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***Research Article***

# FORMULATION AND EVALUATION OF CARBAMAZEPINE SOLID DISPERSIONS WITH POLYETHYLENE GLYCOL 6000 AND THEIR INCORPORATION INTO TABLETS

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## ABSTRACT
The improvement of the physicochemical properties of Carbamazepine (CBZ), a poorly water soluble drug, can be done by forming dispersion with PEG 6000 as water soluble carrier. The solid dispersions(SDs) of CBZ were prepared by solvent evaporation and fusion methods using 1:0.1, 1:0.3, 1:0.5, 1:0.7 and 1:0.9 ratios of drug and polymer (w/w). These SDs were characterized in the solid state by differential scanning calorimetry. Solid state characterizations indicated that CBZ was present as an amorphous material and entrapped in polymer matrix. In contrast to the slow dissolution rate of pure CBZ, the dispersion of the drug in the PEG considerably enhanced the dissolution rate. Furthermore; carbamazepine 200 mg immediate release tablets prepared in a ratio of 1:0.3 (drug: carrier) by the fusion method has resulted in acceptable dissolution results.

***Key Words:*** *Carbamazepine, PEG 6000, Solid Dispersion and Immediate Release Tablets*

## INTRODUCTION
Carbamazepine (CBZ) is considered a first line drug in the treatment of epilepsy and trigeminal neuralgia (Tayel *et al.,* 2008). It is practically insoluble in water. It has at least four different polymorphs (I, II, III and IV) and the dihydrate form (Ali *et al.,* 2013).
Solubility behavior of drugs remains one of the most challenging aspects in formulation development. The term "solid dispersion" refers to the dispersion of one or more active ingredients in an inert carrier or matrix in the solid state prepared by the melting, solvent, or melting/ solvent methods (Leuner *et al.,* 2000).
Polyethylene glycols (PEG) were used to enhance the aqueous solubility or dissolution characteristics of poorly soluble compounds by using solid dispersion technique (Nafee *et al.,* 2003). They have been widely used as vehicles in the preparation of solid dispersions because of their low melting point, rapid solidification rate, capability of forming solid drug solutions, low toxicity and low cost (Bley *et al.,* 2010).
Many published articles concerning CBZ and polyethylene glycol solid dispersions indicate that the minimum ratio of tested CBZ to PEG is 1:1 (Doshi *et al.,* 1997). In this study, the aim was to guide the use of PEG 6000 in very low amounts compared to the amount of the active ingredient used for preparation of immediate release tablets which contain 200 mg of CBZ. Thus the ratios of CBZ: PEG 6000 used were 1: 0.1, 1:0.3, 1:0.5 1:0.7 and 1:0.9 respectively. Immediate release tablets containing carbamazepine 200 mg were developed using the solid dispersions prepared by the fusion method.

## MATERIALS AND METHODS
### *Experimental*
### *Materials*
Carbamazepine USP 33 (Xiamen, China), microcrystalline cellulose PH102 (FMC, Ireland), polyethylene glycol 6000 (PEG 6000) (Lyondel, France), magnesium stearate (Alba chemicals, USA), methanol and acetonitrile for HPLC (Merck, Germany), acetone (El-Nasr pharmaceutical chemicals co, Egypt), Sodium

lauryl sulphate (SLS) (Surfachem, England), Sodium starch glycolate (SSG)(JRS pharma, Germany), empty hard gelatin capsules (the Arab company for gelatin and pharmaceutical products, Egypt).

***Methodology***

***1 Assay of carbamazepine in methanol, distilled water and distilled water containing 1.0 % SLS using HPLC methods***

The HPLC analysis conditions were: $C_{18}$ column; 150 mm x 4.6 mm i.d., mobile phase: Acetonitrile: Potassium dihydrogen phosphate buffer (35: 65 % V/V), column temperature: 25 °C, flow rate: 1.5 ml/ minute, wave-length 254 nm and injection volume: 5 µl (Ali *et al.,* 2013).

***2 Preparation of CBZ / PEG 6000 physical mixtures***

The physical mixtures of carbamazepine and PEG 6000 in a ratio of 1: 0.1, 1:0.3, 1:0.5, 1:0.7 and 1:0.9 were prepared by homogeneous blending of previously sieved and weighed CBZ and PEG 6000 in a glass mortar. The physical mixtures were subsequently passed through sieve 0.355 mm (Verheyen *et al.,* 2001)and stored in capped amber glass vials at room temperature until used (Kalia *et al.,* 2009).

***3 Preparation of CBZ Solid Dispersions***

***3.1. Applying solvent evaporation method***

Carbamazepine and PEG 6000 are soluble in acetone (British Pharmacopea, 2010; Raymond *et al.,* 2009). Thus, acetone was used as a solvent for both the drug and the carrier in the preparation of solid dispersions using solvent evaporation method.

Many researchers used acetone as a solvent for carbamazepine in the preparation of solid dispersions by the solvent evaporation method and the modified solvent evaporation method (Mahalaxmi *et al.,* 2009; Kalyanwat *et al.,* 2011).

Thus CBZ /PEG 6000 solid dispersions were prepared by dissolving PEG 6000 and CBZ in acetone in a ratios of CBZ: PEG 6000 1: 0.1, 1:0.3, 1:0.5 1:0.7 and 1:0.9 w/w respectively, by stirring and slight heating till a clear solution was formed. Drug, polymer and solvent combinations were dried by evaporating on a water bath adjusted at 70˚C until complete drying. The prepared solid dispersions were cooled, crushed in a mortar passed through 0.355 mm sieve and kept in capped amber glass vials away from light and humidity until use.

***3.2. Applying fusion (melting) method***

PEG 6000 was melted on a water bath adjusted at 60˚C, mixed with the drug, triturated till cold. The prepared solid dispersions were passed through 0.355 mm and then treated as mentioned before.

***4 DSC Thermal Analyses for the prepared solid Dispersions***

DSC studies were performed on CBZ alone, a physical mixture in a ratio of 1:0.5 w/w of the CBZ with PEG 6000 and the prepared solid dispersions. Thermograms were obtained at a heating rate of 10˚C /minute over a temperature range of 30 to 220 ˚C (Sethia and Squillante, 2002). Pyris software 8 (Perkin Elmer, USA) was used for analysis.

***5 Dissolution Studies***

Although carbamazepine is practically insoluble in water, the medium used for testing the dissolution of carbamazepine, its physical mixtures and solid dispersions was distilled water. This is to investigate the effect of incorporation of carrier used on dissolution. This is in accordance with Sammour *et al.,* (2006) who used distilled water as a medium for dissolution of a practically insoluble drug rofecoxib as a pure drug, its physical mixtures and solid dispersions.

The prepared mixtures equivalent to 200 mg CBZ were filled in size 00 hard gelatin capsules, placed in apparatus II dissolution vessels with 900 ml distilled water at 37 ± 0.5 ºC and maintained at 75 rpm. Samples of the dissolution medium were taken after 10, 15, 20, 30, 45, 60, 90 and 120 minutes and equal volumes of fresh dissolution medium were added to the dissolution vessels to maintain constant dissolution volume. Each test was performed in triplicate. The amount of drug was analyzed by HPLC method.

***6. Formulation of Carbamazepine Immediate Release Tablet Dosage Forms***

***6.1. Study of the possible interaction between the drug and the chosen additives***

Thermal analyses of carbamazepine alone and with the chosen excipients such as microcrystalline cellulose PH 102 and magnesium stearate were performed in a Perkin Elmer Diamond DSC differential scanning calorimeter (USA) as mentioned before.

***6.2. Preparation of carbamazepine 200 mg tablets using the prepared solid dispersions by the fusion method***

Tablets were prepared according to the proportions given in the following table. The prepared solid dispersions prepared by the fusion method in a ratio of 1: 0.3 (CBZ: PEG 6000 w/w) were then blended with Q.S microcrystalline cellulose PH 102, 2.5 or 5.0 % sodium starch glycolate and 0.5 % magnesium stearate and the resultant blends were then compressed on punch 9.0 mm flat scored using Korsch XL 100 compression machine on target weight 300.0 mg with hardness not less than 60.0 N.

***6.3. Evaluation of the compressed tablets***

The prepared tablets were evaluated by determination of: uniformity of weight, disintegration time, resistance to crushing of tablets, friability, assay, loss on drying and dissolution in distilled water containing 1.0 % SLS according to conditions mentioned in previous studies (Ali *et al.,* 2012 and 2013).

## RESULTS AND DISCUSSION

***1 Evaluation of the Prepared Carbamazepine Solid Dispersions***

***1.1. DSC for the prepared solid dispersions***

Figure (1-a) shows a sharp endothermic onset of peak at 173.75ºC and an exothermic one at 178.42 ºC followed by a sharp endothermic peak at 189.23 ºC corresponding to carbamazepine melting point (Florey *et al.,* 1980). Figure (1-b) shows a sharp endothermic peak at 56.98 ºC corresponding to the melting point of PEG 6000 (Raymond *et al.,* 2009). Figures (1-c:1-h) show sharp endothermic onset peaks at 175.03-188.35ºC corresponding to carbamazepine melting point and sharp endothermic onset peaks at 56.03 : 58.54 ºC corresponding to PEG 6000 melting point. Figures (2-b:2-f) show sharp endothermic onset peaks at 174.44: 188.32 ºC corresponding to carbamazepine melting point and endothermic onset peaks at 57-59 ºC corresponding to melting point of PEG 6000.

The DSC thermograms of carbamazepine in the different prepared solid dispersions show only one endothermic peak that indicates that carbamazepine which is commercially available as form III is transformed to form I. This is in accordance with Rustichelli *et al.,* (2000) who concluded that his attempts to crystallize polymorph III from boiling solvents always produced polymorph I. Barzegar-Jalali *et al.,* (2006) reported that solid-solid transition for CBZ from polymorph III to polymorph I had occurred upon heating.

According to the prepared solid dispersions; it is found that the melting point of PEG 6000 is from 56.03 to 57.66 ºC in case of solid dispersions prepared by solvent evaporation method and from 55.65 to 57.77 ºC in case of solid dispersions prepared by the fusion method. This indicates that PEG 6000 has not been changed in properties from single state to the carrier state in the prepared solid dispersions.

***1.2. Dissolution of carbamazepine from the prepared solid dispersions***

Table (2) shows that the dissolution rate of untreated carbamazepine exhibited 9.142 % dissolution after 10.0 minutes. This is in accordance with Doshi *et al.,* (1997) who concluded that untreated carbamazepine exhibited 10.09 ± 2.92 % dissolution in 10.0 minutes. The low dissolution values for the drug alone may be due to its hydrophobic nature as a practically water-insoluble drug. It was noticed that the plain drug particles float for a long time on the upper surface of the dissolution medium while the prepared physical mixtures and solid dispersions immediately sink to the bottom of the dissolution vessel. It is shown that plain carbamazepine powder has poor dissolution values in comparison with the prepared physical mixture and solid dispersions with PEG 6000.

It was found that CBZ dissolution from the prepared solid dispersions has increased due to the presence of hydrophilic carrier surrounding the drug particles. This is in accordance with Biswal *et al.,* (2009) who

attributed that improvement in the wettability of gliclazide solid dispersions might have resulted from the formation of a film of polyethylene glycol around the particles, thus reducing the hydrophobicity of their surfaces. Also Karanth *et al.,* (2006) stated that when the solid dispersion is exposed to aqueous media, the carrier dissolves and the drug is released as fine colloidal particles and the resulting enhanced surface area produces higher dissolution rate.

Table (3) shows the effect of SD preparation method on dissolution of CBZ which indicates that the dissolution values of carbamazepine SD prepared by the fusion method are higher than those prepared by solvent evaporation method.

The results of this study are in accordance with Doshi D.H. et al (2007) who prepared solid dispersions of carbamazepine in a ratio of 1:6 carbamazepines: PEG 6000 or 4000 and concluded that the fusion method provided significantly higher rate and extent of carbamazepine dissolution than the solvent evaporation method (Verheyen *et al.,* 2001).

### *2. Evaluation of the prepared Carbamazepine 200 mg Tablets*

According to the results obtained from solid dispersions dissolution in distilled water: the ratio 1: 0.3 w/w (CBZ: PEG 6000) was used to prepare the tablets in order to minimize the amount of PEG 6000 used which can aid to add a suitable amount of filler and disintegrant.

### *2.1 Study of the possible interactions between the drug and the chosen additives*

Figure (3-a) shows the DSC thermogram of carbamazepine as mentioned before. Figures (3-b) and (3-c) show endothermic onset of peaks at 173.75 ºC and exothermic onset of peaks at 178.42 ºC followed by sharp endothermic onset of peaks at 189.57 and 186.92 ºC corresponding to carbamazepine melting point. This indicates that carbamazepine is compatible with microcrystalline cellulose PH 102 and magnesium stearate.

### *2.2 Uniformity of weight, disintegration time, friability, resistance to crushing of tablets, assay and loss on drying (LOD)*

Tables (4 & 5) show that the average weight of twenty tablets is very close to the target 300.0. The disintegration time of the prepared tablets varies from 14.0 to 17.0 minutes. Friability results of the prepared tablets are less than 0.4 %. All hardness values are varying from 80.0 to 95.0 N. Assay values are almost 100.0 %. Loss on drying values less than 1.5 %.

### *2.3 Dissolution of carbamazepine 200 mg tablets in distilled water containing 1.0 % SLS*

Table (6) and figure (4) show that the dissolution values of the tablets prepared by 2.5 and 5.0 % sodium starch glycolate (SSG) lie in the required USP range for dissolution test 2 after 15 minutes. The dissolution values of the prepared tablets are more than 95.0 % after 60 minutes. Thus, they are conforming to the second range of dissolution process listed in the USP 33 (2010).

From the dissolution results of CBZ 200 mg immediate release tablets in distilled water and distilled water containing 1.0 % SLS; it is observed that the initial dissolution results of tablets prepared by 5.0 % SSG w/w are higher than those prepared by 2.5 % SSG. It is observed that the dissolution process depends on the disintegration time of the prepared tablets.This is due to the effect of SSG as a super disintegrant which facilitates the breakdown of tablets and lowers the disintegration time which in turn increases the initial dissolution values. These results are in agreement with the results obtained by Mali et al. (2012).

**Table 1: Composition of carbamazepine 200 mg tablets**

| **Ingredients** | **%** |
|---|---|
| Carbamazepine/PEG 6000 SD 1: 0.3 | 66.67 |
| Microcrystalline cellulose PH 102 | Q.S |

| | |
|---|---|
| Sodium starch glycolate (SSG) | 2.5 or 5.0 |
| Magnesium stearate | 0.5 |
| Total | 100.0 |

**Table 2: Dissolution of carbamazepine/PEG 6000 physical mixtures and solid dispersions prepared by solvent evaporation method**

| Time (min) | Percent of CBZ dissoluted | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Drug alone | Physical mixture in a ratio of: | | | | | SD in a ratio of: | | | | |
| | | 1:0.1 | 1:0.3 | 1:0.5 | 1:0.7 | 1:0.9 | 1:0.1 | 1:0.3 | 1:0.5 | 1:0.7 | 1:0.9 |
| **10.0** | 9.14 ± 8.97 | 22.08 ± 2.61 | 26.08 ± 4.04 | 23.92 ± 2.00 | 25.39 ± 4.53 | 29.06 ± 4.81 | 40.47 ± 2.00 | 36.55 ± 2.28 | 35.58 ± 1.20 | 40.32 ± 1.25 | 36.96 ± 2.03 |
| **15.0** | 15.84 ± 6.4 | 29.81 ± 2.13 | 34.48 ± 3.32 | 31.86 ± 1.77 | 34.28 ± 3.72 | 39.49 ± 4.13 | 51.99 ± 3.00 | 47.36 ± 0.94 | 49.06 ± 1.19 | 53.35 ± 1.48 | 51.66 ± 3.25 |
| **20.0** | 21.68 ± 5.91 | 41.84 ± 2.43 | 38.82 ± 2.46 | 38.25 ± 1.61 | 40.54 ± 3.13 | 46.40 ± 4.78 | 58.52 ± 3.26 | 54.86 ± 1.17 | 56.78 ± 3.02 | 64.65 ± 0.85 | 72.98 ± 3.75 |
| **30.0** | 28.64 ± 9.08 | 46.19 ± 2.32 | 44.78 ± 2.92 | 45.46 ± 2.63 | 47.43 ± 3.20 | 54.04 ± 3.56 | 66.99 ± 3.29 | 64.59 ± 1.40 | 71.02 ± 4.13 | 73.94 ± 0.66 | 81.83 ± 0.96 |
| **45.0** | 43.65 ± 8.46 | 50.98 ± 2.31 | 50.02 ± 3.31 | 51.67 ± 3.04 | 53.38 ± 3.24 | 59.41 ± 2.95 | 75.19 ± 2.96 | 73.60 ± 1.11 | 81.31 ± 4.05 | 82.13 ± 1.38 | 85.13 ± 4.10 |
| **60.0** | 48.92 ± 7.22 | 53.16 ± 2.86 | 52.63 ± 2.50 | 55.72 ± 3.23 | 56.08 ± 2.62 | 62.04 ± 2.80 | 78.33 ± 2.37 | 79.55 ± 0.92 | 87.41 ± 3.29 | 86.49 ± 1.94 | 89.07 ± 2.83 |
| **90.0** | 57.78 ± 6.44 | 57.62 ± 3.14 | 57.47 ± 3.26 | 62.08 ± 2.80 | 59.95 ± 2.65 | 66.33 ± 2.84 | 88.50 ± 4.41 | 87.19 ± 0.24 | 93.02 ± 3.75 | 91.13 ± 1.84 | 91.53 ± 3.46 |
| **120.0** | 63.95 ± 5.65 | 69.51 ± 4.09 | 66.31 ± 0.91 | 66.99 ± 0.17 | 69.51 ± 1.22 | 69.51 ± 2.06 | 93.08 ± 0.89 | 91.52 ± 0.01 | 95.01 ± 4.25 | 93.80 ± 1.88 | 93.78 ± 3.06 |

*All values are expressed as mean ± SD (n=12)*

**Table 3: Dissolution of CBZ /PEG 6000 solid dispersions prepared by fusion method.**

| Time (min) | Percent of carbamazepine dissoluted | | | | |
|---|---|---|---|---|---|
| | 1:0.1 | 1:0.3 | 1:0.5 | 1:0.7 | 1:0.9 |
| **10.0** | 31.04 ± 0.11 | 39.93 ± 1.31 | 30.65 ± 1.36 | 36.73 ± 1.08 | 20.00 ± 2.78 |
| **15.0** | 52.26 ± 3.54 | 55.25 ± 2.60 | 53.89 ± 2.55 | 53.07 ± 2.77 | 47.67 ± 1.69 |
| **20.0** | 63.78 ± 2.23 | 63.31 ± 1.70 | 68.21 ± 2.16 | 63.81 ± 3.00 | 64.17 ± 1.98 |
| **30.0** | 74.48 ± 1.64 | 73.63 ± 0.63 | 80.82 ± 2.31 | 76.51 ± 2.10 | 79.48 ± 2.40 |
| **45.0** | 83.81 ± 1.36 | 84.16 ± 0.56 | 88.73 ± 2.81 | 86.23 ± 2.25 | 90.55 ± 3.60 |
| **60.0** | 88.28 ± 1.41 | 90.27 ± 0.49 | 91.55 ± 3.11 | 91.87 ± 2.39 | 94.12 ± 3.16 |

| | | | | | |
|---|---|---|---|---|---|
| **90.0** | 93.97 ± 0.90 | 96.00 ± 0.64 | 96.86 ± 3.03 | 97.42 ± 2.04 | 97.33 ± 2.46 |
| **120.0** | 97.79 ± 1.56 | 99.12 ± 0.81 | 99.79 ± 2.74 | 100.21± 1.81 | 99.64 ± 1.73 |

*All values are expressed as mean ± SD (n=12)*

**Table 4: Average weight, disintegration time and friability for carbamazepine 200 mg tablets prepared from solid dispersions by fusion method**

| Carbamazepine tablets prepared by: | Average weight (mg) ± SD, n = 20 | Disintegration time (minutes) ± SD, n = 6 | Friability (%) ±SD, n = 10 |
|---|---|---|---|
| 2.5 % SSG | 299.2 ± 2.20 | 17.0 ± 1.3 | 0.15 ± 0.03 |
| 5.0 % SSG | 301.0 ± 3.25 | 14.0 ± 0.6 | 0.39 ± 0.05 |

**Table 5: Assay, hardness and loss on drying values for carbamazepine 200 mg tablets prepared from solid dispersions by the fusion method**

| Carbamazepine tablets prepared by: | Assay (%) | Average hardness value (N) | Loss on drying (%) |
|---|---|---|---|
| 2.5 % SSG | 99.68 ± 0.64 | 86.9 ± 5.80 | 1.15 ± 0.02 |
| 5.0 % SSG | 99.87 ± 0.77 | 90.0 ± 4.64 | 1.08 ± 0.03 |

*All values are expressed as mean ± SD (n = 10)*

**Table 6: Dissolution in distilled water containing 1.0 % SLS of carbamazepine 200 mg tablets prepared from solid dispersions by the fusion method**

| Time (minutes) | Percent of carbamazepine dissoluted from its prepared tablets in distilled water containing 1.0 % SLS made with: | |
|---|---|---|
| | 2.5 % SSG | 5.0 % SSG |
| **0** | 0.000 | 0.000 |
| **10** | 41.57 ± 6.84 | 43.62 ± 4.87 |
| **15** | 56.34 ± 6.29 | 59.61 ± 4.51 |
| **20** | 71.05 ± 6.85 | 74.94 ± 3.84 |
| **30** | 87.89 ± 5.37 | 91.46 ± 3.90 |
| **45** | 97.14 ± 1.50 | 97.11 ± 1.87 |
| **60** | 100.31 ± 2.07 | 99.90 ± 0.60 |

| | | |
|---|---|---|
| **90** | 102.26 ± 0.37 | 101.52 ± 0.78 |
| **120** | 103.48 ± 0.47 | 101.92 ± 0.76 |

*All values are expressed as mean ± SD (n = 12)*

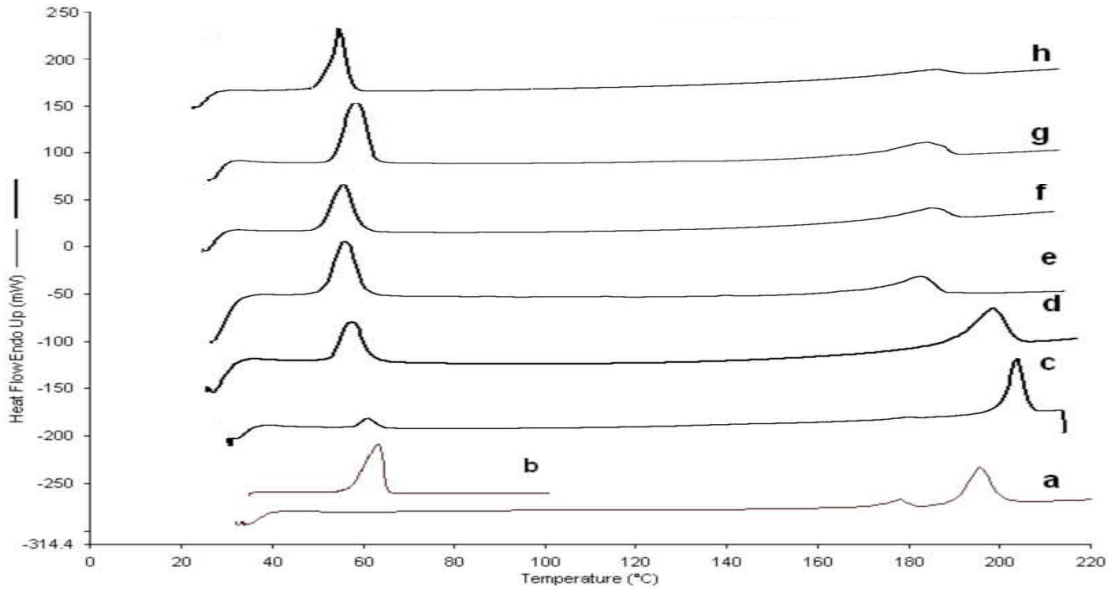


**Figure 1: DSC thermal analysis for: a- carbamazepine alone, b- PEG 6000 alone, c- carbamazepine/ PEG 6000 SD 1:0.1 SE, d- carbamazepine/ PEG 6000 SD 1:0.3 SE, e- carbamazepine/ PEG 6000 SD 1:0.5 SE, f- carbamazepine/ PEG 6000 1:0.5 physical mixture, g-carbamazepine/ PEG 6000 SD 1:0.7 SE and h- carbamazepine/ PEG 6000 SD 1:0.9**

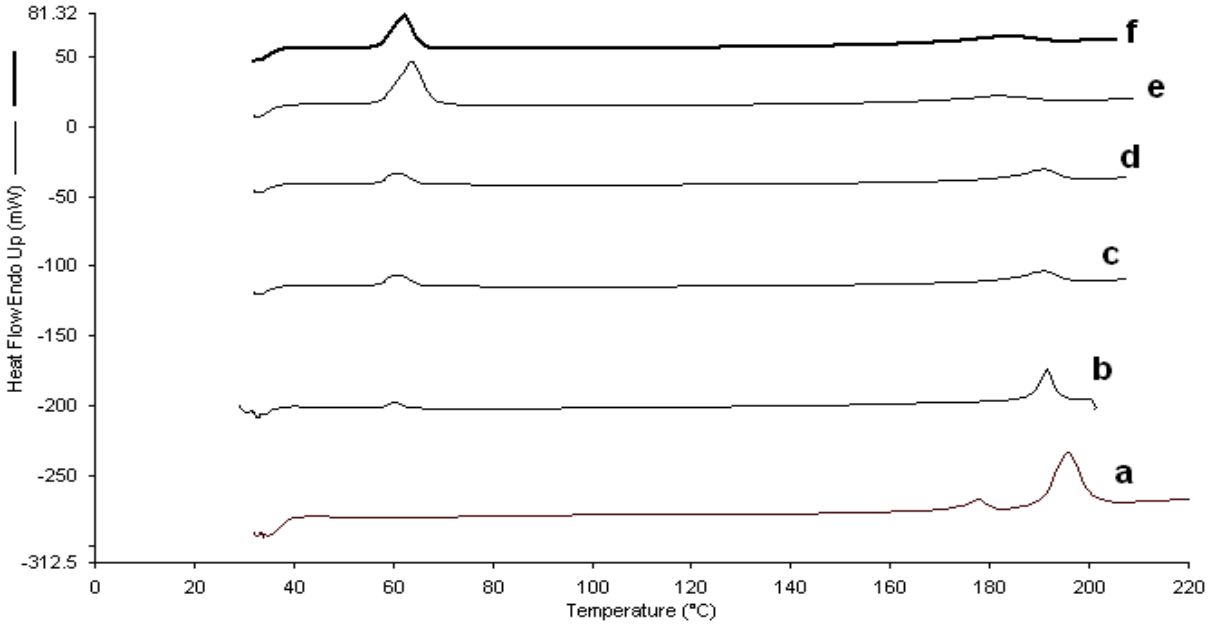

**Figure 2: DSC thermal analysis for: a- carbamazepine alone, b-carbamazepine/ PEG 6000 SD 1:0.1, c- carbamazepine/ PEG 6000 SD 1:0.3 , d- carbamazepine/ PEG 6000 SD 1:0.5 , e-carbamazepine/ PEG 6000 SD 1:0.7 and f- carbamazepine/ PEG 6000 SD 1:0.9 prepared by fusion method**

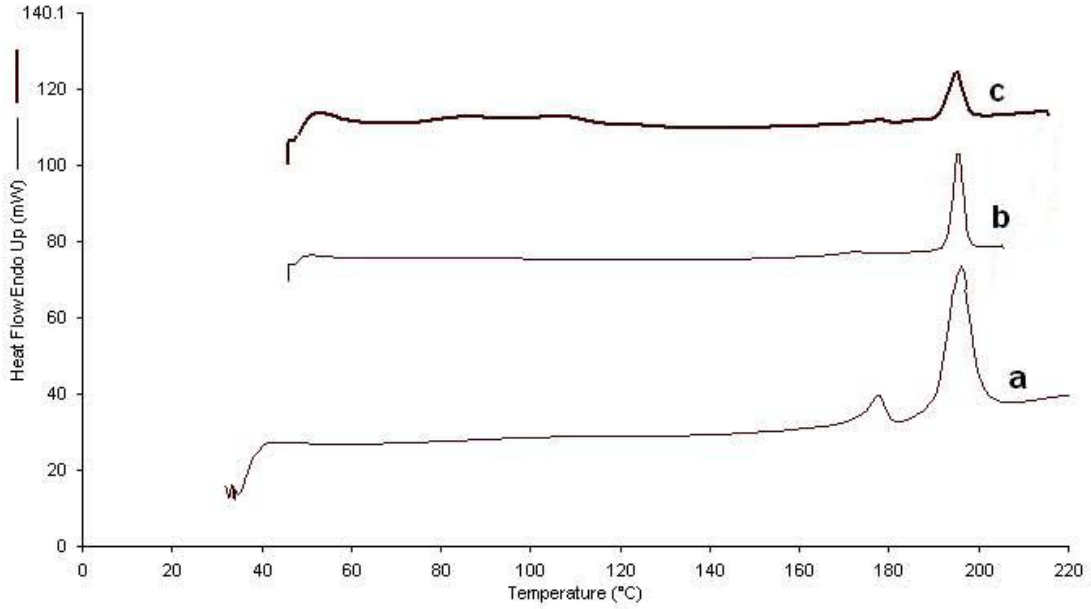


**Figure 3: DSC thermal analysis for: a- CBZ alone. b- CBZ / microcrystalline cellulose physical mixture 1:1, c- CBZ / magnesium stearate physical mixture 1:1**

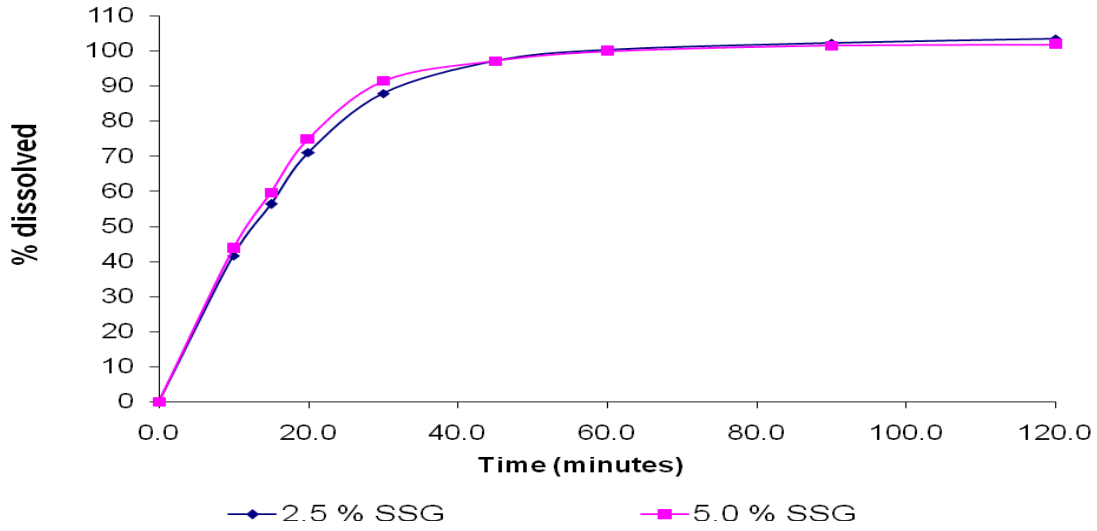


**Figure 4: Dissolution in distilled water containing 1.0 % SLS of carbamazepine 200 mg tablets prepared from solid dispersions by the fusion method**

***Conclusion***

The use of PEG 6000 in small ratios compared to CBZ had enhanced the dissolution rate of the drug in comparison with pure untreated one. All the prepared tablets fulfilled the pharmacopeal requirements concerning uniformity of weight, friability, hardness, loss on drying, drug content and dissolution results. Disintegration time of tablets prepared by 2.5 % SSG were not conforming to USP standard limit while tablets prepared by 5.0 % SSG were conforming to this limit.

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**REFERENCES**

**Ali W, Badawi A, Mahdy M and El-Nahas H (2012).** Formulation and evaluation of carbamazepine 200 mg chewable tablets using cyclodextrins. *International Journal of Pharmacy and Pharmaceutical Sciences* **4**(4).

**Ali W, Badawi A, Mahdy M and El-Nahas H (2013).** Formulation and evaluation of carbamazepine 200 mg controlled release tablets using different HPMC grades. *British Journal of Pharmaceutical Research* **3**(4).

**Ali W, Badawi A, Mahdy M and El-Nahas H (2013).** Formulation and evaluation of carbamazepine 200 mg immediate release tablets using polyethylene glycol 6000. *International Journal of Pharmacy and Pharmaceutical Sciences* **5**(1).

**Barzegar–Jalali M, Nayebi AM, Valizadeh H, Hanaee J, Barzegar-Jalali A, Adibkia K, Anoush M and Sistanizad M (2006).** Evaluation of in vitro–in vivo correlation and anticonvulsive effect of carbamazepine after cogrinding with microcrystalline cellulose. *Journal of Pharmaceutical Sciences* **9**(3) 307-316.

**Biswal S, Sahoo J and Murthy PN (2009).** Characterization of Gliclazide-PEG 8000 solid dispersions. *Tropical Journal of Pharmaceutical Research* **8**(5) 417-424.

**Bley H (2010).** Bernd Fussnegger and Ronald Bodmeir, Characterization and stability of solid dispersions based on PEG/polymer blends. *International Journal of Pharmaceutics* **390** 165-173.

**British Pharmacopea Volume III (2010).** Published by the stationery office on behalf of the Medicines and Healthcare Products regulatory Agency (MHRA).

**Doshi DH, Ravis WR and Betageri GV (1997).** Carbamazepine and polyethylene glycol solid dispersions: preparation, in vitro dissolution, and characterization. *Drug Development and Industrial Pharmacy* **23**(12) 1167-1176.

**Florey K (1980).** Analytical profiles of drug substances, Academic press **9** 87-103.

**Kalia A, Khurana S and Bedi N (2009).** Formulation and evaluation of mouth dissolving tablets of oxcarbazepine, *International Journal of Pharmacy and Pharmaceutical Sciences* **1**(1) 12-23.

**Kalyanwat R, Gupta S, Songara R, Jian D and Patel S (2011).** Study of enhancement of dissolution rate of carbamazepine by solid dispersion, Pharmacy Globale. *International Journal of Comprehensive Pharmacy* **2**(5) 1-4.

**Karanth H, Shenoy VS and Murthy RR (2006).** Industrially feasible alternative approaches in the manufacture of solid dispersions: A technical report. *AAPS PharmSciTech* **7**(4) Article 87.

**Leuner C and Dressman J (2000).** Improving drug solubility for oral delivery using solid dispersions, *European Journal of Pharmaceutics and Biopharmaceutics* **50**(1) 47-60.

**Mahalaxmi R, Ravikumar, Oandey S, Shirwaikar Arun and Shirwair Annie (2009).** Effect of recrystallization on size, shape, polymorph and dissolution of carbamazepine. *International Journal of Pharmtech Research* **1**(3) 725-732.

**Mali P.A., Bharate S.D., Bari M.M., Lohare G. and Janjale M. (2012).** Formulation development and evaluation of fast dissolving tablet of carbamazepine. IJCPR. 4(3), 48-51.

**Nafee NA, Ismail FA, Boraie NA and Mortada LM (2003).** Muco-adhesive buccal patches of miconazole nitrate: in vitro/in vivo performance and effect of ageing. *Journal of Pharmaceutical Sciences* **264**(1-2) 1-14.

**Raymond CR, Paul JS and Marian EQ (2009).** Handbook of pharmaceutical excipients, sixth edition, *Pharmaceutical press* 210- 214.

**Rustichelli C, Gamberini G, Ferioli V *et al.*, (2000).** Solid-state study of polymorphic drugs: carbamazepine. *Journal of Pharmaceutical and Biomedical Analysis* **23** 41-54.

**Sammour OA, Hammad MA, Megrab NA and Zidan AS (2006).** Formulation and optimization of mouth dissolve tablets containing rofecoxib. *AAPS PharmSciTech* **7** 17-31.

**Sethia S and Squillante E (2002).** Physicochemical characterization of solid dispersions of carbamazepine formulated by supercritical carbon dioxide and conventional solvent evaporation method. *Journal of Pharmaceutical Sciences* **91**(9) 1948-1957.

**Tayel SA, Soliman II and Louis D (2008).** Improvement of dissolution properties of carbamazepine through application of the liquisolid tablet technique. *European Journal of Pharmaceutics and Biopharmaceutics* **69** 342-347.

**Verheyen S, Augustijns P, Kinget R and Van den Mooter G (2001).** Melting behavior of pure polyethylene glycol 6000 and polyethylene glycol 6000 solid dispersions containing diazepam or temazepam: a DSC study. *Thermochimica Acta* **380** 153-164.