 2011
14. Matteucci M, Hotze M, Johnston K, Williams R. Drug nanoparticles by antisolvent precipitation:mixing energy vs surfactant stabilization. Langmuir. 2006;22:8951–8959. doi: 10.1021/la061122t. [PubMed] [CrossRef] [Google Scholar]
15. van Eerdenbrugh B, Froyen L, van Humbeeck J, Martens J, Augustijns P, van den Mooter G. Top-down production of drug nanoparticles: nanosuspension stabilization, miniaturization and transformation into solid products. Int J Pharm. 2008;364:64–75. doi: 10.1016/j.ijpharm.2008.07.023. [PubMed] [CrossRef] [Google Scholar]
16. http://www.greatvistachemicals.com/industrial&specialtychemicals/polyvinylpyrrolidone.html. Accessed on 10 Nov 2011ns.

HOW TO CITE THIS ARTICLE

Latika S. Patil*, Archana P. Mahajan. Dissolution Enhancement Technique : Self-Emulsifying Drug Delivery Systems (SEDDS). International Journal of Institutional Pharmacy and Life Sciences, Vol 10[6] November-December 2020 : 40-48.