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By Solvent Evaporation Method, In Vitro Dissolution Study of Glimepiride from Binary and Ternary Solid Dispersion Formulation

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Abstract

Poor aqueous solubility and slow dissolution rate of the glimepiride lead to irreproducible clinical response or therapeutic failure in some cases due to sub therapeutic plasma drug levels. Glimepiride is a poorly water-soluble oral hypoglycemic drug exhibiting poor dissolution pattern. The purpose of this work is to increase the dissolution rate of glimepiride by formation of solid dispersion with different water soluble carriers. In this study, binary and ternary solid dispersion of glimepiride were prepared with poloxamer 407, polyethylene glycol 6000 (PEG 6000), polyethylene glycol 4000 (PEG 4000), and eudragit at different weight ratios using the solvent evaporation and melting method. Solvent evaporation method containing eudargit in ratio 1:2 (Formulation coding: SE2) Showed the best result in comparison of other binary SD formulation by solvent evaporation technique which was released 6.19% after 5 min and 82.29% within 60 mins. Solvent evaporation technique of SD formulation of glimepiride contain poloxomer 407inratio1:9 (Formulationcoding:SE9) showed the best result the other formulation which was 44.71 % after 5 min and 72.68% within 60 mins. was also studied that the release kinetics of glimepiride of different SD formulation with different ratio such as, First order release kinetics, Higuchi, Krosmeyer, Hixoncrowell plot, and also be noted the MDT calculation for improving the solubility of glimepiride. Formulations were characterized by Fourier transform infrared (FTIR) and X-ray diffraction (XRD).No any chemical interaction was

observed between polymer and drugs from IR spectrum. The drug was changed to amorphous form after solid dispersion.

Keywords: - *Glimepiride, Dissolution Study, Formulation, IR spectrum*

INTRODUCTION

The most challenging aspects in the pharmaceutical industry are related to strategies that improve the solubility of poorly soluble drugs. The production of solid dispersions (SDs) is commonly acknowledged as a method to enhance the aqueous solubility, thereby increasing the oral bioavailability of drugs with aqueous low solubility. Especially for substances according to the bio pharmaceutics Classification System, the bioavailability may be enhanced by increasing the solubility and dissolution rate of the drug in the gastrointestinal fluids (1). The rate of dissolution and solubility should not be confused as they are different concepts, kinetic and thermodynamic, respectively. The Solubilization kinetics, as well as apparent solubility can be improved after complexation of an active ingredient with cyclodextrin. This can be used in the case of drug with poor solubility (2).

The use of oral anti diabetic drugs for treatment of type 2 diabetes increases rapidly. It is widely used with the discovery and approval of several new types of oral anti diabetic drugs with different mechanism of pharmacological action(3). Many of the drugs belong to class II of the biopharmaceutical classification system showing poor solubility and high permeability Glimepiride shows low, pH dependent solubility. In acidic and neutral aqueous media, glimepiride exhibits very poor solubility at 370oc (<0.004 mg/ml). In media pH>7, solubility of drug is slightly increased to 0.02 mg/ml. These poorly water soluble drugs provide challenges to deliver them in an active and absorbable form to the desired absorption site using physiologically safe excipients Therefore; one of the most important steps in the development of dosage forms for these drugs is to improve their solubility and/or dissolution rate.

Chiou and Rigelman and Serajuadin et al. have used the solid dispersion (SD) technique for dissolution enhancement of poorly water-soluble drugs (4). Among the various approaches, the SD technique has often proved to be the most successful in improving the dissolution and bioavailability of poorly soluble active pharmaceutical

ingredients because it is simple, economic, and advantageous. Sekiguchi and Obi were the first to propose the SD method using water- soluble carriers to improve the dissolution characteristics of poorly water-soluble drugs. Many water-soluble carriers have been employed for preparation of SD of poorly soluble drugs (5). The most common are polyethyleneglycols, polyvinyl pyrrolidone, mannitol and hydroxypropyl methylcellulose. Due to poor solubility in GI fluids, it results in low and erratic oral bio availability (6). Glimepiride was selected as a model drug for dissolution enhancement studies in the present investigation. Attempts were made to enhance the dissolution of GMP using a SD technique. SDs of GMP with PVP K30 was prepared in different ratios using solvent evaporation method and then tablets of best formulation of SD were formulated by using direct compression method (7).

Tablet formulations were prepared by direct compression technique using super disintegrates povidone in different concentrations. SDs were evaluated for FTIR, XRD, SEM, in vitro dissolution profiles and developed tablet formulations were evaluated for various pharmaceutical characteristics viz. hardness, % friability, weight variation, drug content, disintegration time, in vitro dissolution profiles (8). Priyanka Shrestha, et al, has studied that, Glimepiride is a poorly water-soluble oral hypoglycemic drug exhibiting poor dissolution pattern (9). The purpose of this work is to increase the dissolution rate of glimepiride by formation of solid dispersion with different water soluble carriers. Solid dispersion of glimepiride were prepared with polyvinyl pyrrolidone k-30, poloxamer 407, polyethylene glycol 6000(PEG6000), polyethyleneglycol 4000 (PEG 4000), sodium starch glycolate, ludiflash and lactose at different weight ratios using the solvent evaporation and melting method (10). Physical mixtures of the poloxamer 407 and povidone K-30 with glimepiride at different ratios were also used. In compare to physical mixtures with povidone K-30 and poloxamer 407, drug release from physical mixture PM (1/9) PVP K-30 was higher (65.93%within 5 min) than drug release from physical mixture with poloxamer 407(56% within 5 min) the drug release from pure drug was 6.84%with in5 minute(11).

Solid dispersions showed a better dissolution compared to the pure drugs and physical mixtures, with SD (1/9) PVPK-30 showing the highest dissolution efficiency (91.89% within 5min). Drug release from immediate release tablet containing SD (1/9)

PVP K-30 was59.02% within 5 min and 100% within 30 min. Formulations were characterized by Fourier transform infrared (FTIR) and X-ray diffraction (XRD). No any chemical interaction was observed between polymer and drugs from IR spectrum. The drug was changed to amorphous form after solid dispersion (12).

MATERIALS AND METHODS:

Chemicals Used

Table1: List of ingredients used in experiment

Name of the materials	Functional category	Sources of the chemicals
Glimepiride powder	Active pharmaceutical ingredient(API)	ESKAYEFBANGLADESH LTD,GAZIPUR
Polyethyleneglycol 4000(PEG4000)	Carrier for solid dispersion	ALBION LABOROTORIESLTD.
Polyethyleneglycol 6000(PEG6000)	Carrier for solid dispersion	ALBION LABOROTORIESLTD.
PVP(Polyvinyl pyrrolidone)	Carrier for solid dispersion	LOCALMAEKET
Eudragit	Carrier for solid dispersion	THEACME LABORATORIESLTD.
Poloxomer407	Carrier for solid dispersion	BASF
Potassium dihydrogen phosphate	Major salt of buffer solution	MERCK,MUMBAI
Di-sodium hydrogen Phosphate	Major salt of buffer solution	MERCK, MUMBAI.
Methanol	Aqueous Solvent	UNIVERSITY LABORATORY
Distilled water	Solvent for buffer solution, Used as washing agent too	UNIVERSITY LABORATORY

Solvent Evaporation method

Solvent evaporation is another method used in the enhancement of solid dispersion of Glimepiride and the process is given below:

1) Accurately weighted amount of drug and polymer was taken in screw capped test tube and was dissolved in minimum volume of methanol to obtain clear solution.

2) Then the solutions were kept in room temperature for few days until the solvent was evaporated from the solution. The viscous residues thus obtained were allowed to solidify and the solidified mixture was then grinded to convert powder particles with the help of mortar and pestle

3) The powder particles were passed through a sieve (mesh size 40).

4) Then the resulted solid dispersion formulation were weighted and transferred in fresh vials with proper labeling.

5) Finally all SD formulation was kept in desiccators until further investigation.

Table 2: Formulation of binary solid dispersion of glimepiride prepared by solvent evaporation method using different polymer at different ratio

Serial No.	Carriers	Drug Ratio	Polymer summarized form	Dispensing(mg)	Formulation Coating	Method
43	Eudragit	1:1	Eudragit: Drug	300:300	SE1	Solvent evaporation
44	Eudragit	1:2	Eudragit: Drug	300:600	SE2	Solvent evaporation
45	Eudragit	1:3	Eudragit: Drug	300:900	SE3	Solvent evaporation
46	Eudragit	1:4	Eudragit: Drug	300:1200	SE4	Solvent evaporation
47	Eudragit	1:5	Eudragit: Drug	300:1500	SE5	Solvent evaporation
48	Poloxamer	1:1	Poloxomer: Drug	300:300	SE6	Solvent evaporation

49	Poloxamer	1:2	Poloxomer: Drug	300:600	SE7	Solvent evaporation
50	Poloxamer	1:3	Poloxomer: Drug	300:900	SE8	Solvent evaporation
51	Poloxamer	1:4	Poloxomer: Drug	300:1200	SE9	Solvent evaporation
52	Poloxamer	1:5	Poloxomer: Drug	300:1500	SE10	Solvent evaporation

Preparation of 0.01 M phosphate buffer solution (pH=7.8)

0.58g of monobasic potassium phosphate and 8.86g of dibasic sodium phosphate anhydrous was dissolved in sufficient amount of distilled water. Then pH 7.8was adjusted by adding 1N Sodium Hydroxide (NaOH) for the preparation of 1000ml buffer solution.

Preparation of Standard Curve of Glimepiride

1. 10mg of Glimepiride was accurately weighed and taken in 100mlvolumetric flask.

2. Then phosphate buffer was added upto the mark to prepare primary stock solution.

3. Then 10 ml of this solution was taken in another 100ml volumetric flask and added buffer solution up to the mark. This solution was called stock solution. Then serial dilution was carried out to get different drug concentration.

4. Then 1,2,3,4,5,6,7,8,9 and 10ml of stock solution was gradually taken to the test tube.

5. And 9,8,7,6,5,4,3,2,1 and o ml of buffer solution were added respectively to more 10 ml volume in each test tube.

6. These were then analyzed by UB spectrophotometer at 228 nm and the absorbance value were noted.

7. The absorbance value were plotted against drug concentrations.

8. Finally the standard curve of Glimepiride was produced.

In-vitro dissolution test for Glimepiride and solid dispersion formulation

The in vitro dissolution studies for Glimepiride drug and SD formulation were performed using USP dissolution test apparatus type II (paddle type) method using 900 ml of phosphate buffer (pH 7.8) as dissolution medium. The temperature of the medium was maintained at (37 ±0.5) oc throughout the experiment. The samples contained glimepiride or its equivalent solid dispersion were placed in the dissolution medium.

Paddle was used at a stirring rate of 75 rpm. A 5ml aliquot was withdrawn at predetermined time intervals of 5, 15, 30.45, and 60 min and then 5ml of fresh dissolution medium was replaced to maintain the constant volume of dissolution medium. The absorbance values of the collected samples were measured at 273nm using UV-visible spectrophotometer against dissolution medium as blank. The percent release of drug was calculated using the equation obtained from the standard curve in the media (13).

Fourier Transform Infra-red (FTIR) Spectroscopy

Infra-red studies was 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. FT-IR spectroscopy used to study the possibility of an interaction between drug and polymer in solid-state.

Fourier-transform infrared (FT-IR) spectra were obtained by using a Shimadzu IR 20 Spectrophotometer. The samples (Glimepiride or SDs) were previously grounded and mixed thoroughly with potassium bromide, an infrared transparent matrix, at 1:5 (Sample: KBr) ratio, respectively. The KBr discs were prepared by using corresponding machine. Scans were obtained at a resolution of 4 cm-1, at Wave numbers from 4000 to 500 cm -1.

RESULTS AND DISCUSSION

Glimepiride is an oral blood sugar- lowering drug in a class of medicine for controlling diabetes called Sulfonylurea. The aims of present investigation was to enhance the dissolution rate of poorly water soluble drugs glimepiride by preparing the solid dispersion using poloxomer 407, povidon, PEG 4000, PEG 6000. In this study solvent evaporation method and fusion/melting method was used for the preparation of solid dispersion of glimepiride.

Standard curve of glimepiride (Media: Phosphate buffer, pH7.8)

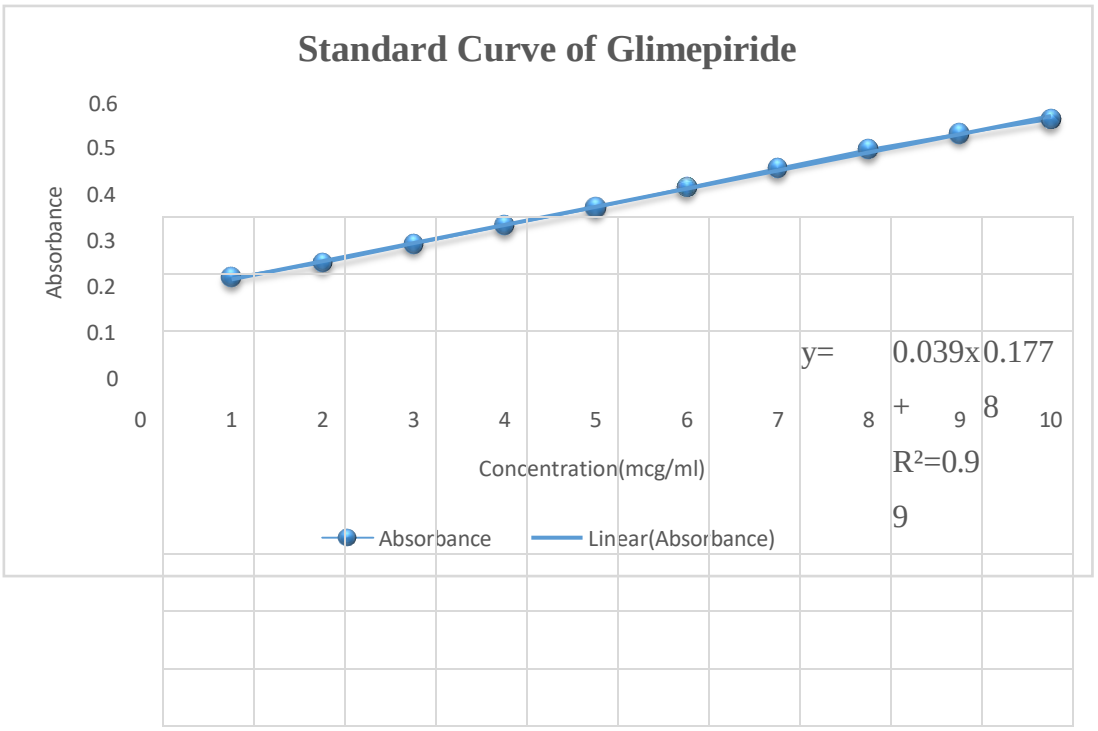

Fig: 1 Standard curve of glimepiride

Dissolution profile of active Glimepiride

10 mg of pure Glimepiride was used for dissolution study. It was found that only 0.46% drug was released after 5 minutes and 15.83% was released within 60 minutes time interval. This showed that dissolution profile of glimepiride was very poorly.

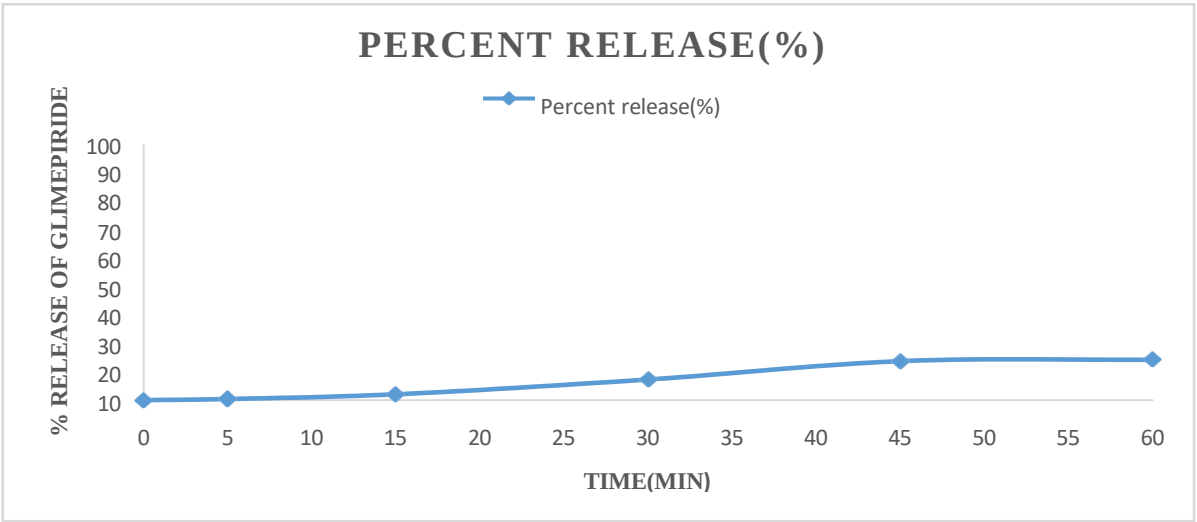

Fig 2: Dissolution profile of Glimepiride (API)

In vitro dissolution study of binary solid dispersion of glimepiride (Solvent evaporation method) containing eudragit and poloxamer

Comparative dissolution profile of active glimepiride and solid dispersion formulation (Glimepiride: Eudragit) for their different ratio

Solid dispersion of glimepiride containing Eudragit at different ratio SE1 (1:1), SE2 (1:2), SE3(1:3),SE4(1:4)andSE5(1:5) were used for dissolution study. It was found 0.69% from SE1, 6.19% from SE2, 2.15%fromSE3, 1.15% from SE4, 22.80% from SE5 and 0.46% from API were released after 5min and 28.48% from SE1, 48.96% from SE2, 19.78% fromSE3, 56.74% from SE4, 55.33% from SE5 and 15.29% from API were released after 45min. Finally 39.02% from SE1,82.29% from SE2, 24.81% from SE3, 54.46% from SE4, 73.22% from SE5 and 17.83% from API were released in an hour time interval. It was observed the rate of dissolution from SD containing eudragit has given comparatively lower release than other SD formulation.

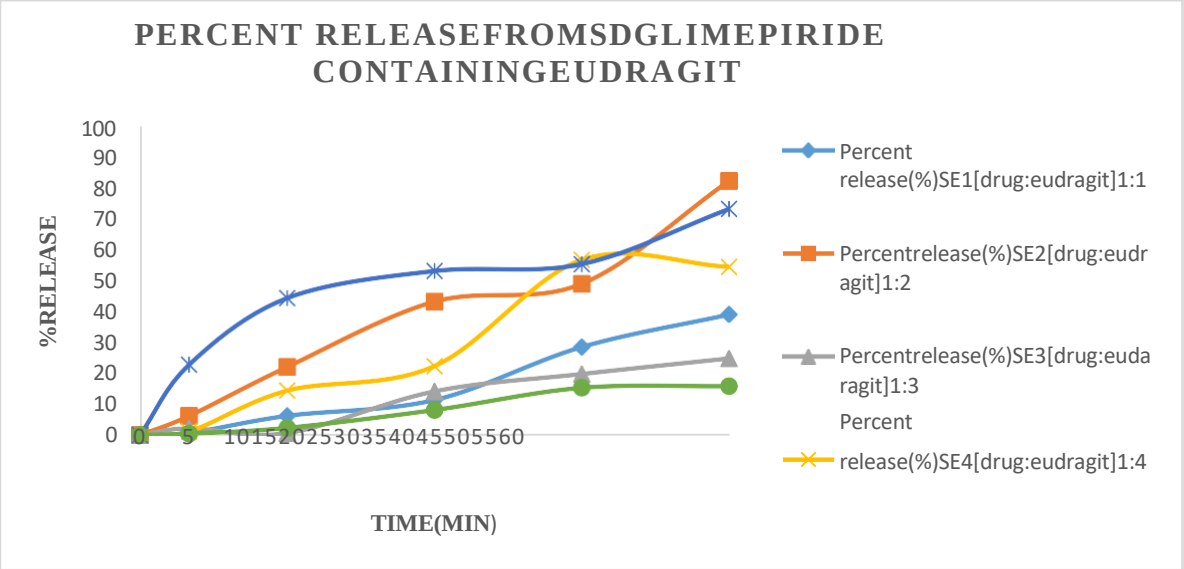

Fig 3: Average % release of drug from binary SD formulation containing eudragit.

Comparative dissolution profile of active glimepiride and solid dispersion formulation (Glimepiride+ Poloxamer) for their different ratio

Solid dispersion of glimepiride containing Poloxamer at different ratio SE6 (1:1), SE7 (1:2), SE8 (1:3), SE9 (1:4), SE10 (1:5) and API were used for dissolution study. It was found that 21% from SE6, 14.46%fromSE7, 34.76%fromSE8, 44.71% from SE9, 22.80% from SE10 and 0.46% from API were released after 5 min and 64.15% from SE6, 22.67% from SE7, 53.69%fromSE8,62.24%fromSE9, 55.28%fromSE10,15.29%fromAPI Were releasedafter45min.Finally56.43% from SE6,52.76%fromSE7,55.83% fromSE8,72.68%fromSE9,73.17% fromSE10and15.83%fromAPIwere released in an hour time interval.

From the below data we can conclude that, the release pattern from SD formulation containing Poloxamer has increased gradually when the amount of drug and poloxamer ratio were increased. It was observed that solid dispersion formulation SE9 showed their better result in 1:4 ratios in comparison to those of SE6, SE7, SE8 and SE10.

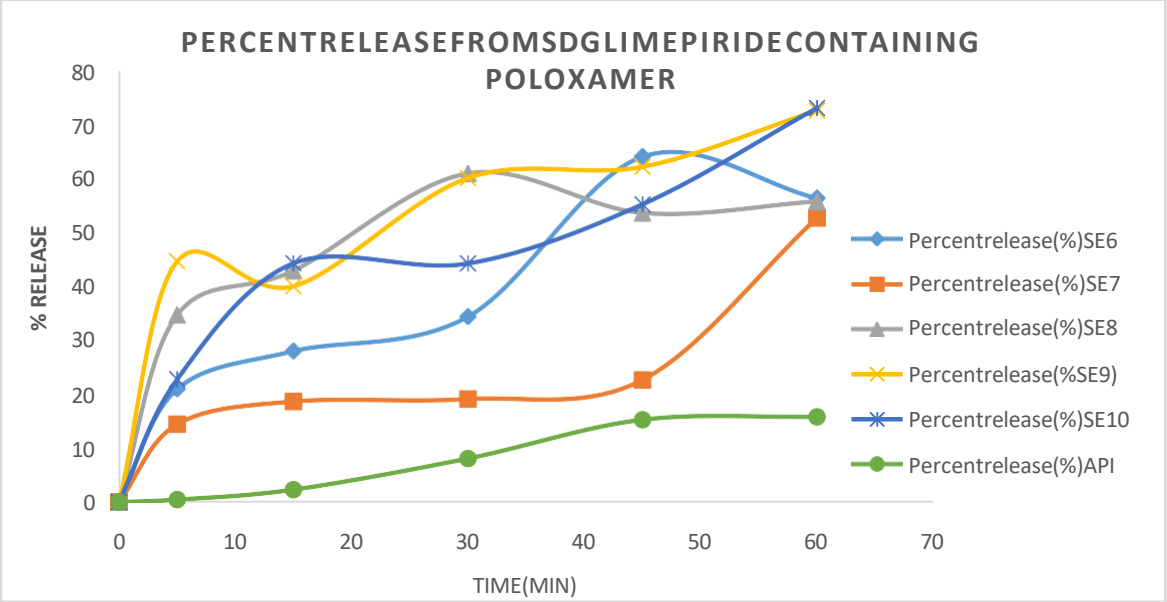

Fig 4: Average % release of drug from binary SD formulations containing Poloxamer.

Effect of the polymer on the improvement of solubility and dissolution rate of poorly water soluble glimepiride

From the above analysis of the result, it was proved that the water soluble polymers were exclusively able to change the drug in the micro level and finally crystal glimepiride was formed to the amorphous state. There is lots of effect to increase the solubility of poorly water soluble drug. Such as polyethylene glycol (PEG) have the ability to solubilize the drug and improve wettability. The solid dispersion of glimepiride with PEG 6000 and PEG 4000 may be useful to increase the stability, solubility, dissolution and bioavailability of poorly water soluble drug (14). Another povidone is suitable for the manufacturing of solid dispersion as it possesses forms water soluble complexes with many active drugs. It also act as binder, bioavailability enhancer and taste master (15). Eudragit has a lower content of quaternary ammonium group in the structure and is considered as more permeable to water.

Poloxamer act as solubilizing agent and plasticizer for enhancing the solubility and bioavailability of poorly soluble drugs in solid dosage forms. This water soluble polymer may operate in the micro environment immediately surrounding the drug particles in the early stage of dissolution, since the carrier completely dissolves in short time thus enhancing the solubility and dissolution of drug.

Finally it can be concluded that dissolution rate of glimepiride was increased by solid dispersion technique which is due to the wettability and spread ability of the precipitated drug by reducing aggregation in the readily soluble state. In this research work, we were prepared total 52 SD dispersion formulation of glimepiride using five water soluble polymer and different drug and polymer ratio. When glimepiride were dispersed in these polymers, its dissolution was enhanced significantly compared with active glimepiride.

Release kinetics study of pure glimepiride and different solid dispersion formulations

We have chosen five SD formulation G5 (Glim + PEG 4000), G8 (Glim + PEG 6000), G13 (Glim+PEG4000+Povidone), SE2 (Glim + Eudragit), SE9 (Glim + Poloxamer), which were given most significant effect on the improvement of dissolution rate. There dissolution data were analyzed by zero order model, First order, Higuch is quare root equation, Hixon crowell.

Zero order kinetics

Table 3: Comparative study of zero order kinetics of five solid dispersion formulations

Time	Percent release(%)SE2	Percent release(%)SE9
0	0	0
5	6.19977	44.71154
15	22.07807	40.05609
30	43.21087	60.18109
45	48.96096	62.24359
60	82.29621	72.68109

First order release Kinetics

Table 4: Comparative study of first order release kinetics of active glimepiride and five solid dispersion formulations

Time (min)	Log of % remaining drug (SE2)	Log of % remaining drug (SE9)	Log of % remaining drug (API)
0	2	2	2
5	1.972204	1.742635	1.997991
15	1.89166	1.777745	1.989849
30	1.754265	1.600089	1.963352
45	1.707902	1.576991	1.927929
60	1.248066	1.436463	1.92512

Higuchi release kinetics

Table 5: Comparative study of Higuchi release kinetics of active glimepiride and five solid dispersion formulations

Square root of time (SQRT)	% release of drug(SE2)	% release of drug(SE9)	%release of drug(API)
0	0	0	0
2.236068	6.19977	44.71154	0.461538

3.872983	22.07807	40.05609	2.310256
5.477226	43.21087	60.18109	8.092308
6.708204	48.96096	62.24359	15.29103
7.745967	82.29621	72.68109	15.83718

Hixoncrowell release kinetics

Table 6: Comparative study of Hixoncrowell release kinetics of active glimepiride and five solid dispersion formulations

Time (min)	Cubic root of % remaining drug (SE2)	Cubic root of % remaining drug (SE9)	Cubic root of % remaining drug (API)
0	4.641589	4.641589	4.641589
5	4.543613	3.809589	4.634437
15	4.271233	3.913647	4.605566
30	3.843749	3.414783	4.512847
45	3.709376	3.354776	4.391806
60	2.606286	3.011765	4.382347

Krosmeyer release kinetics

Table 7: Comparative study of Korsmeyer release kinetics of active glimepiride and five solid dispersion formulations

Log time=LogT	Log fraction of drug release=log(% release/100) SE2	Log fraction of drug release=log(% release/100) SE9	Log fraction of drug release=log(% release/100) API
0.69897	-1.20762	-0.34958	-2.33579
1.176091	-0.65604	-0.39733	-1.63634
1.477121	-0.36441	-0.22054	-1.09193
1.653213	-0.31015	-0.20591	-0.81556
1.778151	-0.08462	-0.13858	-0.80032

Successive fractional dissolution time

Table 8: Table for Mean Dissolution Time (MDT) calculation

Formulation Code	T25%	T50%	T80%	MDT
Pure Drug	69.89354	110.7925	151.4168	105.5033
SE2	18.99841	38.13741	61.17285	38.17681
SE9	0.537879	14.8494	140.8728	70.84047

Mean dissolution time (MDT) value was used to characterized the drug release rate form the dosage forms and the retarding efficiency of the polymer. It was found that, a higher MDT value for the SD. formulation SE9 (glimepiride + PEG4000 + Povidone) which was indicated that higher drug retarting ability of the polymer in the formulation

Table 9: Y equation and R^2 values of five SD formulations and active glimepiride

Formulation coding	Zero Order		1st Order Kinetics		Higuchi model		HixonCrowell model	
	Y equation	R^2 Value	Y equation	R^2 Value	Y equation	R^2 Value	Y equation	R^2 Value
Pure drug	0.3007x-0.77	0.957	-0.0041x+2.0041	0.955	2.3177x+3.0603	0.861	-0.0049x+4.6553	0.956
SE2	1.2855x+0.5822	0.971	-0.011x+2.0473	0.876	10.052x-9.8365	0.900	-0.0306x+4.7255	0.921
SE9	o.9245x+22.763	0.711	-0.0077x+1.8872	0.850	8.351x+10.402	0.879	-0.0217x+4.2527	0.809

The above data showed that R^2 value of active glimepiride, (R^2 = 0.957) and SD formulation SE2 (R2 = 0.971) were found substantially highest result in case of Zero order kinetics than other release kinetics. These R2 value is near about 01, so it can be said that, active glimepiride, SD formulation SE2 were followed zero order release pattern.

Another SD formulation SE9 (R2= 0.879) were displayed best fitting with Higuchi release kinetics pattern. Because R2 value of SE9 was showed better value in case of Higuchi release kinetics.

It was also observed that, in all case no formulation was fitted with Hixon Crowell kinetics model cube root law and Krosmeyer Kinetics.

Glimepiride & polymer interaction study using FT-IR Spectroscopy:

Fourier Transform Infrared Spectroscopic (FTIR) study was concluded four samples-

1) Pure drug /API (Glimepiride)
2) Polymer (PEG 4000)
3) Polymer(Poloxamer407)
4) Solid Dispersion

(SE8= Glimepiride+Poloxamer, 1:3) FT-IR was used to characterize possible interactions between the drug and the carrier in solid Diclofenac Sodium.

FT-IR spectra of Pure Glimepiride

FTIR spectra were employed to be confirmed about the compatibility of Glimepiride with various polymers used to prepare the solid dispersion. According to the chemical structure of Glimepiride shown in below figure FTIR spectra of glimepiride pure drug showed much number of prominent peaks at different wave numbers indicating the presence of different functional groups and substituent.

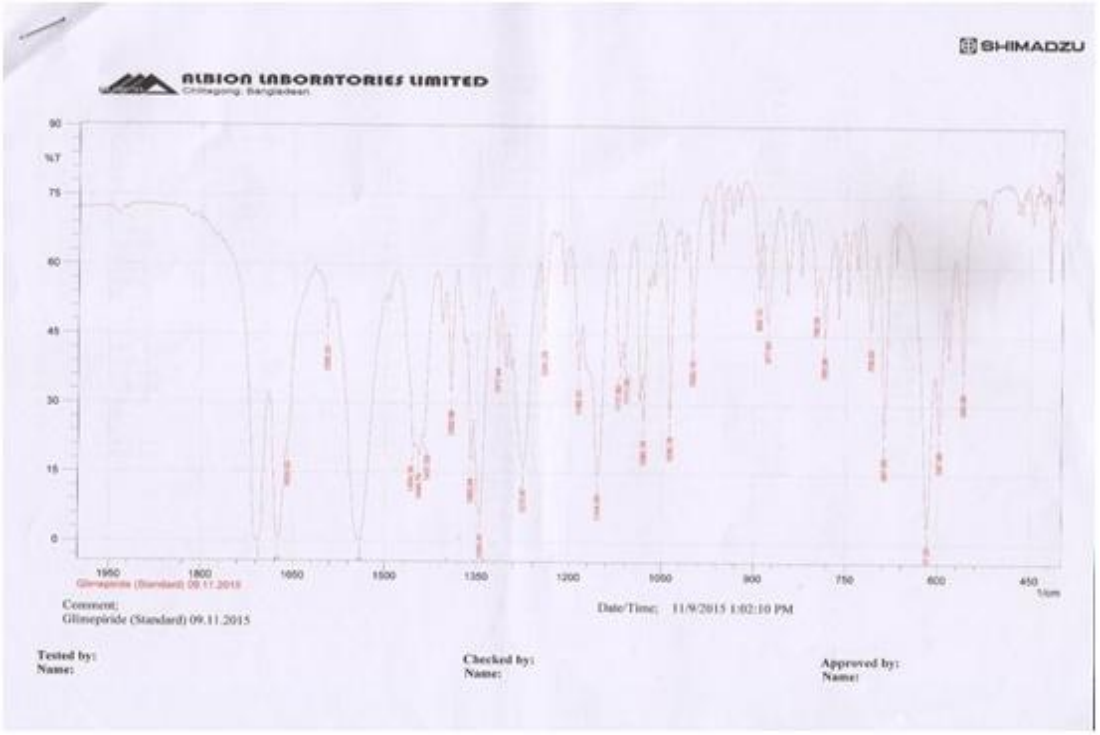

Table: 10

Sr No.	Peak	Indication
01	1454.39cm^{-1} 1444.75cm^{-1} 1437.03cm^{-1}	C-H bending
02	1659.82cm^{-1}	C=OA symmetric Stretching
03	1595.20cm^{-1}	C=OA symmetric Stretching
04	1345.41cm^{-1}	C-N Stretching
05	1317.44cm^{-1}	S=OA symmetric Stretching
06	1150.59cm^{-1}	S=O Symmetric Stretching
07	1472.71cm^{-1}	NH_2 bending

FTIR spectra of glimepiride solid dispersion with Poloxamer 407 prepared by Solvent evaporation method (SE8 = Glim+Poloxamer)

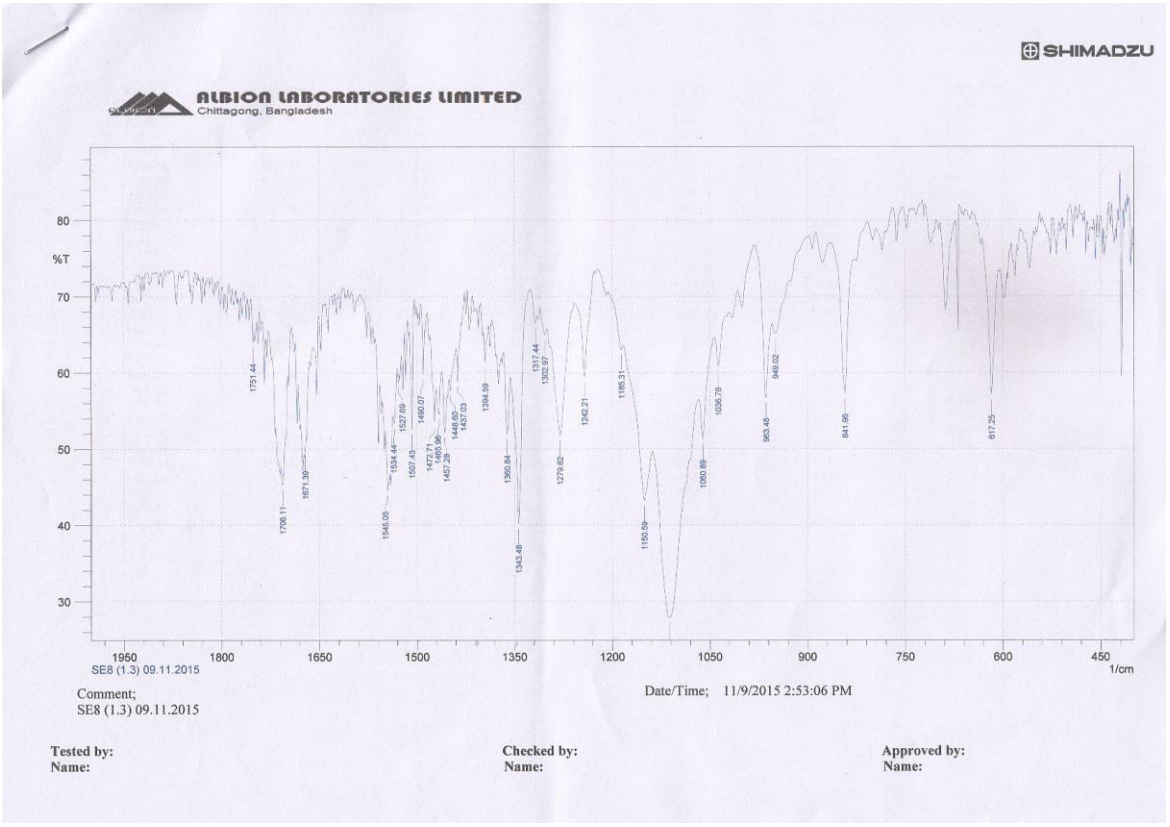

Table: 11

Sr No.	Peak	Indication
01	1060.89cm^{-1}, 1150.59cm^{-1},	C-O(Stretch)
02	1360.84cm^{-1}, 1394.59cm^{-1}, 1437.03cm^{-1}, 1448.60cm^{-1}, 1457.28cm^{-1}, 1456.96cm^{-1},& 1472.71cm^{-1},	-C-H(bending)

03	841.96cm^{-1}, 949.02cm^{-1}, 963.48cm^{-1},	=C-H(bending)
04	1671.39cm^{-1}	C=C(Stretch)
05	1671.39cm^{-1}, 1706.11cm^{-1}, 1751.44cm^{-1},	C=O(Stretch)

From the above shown spectrum, we came to conclude that the spectrum seen in the pure glimepiride was also found in the case of solid dispersion with Poloxamer 407. The spectrum was at same frequency range but some peaks were shifted to their near values. So we can say that there is no significant interaction between the drugs, Poloxamer407, hence there was no chemical change in the Poloxamer 407, when it was in solid dispersion form.

CONCLUSION

In the present study, solid dispersions of Glimepiride with different hydrophilic carriers in different ratios were prepared by physical mixing and fusion method to improve water solubility and dissolution characteristics. The preparation of solid dispersion of Glimepiride by fusion method has been proven to be successful. This research showed that when Glimepiride was dispersed in suitable water-soluble carriers such as PEG 6000, PEG4000 and EudragitE-100, Poloxomer407 and Povidone. Its dissolution was enhanced compared with pure drug. Fusion method of the poloxamer 407 and Eudragit with glimepiride at different ratios were also used. It was found the drug was released 0.46% after 5 minutes and only 15.83% within 60 minutes from active glimepiride. It was found that glimepiride binary SD formulation by Solvent evaporation method containing eudargit in ratio 1:2 (Formulation coding: SE2) Showed the best result in comparison of other binary SD formulation by solvent evaporation technique which was released 6.19% after 5 min and 82.29% within 60 mins. In comparison of other Solvent evaporation technique of SD formulation of glimepiride contain poloxomer 407 in ratio 1:9 (Formulation coding: SE9) showed the best result the other formulation which

was 44.71 % after 5min and 72.68% within 60 mins. It was also studied that the release kinetics of glimepiride of different SD formulation with different ratio such as, First order release kinetics, Higuchi, Krosmeyer, Hixoncrowell plot, and also benoted the MDT calculation for improving the solubility of glimepiride. In-vitro dissolution data also proves that percent release of drug from binary SDs was not similar with ternary SDs. Ternary SDs is more effective to increase the diclofenac sodium release rate. The water soluble carrier may operate in the micro environment (diffusion layer) immediately surrounding the drug particles in the early stage of dissolution, since the carrier completely dissolves in short time thus enhancing the solubility & dissolution of drug.

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