



**RECENT RESEARCH ON SOLID DISPERSIONS - A REVIEW**

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**ABSTRACT**

Solid dispersion technologies are particularly promising for improving the oral absorption and bioavailability of BCS class II drugs. Solid dispersion is a molecular dispersion of an insoluble drug in a hydrophilic polymer/carrier at solid state. When the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug releases as fine colloidal particles. The resulting enhanced surface area produces higher dissolution rate and bioavailability of poorly water-soluble drugs. Literature on solid dispersions, types, methods of preparation, characterization and applications along with recent research on solid dispersions are reviewed in this article.

**Key words:** Solid dispersions, Recent research, Review

**INTRODUCTION**

About 95% of all new potential therapeutic drugs (APIs) exhibit low and variable oral bioavailability due to their poor aqueous solubility at physiological pH and consequent low dissolution rate. These drugs are classified as class II drugs under BCS with low solubility and high permeability characters and pose challenging problems in their pharmaceutical product development process. Several techniques<sup>1</sup> such as micronization, cyclodextrin complexation, use of surfactants and solubilizers, solid dispersion in water soluble and dispersible carriers, use of salts, prodrugs and polymorphs which exhibit high solubility, micro emulsions and self-emulsifying micro and nano disperse systems have been used to enhance the solubility, dissolution rate and bioavailability of BCS class II poorly soluble drugs. Among the various approaches, solid dispersion<sup>2, 3</sup> in water soluble and water dispersible excipients is a simple, industrially useful approach for enhancing the solubility, dissolution rate and bioavailability of poorly soluble drugs.

**Solid Dispersions:**

Chiou and Riegelman defined<sup>4</sup> solid dispersion as “a dispersion involving the formation of eutectic mixtures of drugs with water soluble carriers by melting of their physical mixtures”. The term solid dispersion refers to the dispersion of one or more active ingredient in an inert carrier or matrix at solid state prepared by melting (fusion), solvent, or the melting solvent method. Once the solid dispersion was exposed to aqueous media & the carrier dissolved, the drug was released as very fine, colloidal particles. The term solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug. The matrix can be either crystalline or amorphous. The dispersion of a drug or drugs in a solid diluent or diluents by traditional mechanical mixing is not included in this category<sup>5</sup>. Therefore, based on their molecular arrangement, different types of solid dispersions (SDs) can be distinguished.

**TYPES OF SOLID DISPERSIONS<sup>6</sup>:**

**Eutectic Mixtures:** A simple eutectic mixture consists of two compounds which are completely miscible in the liquid state but only to a very limited extent in the solid state. It is prepared by rapid solidification of fused melt of

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two components that show complete liquid miscibility but negligible solid-solid solution.

**Solid Solutions:**

Solid solutions are comparable to liquid solutions, consisting of just one phase irrespective of the number of components. In the case of solid solutions, the drug's particle size has been reduced to its absolute minimum viz. the molecular dimensions and the dissolution rate is determined by the dissolution rate of the carrier. According to their miscibility two types of solid solution are known.

**Continuous Solid Solutions:** In a continuous solid solution, the components are miscible in all proportions. Theoretically, this means that the bonding strength between the two components is stronger than the bonding strength between the molecules of each of the individual components. Solid solutions of this type have not been reported in the pharmaceutical literature to date.

**Discontinuous Solid Solutions:** In the case of discontinuous solid solutions, the solubility of each of the components in the other component is limited. A typical phase diagram, show the regions of true solid solutions. In these regions, one of the solid components is completely dissolved in the other solid component. Below a certain temperature, the mutual solubilities of the two components start to decrease.

According to the way in which the solvate molecules are distributed in the solvendum the two type of solid solution are known.

**Substitutional Crystalline Solutions:** A substitutional crystalline solid dispersion is a type of solid solutions which have a crystalline structure, in which the solute molecules substitute for solvent molecules in the crystal lattice. Substitution is only possible when the size of the solute molecules differs by less than 15% or so from that of the solvent molecules.

**Interstitial Crystalline Solid Solutions:** In interstitial solid solutions, the dissolved molecules occupy the interstitial spaces between the solvent molecules in the crystal lattice. As in the case of substitutional crystalline solid solutions, the relative molecular size is a crucial criterion for classifying the solid solution type. In the case of interstitial crystalline solid solutions, the solute molecules should have a molecular diameter

that is no greater than 0.59 of the solvent molecule's molecular diameter. Furthermore, the volume of the solute molecules should be less than 20% of the solvent.

**Amorphous Solid Solutions:**

In an amorphous solid solution, the solute molecules are dispersed molecularly but irregularly within the amorphous solvent. Using griseofulvin in citric acid, Chiou and Riegelman were the first to report the formation of an amorphous solid solution to improve a drug's dissolution properties. Other carriers urea and sugars such as sucrose, dextrose and galactose, organic polymers such as polyvinylpyrrolidone (PVP), polyethylene glycol and various cellulose derivatives have been utilized for this purpose.

**Glass Solutions and Glass Suspensions:**

A glass solution is a homogenous, glassy system in which a solute dissolves in a glassy solvent. The term glass can be used to describe either a pure chemical or a mixture of chemicals in a glassy or vitreous state. The glassy or vitreous state is usually obtained by an abrupt quenching of the melt. It is characterized by transparency & brittleness below the glass transition temperature.

**Carriers for Solid Dispersions<sup>7</sup>:**

A carrier should meet the following criteria to be suitable for increasing the dissolution rate of poorly soluble drugs.

1. Freely water-soluble with intrinsic rapid dissolution properties.
2. Non-toxic and pharmacologically inert.
3. Heat stable with a low melting point for the melt method.
4. Soluble in a variety of solvents and pass through a vitreous state upon solvent evaporation for the solvent method.
5. Able to preferably increase the aqueous solubility of the drug and
6. Chemically compatible with the drug and not form a strongly bonded complex with the drug.

**First generation carriers<sup>8</sup>:** Example: Crystalline carriers: Urea, Sugars, Organic acids.

**Second generation carriers<sup>9</sup>:** Example: Fully synthetic polymers include povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates. Natural product based polymers are mainly composed by cellulose

derivatives, such as HPMC, ethyl cellulose or hydroxypropylcellulose or starch derivatives, like cyclodextrine.

**Third generation carriers<sup>10</sup>:** Example: Surface active self emulsifying carriers: Poloxamer 408, Tween 80, and Gelucire 44/14

**Selection of Solvents<sup>10</sup>:**

Solvent to be included for the formulation of solid dispersion should have the following criteria:

1. Both drug and carrier must be dissolved.
2. Toxic solvents to be avoided due to the risk of residual levels after preparation e.g. chloroform and dichloromethane.
3. Ethanol can be used as alternative as it is less toxic.
4. Water based systems are preferred.
5. Surfactants are used to create carrier drug solutions but as they can reduce glass transition temperature, so care must be taken in to consideration.

**METHODS OF PREPARATION OF SOLID DISPERSIONS:**

**Fusion method:**

The first solid dispersions created for pharmaceutical applications were prepared by the fusion method. The fusion process is technically the less difficult method of preparing dispersions provided the drug and carrier are miscible in the molten state. This process employs melting of the mixture of the drug and carrier in metallic vessel heated in an oil bath, immediately after fusion, the sample are poured onto a metallic plate which is kept at ice bath. A modification of the process involves spray congealing from a modified spray drier onto cold metal surface. Decomposition should be avoided and is affected by fusion time and rate of cooling. The fusion method is sometimes referred to as the melt method, which is correct only when the starting materials are crystalline. Therefore, the more general term fusion method is preferred.

The main advantage of direct melting method is its simplicity and economy. In addition melting under vacuum or blanket of an inert gas such as nitrogen may be employed to prevent oxidation of drug or carrier<sup>11</sup>. Firstly, a major disadvantage is that the method can only be applied when drug and matrix are compatible and when they mix well at the heating

temperature. When drug and matrix are incompatible two liquid phases or a suspension can be observed in the heated mixture which results in an inhomogeneous solid dispersion<sup>11</sup>.

**Solvent method:**

The first step in the solvent method is the preparation of a solution containing both matrix material and drug. The second step involves the removal of solvent resulting in formation of a solid dispersion. Mixing at the molecular level is preferred, because this leads to optimal dissolution properties. Using the solvent method, the pharmaceutical engineer faces two challenges. The first challenge is to mix both drug and matrix in one solution, which is difficult when they differ significantly in polarity. To minimize the drug particle size in the solid dispersion, the drug and matrix have to be dispersed in the solvent as fine as possible, preferably drug and matrix material are in dissolved state in solution and solid dispersions are obtained<sup>11</sup>.

The main advantage of the solvent method is that thermal decomposition of drugs or carriers can be prevented because of the low temperature required for evaporation of organic solvents<sup>6</sup>. The disadvantages include the higher cost of preparation, the difficulty in completely removing liquid solvent and possible adverse effect of the supposed negligible amount of the solvent on the chemical stability of drug are some of the disadvantages of this method<sup>11</sup>.

**Supercritical fluid methods:**

Supercritical fluid methods are mostly applied with carbon dioxide, which is used as either a solvent for drug and matrix or as an anti-solvent. When supercritical CO<sub>2</sub> is used as solvent, matrix and drug are dissolved and sprayed through a nozzle, into an expansion vessel with lower pressure and particles are immediately formed. The adiabatic expansion of the mixture results in rapid cooling. This technique does not require the use of organic solvents and since CO<sub>2</sub> is considered environmentally friendly, this technique is referred to as 'solvent free'. The technique is known as Rapid Expansion of Supercritical Solution<sup>11</sup>.

The supercritical anti-solvent rapidly penetrates into the droplets, in which drug and matrix become supersaturated, crystallize and form particles. The general term for this process

is precipitation with compressed anti-oven. More specific examples of PCA are Supercritical Anti Solvent when supercritical CO<sub>2</sub> is used, or Aerosol Solvent Extraction System, and Solution. Enhanced Dispersion by Supercritical fluids<sup>11</sup>. Usually organic solvents like dichloromethane or methanol have to be applied to dissolve both drug and matrix which are more in cost<sup>11</sup>.

#### **Melting solvent method:**

In this method drug is first dissolved in a suitable liquid solvent. Solution is then incorporated directly into the melt of polyethylene glycol obtainable below 70°C, without removing the liquid solvent. It has been shown that 5-10% (w/w) of liquid compound could be incorporated into polyethylene glycol 6000 without significant loss of its solid property<sup>11</sup>.

In this method that thermal decomposition of drugs or carriers can be prevented because of the low temperature required for evaporation of organic solvents<sup>11</sup>. As the practical point of view, the melting-solvent method is limited to drugs with a low therapeutic dose, e.g., below 50mg. Moreover, it is possible that the selected solvent or dissolved drug may not be miscible with the melt of polyethylene glycol. The feasibility of the method has been demonstrated on spironolactone polyethylene glycol 6000 system<sup>11</sup>.

#### **Lyophilization Technique:**

Lyophilization has been thought of a molecular mixing technique. The drug and carrier are co dissolved in a common solvent, Frozen and sublimed to obtain a lyophilized molecular dispersion<sup>11</sup>.

#### **Melt agglomeration method:**

This technique has been used to prepare where in the binder acts as a carrier. In addition, are prepared either by Heating binder, drug and excipient to a temperature above the melting point of the binder or by spraying a dispersion of drug in molten binder on the heated excipient by using a high shear mixer-35. A rotary processor has been shown to be alternative equipment for melt agglomeration. The rotary processor might be preferable to the high melt agglomeration because it is easier to control the temperature and because a higher binder content can be incorporated in the agglomerates. In

addition the melt in procedure also results in homogenous distribution of drug in agglomerate. Larger particles results in densification of agglomerates while fine particle cause complete adhesion. The mass to bowl shortly after melting attributed to distribution and coalescence of the fine particles<sup>11</sup>.

#### **Electrospinning:**

Electrospinning is a process in which solid fibers are produced from a polymeric fluid stream solution or melt delivered through millimeter scale nozzles. This process involves the application of a strong electrostatic field over a conductive capillary attaching to a reservoir containing a polymer solution or melt and a conductive collection screen. Upon increasing the electrostatic field strength up to but not exceeding a critical value, charge species accumulated on the surface of a pendant drop destabilize the hemispherical shape into a conical shape. Beyond the critical value, a charged polymer jet is ejected from the apex of the cone.

The ejected charged jet is then carried to the collection screen via the electrostatic force. The Coulombic repulsion force is responsible for the thinning of the charged jet during its trajectory to the collection screen. The thinning down of the charged jet is limited by the viscosity increase, as the charged jet is dried<sup>11</sup>. This technique has tremendous potential for the preparation of nanofibres and controlling the release of biomedicine. Process is simplest, the cheapest. This technique can be utilized for the preparation of solid dispersions in future<sup>11</sup>.

#### **Gel entrapment technique:**

Carrier which have tendency to swell is dissolved in suitable organic solvent to form a clear and transparent gel. The drug is then dissolved in gel by sonication for few minutes. Organic solvent is evaporated under vacuum. Solid dispersions are reduced in size by glass mortar and sieved.<sup>12</sup>

#### **Direct capsule filling:**

Direct filling of hard gelatin capsules with the liquid melt of solid dispersions avoids grinding-induced changes in the crystallinity of the drug<sup>13</sup>. This molten dispersion forms a solid plug inside the capsule on cooling to room temperature, reducing cross contamination and operator exposure in a dust-free environment, better fill weight and content uniformity was

obtained than with the powder-fill technique. However, PEG was not a suitable carrier for the direct capsule-filling method as the water-soluble carrier dissolved more rapidly than the drug, resulting in drug-rich layers formed over the surface of dissolving plugs, which prevented further dissolution of the drug<sup>14</sup>.

**Solvent evaporation method:**

The solvent-based process uses organic solvent to dissolve and intimately disperse the drug and carrier molecule. Identification of a common solvent for both drug and carrier can be problematic, and complete solvent removal from the product can be a lengthy process. Moreover suitable alterations in the concentrations used for solvent evaporation may lead to large changes in the product performance. In addition large volumes of solvents are generally required which can give rise to toxicological problems. Many investigators studied solid dispersions of Meloxicam, Naproxen, Rofecoxib, Felodipine, Atenolol, and Nimesulide using solvent evaporation techniques. These findings suggest that the above-mentioned technique can be employed successfully for improvement and stability of solid dispersions of poor water soluble drugs. Bhanbhun M Suhagic suggested a method for preparation of solid dispersions of etorocoxib employing solvent evaporation process where in carrier is poly ethyl glycol (PEG) and PVP along with drug were dissolved in 2-propanol to get a clear solution and solvent was evaporated. The prepared solid dispersions exhibited improved dissolution attributed to decreased crystallinity, improved wetting and improved bioavailability.

**Extruding method:**

The extruding method was originally designed as an extraction casting method for polymer alloys in plastic industry, is now used to process cereals and functionalize food materials, such as tissue products from animal proteins<sup>15</sup>. Hot melt extrusion approach represent the advantageous mean of preparation of SD(s) by using the twin screw hot melt extruder where only thermo stable components are relevant<sup>16</sup>. The extruder consists of a hopper, barrel, a die, a kneading screw and heaters. The physical mixture is introduced into the hopper that is forwarded by feed screw and finally is extruded from the die<sup>17</sup>. The effect of

screw revolution speed and water content on the preparation of SD(s) should be investigated, since these parameters have profound impact on the quality of SD(s). Nakamichi et al<sup>18</sup>, studied that presence of kneading paddle element of screw results in super saturation on dissolution testing while slow revolution rate of screw and addition of the suitable amount of water increased rate of dissolution although no super saturation occurred.

**Spray drying:**

The manufacture of milk powder was one of the first applications of spray drying when the method was developed in 1920. Today, spray drying finds great utility in pharmaceutical industry because of the rapid drying and specific characteristics such as particle size and shape of the final product. In addition, it is simple and cost effective, as it is 30-50 times less expensive than freeze-drying. It is an established method that is initiated by atomizing suspensions or solutions into fine droplets followed by a drying process, resulting solid particles. The process allows production of fine, dust free powder as well as agglomerated one to precise specifications. The operating conditions and dryer design depends upon the drying characteristics of the product and require powder specifications<sup>19,20</sup>. Rankell et al. prepared SD(s) of loperamide with PEG 6000 by this technique wherein solutions containing different concentrations of PEG 6000 and constant amount of loperamide were spray dried. Chouhan et al<sup>21</sup> studied the suitability of this technique for preparation of SD(s) of glibenclamide polyglycolized glycerides.

**Physical Mixture Method<sup>22</sup>:**

The physical mixtures were prepared by weighing the calculated amount of drug and carriers and then mixing them in a glass mortar by triturating. The resultant physical mixtures were passed through 44-mesh sieve and stored in desiccators until used for further studies.

**Co-Grinding Method:**

The calculated amounts of drug and carriers were weighed and mixed together with one ml of water. The damp mass obtained was passed through a 44-mesh sieve; the resultant granules were dispersed in Petri dishes and dried at 60°C under vacuum, until a constant weight was obtained.

### **Kneading method<sup>23</sup>:**

A mixture of accurately weighed drug and carrier is wetted with solvent and kneaded thoroughly for some time in a glass mortar. The paste formed is dried and sieved.

### **Evaluation & Characterization of Solid Dispersions:**

#### **1. Physical appearance:**

Includes visual inspection of solid dispersions.

#### **2. Percent Practical Yield<sup>24</sup>:**

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus its help in selection of appropriate method of production. SDs were collected and weighed to determine practical yield (PY) from the following equation  $PY (\%) = \frac{[\text{Practical Mass (Solid dispersion)}]}{[\text{Theoretical Mass (Drug+ Carrier)}]} \times 100$

#### **3. Drug content<sup>25</sup>:**

In this method definite amount of solid dispersion is taken and dissolved in a suitable solvent in which drug is freely soluble, then after appropriate dilution, concentrations are measured by UV Spectro-photometry.

#### **4. Aqueous solubility studies<sup>26</sup>:**

It was carried out to determine solubility drug alone in aqueous medium and also in presence of carriers. This was done by dissolving excess drug in different flasks containing different concentration of carrier in distilled water. The flasks were shaken thoroughly for 6 hours and kept aside for 24 hours. The suspensions were filtered, diluted suitably and absorbance was measured at suitable wavelength.

#### **5. Dissolution Studies<sup>27</sup>:**

Dissolution studies are the most significant evaluation parameter for any solid dosage form. Dissolution study is carried out to determine the rate and extent of dissolution. The dissolution studies of solid dispersion were performed in 500ml at 37°C by the USP- II paddle apparatus at 75 rpm. Drug was dispersed in medium. Aliquots of 5 ml from the dissolution medium were withdrawn at different time interval and replenished by an equal volume of fresh dissolution medium. The samples were filtered through Whatman filter paper and analyzed for drug contents by measuring the absorbance at suitable wavelength using Shimadzu 1700 UV/visible Spectrophotometer.

### **6. Drug carrier compatibility<sup>28</sup>:**

This study is done to determine the interactions if any between the drug and carrier and to determine the formation of inclusion complexes. Methods used for this purpose are:

#### **(a) Fourier Transform Infra Red (FTIR) Spectroscopy:**

Infra red studies were carried out to rule out interaction between drug and carrier used in formulation of solid dispersion by potassium bromide disc method using Infra red spectrophotometer.

#### **(b) Differential Scanning Calorimetry:**

Differential scanning calorimetry was performed by Differential scanning calorimeter 60 Shimadzu to obtain suitable thermograms. The accurately weighed sample was placed in an aluminium pan and an empty aluminium pan was used as reference. The experiment was performed under nitrogen flow, at a scanning rate 300°C/min. in range of 50-3500°C.

#### **(c) Powder X-ray diffraction:**

The detection of crystalline phases in mixed systems can be analyzed by powder X-ray diffraction. However, too much crystallinity causes brittleness. The crystallinity parts give sharp narrow diffraction peaks and the amorphous component gives a very broad peak. The ratio between these intensities can be used to calculate the amount of crystallinity in the material.

#### **Mechanisms of Increased Dissolution Rate<sup>29</sup>:**

The main reasons postulated for the observed improvements in dissolution of these systems are as follows:

##### **a) Reduction of particle size:**

In case of glass, solid solution and amorphous dispersions, particle size is reduced to a minimum level. This can result in an enhanced dissolution rate due to an increase in both the surface area solubilization.

##### **b) Solubilization effect:**

The carrier material, as it dissolves may have a solubilization effect on the drug. This was shown to be the case for acetaminophen and chlorpropamide in urea as well as for numerous other drugs.

##### **c) Wettability and dispersibility:**

The carrier material may also have an enhancing effect on the wettability and dispersibility of the drug in the dissolution

media. This should retard any agglomeration or aggregation of the particles, which can slow the dissolution process.

**d) Meta stable Forms:**

Formation of metastable dispersions with reduced lattice energy would result in faster dissolution rates. It was found that the activation energies for dissolution for furosemide was 17 K Cal per mol, whereas that for 1:2 furosemide: PVP coprecipitate was only 7.3 K Cal per mol.

**Pharmaceutical Applications of Solid Dispersions:**

The pharmaceutical applications of solid dispersions are numerous. They may be employed

1. To enhance the absorption of drugs.
2. To obtain a homogeneous distribution of a small amount of drug in solid state.
3. To stabilize unstable drugs and protect against decomposition by processes such as hydrolysis, oxidation, racemization, photooxidation etc.
4. To dispense liquid or gaseous compounds.
5. To formulate fast release priming dose in a sustained release dosage form.
6. To formulate sustained release preparation of soluble drugs by dispersing the drug in poorly soluble or insoluble carrier.
7. To reduce side effects- (a) the binding ability of drugs for example to the erythrocyte membrane is decreased by making its inclusion complex, (b) the damage to the stomach mucous membranes by certain non-steroidal anti-inflammatory

drugs can be reduced by administration as an inclusion compound.

8. To mask unpleasant taste and smell. The very unpleasant taste of anti-depressant famoxetine hindered the development of liquid oral formulations. The bitter taste was greatly suppressed when the solid complex of famoxetine was formulated as aqueous suspension.
9. To convert liquid compounds into formulations. Liquid drugs can be manufactured as solid drug formulations such as powders, capsules or tablets e.g., unsaturated fatty acids, essential oils, nitroglycerin, benzaldehyde, prostaglandin, clofibrate etc.

**Recent Research on Solid Dispersions:**

Several studies are reported on preparation and evaluation of solid dispersions of poorly soluble drugs for enhancing their solubility, dissolution rate and bioavailability in their formulation development. A summary of recent research on solid dispersions is given in Table 1.

**CONCLUSION**

BCS class II drugs with low solubility and high permeability characters pose challenging problems in their pharmaceutical product development process. Solid dispersion is a promising technology for formulation development of these poorly soluble drugs. Though several studies are reported on solid dispersions, intensive research in this area is still needed for making the technology applicable to industry needs.

**Table 1: Summary of Recent Research on Solid Dispersions**

S. No	Drug (Therapeutic Category)	Technique/ Method Used	Polymers/ Carriers Used	Result	Reference
1	Terbinafine Hydrochloride (antiviral)	Solid dispersion (simple trituration)	PEG-6000, PVP K30	Better release.	30
2	Terbinafine hydrochloride (antiviral)	Fusion method	Mannitol, PEG.	Increase the dissolution rate.	31
3	Simvastatin (hyper lipidemia)	Evaporation and kneading method	PEG-4000, PVP K30	Enhance the dissolution rate of poorly soluble drug.	32
4	Curcumin (antibiotic)	Hot melt, solvent evaporation methods	PEG-6000, PEG-4000, PVP K30, MCC.	Maximum dissolution in ten minutes (98.78%).	33
5	Cefixime (antibiotic)	Solvent evaporation method.	Guar gum	Improved solubility and dissolution rate.	34
6	Verapamil hydrochloride(antihypertension)	Solid dispersion.	Eudragit-RSPO, their combinations	HPMC K <sub>4</sub> M acts as a better release retardant.	35
7	Simvastatin (hypercholeemia)	Solid dispersion.	PEG-(6000, 12000, 20000).	Influence of PEG molecular weight on drug dissolution rate.	36

8	Ketaconazole (antifungal)	Melt-fusion and solvent evaporation.	Pluronic F127, PVP K30.	Rate of dissolution was improved.	37
9	Aceclofenac (NSAID)	Dropping method.	PEG-8000, NaOH and KH <sub>2</sub> PO <sub>4</sub> .	Fast dissolution rate.	38
10	Hydrochlorothiazide (diuretic)	Solvent evaporation technique	HPMC C5 and PVP K30.	Improvement of solubility profile.	39
11	Glibenclamide (antidiabetic)	Solvent evaporation technique	PEG6000, PVP K30 and poloxamer.	Better dissolution profile than commercial tablets.	40
12	Piroxicam (NSAID)	Spray drying.	HPMC K <sub>100</sub> m.	Improved bioavailability	41
13	Simvastatin (hyperlipidemic)	Solid dispersion.	Xanthan gum, guar gum, Karaya.	Enhanced solubility.	42
14	Aceclofenac (NSAID)	Solid dispersion and solvent wetting.	Lactose and corn starch.	Increased dissolution rate.	43
15	Carbamazepine (antidepressant)	Solid dispersion.	HPMC, croscopolvidone	Enhanced solubility.	44
16	Olanzapine (antidepressant)	Solid dispersion	Pregelatinised starch, sodium starch glycollate	Increase in aqueous solubility and dissolution parameters than that of the pure drug.	45
17	Naproxen sodium. (NSAID)	Solid dispersion.	PEG (4000, 6000) and urea.	Faster dissolution rate.	46
18	Meloxicam (NSAID)	Co-grinding and solvent evaporation.	PEG6000 and PVP.	Improved dissolution.	47
19	Melitracen (antidepressant)	Solvent evaporation and kneading method	PEG 6000, PEG 4000 and $\beta$ -CD	Enhanced solubility and dissolution rate and hence better patient compliance.	48
20	Lacidipine (antihypertensive)	Physical mixture and solid dispersion.	PEG 6000, PEG 4000, HEC, DX.	Rate of dissolution was improved.	49
21	Itraconazole (antifungal)	Super saturation and spray drying.	Polyvidone K25, PVP A 64, HPMC2910E5, PEG 6000 and 100,000; Eudragit E100; Kollicoat IR, Poloxamer (188,407).	Enhanced solubility and dissolution rate.	50
22	Irbesartan. (antihypertensive)	Fusion and co-solvent methods	PVP, PEG 6000.	Rate of dissolution was improved.	51
23	Glipizide. (antidiabetic)	Solid dispersion, solvent evaporation.	Crosscarmellose sodium, HPMC,	Increases in the polymer concentration increases the drug release from solid dispersions.	52
24	Gliclazide. (antidiabetic)	Physical mixture, freeze dried method	Poloxamer 407	Rapid solubility and dissolution.	53
25	Gliclazide. (antidiabetic)	Solid dispersion, physical mixture	PEG 8000.	Increased solubility.	54
26	Furosimide (antihypertensive)	Solid dispersion	Cross povidone	Enhanced dissolution rate.	55
27	Acyclovir (antiviral)	Solid dispersion	PEG -6000	Enhance the solubility and dissolution rate	56
28	Acyclovir (antiviral)	Solid dispersion, physical mixture, inclusion method.	PEG -6000 and PVP K30 and $\beta$ -CD	Improve the dissolution characteristics and better bioavailability.	57
29	Aceclofenac (NSAID)	Solid dispersion.	Lactose, mannitol and urea.	Increase in the dissolution rate.	58

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