Formulation, Physicochemical Evaluation, and Dissolution Studies of Carbamazepine Solid Dispersions

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ABSTRACT

Carbamazepine is a water-insoluble antiepileptic drug. Being a BCS class-II drug, its absorption is dissolution rate limited. Solid dispersions were prepared to enhance the dissolution rate of the drug. Crospovidone and croscarmellose sodium were used as the hydrophilic carriers. Solid dispersions showed a remarkable enhancement in the dissolution rate of the drug. In the present research work, the solid dispersions were formulated in to fast dissolving tablets. The prepared tablets were evaluated for hardness, friability, drug content, disintegration time and the in vitro dissolution rate. The solid dispersions were characterized by Fourier Transform Infrared Spectroscopy (FTIR), differential scanning calorimetry (DSC) and thermo-gravimetric analysis (TGA). The DSC study revealed a marked reduction in the crystallinity of the drug. The faster dissolution rate of the solid dispersion is attributed to a marked reduction in the crystallinity of the drug. The FTIR and DSC studies demonstrated the absence of drug-polymer interaction. The formulated tablet (F2) achieved a 7 fold faster dissolution rate compared to the marketed tablet.

KEYWORDS: Carbamazepine; solid dispersions; dissolution; fast dissolving tablets.

Introduction

The progress in treatment of diseases has been evident with the upsurge in the development of new drugs. An estimated 40% of these drugs are poorly water soluble. The enhancement of oral bioavailability of such poorly water soluble drugs remains one of the most challenging aspects of drug development. The development of solid dispersions as a practically viable method to enhance the bioavailability of poorly water-soluble drugs can overcome the limitations of the previous approaches such as salt formation, solubilization by cosolvents, and the particle size reduction (Chiou and Riegelman, 1971). Much of the research that has been reported on solid dispersion technologies involves drugs that are poorly water-soluble and highly permeable to biological membranes, as with these drugs, the dissolution is the rate limiting step to absorption (Ford, 1986).

Solid dispersion technologies are particularly promising for improving the oral absorption and bioavailability of BCS Class II drugs (Sinha et al., 2010). 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 drug can be dispersed molecularly, in amorphous particles (clusters) or in crystalline particles. Solid dispersion technology is the science of dispersing one or more active ingredients in an inert matrix in the solid state in order to achieve increased dissolution rate, sustained release of drugs, altered solid state properties and enhanced bioavailability (Leuner and Dressman, 2000; Sheu et al., 1994). The solid dispersion approach has been widely and successfully applied to improve the solubility, dissolution rate and consequently the bioavailability of poorly soluble drugs (Craig, 2002; Sudha et al., 2002; Varma and Pandit, 2005). Many hydrophilic excipients like PVP, cyclodextrins, PEG 4000, PEG 6000, mannitol, and poloxamers can be used to enhance the dissolution of poorly soluble drugs (Dahlberga et al., 2010). 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.

The carbamazepine is an anticonvulsant and mood-stabilizing drug used primarily in the treatment of epilepsy and bipolar disorder, as well as trigeminal neuralgia (Raid et al., 1986). It is practically insoluble in water. Being a BCS class-II drug, it has dissolution dependent oral bioavailability. The absorption of carbamazepine from immediate-release tablets is slow, erratic and unpredictable (Aldenkamp et al., 1988; Martindale, 2005). Solid dispersions of carbamazepine in sodium starch glycolate and HPMC have been developed to increase the dissolution rate (Rane et al., 2008).
In the present study, attempt was made to increase the dissolution rate of poorly water soluble drug, carbamazepine by solid dispersion technique using cross-povidone and Ac-di-Sol as the hydrophilic carriers. The solid dispersions were characterized by FTIR, DSC and TGA. The solid dispersions were formulated in to fast dissolving tablets (FDT). The prepared tablets were evaluated for hardness, friability, drug content, disintegration time and the in vitro dissolution rate.

Materials and Methods

Drugs and Chemicals

Carbamazepine was obtained as a generous gift sample from Sun Pharmaceuticals Ltd, Vadodra. Cross-povidone (CP), magnesium stearate, talc, aerosol, tween 80, croscarmellose sodium/AC-di-Sol (CCS), microcrystalline cellulose (MCC) and sodium lauryl sulphate (SLS) were procured from SD Fine Chemicals Ltd, Mumbai. The marketed tablet B1 was purchased from the local pharmacy store. All other chemicals used were of analytical grade.

Formulation and Evaluation Methodology

Preparation of Calibration Curve of Carbamazepine

The 100 mg of carbamazepine was accurately weighed and dissolved in 20 mL of alcohol in a 100 mL volumetric flask and finally the volume was adjusted to 100 mL with distilled water (1000 µg/mL). The standard solution of carbamazepine was subsequently diluted to obtain a series of dilutions containing 2, 4, 6, 8, 10 µg/mL. The absorbance of the above dilutions was measured on a UV spectrophotometer (Lab. India) at 286 nm using distilled water as the blank. The absorbance was plotted against concentration, and the calibration curve was constructed. Similarly, the calibration curve of carbamazepine in 0.1 N HCl (286 nm) and 1% aqueous SLS (288 nm) was prepared.

Preparation of solid dispersions by kneading method

Solid dispersions were prepared in the ratios of 1:1, 1:3 (drug: carrier) with CCS and CP. Initially weighed amount of drug and carrier (CCS/CP) were placed in a mortar and were ground with pestle for few minutes. Then few mL of alcohol: water (1:1) solvent blend was added and then triturated until alcohol: water gets evaporated. The dispersions were preserved in desiccators for complete drying. The dry dispersion was then passed through the 100# mesh sieve and was stored in the moisture free area till further use. Similarly, the ternary solid dispersions of carbamazepine: CP/CCS: Tween 80 (two ratios, 1:1:0.1, 1:3:0.1) were prepared by the above kneading method (Table 1). The physical mixtures were prepared by mixing the drug and the carrier (in a mortar) without using the solvent, the resulting sample was passed through the 100# mesh sieve.

Formulation of Fast Dissolving Tablets (FDT) of Carbamazepine

The solid dispersions equivalent to 100 mg of drug was taken, it was mixed with directly compressible diluent in a plastic bag. The magnesium stearate, talc and aerosil were passed through sieve no. 60, mixed and blended with the initial mixture in the plastic container followed by compression of the blend using a single punch Cadmach machine to produce the round tablets (Table 2).

Evaluation of Solid Dispersions

Drug content uniformity

The solid dispersion sample equivalent to 100 mg of drug was weighed, transferred into a 100 mL volumetric flask, the dispersion was solubilized in 20 mL alcohol and finally the volume was adjusted to 100 mL with distilled water. From the obtained stock, the dilutions were made such that we finally obtain 10 µg/mL solution. The obtained solution was assayed for drug content using a UV spectrophotometer at 286 nm. The drug content was calculated from the absorbance obtained with the help of the calibration curve.

In Vitro dissolution studies

The dissolution rate of pure drug, solid dispersions and the physical mixtures were evaluated using the USP
paddle type dissolution testing apparatus. The dissolution fluid was 900 mL of distilled water/0.1 N HCl, a speed of 75 rpm and a temperature of 37°C ± 0.5°C was used in each test. Samples of dissolution medium (5 mL) were withdrawn at different time intervals (5, 10, 20, 30, 45 and 60 minutes), suitably diluted and assayed for carbamazepine by measuring the absorbance at 286 nm. The dissolution experiments were conducted in triplicate and the results are shown in Figure 1-6.

Evaluation of Fast Dissolving Tablets (FDT)

All the prepared tablets were evaluated for the following parameters as per the IP guidelines and the results are given in the Table 3.

**TABLE 3**
Evaluation of carbamazepine fast dissolving tablets.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>F1</th>
<th>F2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg. wt (mg)±SD (n=20)</td>
<td>298±0.54</td>
<td>298.5±0.32</td>
</tr>
<tr>
<td>Hardness (Kg/cm²) (n=3)</td>
<td>4.5±0.12</td>
<td>4.5±0.34</td>
</tr>
<tr>
<td>Friability (%) (n=10)</td>
<td>0.19</td>
<td>0.21</td>
</tr>
<tr>
<td>In-vitro Disintegration</td>
<td>88sec</td>
<td>65sec</td>
</tr>
<tr>
<td>time (sec) (n=6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drug content (%) (n=3)</td>
<td>98.6±0.26</td>
<td>100.34±0.45</td>
</tr>
</tbody>
</table>

**Weight variation**

Twenty tablets were randomly selected from each batch, individually weighed, the average weight and the standard deviation of 20 tablets was calculated.

**Hardness**

The hardness or tablet crushing strength (F<sub>c</sub>); the force required to break a tablet in a diametric compression was measured using a Monsanto tablet hardness tester.

**Friability**

The friability of the tablets was determined using the Roche friabilator (USP). Preweighed sample of tablets (n=10) was placed in the friabilator and was subjected to 100 revolutions at 25 rpm. The tablets were dedusted using a soft muslin cloth and reweighed. Percent friability = [initial weight – final weight/initial weight] × 100

**Drug content**

The five tablets from each formulation were weighed accurately and powdered. The powder equivalent to 100 mg of carbamazepine was dissolved in 20 mL alcohol and the volume was adjusted to 100 mL with distilled water. The resulting solution was then subsequently diluted with distilled water and assayed for the drug by using the UV spectrophotometer at 288 nm.

**Disintegration test**

The USP disintegration test apparatus (Electrolab) was used. The experiment was conducted in 900 mL of distilled water at 37°C ± 0.5°C. Each time six (n = 6) tablets were used.

**Dissolution studies**

The dissolution rate of carbamazepine from all the formulations was performed using the USP dissolution testing apparatus (paddle). The dissolution fluid was 900 mL of distilled water/0.1 N HCl/1% SLS, a speed of 75 rpm and a temperature of 37°C ± 0.5°C was used in each test. Samples of dissolution medium (5 mL) were withdrawn at different time intervals (5, 10, 20, 30, 45 and 60 minutes), suitably diluted and assayed for carbamazepine by measuring the absorbance at 286/288 nm. The dissolution experiments were conducted in triplicate and the results are shown in Figure 24-26. As per the USP dissolution specification (USP,2007), the carbamazepine tablets should dissolve not less than 75% in 60 minutes at 75 rpm (paddle method) in 900 mL of aqueous solution of 1% SLS. The values of dissolution efficiency up to 10 minutes (DE<sub>10</sub>) and up to 30 minutes (DE<sub>30</sub>) were calculated by the method reported by Khan and Rhodes, 1975.

**TABLE 4**
Dissolution parameters of fast dissolving tablets.

<table>
<thead>
<tr>
<th>Batch codes</th>
<th>DE&lt;sub&gt;10&lt;/sub&gt; (%)</th>
<th>DE&lt;sub&gt;30&lt;/sub&gt; (%)</th>
<th>T&lt;sub&gt;90&lt;/sub&gt; (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>95.95</td>
<td>-</td>
<td>8</td>
</tr>
<tr>
<td>F2</td>
<td>95.82</td>
<td>-</td>
<td>5.5</td>
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<tr>
<td>B1</td>
<td>83.8</td>
<td>92.56</td>
<td>27</td>
</tr>
<tr>
<td>D</td>
<td>19.5</td>
<td>53.35</td>
<td>90</td>
</tr>
</tbody>
</table>

**Characterization of Solid Dispersions**

**FTIR studies**

The FTIR study was undertaken to assess the drug-polymer interaction. FTIR spectra of pure drug, physical mixtures and the solid dispersions were recorded on a Bruker FTIR spectrophotometer. The potassium bromide pellet method was employed. Each spectrum was recorded in the region 400-4000 cm⁻¹ at spectral resolution of 2 cm⁻¹.

**DSC studies**

The DSC measurements were carried out to evaluate the drug-polymer interaction. The accurately weighed sample was placed in an aluminum pan. An empty aluminum pan was used as the reference. The experiment was carried out in nitrogen atmosphere at a scanning rate of 10°C/minute, in the range: 20°C–400°C.

**TGA studies**

Thermo-gravimetric analysis (TGA) records the decrease in the weight of the sample as a function of the temperature (time range: 0-100 minutes, temperature range: – 20°C–400°C). TGA indicates the dehydration and decomposition of the sample.

**Results and Discussion**

**Preparation of Solid Dispersions**

The objective of the present study was to improve the dissolution rate of carbamazepine and formulate it into
fast dissolving tablets. In the present study, CP and CCS were employed in the preparation of solid dispersions as they act as hydrophilic carriers, thereby enhancing the dissolution rate of the drug. The solid dispersions were prepared by the kneading method. The composition of the different batches of solid dispersions is represented in Table 1. As physical mixtures that are prepared at high drug-polymer ratios, haven't shown good dissolution profile, the solid dispersion technique was employed. Totally, six solid dispersions were prepared (Sd1, Sd2, Sd3, Sd4, Sd5, and Sd6) with varying drug:polymer ratios. For the prepared dispersions, the drug content and the in vitro dissolution studies were performed. The dissolution profiles of the solid dispersions are depicted in Figure 1-6. All the prepared batches of solid dispersions were found to be non-hygroscopic and free flowing powders. All the prepared solid dispersions exhibited uniformity of drug content. The drug content of the solid dispersions was found in the range: 96%-102%. The solid dispersions showed remarkable increase in the dissolution rate compared to the pure drug. Based on the drug-carrier ratio and the results of the dissolution study, the batches, Sd1 and Sd5 were selected for the formulation of fast dissolving tablets.

Fig. 1. Dissolution Profiles of solid dispersions (Sd1, Sd2, Sd3, Sd4) and pure drug in water.

Fig 2. Dissolution profiles of physical mixtures (PM1, PM2, PM3 and PM4) in water.
Fig. 3. Dissolution Profiles of solid dispersions (Sd1, Sd2, Sd3, Sd4) and pure drug in 0.1N HCl.

Fig. 4. Dissolution profiles of physical mixtures: PM1, PM2, PM3, PM4 in 0.1N HCl.

Fig. 5. Dissolution profiles of Sd5, Sd6, PM5 and PM6 in distilled water.
Evaluation of Tablets

The fast release solid dispersions were formulated in to fast dissolving tablets by the direct compression method. The composition of the formulated tablets is indicated in Table 2. The tablet formulations exhibited uniform drug content. The quality control parameters of all the tablet formulations are represented in Table 3. The drug content of the formulated tablets was found in the range: 98.63%-100.34%. The formulated tablets fulfilled the compendial limits of weight variation, hardness, friability and the disintegration time (Table 3). The friability values of the formulated tablets ranged from 0.19%-0.21%. The hardness of the formulated tablets ranged was found to be 4.50 Kg/cm². The disintegration time (DT) of the fabricated tablets ranged from 65-88 seconds.

Dissolution Studies

The dissolution profiles of the solid dispersions are represented in Figure 1-6. The dissolution profiles of the formulated tablets are depicted in Figure 24-26. The dissolution parameters of the formulated tablets are indicated in Table 4. In the present research work, kneading technique was employed to prepare the solid dispersions and water: alcohol blend in 1:1 volume ratio was used as a solvent. During the preparation, the volatile solvent will evaporate and forms a semisolid mass at the end by dispersing the fine drug particles in the hydrophilic polymer matrix, there by an increase in the dissolution rate was observed. The dissolution studies of the solid dispersions were conducted by using different dissolution media (distilled water and 0.1 N HCl was used). The pure drug exhibited very poor dissolution rate due to its hydrophobic nature and poor wettablility. Also, the physical mixtures exhibited better dissolution rate compared to the pure drug when 0.1 N HCl was used as the dissolution medium. The faster dissolution rate of the drug from the solid dispersions is attributed to the enhancement of wettability (as hydrophilic carriers were used) and decrease in the aggregation of the hydrophobic drug particles. The decrease in the particle size and the increase in the surface area of the hydrophobic drug particles (in the solid dispersions) may contribute to the enhancement of the dissolution rate of the drug. Also, the pure drug demonstrated extremely poor dissolution when 0.1 N HCl was used as the dissolution medium. The pure drug showed only 40% drug release in 30 minutes and 60% drug release in 1 hour. The pure drug did not attain 80% drug release even at the end of 1 hour. Based on the percent drug dissolved in 5 minutes, the solid dispersion (SD1) achieved 17 fold increase in the dissolution rate compared to the pure drug when 0.1 N HCl was used as the dissolution medium.

The pure drug exhibited very poor dissolution rate due to the hydrophobic and the crystalline nature of the carbamazepine. Also, the physical mixtures exhibited better dissolution rate compared to the pure drug when 0.1 N HCl was used as the dissolution medium. The faster dissolution rate of the drug from the solid dispersions is attributed to the enhancement of wettability (as hydrophilic carriers were used) and decrease in the aggregation of the hydrophobic drug particles. The decrease in the particle size and the increase in the surface area of the hydrophobic drug particles (in the solid dispersions) may contribute to the enhancement of the dissolution rate of the drug. Hydrophilic polymer drug solid dispersions increase drug dissolution because of the following possible reasons: usually in solid dispersions, the drug is partially dissolved in melted or
dissolved polymer. After drying of these solid dispersions, the drug will not nucleate to form firm crystals resulting in formation of microcrystals. Drug microcrystals are embedded in the water-soluble matrix, where hydrophilic polymers present the ability of rapid wetting and thereby increase the dissolution rate of the drug. Generally PEGs and PVP solid dispersions follow this principle (Arias et al., 1996). For solid dispersions of crospovidone and Ac-di-Sol, higher dissolution rates observed when compared with the pure drug may be owing to their easy and rapid dispersibility in the aqueous dissolution fluids. Similar results were obtained when sodium starch glycolate was used as a carrier to enhance the dissolution rate of hydrophobic drugs (Rane et al., 2007; Chowdary and Rao, 2000).

Totally, two different FDT (F1, F2) of carbamazepine were formulated using Sd1 and Sd5. Out of the two prepared formulations, F2 showed better dissolution rate than F1. The formulated tablets were evaluated for the dissolution rate in different dissolution media: distilled water, 0.1 N HCl and 1% SLS. As per the USP dissolution specification (USP, 2007), the carbamazepine tablets should dissolve not less than 75% in 60 minutes at 75 rpm (paddle method) in 900 mL of aqueous solution of 1% SLS. The dissolution rate of the branded tablet, B1 was compared with the formulated tablets, when 1% SLS was used as the dissolution medium. Dissolution parameters such as (DE10), (DE30) and T90 (minutes) were estimated. The formulated tablets F1 and F2 demonstrated more than fourfold increase in the (DE10) values when compared with the pure drug (D). Also, the formulated tablets: F1, F2 showed higher (DE10) values compared to the brand, B1. Based on the time taken for 90% drug release, T90 (minutes), the formulated tablet, F1 showed a 12 fold and F2 showed 28 fold increases in the dissolution rates compared to the pure drug (Figure 24-26). Based on the T90 (minute) values, the optimized formulation F2 showed a 7 fold increase in the dissolution rate compared to the marketed brand B1. Formulations F1 and F2 fulfilled all the specifications prescribed for fast dissolving tablets of carbamazepine.

The different manufactures may use different excipients (hydrophilic or hydrophobic) which can influence the drug release of the hydrophobic carbamazepine, hence the dissolution rate of the formulated tablets was compared with the branded tablet, B1. The results of the dissolution study indicate an improvement of dissolution rate of carbamazepine in the solid dispersion tablets. The improvement in the dissolution rate is achieved due to several factors. Such factors are: the strong hydrophilic property of the polymeric carriers, which improves the water penetration and the wettability of the hydrophobic drug; the optimal dispersion of the drug in the hydrophilic polymeric carrier; the absence of crystals (amorphous dispersions) corresponds to lower energy required for dissolution; the molecular dispersion of drug on the polymeric carrier improves the hydrophilic characteristics of the hydrophobic drug (Karavas et al., 2003). Also, the decrease in the particle size, decrease in the aggregation and the agglomeration of the hydrophobic drug particles and the improvement in the dispersibility of the hydrophobic drug particles can improve the dissolution rate of the drug (Ford, 1986; Varma and Pandit, 2005).

FTIR studies

The FTIR spectra of carbamazepine, solid dispersions and the physical mixtures are depicted in Figure 7-13. The pure drug showed characteristic absorption bands cm\(^{-1}\) at 3467 (NH stretching of NH\(_2\)), 3080 (aromatic CH stretching), 1678 (C=O stretching of CONH\(_2\)) and 1605, 1489 (C=C ring stretching). The same peaks were observed in the drug substance, physical mixtures and in the solid dispersions. The absence of any new peaks in the solid dispersions indicates that there are no polymorphic changes in the drug substance during the preparation of the solid dispersions. Furthermore, the absence of shifts in the wave numbers of the FTIR peaks of the solid dispersions compared to the physical mixtures indicates the lack of significant interaction between the drug and the polymer components in the solid dispersion at the molecular level. The FTIR studies revealed that there was no chemical interaction between the drug and the polymer (crospovidone or the Ac-di-Sol) in the physical mixtures and in the solid dispersions.

DSC and TGA studies

The DSC thermograms of pure drug, physical mixtures and the solid dispersions are shown in Figure 14-18. A sharp endothermic peak at 196.4°C was observed indicating the melting point of the crystalline drug, carbamazepine. The melting point was observed at 193.7°C in the drug-crospovidone (1:1 weight ratio) solid dispersion and the melting point of the drug-crospovidone (1:1 weight ratio) physical mixture was observed at 195.5°C. The presence of the endotherm clearly indicates the absence of the drug-polymer interaction in the drug-crospovidone solid dispersion and also in the drug-crospovidone physical mixture. The melting point was observed at 195.5°C in the drug-Ac-di-Sol (1:1 weight ratio) solid dispersion and the melting point of the drug-Ac-di-Sol (1:1 weight ratio) physical mixture was observed at 195.4°C. The presence of the endotherm clearly indicates the absence of the drug-polymer interaction in the drug-Ac-di-Sol solid dispersion and also in the drug-Ac-di-Sol physical mixture.

The two broad endothermic peaks were observed at 70°C (attributed to the evaporation of absorbed water) and 193.7°C (lower melting point is ascribed to the melting point depression) in the drug-crospovidone (1:1 weight ratio) solid dispersion. As the intensity of the endotherm was drastically decreased, this clearly indicates the marked reduction in the crystallinity of the drug in the crospovidone solid dispersion. Also, two endothermic peaks were observed at 70°C (due to evaporation of absorbed water) and 195.5°C (melting point of drug) in the drug-crospovidone (1:1 weight ratio) physical mixture. Appearance of the endothermic peak at
195.5°C in the drug-crospovidone physical mixture demonstrated the absence of the drug-polymer interaction. Also, in the drug-Ac-di-Sol solid dispersion (and in the physical mixture) a broad endothermic peak was observed at 70°C (attributed to the evaporation of absorbed water). In the drug-Ac-di-Sol solid dispersion, as the intensity of the endotherm was markedly decreased, the faster dissolution rate of the drug from the solid dispersion is attributed to the reduction in the crystallinity of the drug. Crystallization inhibition is attributed to the entrapment of drug molecules in the polymer matrix during the solvent evaporation (Bettinetti et al., 1991). Numerous studies have shown that polymers like HPMC, PVP used in the solid dispersions can inhibit the crystallization of drugs resulting in an amorphous form of the drug in the solid dispersions (Yamashita et al., 2003; Tantishaiyakul et al., 1999). The microcrystals are formed as a consequence of evaporation of solvent during the preparation of solid dispersions. Evaporation of solvent increases the viscosity very rapidly leading to a decrease in drug mobility preventing recrystallization. When the solvent is evaporated completely drug molecules are frozen in the polymer. A crystal lattice is not formed, but the drug molecules are of randomly dispersed order (Van den Mooter et al., 1998) over only a few molecular dimensions. The TGA indicated slight decrease in weight of the sample around 100°C due to dehydration of the solid dispersion. But beyond the melting point of the drug (190°C), the decrease in weight may be due to the melting (liquifaction) and the decomposition of the drug (Figure 19-23).

Fig. 7. FTIR spectrum of car-bamazepine.

Fig. 8. FTIR spectrum of crospovidone.
Fig. 9. FTIR spectrum of carbamazepine:crospovidone (1:1) solid dispersion.

Fig. 10. FTIR spectrum of carbamazepine:crospovidone (1:1) physical mixture.
Fig. 11. FTIR spectrum of Ac-di-Sol.

Fig. 12. FTIR spectrum of carbamazepine:Ac-di-Sol (1:1) solid dispersion.
Fig. 13. FTIR spectrum of carbamazepine:Ac-di-Sol(1:1) physical mixture.

Fig. 14. DSC thermogram of carbamazepine.
Fig. 15. DSC thermogram of carbamazepine: crospovidone (1:1) solid dispersion.

Fig. 16. DSC thermogram of carbamazepine: crospovidone (1:1) physical mixture.
Fig. 17. DSC thermogram of carbamazepine:Ac-di-Sol (1:1) solid dispersion.

Fig. 18. DSC thermogram of carbamazepine:Ac-di-Sol (1:1) physical mixture.
Fig. 19. TGA scan of carbamazepine.

Fig. 20. TGA scan of carbamazepine: crospovidone (1:1) solid dispersion.
Fig. 21. TGA scan of carbamazepine:crospovidone (1:1) physical mixture.

Fig. 22. TGA scan of carbamazepine:Ac-di-Sol (1:1) solid dispersion.
Fig 23. TGA scan of carbamazepine:Ac-di-Sol (1:1) physical mixture.

Fig 24. Dissolution profiles of F1 tablet in different media.
Conclusions

The optimized formulations were F1 and F2. The study shows that the dissolution rate of carbamazepine can be enhanced to a great extent by the solid dispersion technique using an industrially feasible kneading method. Based on the time taken for 90% drug release, the optimized tablet formulation, F2, achieved a 7 fold faster dissolution rate compared to the marketed brand B1. The DSC study exhibited a marked reduction in the crystallinity of the drug in the solid dispersions. The faster dissolution rate of solid dispersions is ascribed to a marked reduction in the crystallinity of the drug. Hence, carbamazepine-CP, carbamazepine-CCS binary systems could be considered for formulations of fast dissolving tablets of carbamazepine. The FTIR and DSC studies revealed the absence of drug-polymer interaction.

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