Research Article

[Rahman *et al.*, 3(3): Mar., 2012]

ISSN: 0976-7126

INTERNATIONAL JOURNAL OF PHARMACY & LIFE SCIENCES

Enhancement of solubility and dissolution properties of clonazepam by solid dispersions

Md. Armin Minhaz[1], Md. Mofizur Rahman[2*], Md. Qamrul Ahsan[1], Md. Habibur Rahman[2] and Md. Raihan Chowdhury[1]

1, Department of Pharmacy, University of Asiapacific, Dhaka, Bangladesh

2, Department of Pharmacy, Bangladesh University, Dhaka, Bangladesh

Abstract

The aim of the present study was to improve the solubility and dissolution rate of a poorly water-soluble drug by a solid dispersion technique, in order to investigate the effect of these polymers on release mechanism from solid dispersions. Clonazepam was used as a model drug to evaluate its release characteristics from different matrices. Solid dispersions were prepared by using polyethylene glycol 6000 (PEG- 6000), HPMC, HPC and Poloxomer in different drug-to-carrier ratios (1:2, 1:4, 1:6, 1:8, 1:10). The solid dispersions were prepared by solvent method. The pure drug and solid dispersions were characterized by in vitro dissolution study. Distilled water was used as dissolution media, 1000 ml of distilled water was used as dissolution medium in each dissolution basket at a temperature of 37° C and a paddle speed of 100 rpm. The very slow dissolution rate was observed for pure Clonazepam and the dispersion of the drug in the polymers considerably enhanced the dissolution rate. This can be attributed to improved wettability and dispersibility, as well as decrease of the crystalline and increase of the amorphous fraction of the drug. Solid dispersions prepared with PEG-6000, Poloxomer showed the highest improvement in wettability and dissolution rate of Clonazepam. Solid dispersion containing polymer prepared with solvent method showed significant improvement in the release profile as compared to pure drug, clonazepam.

Key-Words: Clonazepam, Solid dispersions, PEG 6000, HPMC 6cps, Poloxomer 407

Introduction

In solid dispersion systems, a drug may exist as an amorphous form in polymeric carriers, and this may result in improved solubility and dissolution rates compared with crystalline material. The mechanisms for the enhancement of the dissolution rate of solid dispersions have been proposed by several investigators. Molecular dispersion of drug in polymeric carriers may lead to particle size reduction and surface area enhancement, which result in improved dissolution rates. Furthermore, no energy is required to break up the crystal lattice of a drug during dissolution process and improvement in drug solubility and wettability due to surrounding hydrophilic carriers [1].

*** Corresponding Author**
E-Mail: rmfi02@yahoo.com
Tel: +8801911605139

Most of the recently introduced drugs suffer from poor solubility as they are developed by combinatorial chemistry and high throughput screening techniques. Solid dispersions are useful for solving the solubility and bioavailability problem of such drugs [2]. By definition solid dispersions are formulations of finely crystalline or amorphous drug dispersed in an inert matrix [3].

Reduction or absence of aggregation and agglomeration may also contribute to increased dissolution. The methods used to prepare solid dispersions include the melting method, the solvent method, and the solvent wetting method [4, 5].

Among the various approaches employed to improve the dissolution of poorly soluble drugs, solid dispersion has been proven successful. Fast or immediate drug dissolution from solid dispersions has been observed due to increased wettability, improved dispersibility of drug particles, existence of the drug in amorphous form with improved solubility and absence of aggregation of drug particles [6]. Literature shows that the solvent evaporation method has been used for the preparation of solid dispersions for dissolution enhancement [7].

Polymeric carriers have been the most successful for solid dispersions, because they are able to originate amorphous solid dispersions. They are divided into fully synthetic polymers and natural product-based polymers. Fully synthetic polymers include povidone (PVP), polyethyleneglycols (PEG) and polymethacrylates . Natural productbased polymers are mainly composed by cellulose derivatives, such as hydroxypropylmethylcellulose (HPMC), ethylcellulose or hydroxypropylcellulose or starch derivates, like cyclodextrins . Amorphous solid dispersions can be classified according to the molecular interaction of drug and carriers in solid solutions, solid suspensions or a mixture of both. In amorphous solid solutions, drug and carrier are totally miscible and soluble, originating a homogeneous molecular interaction between them. In these systems, the drug and carrier interaction energy is extremely high, resulting in a really true solution [8].

In the present experiment Clonazepam belongs to a class of anticonvulsants that enhances gamma-aminobutyric acid (GABA) receptor responses. Anticonvulsants used for several types of seizures, including myotonic or atonic seizures, photosensitive epilepsy, and absence seizures. Clonazepam exerts its action by binding to the benzodiazepine site of the GABA receptors, which causes an enhancement of the electric effect of GABA binding on neurons resulting in an increased influx of chloride ions into the neurons. This results in an inhibition of synaptic transmission across the central nervous system [9, 10]. Clonazepam is a light yellow crystalline powder which is practically odorless. It is freely very soluble in methanol, ethanol, and acetone, and practically insoluble in water (at 25°C < 0.1 mg/ml). It is generally considered that compounds with very low aqueous solubility will show dissolution rate-limited absorption and, hence, poor absorption, distribution, and target organ delivery [11]. Improvement of aqueous solubility in such a case is a valuable goal to improve therapeutic efficacy.

Several attempts have been reported in literature using solid dispersion technique to increase the dissolution characteristics where Hydroxy Propyl methyl cellulose (HPMC), polyvinylpyrrolidone (PVP), polyethylene glycol, sodium carboxymethyl cellulose, sodium starch glycolate, pregelatinized starch were used as solubilizing agents [12-14].

In this study solid dispersions were formulated with three water soluble polymers by solvent evaporation technique. Micronized poloxamer 407, HPMC 6 cps and HPC were utilized for this purpose. Poloxamers are nonionic polyoxyethylene-poly-oxypropylene copolymers used primarily as emulsifiers, solubilizing agents, wetting agents and have been reported for enhancing the solubility and bioavailability of sparingly soluble drugs in solid dosage forms [15-17]. Solid dispersions were prepared with poloxamer by melting method for rofecoxib [18] and ibuprofen [18] Reduced crystalline structure and improved wettability [19, 20] were mentioned as the mechanism by which poloxamer can enhance dissolution from solid dispersions. On the other hand, both HPMC and PVP are known to act as crystallization inhibitors and thus they help to produce solid solutions [21-24]. They improve the dissolution characteristics due to interaction through hydrogen bonding.

The objective of the present study was to improve the solubility of Clonazepam by using three different types of water soluble polymers. The formulations were characterized by in vitro dissolution study to compare the effects of polymers on the preparation of solid dispersion and dissolution enhancement.

Material and methods

Materials

Clonazepam was a gift sample from Rangs Pharmaceuticals Ltd., Dhaka, Bangladesh. Poloxamer 407 (Lutrol 127) was gifted by BASF, Germany. HPMC 6 cps (Shin Etsu Chemical Company Ltd., Japan), HPC (Samsung, Korea) and reagent grade methanol (Merck, Germany) were purchased from the market.

Preparation of solid dispersions

The solvent process (Figure 1) either comprises dissolving a sparingly water-soluble drug and a water-soluble polymer, i.e. the carrier, in an organic solvent capable of dissolving both and removing the solvent by evaporation or comprises dissolving the drug in an organic solvent, dispersing the solution in the carrier and removing the solvent by evaporation to provide the desired solid dispersion.

Formulation of clonazepam solid dispersion with different polymer showed in the table 1-3. 50 mg of clonazepam was taken in the vial and 4ml acetone was added in each. The drug was completely dissolved in the solvent. Then different types of polymer were added in the solution and sonicated it for 1 min. All solutions were dried by hot air. When the solutions were evaporated completely, they were stored in a dessicator. The formulations were withdrawn from vials, crushed in morter and pestle, passed through 36 microne sieves. Finally lactose was added in the formulation. Then formulations were transferred in vials and stored in a dessicator. A slightly different approach was warranted for solid dispersions containing poloxamer as it is low melting substance (m.pt. 52-57oC) and melting method was most suitable

ISSN: 0976-7126

for this polymer [18, 19]. The drug was dispersed with methanol in a glass flask and heated in a water bath at 50oC. Poloxamer was added to the dispersion and it was melted at that temperature. The solvent was evaporated during constant mixing and the resulting solid mass was dried at 40oC in hot air oven. The dried samples were crushed in mortar and pestle followed by sieving through 30 mesh screen. The ratio between drug and polymer for all polymers was kept at 1:2, 1:4, 1:6, 1:8 and 1:10.

Preparation of standard curve of clonazepam in distilled water

To prepare a standard curve for Clonazepam, 10mg of Clonazepam was accurately weighted & dissolved in 100 ml of Methanol to produce a solution 0.1 mg/ml. Then 20ml of preparation was taken and made up to 100ml with distilled water. Then 1, 2, 3, 4, 5, 6, 7, 8, 9 & 10 ml of this solution was taken in 10ml volumetric flask & 9, 8, 7, 6, 5, 4, 3, 2, 1 & 0 ml distilled water was added to them for the purpose of serial dilution. This serial dilution was carried out to get different Clonazepam concentration. These were then analyzed by UV spectrophotometer at 254 nm and absorbance was noted. Then the absorbance values were plotted against drug concentration and standard curve of Clonazepam was produced.

Quantitative assay

Formulation containing clonazepam was taken in a morter and triturated properly until fine powder was formed. 5 mg equivalent of fine powder was taken in a 10 ml volumetric flask with the help of a funnel. 5 ml methanol and 5 ml distilled water was added with the powder, sonicated in a sonicator to make a clear solution and then finally was filtered. From this solution 2 ml drug solution was withdrawn and taken in a 100 ml volumetric fiask. The volume of drug solution was then adjusted up to 100 ml with distilled water.

In the same way, 10 mg equivalent of fine powder was taken in a 25 ml volumetric flask with the help of a funnel. 10 ml methanol and 15 ml distilled water was added with the powder, sonicated in a sonicator to make a clear solution and then finally was filtered. From this solution 2 ml drug solution was withdrawn and taken in a 100 ml volumetric fiask. The volume of drug solution was then adjusted up to 100 ml with distilled water. For reagent blank 1 ml methanol was transferred into a 100 ml volumetric flask, diluted to 100 ml with distilled water.

Absorbance value was determined using UV-spectrophotometer (UV-mini-1240, SHIMADZU CORP., Kyoto, Japan), at 254 nm. Solutions were also diluted if necessary. Using the absorbence value, the amount of clonazepam entrapped was determined with the help of standard curve.

***In-vitro* release study of Clonazepam from solid dispersion**

In-vitro dissolution study was performed in a paddle type Dissolution Apparatus (USP Type II Dissolution Apparatus, VEEGO, INDIA). A fixed amount of solid dispersion containing 10 mg equivalent clonazepam from each batch was calculated for dissolution purpose. Distilled water was used as dissolution media. 1000 ml of distilled water was used as dissolution medium in each dissolution basket at a temperature of 37° C and a paddle speed of 100 rpm. The fixed amount of solid dispersion from each batch was weighed and transferred in each dissolution basket. The dissolution was carried out for 1 hour and 5 ml sample was withdrawn at predetermined intervals of 5, 10, 15, 20, 30, 40, 50 & 60 minutes. Each and every time 5 ml dissolution sample was compensated by another fresh 5 ml distilled water.

Dissolution samples were withdrawn with the help of disposable syringe filter and were kept in a test tube. The dissolution samples were then analyzed spectrophotometrically by UV-VIS spectrophotometer (UV-mini-1240, SHIMADZU CORP., Kyoto, Japan) at 254 nm and absorbance was noted. The dissolution study for each batch was performed in triplicate. These were then analyzed by UV spectrophotometer

Results and Discussion

The effects of three water soluble polymers (HPMC, HPC and poloxamer) on the formulations of Clonazepam solid dispersions were compared. The potencies of Clonazepam in prepared solid dispersions were analyzed by UV spectrophotometer and the results were within 99-100% in all cases which indicates uniform mixing of the dispersions.

Dissolution studies

The in vitro dissolution testing was performed for 45 minutes to ascertain the effect of formulations on immediate drug release enhancement. The enhancement of polymers on drug release from solid dispersion was evaluated by comparing the solubility of drug present in the mixtures as well as of pure drug. Theoretically the solid dispersions improve drug dissolution by decreasing particle size, formation of amorphous forms and improved wettability [2].

HPMC show retarded dissolution rate. Rane Y., et al., reported that in the case of HPMC solid dispersions, an increase in the amount of polymer up to a certain level resulted in enhanced dissolution rate but further addition of polymer resulted in a decrease of dissolution rate. This finding may be correlated to

ISSN: 0976-7126

matrix-forming ability of HPMC. Solid dispersions of hydrophilic swellable polymers such as HPMC become gelatinized in the dissolution medium. HPMC showed retarded drug dissolution, which may be owing to the formation of highly viscous barrier layer at the interface of drug and dissolution medium [14].

The better dissolution rate of solid dispersion may be due to an improved wettability of drug particles, a significant reduction in particle size during formation of solid dispersion and dissolution due to increase in the surface area of drug, proper dispersion and increase in the amorphicity of drug by adsorption on the surface of adsorbent. High rate of dissolution of soluble polymer component of solid dispersion which would pull along more insoluble but finely mixed drug into dissolution medium. Similar studies was performed by Hsiu-O Ho et., al [25] the dissolution rate of nifedipine increased as more HPMC was added to the solid dispersions.

Comparison of % release of HPMC 6cps

From the curve it is observed that increases the HPMC with other polymer were fixed and the drug release was increase significantly. In the case of pure drug, release was decreased than drug with the combination of other polymer. When HPMC is increased drug release from solid dispersion increase significantly due to wetting ability and convert crystalline to amorphous. The formulation containing increased HPMC increased drug release.

The drug release was reduced by higher amount of HPMC. The polymer, when used at high concentration, forms a gelatinous layer around drug particles upon contact with aqueous media and which acts as a barrier to drug release. The drug is released slowly from such matrix by diffusion process. Usually the higher molecular weight HPMC (such as HPMC K15, K100) are used for sustained release effect in tablet formulations but in case of solid dispersions the low molecular weights are capable of achieving the enhance drug release.

The formulation containing 1:10 drug-polymer, the drug release was highest due to wetting ability (Fig. 3). At high concentration HPMC provides wetting of drug and improves dissolution. It is supported by the fact that increased drug release was observed with formulations containing drug/polymer 1:10 ratio (Fig. 3). This formulation contained small amount of crystal lattice compared to pure drug alone which indicates reduction of drug particle size may be responsible for improved dissolution.

Comparison of % release of HPC

From the curve (Fig. 4) it is observed that increases the HPC with other polymer were fixed and the drug release was increase significantly. In the case of pure drug, release was decreased than drug with the combination of other polymer. When HPC is increased drug release from solid dispersion increase significantly due to wetting ability and convert crystalline to amorphous. The formulation containing increased HPC increased drug release.

Comparison of % release of Poloxomer 407

From the curve (Fig 5) it is observed that increases the Poloxomer with other polymer were fixed and the drug release was increase significantly. In the case of pure drug, release was decreased than drug with the combination of other polymer. When poloxomer is increased drug release from solid dispersion increase significantly due to wetting ability and convert amorphous to crystalline. The formulation containing increased poloxomer increased drug release.

Poloxamer 407 can act as gelling agent at high concentration and it can affect drug dissolution from solid dispersions. Drug release was very rapid compared to other polymers ratios. But similar to HPMC, higher amount of poloxamer facilitated drug release. When the poloxomer concentration was decreased the drug release was also decreased.

Although dissolution rate for poorly water-soluble drug can be enhanced by converting the drug into its amorphous form [26] but it can be thermodynamically unstable, and under certain levels of heat and humidity, could recrystallize into a more stable, poorly water-soluble form [27]. Clonazepam could be crystallized out of the formulations from poloxamer containing solid dispersions after contact with aqueous media. Poloxomers rapidly dissolved away from the solid dispersions and amorphous clonazepam reverted back to its crystalline state.

It was reported that molecular dispersion is one of the important roles of drug release from the polymer-drug system. The present work shows that the dissolution rate of Clonazepam from solid dispersions with PEG 6000 and poloxomer improved compared to the pure drug. Further, solid dispersions performed better than the corresponding physical mixtures. Various studies have shown that freely water soluble carriers inhibit crystallization of drugs in solid dispersions resulting in amorphous form of the drug in the solid dispersions [28, 29]. Crystallization inhibition is attributed to two effects: interactions, such as hydrogen bonding between the drug and the polymer and the entrapment of the drug molecules in the polymer matrix during solvent evaporation or a combination of both. The present study confirmed the advantage of improved aqueous solubility of Clonazepam in its solid

ISSN: 0976-7126

dispersions form, which can be formulated as tablets with better dissolution characteristics.

Solid dispersion is proven to be a useful technique to improve the solubility of poorly soluble drugs like Clonazepam. Solid dispersions prepared from hydrophilic polymers using the solvent evaporation method were effective in improving drug dissolution. The dispersion containing Poloxomer (Table 2.) shows acceptable dissolution compared to the HPMC, HPC dispersion or pure drug. The study revealed that optimum levels of hydrophilic carriers and hydrophillic porous adsorbants ensure a prompt and complete dissolution of clonazepam from solid dispersions that are used in oral pharmaceutical formulations. Depending on experimental data it is concluded that the type of polymer and drug-polymer ratio are the critical factors for the development of solid dispersions.

Acknowledgement

The authors are thankful to Rangs Pharmaceuticals Ltd., Dhaka, Bangladesh for their generous donation of Clonazepam. The authors are also thankful to Bangladesh University, University of Asiapacific and the University of Dhaka for their supports and co-operations.

References

1. Yamashita, K.; Nakate, T.; Okimoto, K.; Ohike, A.;et al Establishment of new preparation method for solid dispersion formulation of tacrolimus. Int. J. Pharm. **2003**, *267*, 79–91.
2. Leuner. C, Dressman. J. Improving drug solubility for oral delivery using solid dispersions. *Eur J Pharm Biopharm*. **2000**, 50, 47–60.
3. Chiou, WL, Rigelman, S. Pharmaceutical application of solid dispersion system. *J Pharm Sci.* **1971**, 60, 1281-1302.
4. Yh-Nam, P.; Jing-Huey, C.; Russel, R.C.et al. Enhancement of dissolution and bioavailability of piroxicam in solid dispersions systems. *Drug Dev. Ind. Pharm.* **2000**, *26*, 989–994.
5. Van den Mooter, G.; Augustijns, P.; Blaton, et al. Physicochemical characterization of solid dispersions of temazepam with polyethylene glycol 6000 and PVP K30. *Int. J. Pharm.* **1998**, *164*, 67–80.
6. Gohel, M. C.; Patel, L. D. Improvement of nimesulide dissolution from solid dispersions containing crosscarmellose sodium and Aerosil® 200. *Acta Pharm.* **2002**, 52, 227–241.
7. *United States Pharmacopoeia*, 23, NF 18. The USP Convention, Rockville **1995**, pp. 1791–1799.
8. Costantino, HR.; Firouzabadian, L. Wu. C.; Carrasquillo, KG.; Griebenow, K.; Zale SE.; Tracy, MA. Protein spray freeze drying. 2. Effect of formulation variables on particle size and stability. *J. Pharm. Sci.* **2002**, 91**,** 2, 388-395.
9. Skerritt, JH.; Johnston, GA. Enhancement of GABA binding by benzodiazepines and related anxiolytics. *Eur J Pharmacol*. **1983**, 89, 3–4, 193–198.
10. Lehoullier, PF.; Ticku, MK. Benzodiazepine and beta-carboline modulation of GABA-stimulated 36Cl-influx in cultured spinal cord neurons. *Eur J Pharmacol.* **1987**, 135, 2, 235–238.
11. Proudfoot, S. Factors affecting bioavailability: factors influencing drug absorption from the gastrointestinal tract. In: Aulton ME, editor. Pharmaceutics: the science of dosage from design. Edinburgh: Churchill Livingstone. **1991**. pp. 135–173.
12. Douroumis, D.; Bouropoulos, N.; Fahr, A. Physicochemical characterization of solid dispersions of three antiepileptic drugs prepared by solvent evaporation method. *J Pharm Pharmacol*. **2007**, 59, 645–653.
13. Nair, R.; Gonen, S.; Hoag, SW. Influence of polyethylene glycol and povidone on the polymorphic transformation and solubility of carbamazepine. *Int J Pharm*. **2002**, 240, 11–22.
14. Rane, Y.; Mashru, R.; Sankalia, M.; Sankalia, J. Effect of Hydrophilic Swellable Polymers on Dissolution Enhancement of Carbamazepine Solid Dispersions Studied Using Response Surface Methodology. *AAPS PharmSciTech.* **2007**, 8, 2, Article 27.
15. Chen, Y.; Zhang, GGZ.; Neilly, J.; Marsh, K.; Mawhinney, D.; Sanzgiri, YD. Enhancing the bioavailability of ABT-963 using solid dispersion containing pluronic F-68. *Int J Pharm* **2004**, 286, 69-80.
16. Passerini, N.; Gonzalez-Rodriguez, ML.; Cavallari, C.; Rodriguez, L.; Albertini, B. Preparation and characterization of ibuprofen-poloxamer 188 granules obtained by melt granulation. *Eur J Pharm Sci*. **2002**, 15, 71-78.
17. Yu, H.; Chun, MK.; Choi, HK. Preparation and characterization of piroxicam/poloxamer solid dispersion prepared by melting method and solvent method. *J Kor Pharm Sci,* **2007,** 37, 1-5.
18. Newa, M.; Bhandari, KH.; Oh, DH.; Kim, YR.; Sung, JH.; Kim, JO.; Woo, JS.; Choi, HG.; Yong, CS. Enhanced Dissolution of Ibuprofen Using Solid Dispersion with Poloxamer 407. *Arch Pharm Res* **2008**, 31, 11, 1497-1507.

ISSN: 0976-7126

19. Shah, TJ.; Amin, AF.; Parikh, JR.; Parikh, RH. Process Optimization and Characterization of Poloxamer Solid Dispersions of a Poorly Water-soluble Drug. *AAPS PharmSciTech*, **2007**, 8, 2, Article 29.
20. Chokshi, RJ.; Zia, H.; Sandhu, HK.; Shah, NH.; Malick, WA. Improving the Dissolution Rate of Poorly Water Soluble Drug by Solid Dispersion and Solid Solution-Pros and Cons. *Drug Delivery*, **2007**, 14, 33–45.
21. Konno, H.; Handa, T.; Alonzo, DE.; Taylor, LS. Effect of polymer type on the dissolution profile of amorphous solid dispersions containing felodipine. *Eur J Pharm Biopharm*, **2008**, 70, 2, 493-9.
22. Gao, P.; Rush, BD.; Pfund, WP.; Huang, T.; Bauer, JM.; Morozowich, W.; Kuo, MS.; Hageman, MJ. Development of a supersaturable SEDDS (S-SEDDS) formulation of paclitaxel with improved oral bioavailability. *J Pharm Sci*, **2003**, 92, 12, 2386-98.
23. Iervolino, M.; Cappello, B.; Raghavan, SL.; Hadgraft, J. Penetration enhancement of ibuprofen from supersaturated solutions through human skin. *Int J Pharm.* **2001,** 212, 1, 131-41.
24. Lipp, R. Selection and use of crystallization inhibitors for matrix-type transdermal drug-delivery systems containing sex steroids. *J Pharm Pharmacol*. **1998**, 50, 12, 1343-9.
25. Hsiu-O, Ho. ; Huei-Lin, Su.; Tsuimin, Tsai.; Ming-Thau, Sheu. The preparation and characterization of solid dispersions on pellets using a fluidized-bed system. International Journal of Pharmaceutics. **1996**, 139, 1-2, 223-229
26. Hancock, BC.; Parks, M. What is the true solubility advantage for amorphous pharmaceuticals? *Pharm Res*, **2000**, 17, 397-404.
27. Matsuda, Y.; Kawaguchi, S. Physicochemical characterization of oxyphenbutazone and solid-state stability of its amorphous form under various temperature and humidity conditions. *Chem Pharm Bull*, **1986**, 34, 1289-1298.
28. Van, DMG.; Augustijns, P.; Blaton, N.; Kinget, R. Physicochemical characterization of solid dispersions of temazepam with polyethylene glycol 6000 and PVP K30. Int J Pharm. **1998**, 164, 67–80.
29. KPR; Murthy, KVR.; Hayman, AR.; Becket, G. Physicochemical characterization of nimesulide- cyclodextrin binary systems. *AAPS PharmSciTech*. **2003**, 4, 1, article 7, 1-12.

Table 1: Formulation of clonazepam solid dispersion by changing the amounts of HPMC 6cps with PEG 6000

Formulation of solid dispersion						
Component	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Clonazepam	50	50	50	50	50	50
PEG 6000	100	100	100	100	100	100
HPMC 6cps	500	400	300	200	100	0
Lactose	3	3	3	3	3	3

Table 2: Formulation of clonazepam solid dispersion by changing amounts of HPC with PEG 600

Formulation of solid dispersion						
Component	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Clonazepam	50	50	50	50	50	50
PEG 6000	100	100	100	100	100	100
HPC	500	400	300	200	100	0
Lactose	3	3	3	3	3	3

ISSN: 0976-7126

Table 3: Formulation of clonazepam solid dispersion by changing the amounts of Poloxomer 407 with PEG 6000

Formulation of solid dispersion						
Formulation	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)
Clonazepam	50	50	50	50	50	50
PEG 6000	100	100	100	100	100	100
Poloxomer 407	500	400	300	200	100	0
Lactose	3	3	3	3	3	3

Poorly water soluble drug

(Clonazepam)

+

Solvent

(Acetone)

+

Polymers

(HPMC 6 CPS / HMC / POLOXOMER)

⇩

Solvent evaporation resulting Solid Dispersion

+

Adsorbents

(Lactose)

⇩

Prepared formulations

Fig. 1: Flow chart for the process of preparation of Solid Dispersion (Solvent method)

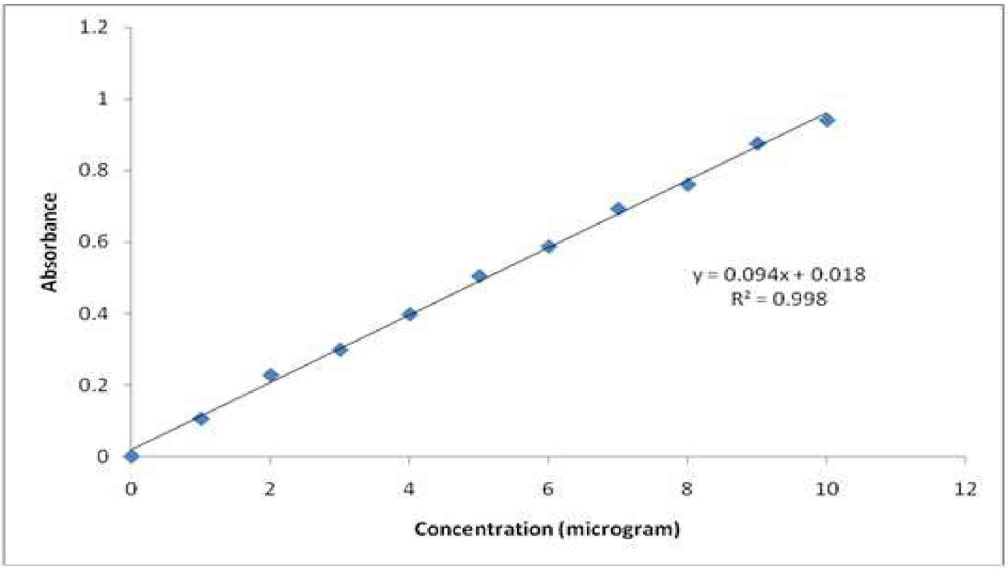

Fig. 2: Standard curve of clonazepam in distilled water

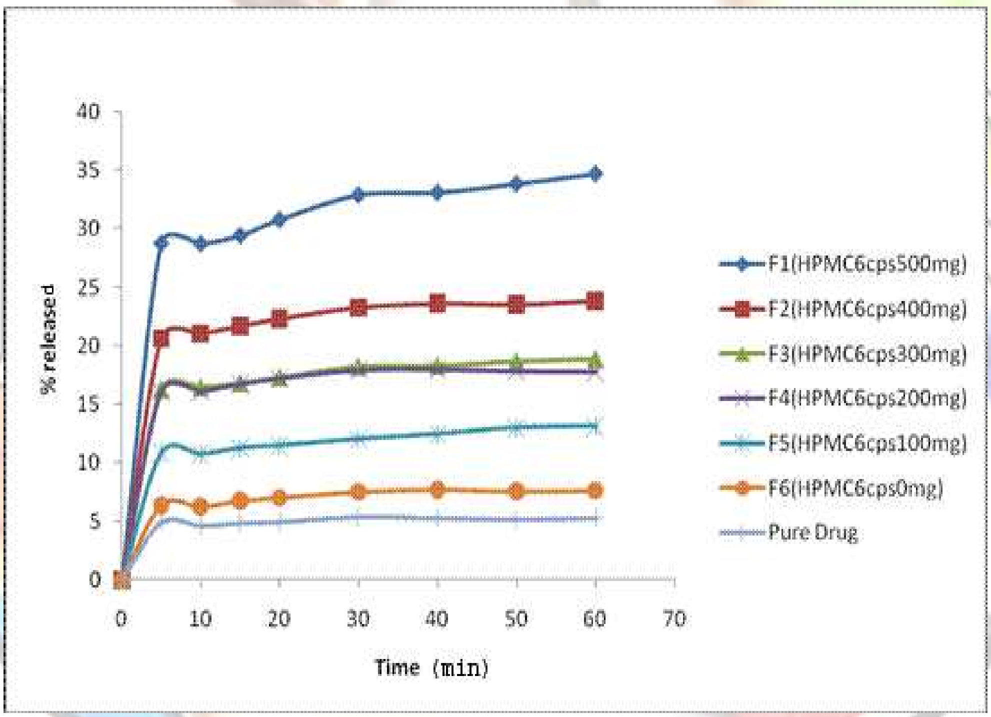

Fig. 3: Drug release from HPMC 6 cps formulations

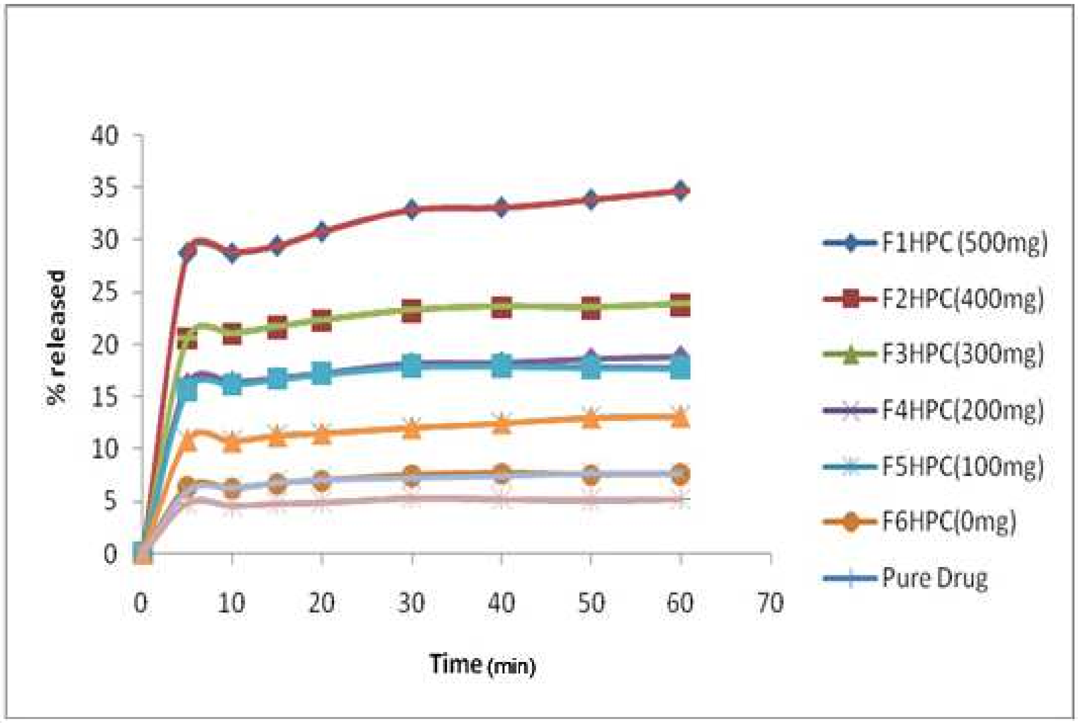

Fig. 4: Drug release from HPC formulations

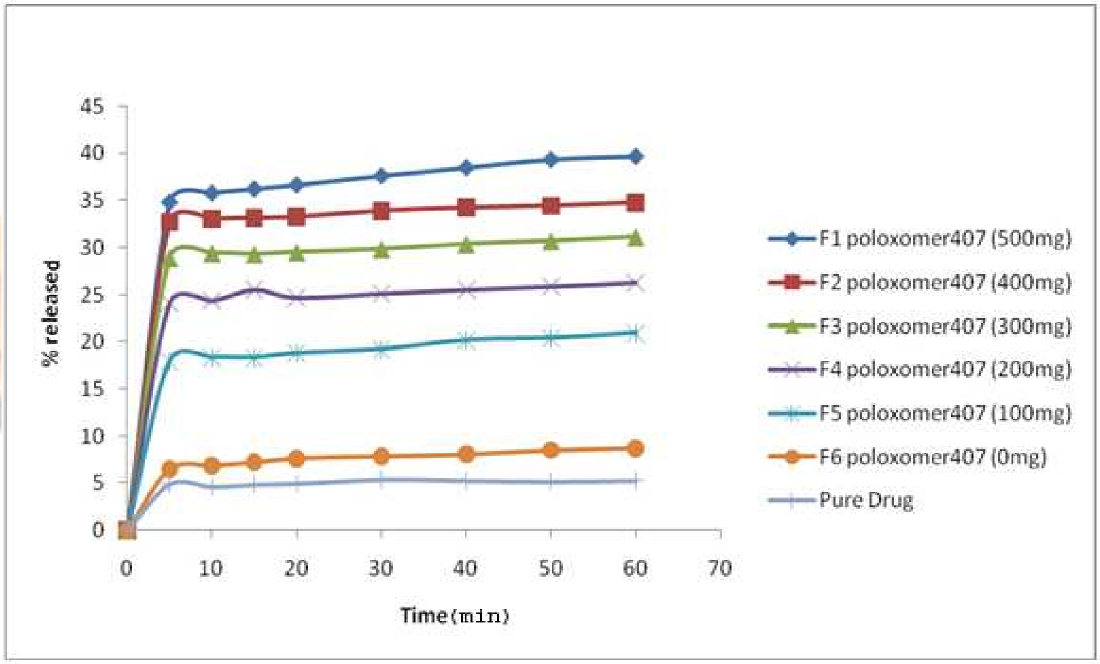

Fig. 5: Drug release from ploxomer 407 formulations