

# Solid Dispersion Technique: An Emerging Approach to Enhance Solubility and Bioavailability of Poorly Water-Soluble Drugs

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## ABSTRACT

Improving oral bioavailability of medicine those given as solid dosage forms remains a challenge for the formulation of scientists because of solubility problems. The dissolution rate can be the rate-limiting process within the absorption of a drug from a solid dosage sort of relatively insoluble drug.

The historical background of solid dispersion technology, has limitations, classification, and various preparation techniques with its advantages and drawbacks. This review also discusses the recent advances within the field of solid dispersion technology. Supported the prevailing results and authors reflection, this review gives rise to reasoning and suggested choices of carrier or matrix and solid dispersion procedure.

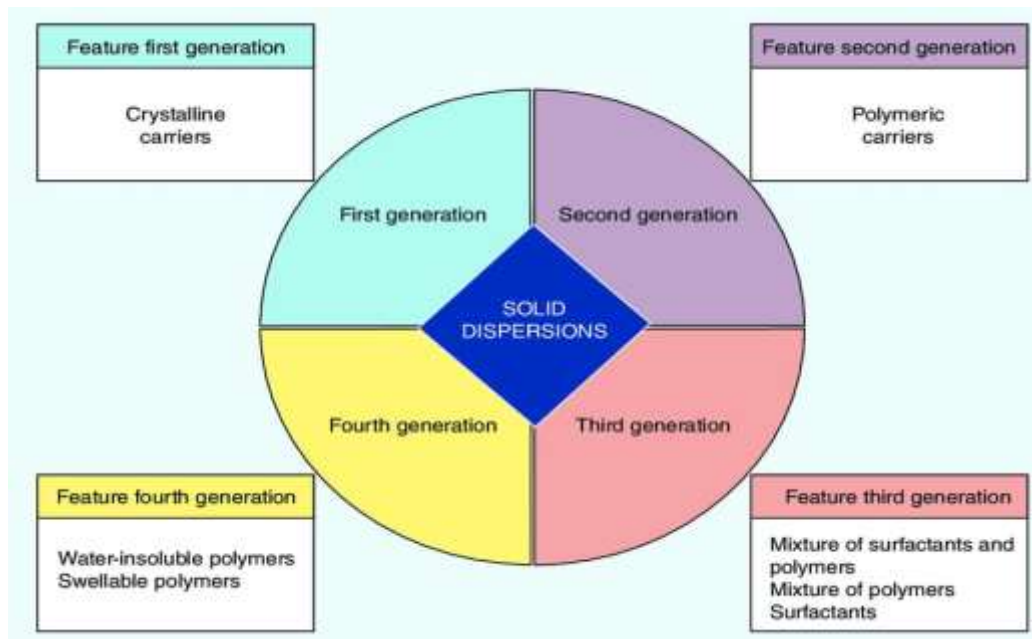
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## INTRODUCTION

Oral bioavailability of drugs depends on its solubility and/or dissolution rate, therefore major problems associated with these drugs was its very low solubility in biological fluids, which results into poor bioavailability after oral administration .<sup>[1-5]</sup>

An ideal drug delivery system should be able to deliver an adequate amount of drug, preferably for an extended period of time for its optimum therapeutic activity. Most drugs are inherently not long lasting in the body and require multiple daily dosing to achieve the desired blood concentration to produce therapeutic activity. To overcome such problem, controlled release and sustained release delivery systems are receiving considerable attention from pharmaceutical industries worldwide. A controlled release drug delivery system not only prolongs the duration of action, but also results in predictable and reproducible drug-release kinetics. One advantage of controlled release dosage forms is enhanced patient compliance. Drug delivery systems based on the principles of solid dispersion .<sup>[6]</sup>

## 1) CLASSIFICATION -



[https://www.researchgate.net/figure/Classification-of-solid-dispersions\\_fig3\\_333144751](https://www.researchgate.net/figure/Classification-of-solid-dispersions_fig3_333144751)<sup>[7]</sup>

## 2) MECHANISM OF SOLID DISPERSION -

There are two sets of observations with regard to the mechanism of drug release from solid dispersions.

**2.1 Carrier-controlled Release** - Corrigan (1986) provided a very valuable contribution by not only measuring the dissolution rate of the incorporated drug but also assessing that of the polymer itself, in this case PEG. He found that the dissolution rate of the drug in the polymer and the polymer alone were in fact equivalent, leading to the suggestion of carrier-controlled dissolution whereby the dissolution rate of the drug is controlled by that of the inert carrier.

**2.2 Drug-controlled Release** - Sjokvist and Nystrom (1991) measured the particle size of the griseofulvin particles released from the dispersions and produced strong evidence that dissolution rate enhancement was a direct function of the size of the released particles. In an attempt to reconcile these contradictions Sjokvist-Saers and Craig (1992) used a homologous series of drugs (paraaminobenzoates) in PEG 6000 in an attempt to interrelate the solid state structure, drug solubility and dissolution rate.<sup>[8-9]</sup>

## 3) Applications of Solid Dispersion in Pharmaceutical -

Field Aside from absorption improvement, the solid dispersion method may have various pharmaceutical applications, which ought to be additionally investigated. Such a procedure might be utilized.

1. To obtain a homogeneous distribution of a small amount of drug in a solid-state.
2. To stabilize the unstable drug.
3. To dispense liquid (up to 10%) or vaporous mixes in a solid dosage.
4. To plan a quick-release primary dose in a sustained release dosage form.
5. To plan continued a sustained release regimen of soluble drugs by utilizing ineffectively dissolvable or insoluble carriers.
6. To reduce pre systemic inactivation of drugs like morphine and progesterone.<sup>[10-11]</sup>

#### 4) Characterization -

The characterization of amorphous solids differs from that for crystalline solids. It is customary to characterize an amorphous material both below and above the glass transition temperature, i.e., both as the frozen solid and as the supercooled viscous liquid. The physical characterization of amorphous solids utilizes a wide range of techniques and offers several types of information.

##### 4.1 Powder X-ray diffraction

Powder X-ray diffraction can be used to qualitatively detect material with long-range order. Sharper diffraction peaks indicate more crystalline material. Diffraction techniques are perhaps the most definitive method of detecting and quantifying molecular order in any system, and conventional, wide-angle and small-angle diffraction techniques have all been used to study order in systems of pharmaceutical relevance. Conventional X-ray powder diffraction, also known as PXRD can be used to quantify non crystalline material down to levels of 5% and with temperature and environmental control can also be used to follow the kinetics of phase transformation.

##### 4.2 Differential scanning calorimetry (DSC)

Frequently used technique to detect the amount of crystalline material is differential scanning calorimetry (DSC). In DSC, samples are heated with a constant heating rate and the amount of energy necessary for that is detected. With DSC the temperatures at which thermal events occur can be detected. Thermal events can be a glass to rubber transition, (re)crystallization, melting or degradation.

##### 4.3 Solid state NMR (ss-NMR)

High-resolution  $^{13}\text{C}$  ss-NMR spectra are obtained using proton decoupling and magic angle spinning (MAS) and sensitivity enhancement is achieved by cross-polarization (CP).  $^{13}\text{C}$  ss-NMR has the advantage of being a non destructive test method that provides information about the structure of the material. Like in any other one-dimensional NMR method, it is possible to relate straightforwardly the integral of the CPMAS NMR signal to the number of  $^{13}\text{C}$  atoms involved, provided relaxation rates, Hartmann–Hahn conditions and cross-polarization rates are properly investigated for each species in the sample.

##### 4.4 Temperature modulated differential scanning calorimetry (TMDSC)

In MTDSC, a sinusoidal wave modulation is superimposed over the conventional linear (or isothermal) heating or cooling temperature program. MTDSC is based on the same theory as conventional DSC, in which the heat flow signal is a combination of the specimen heat capacity  $C_p$ ,  $t$  (heat-rate dependent component) and of any temperature dependent, often irreversible, ‘kinetic’ component. Quantification of amorphous content of a sample using MTDSC is based on the measurement of heat capacity jump associated with the amorphous phase glass transition by preparing a calibration curve based on the heat capacity jumps of physical mixtures of known crystallinity.

##### 4.5 Inverse gas chromatography (IGC)

IGC is a vapor sorption technique in which the powder is packed in a column and known vapors (usually at infinite dilution in a carrier gas) are injected. From the retention times of the probes it is possible to assess the surface nature of the material in the column. IGC is a highly sensitive technique and has been used to determine the specific energies of adsorption of polar probes DGSP A, which can then be used to calculate the basic/acidic parameter ratio  $K_D/K_A$ .

##### 4.6 Dynamic vapor sorption (DVS)

Water sorption or gravimetric techniques have been extensively used in the study of many amorphous and partially amorphous powders. It is a useful method for standardizing the amorphous content either as a

single component or in combination. Dynamic vapor sorption (DVS) is based on the concept of exploitation of crystallization of amorphous materials with changes in humidity, with consequent expulsion of water. Extent of water sorption and desorption is related to the amorphous content of the sample. DVS works simply by detecting the crystallization response for the amorphous material component.

#### 4.7 Dissolution calorimetry

Dissolution calorimetry measures the energy of dissolution, which is dependent on the crystallinity of the sample. Usually, dissolution of crystalline material is endothermic, whereas dissolution of amorphous material is exothermic.

#### 4.8 Confocal Raman spectroscopy

Confocal Raman spectroscopy is used to measure the homogeneity of the solid mixture. It is described that a standard deviation in drug content smaller than 10% was indicative of homogeneous distribution. Because of the pixel size of 2  $\mu\text{m}^3$ , uncertainty remains about the presence of nano-sized amorphous drug particles.<sup>[12-23]</sup>

### 5. Common Methods Used for Preparation of Solid Dispersion -

Various methods used for preparation of solid dispersion system. These methods are given below.

1. Melting method
2. Solvent methods
3. Melt extrusion methods
4. Super Critical Fluid (Scf) technologies
5. Spray Drying
6. High pressure homogenization
7. Polymeric alteration

#### 5.1 Melting method

The melting or fusion method is the preparation of physical mixture of a drug and a water-soluble carrier and heating it directly until it melted. The melted mixture is then solidified rapidly in an ice-bath under vigorous stirring. The final solid mass is crushed, pulverized and sieved. Appropriately this has undergone many modifications in pouring the homogenous melt in the form of a thin layer onto a ferrite plate or a stainless steel plate and cooled by flowing air or water on the opposite side of the plate

#### 5.2 Solvent method

In this method, the physical mixture of the drug and carrier is dissolved in a common solvent, which is evaporated until a clear, solvent free film is left. The film is further dried to constant weight. The main advantage of the solvent method is thermal decomposition of drugs or carriers can be prevented because of the relatively low temperatures required for the evaporation of organic solvents. However, some disadvantages are associated with this method such as

- a. The higher cost of preparation.
- b. The difficulty in completely removing liquid solvent.
- c. The possible adverse effect of traces of the Solvent on the chemical stability
- d. The selection of a common volatile solvent.
- e. The difficulty of reproducing crystal form.
- f. In addition, a super saturation of the solute in the solid system cannot be attained except in a System showing highly viscous properties.

### 5.3 Melt extrusion method

The drug/carrier mix is typically processed with a twin screw extruder. The drug/carrier mix is simultaneously melted, homogenized and then extruded and shaped as tablets, granules, pellets, sheets, sticks or powder. The intermediates can then be further processed into conventional tablets. An important advantage of the hot melt extrusion method is that the drug/carrier mix is only subjected to an elevated temperature for about 1 min, which enables drugs that are somewhat thermo labile to be processed.

### 5.4 Super Critical Fluid (Scf) Technology

The supercritical fluid antisolvent techniques, carbon dioxide are used as and antisolvent for the solute but as a solvent with respect to the organic solvent. Different acronyms were used by various authors to denote micro ionization processes: aerosol solvent extraction system, precipitation with a compressed fluid anti solvent, gas anti-solvent, and solution enhanced dispersion by supercritical fluids, and supercritical antisolvent.

### 5.5 Spray Drying

Dissolve the various amounts of carriers in water. Then disperse the 10gm of drug, pre-sieved through a 60-mesh screen in the solution. The resulting dispersion is subjected towards the nozzle at a flow rate previously fixed using a peristaltic pump & spray dry it at an inlet temperature of about 1200C & an outlet temperature of about 65-700C. Fix the spray pressure. Maintain the flow rate of drying air at the aspirator. After spray-drying, collect each resulting powders by cyclone separation and transferred to glass vials.

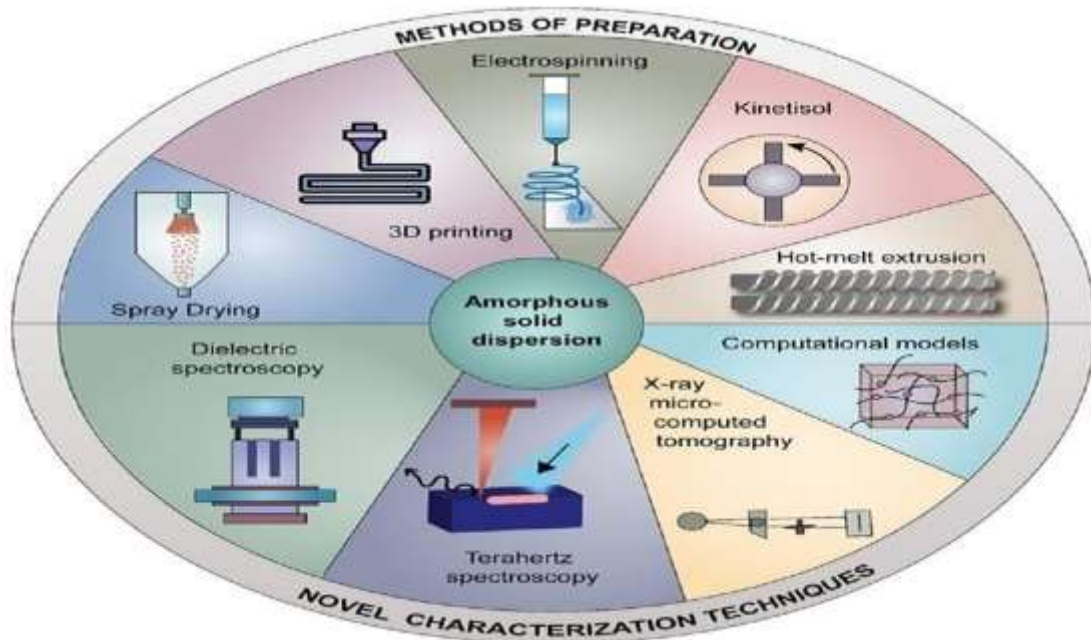
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### 5.6 High - pressure homogenization

The high pressure homogenization involves dispersing a drug powder in an aqueous surfactant solution and passing through a high-pressure homogenizer, subsequently Nano suspensions are obtained. The cavitation force experienced is sufficient to disintegrate drug from micro particles to nanoparticles. The particle size is dependent on the hardness of the drug substance, the processing pressure and the number of cycles applied. However, only brittle drug candidates might be broken up into nanoparticles by this technique.

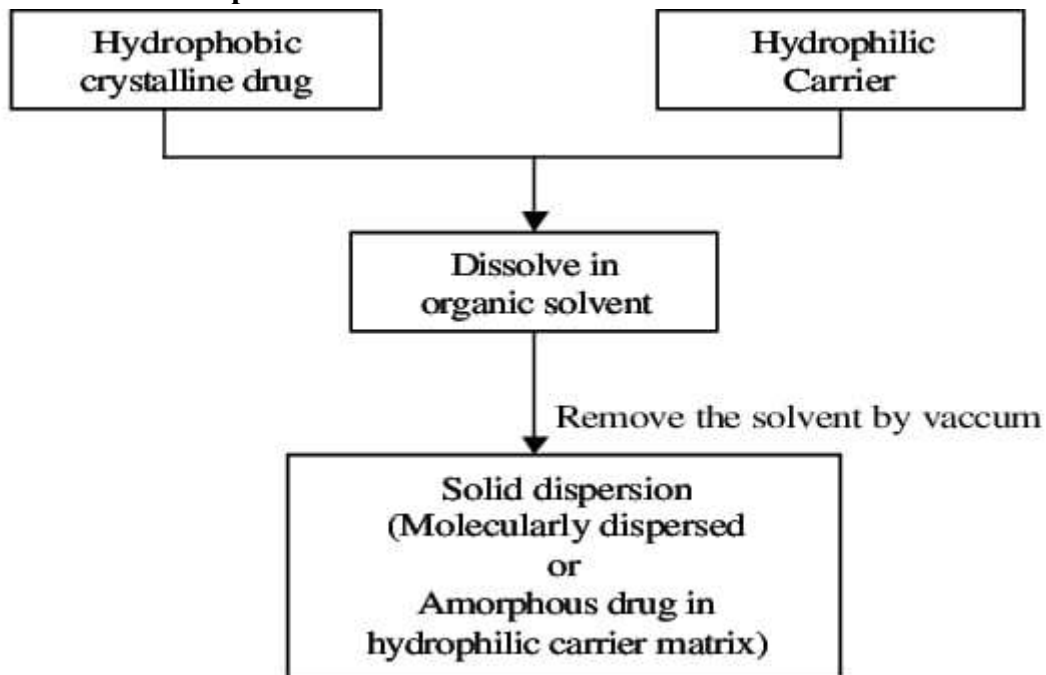
### 5.7 Polymeric alteration

Polymorphs may differ in physicochemical properties such as physical and chemical stability, shelf-life, melting point, vapour pressure, intrinsic solubility, dissolution rate, morphology, density and biological activities as well as bioavailability. It is preferable to develop the most thermodynamically stable polymorph of the drug to assure reproducible bioavailability of the product over its shelf-life under a variety of real-world storage conditions <sup>[24-33]</sup>



<https://www.mdpi.com/1999-4923/14/10/2203#><sup>[34]</sup>

## 6 Preparation of Solid Dispersion –



[https://www.researchgate.net/figure/A-schematic-representation-of-preparation-of-solid-dispersion-by-solvent-evaporation\\_fig1\\_232708790](https://www.researchgate.net/figure/A-schematic-representation-of-preparation-of-solid-dispersion-by-solvent-evaporation_fig1_232708790)<sup>[35]</sup>

## 7 Future Prospects -

Solid dispersion technology continues to evolve rapidly with the introduction of novel polymers, continuous manufacturing, and advanced analytical tools. Integration with nanotechnology, 3D printing, and computational modeling is expected to revolutionize formulation design.

## 8. Future focus areas include-

Development of stable co-amorphous systems.

Exploration of biodegradable and stimuli-responsive polymers.

Application of Quality by Design (QbD) and Artificial Intelligence (AI) for predicting drug-carrier behavior.

Expanding use in personalized medicine and targeted delivery.

## 9. Conclusion -

Solid dispersion is an efficient and reliable strategy for enhancing the solubility and bioavailability of poorly water-soluble drugs. With the help of new polymers and advanced processing technologies, SDT has moved from a laboratory concept to a viable industrial approach. Continuous research and optimization can further improve the stability, scalability, and therapeutic performance of solid dispersion systems, making them a cornerstone of modern formulation science.

## REFERENCES

1. K. Sekiguchi, and N. Obi, "Studies on absorption of eutectic mixture" I. A comparison of the behavior of eutectic mixture of sulfathiazole and that of ordinary sulfathiazole in man," *Chem. Pharm. Bull.*, vol. 9, 1961, pp. 866-872.
2. W. L. Chiou, and S. Riegelman, "Pharmaceutical applications of solid dispersion systems," *J. Pharm. Sci.*, vol. 60, no. 9, 1971, pp. 1281-1302, doi: 10.1002/jps.2600600902.
3. D. M. Brahmkar, and S. B. Jaiswal, *Biopharmaceutics and Pharmacokinetics: A Treatise*, 1st ed., Delhi: Vallabh Prakashan, 1995, pp.171-172.
4. B. Swarbrick, 2002. *Encyclopedia of Pharmaceutical Technology*, 2nd ed., vol.1, New York: Marcel Dekker Inc, pp. 641-647.
5. C. Leunner, and J. Dressman, "Improving drug solubility for oral delivery using solid dispersions," *Eur. J. Pharm. Biopharm.*, vol. 50, no.1, J88uly 2000, pp. 47-60.
6. Iqbal, Z.; Babar, A.; Muhammad, A. Controlled release Naproxen using micronized Ethyl Cellulose by wet-granulation and solid dispersion method. *Drug Dev. Ind. Pharm.* 2002, 28 (2), 129-134.
7. [https://www.researchgate.net/figure/Classification-of-solid-dispersions\\_fig3\\_333144751](https://www.researchgate.net/figure/Classification-of-solid-dispersions_fig3_333144751)
8. Duncan QM Craig. The Mechanism of Drug release from Solid Dispersions and Water soluble polymers. *International Journal of Pharmaceutics*, 2002;231:131 144.
9. Leuner C, Dressman J. Improving drug solubility for oral delivery using solid dispersions. *European Journal of Pharmaceutics and Biopharmaceutics*,2000;50:47 60,
10. Karavas E, Georgarakis E, Sigalas MP, Avgoustakis K, Bikiaris D (2007) Investigation of the release mechanism of a sparingly water-soluble drug from solid dispersions in hydrophilic carriers based on the physical state of drug. particle size distribution, and drug-polymer Interactions. *Eur J Pharm Biopharm*, 66(3): 334-347.
11. Kapoor B, Kaur R Kaur S (2012) Solid Dispersion An Evolutionary Approach for Solubility Enhancement of Poorly Water-Soluble Drugs. *Int J Rec Adv Pharm Res*, 2(2):16
12. Lian Yu Amorphous pharmaceutical solids: preparation, characterization and stabilization Elsevier *Adv Drug Deliv Rev*, 48 (2001), pp. 27-42
13. Tao Feng, Rodolfo Pinal, M. Teresa Carvajal Process induced disorder in crystalline materials: differentiating defective crystals from the amorphous form of griseofulvin *J Pharm Sci*, 97 (2008), pp.

3207-3221

14. Gregory A. Stephenson, Robert A. Forbes, Susan M. Reutzel-Edens Characterization of the solid state: quantitative issues Elsevier Adv Drug Deliv Rev, 48(2001), pp. 67-90
15. Ann Newman, David Engers, Simon Bates, Igor Ivanisevic, Ron C. Kelly, George Zografi Characterization of amorphous API: polymer mixtures using X-ray powder diffraction J Pharm Sci, 97 (2008), pp. 4840-4856
16. Bruno C. Hancock, George Zografi Characteristics and significance of the amorphous state in pharmaceutical systems J Polym Soc, 86 (1) (1997)
17. Birju Shah, Vasu Kumar Kakumanu, Arvind K. Bansal Analytical techniques for quantification of amorphous/crystalline phases in pharmaceutical solids J Pharm Sci, 95 (2006), pp. 1641-1665
18. S. Guinot, F. Leveiller The use of MTDSC to assess the amorphous phase content of a micronised drug substance Int J Pharm, 192 (1999), pp. 63-75
19. [19] S.E. Hogan, G. Buckton The quantification of small degrees of disorder in lactose using solution calorimetry Int J Pharm, 207 (2000), pp. 57-64
20. M. Ohta, G. Buckton Determination of the changes in surface energetics of cefditoren pivoxil as a consequence of processing induced disorder and equilibration to different relative humidities Int J Pharm, 269 (2004), pp. 81-88
21. G. Buckton, P. Darcy Assessment of disorder in crystalline powders—a review of analytical techniques and their application Int J Pharm, 179 (1990), pp. 141-158
22. David E. Bugay Characterization of the solid-state: spectroscopic techniques Adv Drug Deliv Rev, 48 (2001), pp. 43-65
23. Sameer Singh, Raviraj Singh Baghel, Lalit Yadav A review on solid dispersion Int J Pharm Life Sci, 2 (9) (2011), pp. 1078-1095
24. Yogesh S. Thorat, et. al, 2017, solubility enhancement conventional and novel
25. approaches pharmaceuticals science and research, project impact factor, 15: 725-735.
26. Poovi Ganesan, et. al. -2015 Developed methods for characterization and solubility, Asian journal of pharmaceuticals science, 10(5): 433-441.
27. Jain N K, the textbook of Pharmaceutical product development published by CBS publishers and distributors Pvt. Ltd., New Delhi, first edition, 2006; 335.
28. Tripathi K.D., the textbook of essential medical pharmacology, published by Jaypee Brothers Medical Publishers, New Delhi, India, 14th edition, 2010.
29. Kom muru, T. R., et. al, 2001 Self-emulsifying drug delivery system of coenzyme Q10: Formulation development and bioavailability assessment. Int. J. Pharm, 212: 233-246.
30. Nagar Priyanka, et, al. 2011, orally disintegrating tablets: formulation, preparation techniques, and evaluation, Journal of applied pharmaceutical science, 01(04): 35-45.
31. Singh & Sarangi, 2017, solid dispersion a novel approach for enhancement of bioavailability of poorly soluble drugs in oral drug delivery system, Global journal of pharmacy & pharmaceutical science, 3(2): 01-10.
32. Krishnamoorthy V, Nagalingam A, Priya Ranjan Prasad V, Parameshwaran S, George N, et al. (2011) Characterization of Olanzapine-Solid Dispersions. Iran J Pharm Res, 10(1): 13-24.
33. Leuner C, Dressman J (2000) Improving drug solubility for oral delivery using solid dispersions. Eur J Pharm Biopharm, 50(1): 47-60.

34. Aulton ME (1998) *Pharmaceutics: The science of dosage form design*(10th edn). Edinburgh: Churchill Livingstone, 63-64.
35. <https://www.mdpi.com/1999-4923/14/10/2203#>
36. [https://www.researchgate.net/figure/A-schematic-representation-of-preparation-of-solid-dispersion-by-solvent-evaporation\\_fig1\\_232708790](https://www.researchgate.net/figure/A-schematic-representation-of-preparation-of-solid-dispersion-by-solvent-evaporation_fig1_232708790)