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SOLID DISPERSION: A MAGNIFICENT APPROACH TO IMPROVE SOLUBILITY OF POORLY SOLUBLE DRUGS

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ABSTRACT
The solubility conduct of drugs stays perhaps the most testing viewpoints in formulation advancement with the appearance of combinatorial science and high throughput screening, The quantity of inadequately water dissolvable mixtures has significantly expanded. Accordingly, a drug with poor water solubility will commonly show pervasion rate restricted ingestion. Albeit solid arrangements have gigantic potential for improving drug solvency, 40years of exploration have brought about a couple advertised item utilizing this methodology. In this manner a more noteworthy comprehension of disintegration and retention conduct of drug with low water solubility is needed to effectively figure them into more soluble and thus bioavailable drug item if there should be an occurrence of inadequately water-soluble drug. Disintegration might be the rate restricting advance during the time spent drug ingestion. Drug with helpless water solubility have been demonstrated to be capriciously and gradually ingested contrasted and drugs of higher solubility. The different procedures are accessible for improvement of solubility. Solid dispersion is quite possibly the most encouraging methodology for solubility improvement. Solid dispersion alludes to a gathering of solid items comprising of in any event two distinct parts, by and large hydrophilic network and a hydrophobic drug. The framework can be either glasslike or undefined. This article gives an outline of solid dispersion systems, preparation strategies (like fusion or melting method solvent evaporation co-precipitation, etc), characterization and applications of solid dispersions.

KEYWORDS: Bioavailibility, Solid dispersion, fusion method, solvent evaporation, solubility.

INTRODUCTION
Presently a Days, numerous hydrophobic drugs were coming into the market. Significant downsides of these drugs are its bioavailability issues because of poor fluid dissolvability. In this way, it is important to improve its solvency & its penetrability in this manner improving the disintegration, absorption& bioavailability of the drugs.[1] At the point when a drug managed orally, its rate and degree of assimilation relies upon rate and degree of disintegration of dynamic fixing from the dose structure. The drug should disintegrate in gastric liquids and then it saturates through layer. Drugs which are hydrophobic and low porousness show disintegration rate restricted and saturation rate restricted absorption.[2] Different techniques are accessible to upgrade disintegration are salt development, micronisation, expansion of dissolvable or surface dynamic specialists Recent progressions were completing in solid dispersions which is a powerful disintegration upgrading technique. Solid dispersion includes a dispersion of at least one dynamic fixings in an idle transporter or lattice in solid state by various techniques. Readiness of solid dispersion incorporates combination or dissolving technique, dissolvable vanishing strategy, freeze drying, lyophilisation, hot dissolve expulsion etc.[3] As per BCS classification, drugs are ordered by their dissolvability, penetrability and disintegration into class I, II, III and IV. Class II drugs are better drug applicants yet their low dissolvability nature is a limit to their retention and bioavailability. So, it is necessary to improve their disintegration through solid dispersion.[4]

Table 1: Biopharmaceutical Classification System.

BCS Class	Solubility	Permeability
Class I	High	High
Class II	Low	High
Class III	High	Low
Class IV	Low	Low

Merits of Solid Dispersion
1. Improved drug bioavailability and change in water solvency are conceivable.
2. More effective than molecule size decrease methods, since the last have a molecule size decrease limit around 2–5 mm which every now and again isn't sufficient to improve significantly the drug solvency

or then again drug discharge in the small digestive tract.[5]
3. Expansion in disintegration rate and degree of retention and decrease in pre-foundational digestion.
4. Change of fluid type of drug into strong structure.
5. Boundaries, for example, transporter atomic weight and arrangement, drug crystallinity and molecule porosity and wettability, when effectively controlled, can deliver enhancements in bioavailability.[6]

Demerits of Solid Dispersion

1. Changes in crystallinity and a decrease in dissolution rate with maturing.[7]
2. Moisture and temperature have crumbling impact on SD than on actual combinations.
3. Some SD may not loan them to simple dealing with due to tackiness.
4. Disadvantage of SD is their helpless scale-up for the motivations behind manufacturing.[8]

Choice standards for carrier

- The carrier should be freely soluble in water with a high pace of dissolution.
- It should be non poisonous in nature.
- It should be pharmacologically inactive.
- should have heat soundness with a low Liquifying point.
- It should have the option to improve aqueous dissolvability of the drug.
- Economical.[9]

Table 2: Classification of Carriers.

Category	Examples of carriers
Sugars	Dextrose, sucrose, lactose, maltose, sorbitol, mannitol, galactose.
Acids	Citric acids, Succinic Acids.
Polymeric material	Povidone, polyethylene glycol, Hydroxyl propyl methyl cellulose, hydroxyl ethyl cellulose, pectine, galactomannan.
Enteric polymers	Hydroxypropyl methyl cellulose, phthalate, Eudrgit RS.
Surfactants	Polyoxyethylene stearate, Renex, Poloxamer 188, Texofor AIP, deoxycholioic acids, Tweens, spans miscellaneous urea, hydroxyalkylxanthins, urethans

Ideal candidates for solid dispersion

Solid dispersion advances utilize those drugs which are having poor aqueous dissolvability and are porous through the organic layer. Because of their poor dissolvability dissolution gets troublesome and along these lines' retention and bioavailability decreases. Solid dispersions are ideal for the class II drugs of the BCS classification which have poor aqueous solvency yet high layer penetrability.[10]

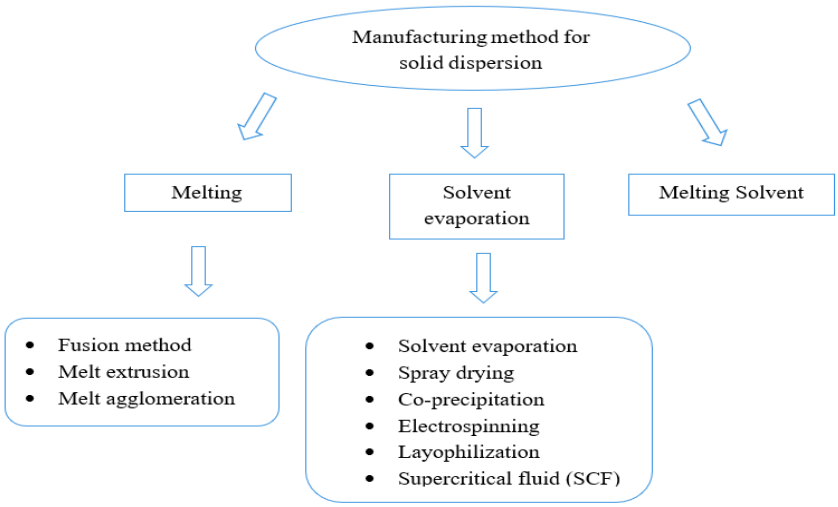

Fig. 1: Method of Preparation of Solid Dispersion.

A. Melting

a. Melting method (fusion method)

In melting or fusion strategy, a physical combination of the drug and a water-soluble carrier is readied, by warming it straightforwardly until it softens. The last solid mass that is gotten is squashed, pounded and sieved. Anyway, substances either the drug or the carrier may deteriorate because of high temperature during the melting interaction. A strategy to defeat this issue could be warming the combination in a fixed compartment or under vacuum or within the sight of dormant gases like nitrogen. The benefit is its effortlessness and conservative nature. The first SD was created by this technique for pharmaceutical applications. This was a combination of sulfathiazole and urea which combined and later cooled to get the last dispersion. The eutectic

composition was picked to accomplish achieve simultaneous crystallization of drug and matrix during cooling.[11-13]

b. Hot melt Extrusion method

In this strategy extruder is used for serious mixing of parts. The segments of the extruder are barrel, hopper, a kneading screw, warming jacket, and a diet.[14] By and large actual combination of both the carrier and drug is brought into the hopper at that point went through screw lastly it is expelled from the die. The upside of the strategy is to get different shapes and plans of the warmed drug-matrix blend into ophthalmic inserts, implants, or oral dosage form.[15] Other benefit like the nonstop production of SD is conceivable so that huge scope production can without much of a stretch be accomplished. The item created by this strategy can without much of a stretch be taken care of on the grounds that any shape can be received.[16] Like different strategies, miscibility of drug and matrix likewise makes an issue. Thermolabile mixtures can be corrupted because of the production of warmth created by the extruder.[17,18]

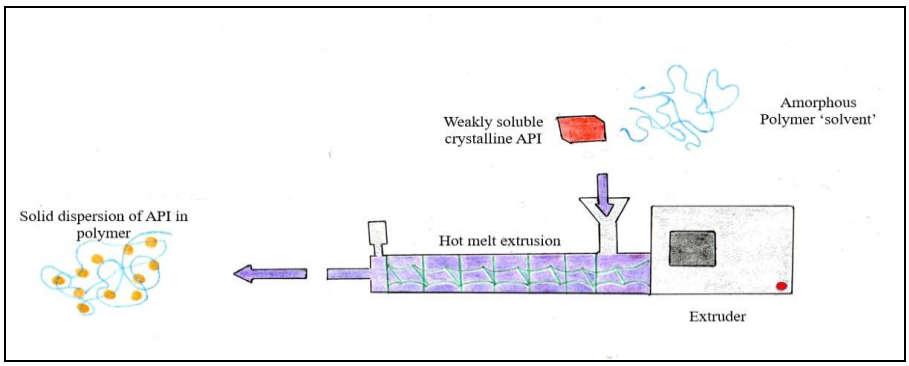

Fig. 2: Hot Melt Extrusion Method.

c. Melt agglomeration process

In this technology, drug and polymer or binder is put in persistent mixing chamber. At that point generates heat dependent on the melting point of drug. at that point drug and inert carrier mixing together and formulates an agglomerates. In this interaction discover particles are melted together and structures an agglomerates. By improving dissolution rates use surfactants moreover. In this technique coming about flowable material gets to builds flow properties.[19-20]

B. Solvent Evaporation Method

In this method, drug and polymer dissolve in common organic solvent and the solvent is evaporated at low temperature. At that point, the subsequent blend is milled through reasonable screens. A portion of the items are not appropriate in this technique on the grounds that solitary single solvent is used in this cycle. In the event that drug is solvent in one solvent and polymer is broken down in one more solvent at the hour of evaporation, solvents are evaporated dependent on boiling point, so drug or polymer solidified immediately dependent on the solvent utilized. It will prompt not complete polymorphic change happens. So, at long last makes a low soluble and low dissolution rate. Subsequently, drug and polymer disintegrate in single solvent as it were. The selection of polymer depends on drug nature and soluble of drug in organic solvent. All in all, solvents utilized ethanol, acetone, isopropyl alcohol, and dichloromethane.[21,22]

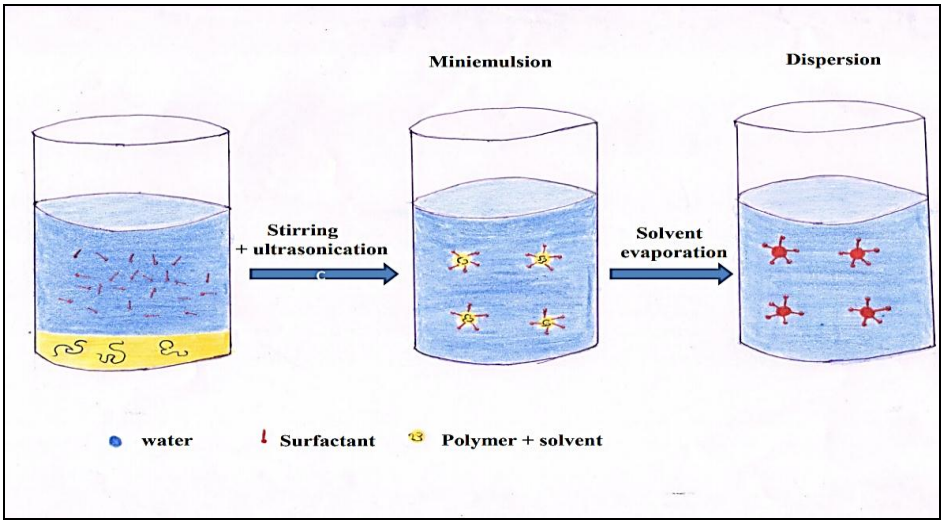

Fig. 3: Solvent Evaporation Method.

a. Spray drying method

Spray drying procedure is perhaps the best and regularly utilized solid dispersion techniques. It is a solitary advance, advantageous, and simple to reproducible cycle. Predominantly rule associated with spray dry procedure is nonstop change of changing material from liquid state over to solid state utilizing a heat drying chamber. In this interaction drug, polymer, at times surfactants, dissolves in solvent and constant spraying in heating chamber where solvent is dissipated and changed over into solid state.[23] In this drying chamber, solvent is sprayed utilizing atomization air. The solvent is changed over into fine droplets because of atomization air and converts solid particles in drying chamber. In this technique, drug and inert carriers were finished dissolve in reasonable solvent. The solvent utilized was single solvent or mixture of solvents dependent on the solubility of drug and inert carriers. Because of the solubility of drug and inert carriers, drug particles changed over its crystalline nature to amorphous nature and it improves the solubility and bioavailability.[24]

b. Co-precipitation method

Co-precipitation is a recognized procedure for expanding the dissolution of ineffectively water dissolvable drugs, in order to consequently improve bioavailability. In this technique nonsolvent is added drop wise to the drug and carrier solution, under constant stirring.[25] In the course of the nonsolvent expansion, the drug and carrier are co-accelerated to frame micro particles. Toward the end, the came about micro particle suspension is filtered and dried40. The necessary amount of polymer and the drug were blended and afterward solvent was added to acquire clear solution. The Solution was first dried under vacuum at room temperature and kept inside hatchery (370c) for 12 hrs. At last it was gone through sieves41.[26]

c. Electrospinning method-

This is a nanotechnology significantly utilized for polymer industry. In this strategy, a liquid stream of drug and polymer solution includes into potential somewhere in the range of 5 and 30 Kv. At the point when electric forces defeat to surface tension of drug and polymer solution at air interface, it includes the solid electrostatic field over a polymer solution to frame a submicron diameter fiber. The fiber diameter totally relies upon dielectric consistent, surface tension, electric field strength, and feeding rate.[27-29]

d. Lyophilization techniques

It is additionally called as freeze-drying in this cycle drug, and inert carrier disintegrates in like manner dissolvable. The solution is frozen and sublimation under vacuum. The frozen state material is pin low air pressure and it changes over in smooth like structure. The upside of this interaction is insignificant thermal stress and risk of stage partition is low. It is an innovation that the drug substance keeps up quality and stable.[30,31]

e. Supercritical fluid (SCF) technology

Utilizing SCF technology to plan solvent free dosage structures. It is a solitary fluid stage over the basic temperature and pressing factor. Carbon dioxide is generally utilized for supercritical fluid as artificially idle nature, non-flammable, and non-harmful. In this interaction, drug particles soluble with supercritical fluid and afterward recrystallization with diminished molecule size according to necessity.The carbon dioxide is utilized for anti-solvent reason.[32-34]

C. Melting solvent method

Melting solvent method is a blend of the two cycles all at once, i.e., melting and solvent evaporation technique. In this innovation, drug is broken up in reasonable solvent subsequent to getting clear solution straightforwardly joined into melt of appropriate carrier. At that point, persistent low heat circled in outside until the total solvent is dissipated. The subsequent residue is the blend of drug and inert carrier at that point solidified it appropriately.[26] The solid material is milled with appropriate screen and mixed with other excipients. The principle benefit of this technique is drugs which are having low melting and high temperature-sensitive drugs which are appropriate in this strategy.[35]

- **Characterization of solid dispersion[36]**

1) Physical Appearance
2) Drug content
3) Dissolution
4) Fourier Transform infra-red (FTIR) Spectroscopy
5) Differential scanning calorimetry (DSC)
6) Scanning electron Microscopy

Physical Appearance

It includes the appearance of solid dispersion by visual examination.

Drug content

It is an analysis of the amount of drug present in solid dispersion. The examine technique for drug is taken and dissolved in appropriate solvents which guarantee that freely soluble in nature and dilute it in fitting fixation. At last drug content estimated by UV or high-performance liquid chromatography (HPLC) strategy.

DISSOLUTION

Dissolution estimates the dissolve component at specific time span. The percentage of drug release at specific time-frame estimated by fundamentally UV or HPLC strategies. The examination is performed at pre-decided volume and RPM at 37±0.5°C. According to USP 7 dissolution apparatus are accessible. Generally, basket or paddle apparatus is utilized for strong oral dosage form.

Fourier transform infra-red (FTIR) spectroscopy

FTIR spectroscopy gives a reasonable picture of interaction between drug to drug and drug to excipients. It estimates intensity over a narrow range of frequencies all at once.

DSC

DSC is a thermoanalytical technique which estimates endothermic and exothermic reactions by expanding temperature progressively. Endothermic reactions measure melting and edges of boiling over. Exothermic reactions measure crystallization and polymerization.

Scanning electron microscopy

It is utilized to discover the images of sample by scanning to surface of material with focused beam. Electron microscopy is useful to morphological structure of material.

Application of solid dispersion[37]

- It expands the solubility of ineffectively solvent drugs and along these lines builds the dissolution rate, which upgrades the absorption and bioavailabilty of the drug.
- For stabilization of the unstable drugs against different deterioration systems like hydrolysis, oxidation and so on.
- Masking of upsetting taste and smell of drugs.
- To stay away from bothersome incompatibilities.
- To get a homogeneous dispersion of a restricted amount of drug in solid state.
- Dispensing of liquid (up to 10%) or gaseous compounds in a solid dosage.
- Formulation of sustained release dosage form.

CONCLUSION

Solubility is the significant models for a drug formulation and its therapeutic adequacy. One of the significant methods to enhance the solubility of drug is Solid dispersion procedure. It is a promising method for the enhancement of bioavailability of poorly fluid soluble drugs. It targets improving the dissolution and absorption of drugs by different methods like fusion, solvent evaporation, and so forth Choice of reasonable carrier and readiness method are legitimate for the better enhancement of bioavailability. Advancement of Self emulsifying carriers and filling of solid dispersion in a hard gelatin capsule as melts improved the benefits of solid dispersion framework. A significant spotlight on the future will turn into the recognizable proof of new surface dynamic carriers and self emulsifying carriers for solid dispersion. Aside from every one of the disadvantages it has promising future in the enhancement of bioavailability of poorly soluble drugs.

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REFERENCES

1. A.Arunachalam, M.Karthikeyan, Kishore Konam, Pottabathula Hariprasad, S.Sethuraman, S.Ashutoshkumar. Solid Dispersion: A review. Current Pharma Research, 2010; 1(1): 83-90.
2. Serajuddin, A.T.M., Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs. J. Pharm. Sci., 1999; 88: 1058-1066
3. Sanjoy Kumar Das, Sudipta Roy, Yuvaraja Kalimuth, Jasmina Khanam, Arunabha Nanda. Solid Dispersion: An approach to enhance the bioavailability of poorly water-soluble drugs, 2011; 1(1): 37-46.
4. Meenakshi Joshi, Gaurav Tiwari, Ruchi Tiwari, Saurav Pandey, Preeti Pandey, A.K.Rai. Solid dispersion: A Technology for the Improvement of Oral Bioavailability of Poorly Soluble Drugs. Review Article Current Pharma Research, 2012.
5. Vasconcelos T, Sarmento B, Costa P. Solid dispersion as a strategy to improve bioavailability of poorly water-soluble drugs. Drug Discovery Today, 2007; 12: 1068-75.
6. Price JC. Polyethylene glycol. In : Wade A, Weller PJ.Ed. Handbook of Pharmaceutical Excipients, Washington DC/London: Ameri Pharm Asso/The Pharm Press, 1994; 355-61.
7. Shah JC, Chen JR, Chow D. Preformulation study of etoposide increased solubility and dissolution rate by solid-solid dispersions. Int J Pharm, 1995; 113: 103-11.
8. Singh S, Baghel RS, Yadav L. A review on solid dispersion. Int J Pharm Life Sci., 2011; 2: 1078-95.
9. Yoshihashi Y. Estimation of physical stability of amorphous solid dispersion using differential scanning calorimetry. J Therm Anal Calorim, 2006; 85: 689-92.
10. Eriksson HJC, Hinrichs WLJ, Veen B, Somsen GW, Jong GJ, Frijlink HW. Investigations into the stabilization of drugs by sugar glasses: I, Tablets prepared from stabilized alkaline phosphateise. Int J Pharm, 2002; 249: 59-70.
11. Singh J, Walia M, Harikumar SL. Solubility enhancement by solid dispersion method: a review. J Drug Delivery Ther, 2013; 3: 148-55.
12. Narang A, Shrivastava A. Melt extrusion solid dispersion technique. Drug Dev Ind Pharm, 2002; 26: 111-5.
13. Gandhi S, Chandrul K. Pharmaceutical solid polymorphism in abbreviated new drug applications-a regulatory perspective. J Chem Pharm Res., 2011; 3: 6-17.
14. Ingle US, Gaikwad PD, Banker VH, Pawar SP. Review on solid dispersion: A dissolution enhancement technique. Int J Res Ayurveda Pharm, 2011; 2: 751-7.
15. Rajmalle RK, Zameeruddin M, Jadhav SB, Kadam VS, Bharkad VB. Recent approaches solubility and dissolution enhancement of atorvastatin: a review. World J Pharm Sci., 2014; 3: 534-44.
16. Allawadi D, Singh N, Singh S, Arora S. Solid dispersions: a review on drug delivery system and solubility enhancement. Int J Pharm Sci Res., 2013; 4: 2094-105.

17. Rankell AS, Liberman HA, Schiffmann RF, Lachman L, Liberman HA, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. Bombay: Varghese Publishing house, 1987; 61.
18. Serajuddin A. Solid dispersion of poorly water-soluble drugs: early promises, subsequent problems, and recent breakthroughs. J Pharm Sci., 1999; 88: 1058-66.
19. Dixit AK., Singh RP; solid dispersion – A strategy for improving the solubility of poorly soluble drugs; IJRPBS, 2012; 3(2); 960-966.
20. Thakur et al; A review on solid dispersion; World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(9): 173-187.
21. Hasegawa S, Hamaura T, Furuyama N, Kusai A, Yonemochi E, Terada K, *et al*. Effects of water content in physical mixture and heating temperature on crystallinity troglitazone-PVP K-30 solid dispersions prepared by closed melting method. Int J Pharm, 2005; 302: 103-12.
22. Yoshihashi Y. Estimation of physical stability of amorphous solid dispersion using differential scanning calorimetry. J Therm Anal Calorim, 2006; 85: 689-92.
23. Chauhan B, Shimpi S, Paradkar A. Preparation and evaluation of glibenclamide-polyglycolized glycerides solid dispersion with silicon dioxide by spray drying technique. Eur J Pharm Sci., 2005; 26: 219-30.
24. Seo A, Schaefer T. Melt agglomeration with polyethylene glycol beads at a low impeller speed in a high shear mixer. Eur J Pharm Biopharm, 2001; 52: 315-25.
25. Vilhelmsen T, Eliasen H, Schaefer T. Effect of melt agglomeration process on agglomerates containing solid dispersion. Int J Pharm, 2005; 303: 132-42.
26. Pouton CW. Formulation of poorly water-soluble drugs for oral administration:Physicochemical and physiological issues and the lipid formulation classification system. Eur J Pharm Sci., 2006; 29: 278-87.
27. Dixit ND, Niranjan SK. A review: Solid dispersion. World J Pharm Sci., 2014; 3: 238-57.
28. Singh J, Walia M, Harikumer SL. Solubility enhancement by solid dispersion method: A review. J Drug Deliv Ther, 2013; 3: 148-55.
29. van Drooge DJ, Hienrichs WL, Visser MR, Frijlink HW. Characterization of the molecular distribution of drugs in glassy solid dispersions at the nano-meter scale, using differential scanning calorimetry and gravometric water vapour sorption techniques. Int J Pharm, 2006; 310: 220-9.
30. Hohman MM, Shin M, Rutledge G, Brennera MP. Electrospinning and electrically forced jets. II. Applications. Phys Fluids, 2001; 13: 2221-36.
31. Neamnark A, Rujiravanit R, Supaphol P. Electrospining of hexanoyl chitosan. Carbohydrate polymers. Int J Pharm 2006; 66: 298-305.
32. Zhang W, Yan E, Huang Z, Wang C, Xin Y, Zhao Q, *et al.* Preparation and study of PPV/PVA nanofibers via electrospinning PPV precursor alcohol solution. Eur Poly, 2007; 43: 802-97.
33. Taki S, Badens E, Charbit G. Controlled release system formed by supercritical anti-solvent coprecipitation of a herbicide and a biodegradable polymer. J Supercrit Fluids., 2001; 21: 61-70.
34. Dohrn R, Bertakis E, Behrend O, Voutsas E, Tassios D. Melting point depression by using supercritical CO_2 for a novel melt dipersionmicronization process. J Mol Liq., 2007; 131-2: 53-9.
35. Yadav PS, Kumar V, Singh UP, Bhat HR, Mazumder B. Physicochemical characterization and in vitro dissolution studies of solid dispersions of ketoprofen with PVP K30 and d-mannitol. Saudi Pharm J., 2013; 21: 77-84.
36. Ali W, Williams AC, Rawlinson CF. Stochiometrically governed molecular interactions in drug: Poloxamer solid dispersions. Int J Pharm, 2010; 391: 162-8.
37. Walker SE, Ganley JA, Bedford K and Eaves T J.Pharm. Pharmacol., 1980; 32: 389-393.