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Dissolution Enhancement of Glimepiride by Solid Dispersion Technique.

Priyanka Shrestha[1]*, Shiva Kumar Bhandari[1], SM Ashraful Islam[1], and Santosh Adhikari[2].

[1]Department of Pharmacy, University of Asia Pacific, Dhanmondi, Dhaka-1209, Bangladesh.
[2]Department of Pharmacy, Rajiv Gandhi University of Health Science, Banglore-560 041.

ABSTRACT

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. Solid dispersion of glimepiride were prepared with polyvinyl pyrrolidone k-30, poloxamer 407, polyethylene glycol 6000 (PEG 6000), polyethylene glycol 4000 (PEG 4000), sodiumstarch glycolate, ludiflash and lactose at different weight ratios using the solvent evaporation and melting method. 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 in 5 minute. Solid dispersions showed a better dissolution compared to the pure drugs and physical mixtures, with SD (1/9) PVP K-30 showing the highest dissolution efficiency (91.89% within 5min). Drug release from immediate release tablet containing SD (1/9) PVP K-30 was 59.02% 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.

Key words: Glimepiride, solid dispersion, hydrophilic carrier, *in-vitro* study, interaction, compatibility.

Corresponding author

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INTRODUCTION

The most challenging aspects in the pharma 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 [1]. Various approaches available to improve drug solubility as well as drug dissolution of poorly aqueous soluble drugs include micronization [2], formation of inclusion complexes with cyclodextrins [3], formation of amorphous drugs [4] and formation solid dispersions of drugs using various hydrophilic carriers [5, 6]. Among them, solid dispersion technique has attracted substantial interest as an efficient means of improving the dissolution rate as well as the bioavailability of a wide range of poorly aqueous soluble drugs [1, 7, 8].

The poor solubility and low dissolution rate of poorly water soluble drugs in the aqueous gastro intestinal fluids often cause insufficient bioavailability. This may be achieved by incorporating the drug in a hydrophilic carrier material obtaining products called solid dispersions. Depending on the properties of both, drug and carrier, and depending on their ratio, a solid solution or a solid suspension of the drug in the carrier material may be formed. The mechanisms involved in solubility and dissolution rate enhancement include transformation of unstable modifications into more stable ones or even into the amorphous state, reduction of particle size possibly to the molecular level as well as enhancement of wettability and solubility of the drug by the carrier material. However, if a solid dispersion represents a thermodynamically unstable system, it is prone to convert into a more stable state. Especially for substances according to the Biopharmaceutics Classification System, the bioavailability may be enhanced by increasing the solubility and dissolution rate of the drug in the gastrointestinal fluids [9].

MATERIALS AND METHODS

Materials

Glimepiride was a gift sample from General Pharmaceutical Limited, Polymers-Poloxamer407, Povidone K-30, PEG 6000, PEG 4000 (Unichem Chemical Reagents), Distilled water (University Laboratory), Na-starch glycolate (Ming Ti, Taiwan), Excipients- Ludiflash, Purified Talc, Magnesium stearate, Lactose (Ming Ti, Taiwan), Solvent – Methanol (MERCK, Germany), Distilled water (University Laboratory)

METHOD

Table 1: Formulation for preparation of physical mixture of glimiperide using different concentration of polymers.

Formulation Code	Glimepiride	Poloxamer 407	Povidone K-30
PM(1/1) poloxamer	10mg	10mg	
PM(1/5) poloxamer	10mg	50mg	
PM(1/9) poloxamer	10mg	90mg	
PM(1/1) PVP K-30	10mg		10mg
PM(1/5) PVP K-30	10mg		50mg
PM(1/9) PVP K-30	10mg		90mg

Preparation of solid dispersion of glimepiride by solvent evaporation and melting method

The solvent process comprises of either dissolving water insoluble drug and water soluble polymers in an organic solvent capable of dissolving both and removing the solvent by evaporation or 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. Glimepiride and different concentration of polymer at 1:1, 1:3, 1:5, 1:9 and 1:9:5 ratio indicating as different formulation code were weighted accordingly the formulation mentioned in the

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Table2 and added in beakers. Methanol was added to dissolve the mixture. The mixture was dried in water bath at 40°C when the solvent was evaporated completely; the prepared solid dispersion was sealed and stored in a desicator till further use.

Table2: Formulation for preparation of solid dispersion of glimiperide using different concentration of polymers.

Formulation Code	Glimepiride	Poloxamer	Povidone K-30	Ludiflash	Sodium starch glycolate	PEG 4000	PEG 6000	Lactose
SD(1/1) poloxamer	10mg	10mg	-	-	-	-	-	-
SD(1/5) poloxamer	10mg	50mg	-	-	-	-	-	-
SD(1/9) poloxamer	10mg	90mg	-	-	-	-	-	-
SD(1/3) PVP K-30	10mg	-	30mg	-	-	-	-	-
SD(1/9) PVP K-30	10mg	-	90mg	-	-	-	-	-
SD(1/1) PEG 6000	10mg	-	-	-	-	10mg	-	-
SD(1/3) PEG 6000	10mg	-	-	-	-	30mg	-	-
SD(1/5) PEG 6000	10mg	-	-	-	-	50mg	-	-
SD(1/3) PEG 4000	10mg	-	-	-	-	-	30mg	-
SD(1/1) LDF	10mg	-	-	10mg	-	-	-	-
SD(1/3) LDF	10mg	-	-	30mg	-	-	-	-
SD(1/3) SSG	10mg	-	-	-	30mg	-	-	
SD(1/9/5)PVP K-30, LDF	10mg	-	90mg	50mg	-	-	-	-
SD(1/9/5)PVP K-30, Lactose	10mg	-	90mg	-	-	-	-	50mg

Table 3: Preparation of solid dispersion of glimepiride using different carriers in different ratios by different methods.

Formulation code	Method of preparation	Drug:POLX 407	Drug: PEG 4000	Drug: PEG 6000	Drug: PVPK30	Drug:LDF	Drug:SSG	Drug:PVPK30:LDF	Drug:PVPK30:Lactose
POL1/1	Solvent evaporation	1:1	-	-	-	-	-	-	-
POL 1/5	Solvent evaporation	1:5	-	-	-	-	-	-	-
POL 1/9	Solvent evaporation	1:9	-	-	-	-	-	-	-
PVP 1/3	Solvent evaporation	-	-	-	1:3	-	-	-	-
PVP 1/9	Solvent evaporation	-	-	-	1:9	-	-	-	-
LDF 1/1	Solvent evaporation	-	-	-	-	1:1	-	-	-
LDF 1/3	Solvent evaporation	-	-	-	-	1:3	-	-	-
SSG 1/3	Solvent evaporation	-	-	-	-	-	1:3	-	-
PVP-LDF 1/9/5	Solvent evaporation	-	-	-	-	-	-	1:9:5	-
PVP-LCT 1/9/5	Solvent evaporation	-	-	-	-	-	-	-	1:9:5
PEG 4 1/1	Melting method	-	1:1	-	-	-	-	-	-
PEG 4 1/3	Melting method	-	1:3	-	-	-	-	-	-
PEG 4 1/5	Melting method	-	1:5	-	-	-	-	-	-
PEG 6 1/3	Melting method	-	-	1:3	-	-	-	-	-

Immediate release tablet formulations

Preparation of immediate release (IR) tablets from solid dispersion powder

The formulation containing povidone K 30 carrier in 1:9 ratio (SD 1/9 PVP K-30) shows the best release profile after dissolution test so it was selected for immediate release tablet formulation. Solid dispersion equivalent to 10 mg glimepiride and other excipients were weighed and mixed accurately using mortar and pastel. Then it was mixed in a container for 20 minutes manually. Finally tablets were prepared by direct compression technique.

Table 4: Composition of glimepiride IR (immediate release) tablet formulation containing 10 mg glimepiride.

Ingredients	Amount
Glimepiride SD (1/9) PVP K-30	100 mg
Lactose	250 mg
Ludiflash	40 mg
Purified Talc	5 mg
Magnesium stearate	5 mg

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In-vitro dissolution studies of Glimepiride immediate release (IR) tablets from solid dispersion powder

The in-vitro dissolution tests were performed for the pure glimepiride, physical mixture and solid dispersions and formulations using USP dissolution test apparatus type II (Paddle type) using 900 ml of dissolution medium. Phosphate buffer pH 7.8 was used as dissolution medium. The temperature of the medium was maintained at 37°C ± 0.5°C throughout the experiment. The sample containing 10 mg of the glimepiride or its equivalent in solid dispersions or physical mixtures were placed in the dissolution medium. Paddle was used at a stirring rate of 75 rpm. A 5 ml aliquot was withdrawn at predetermined time intervals of at 5, 10, 15, 20, 30, 40, 50 and 60 minutes and then 5 ml of fresh dissolution medium was placed to maintain the constant volume of dissolution medium. From the samples collected, absorbance were measured at 228 nm using Shimadzu UV – 1700 UV/Visible Double Beam Spectrophotometer (Shimadzu, Japan) against dissolution medium as blank. Percentage of the drug release was calculated using the equation obtained from the standard curve preparation in the same media.

RESULTS AND DISCUSSION

Glimepiride is an oral blood sugar-lowering drug in a class of medicines for controlling diabetes called sulfonylureas. The aims of present investigation was to enhance the dissolution rate of poorly water soluble drugs glimepiride by preparing the solid dispersion with different water soluble carriers in different ratios. The carriers used for solid dispersion are poloxamer 407, povidone K-30, ludiflash and sodium starch glycolate. In this study, solvent evaporation method and melting method was used for the preparation of solid dispersion of glimepiride.

Preparation of standard curve of Glimepiride

To prepare a standard curve for glimepiride, serial dilution was carried out to get different concentration of glimepiride. Absorbance was measured against dissolution medium as blank and absorbance value were plotted against drug concentration and standard curve of glimepiride was produced which was shown in Figure1.

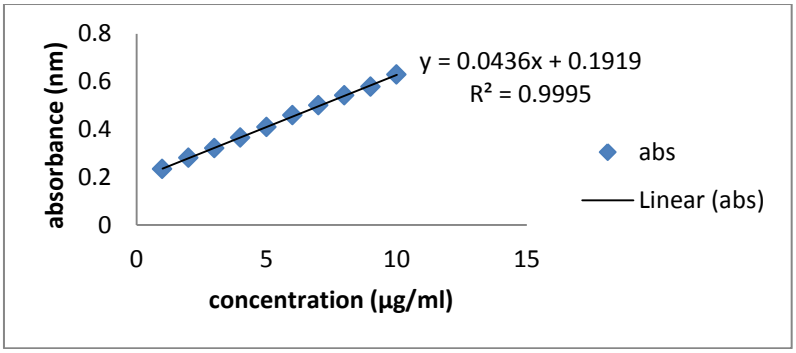

Figure1: Standard curve of glimepiride at pH 7.8

The drug shows low, pH dependent solubility. In acidic and neutral aqueous media, glimepiride exhibits very poor solubility at 37°C (<0.004 mg/ml). In media pH>7, solubility of drug is slightly increased to 0.02 mg/ml. This poor solubility may cause poor dissolution and unpredicted bioavailability [10]. So in the experiment phosphate buffer at pH 7.8 was used.

Dissolution profile of active Glimepiride

Dissolution profile of active glimepiride was found very poor i.e. .84% was released after 5 minutrs and 27.35% was released after an hour as shown in Figure2.

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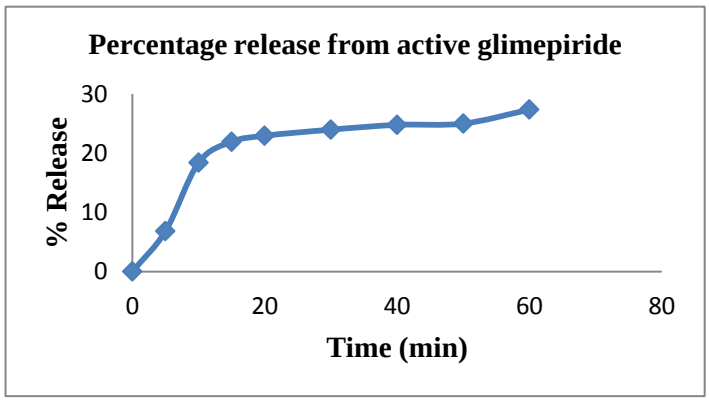

Figure2: Percentage release from active glimepiride

Dissolution profile of physical mixture of glimepiride and poloxamer 407

The percent release after the dissolution of mixture of glimepiride and poloxamer 407 was found 40%, 60% and 56% after 5 min, 60.2%, 82% and 78% were released after 40 min and after an hour 77.11%, 84% and 80% were released at ratio of 1:1 (PM (1/1), 1:5 (PM (1/5) and (PM (1/9) poloxamer respectively as shown in Figure. This result shows that the rate of dissolution of glimepiride was increased after making the physical mixture with poloxamer 407. The rate by which dissolution rate was increased from PM (1/1) poloxamer to PM (1/5) poloxamer was not same to PM (1/9) poloxamer, which means further increase in the amount of polymers, do not give the significiant change in dissolution rate. The ratio of physical mixture PM (1/5) poloxamer shows the best result in compare to PM (1/1) poloxamer and PM (1/9) poloxamer.

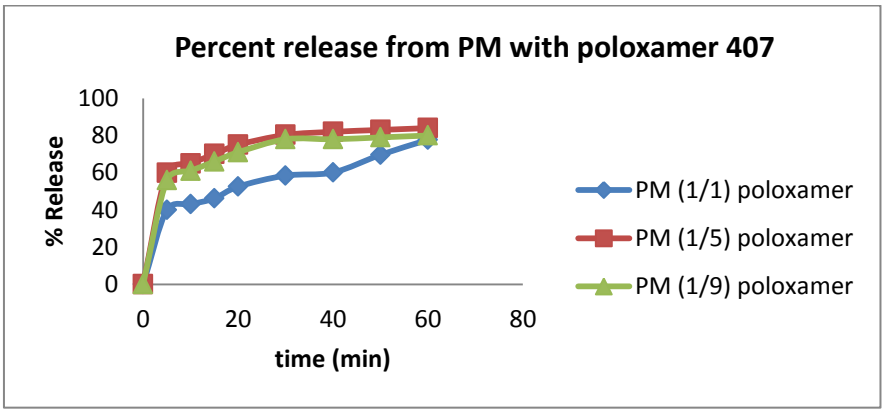

Figure3: Percent release from physical mixture of Glimepiride and Poloxamer 407 in different ratio

Dissolution profile of physical mixture of glimepiride and povidone K-30

The percent release after the dissolution of mixture of glimepiride and povidone k-30 at ratio of 1:1 (PM (1/1) PVP K-30), 1:5 (PM (1/5) PVP K-30) and 1:9 (PM (1/9) PVP K-30) were found 31.19 %, 56.72 % and 65.93 % respectively after 5 min, 67%, 75% and 88.45% respectively were released after 40 min and 72.95 %, 80 % and 103 % respectively were released after an hour as shown in Figure. From this data we can conclude that the release pattern from the physical mixture with povidone K-30 increases gradually. After increasing the amount povidone K-30 there was increase in the dissolution rate in each physical mixture. The PM (1/9) PVP K-30 gives the best result in comparison to PM (1/1) PVP K-30 and PM (1/5) PVP K-30.

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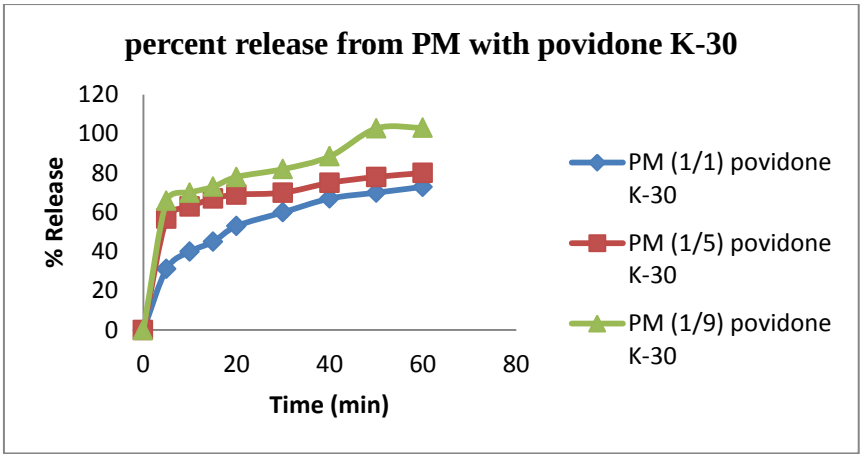

Figure4: Percent release from physical mixture of Glimepiride and Povidone K-30 in different ratio.

Comparision of dissolution profile of physical mixture (PM) of glimepiride with different polymers in different ratios

The physical mixture (PM) of glimiperide was prepared with poloxamer 407 and povidone K-30 at different ratios 1:1 (PM (1/1) poloxamer, (1/1) PVP K-30), (PM (1/5) poloxamer, (1/5) PVP K-30) and (PM (1/9) poloxamer, (1/9) PVP K-30) were used for dissolution study and result were compared. The data shows that in one hand the physical mixture PM (1/5) poloxamer shows the better result while in another hand the PM (1/9) PVP K-30 shows the better result. Within 5 min the release rate from PM (1/5) poloxamer was 60%, while from PM (1/9) PVP K-30 was 66%. Within 60 min the release rate from PM (1/5) poloxamer was 84%, while from PM (1/9) PVP K-30 was 103%. While comparing both the result it was found that the dissolution rate was significantly increased by physical mixture with povidone K-30 than poloxamer 407 as shown in Figure5.

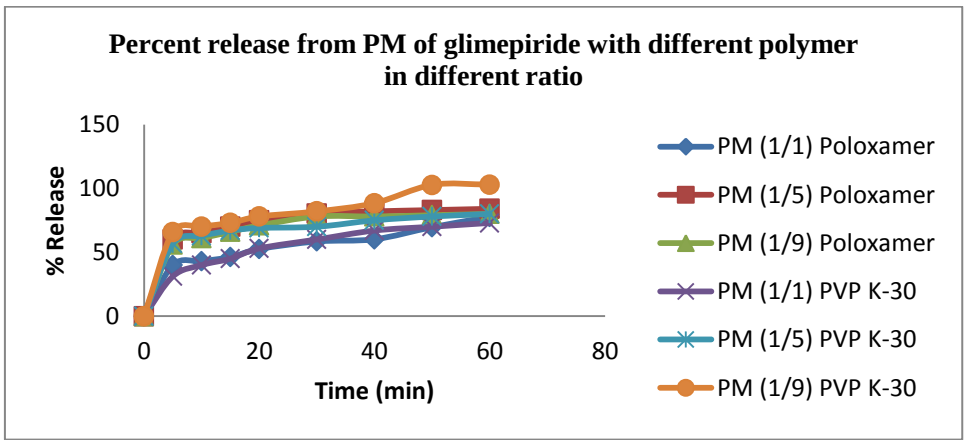

Figure5: Comparision of dissolution profile of solid dispersion of glimepiride with different polymers in different ratios

Dissolution profile of solid dispersion of glimepiride with poloxamer 407

Solid dispersion of glimepiride with poloxamer 407 at different ratios 1:1 (SD (1/1) poloxamer), 1:5 (SD (1/5) poloxamer) and 1:9 (SD (1/9) poloxamer) were used for dissolution study. Drug released were found 32.02%, 55.93 respective ratios within 40 min and 56.12 %, 84.75% and 99.22 % at respective ratio within an hour as shown in Figure. The above data shows that the dissolution rate of the glimepiride was not significantly increased after making the solid dispersion with poloxamer 407. The result was found to be quite same as the result of physical mixture of glimepiride with poloxamer 407. Generally the dissolution pattern should be increased after making the solid dispersion. The low dissolution rate of solid dispersion may be due to physical instability of solid dispersion.

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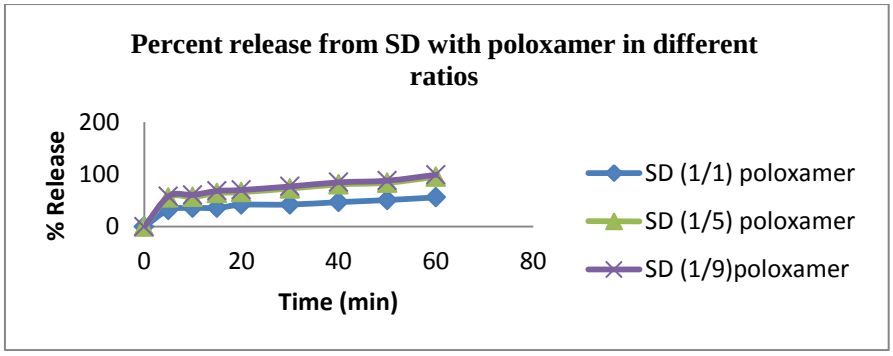

Figure6: Percent release from SD with poloxamer in different ratios

Dissolution profile of solid dispersion of glimepiride with povidone K-30

Solid dispersion of glimepiride with povidone K-30 at different ratios 1:3 (SD (1/3) PVP K-30) and 1:9 (SD (1/9) PVP K-30) were used for dissolution study. Drug released were found 47.51% and 91.89% at respective ratio within 5 min, 74.84% and 102% within 40 min and 98 % and 102% within an hour as shown in Figure. From the result we can conclude that the dissolution rate of the solid dispersion increases when prepared with povidone K-30. As the soluble carrier dissolves, the insoluble drug is exposed to dissolution medium as very fine particles leading to an increase in both surface area and solubilization for fast dissolution and absorption. SD (1/9) PVP K-30 shows the best result which was 91 % within 5 min.

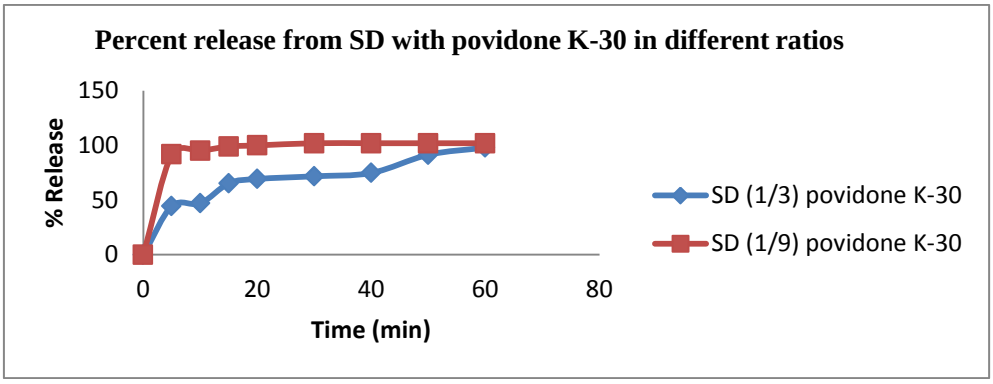

Figure7: Percent release from SD with povidone K-30 at different ratios

Comparision of dissolution profile of solid dispersion (SD) of glimepiride between poloxamer 407 and povidone k-30 in different ratios

The solid dispersion prepared with poloxamer 407 and povidone K-30 in different ratios was compare with each other. When comparing the solid dispersions prepared with poloxamer 407, SD (1/9) poloxamer gives the best result which was 58.12% release within 5 min and 99.21% within an hour. When comparing the solid dispersions prepared with povidone K-30, SD (1/9) PVP K-30 gives the best result which was 91.88% release within 5 min and 102% within an hour. While comparing the solid dispersion SD (1/9) poloxamer and SD (1/9) PVP K-30, the percentage release from povidone k-30 was found to be maximum.

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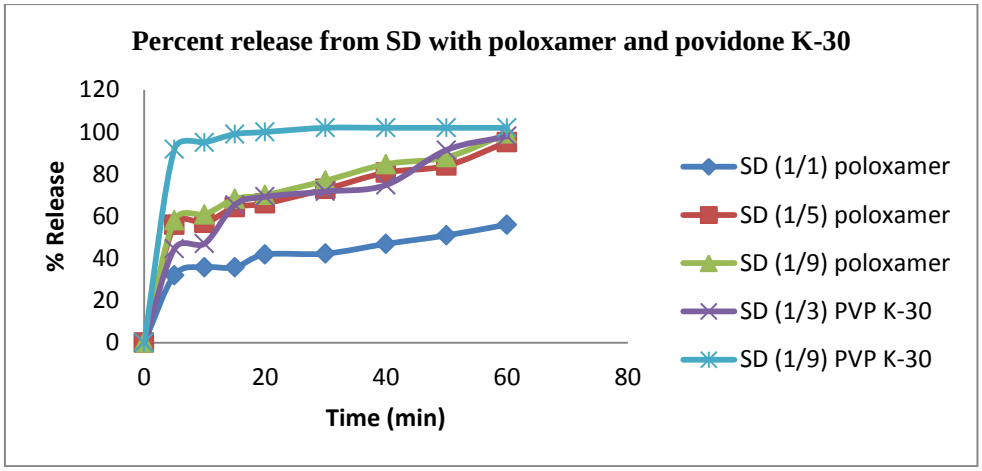

Figure8: Percent release from SD with poloxamer and povidone K-30

Dissolution profile of solid dispersion of glimepiride with sodium starch glycolate

Solid dispersion of glimepiride with sodium starch glycolate at 1:1 (SD (1/1) SSG) was used for dissolution study. Drug release from SD (1/1) SSG was found 34.53% within 5 min, 53.71% within 40 min and 55.24 % within an hour.

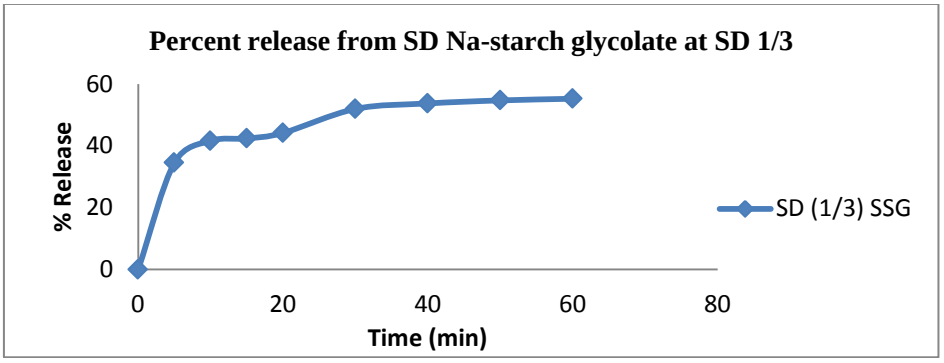

Figure9: Percent release from SD with Na-starch glycolate

Dissolution profile of solid dispersion of glimepiride with PEG 6000

Solid dispersion of glimepiride with PEG 6000 at different ratios 1:1 (SD (1/1) PEG 6000), 1:3 (SD (1/3) PEG 6000) and 1:5 (SD (1/5) PEG 6000) were used for dissolution study. Drug released were found 61.53%, 55.47 % and 60.91% at respective ratio within 5 min, 70.10%, 77.93% and 84.01% within 40 min and 73.46 %, 84.03% and 88.67% within an hour as shown in Figure. The SD (1/5) PEG 6000 gives the best result in comparision to SD (1/1) PEG 6000 and SD (1/3) PEG 6000 which was 88.6% within an hour.

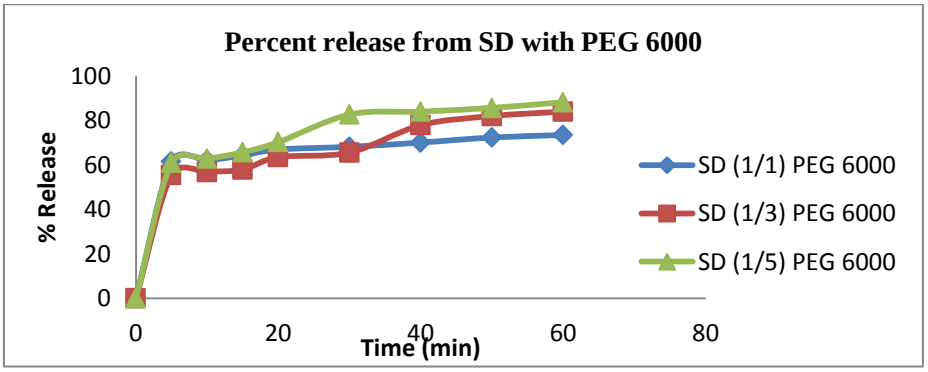

Figure10: Percent release from SD with PEG 6000 at different ratios

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Dissolution profile of solid dispersion of glimepiride with PEG 4000

Solid dispersion of glimepiride with PEG 4000 at ratio 1:3 (SD (1/3) PEG 4000) was used for dissolution study. Drug release from SD (1/3) PEG 4000 was found 27% within 5 min, 48.95 % within 40 min and 56.48% within an hour.

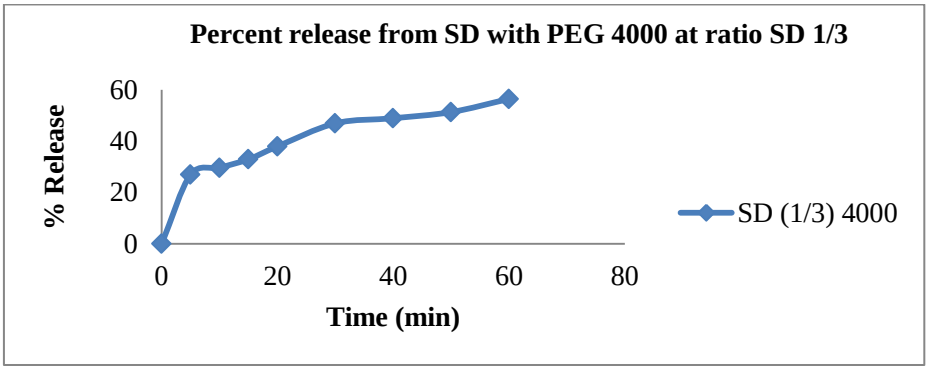

Figure11: Percent release from SD with PEG 4000

Comparison of dissolution profile of solid dispersion (SD) of glimepiride among PEG 6000, PEG 4000, sodium starch glycolate and povidone k-30 in different ratios

In comparison to the poloxamer 407 and povidone K-30 we found that solid dispersion prepared from povidone K- 30 gave the best result. So, now we will compare the solid dispersion with povidone K-30 with other polymer like PEG6000, PEG4000 and sodium starch glycolate. Within solid dispersion prepared with PEG 6000 in different ratio, SD (1/5) PEG 4000 gave the best result. The best result obtained from the each solid dispersion was compared with each other. The release rate was found 60.90% within 5 min and 88.27% within an hour from SD (1/5) PEG 6000, 27% within 5 min and 56.48% within an hour from SD (1/3) PEG 4000, 34.53% within 5 min and 55.24% within an hour from SD (1/3) SSG and 91.88% within 5 min and 102% within an hour from SD (1/9) PVP K-30. So, from the above data we can conclude that solid dispersion SD (1/9) PVP K-30 gave the best result in compare to PEG 6000, PEG 4000 and sodium starch glycolate.

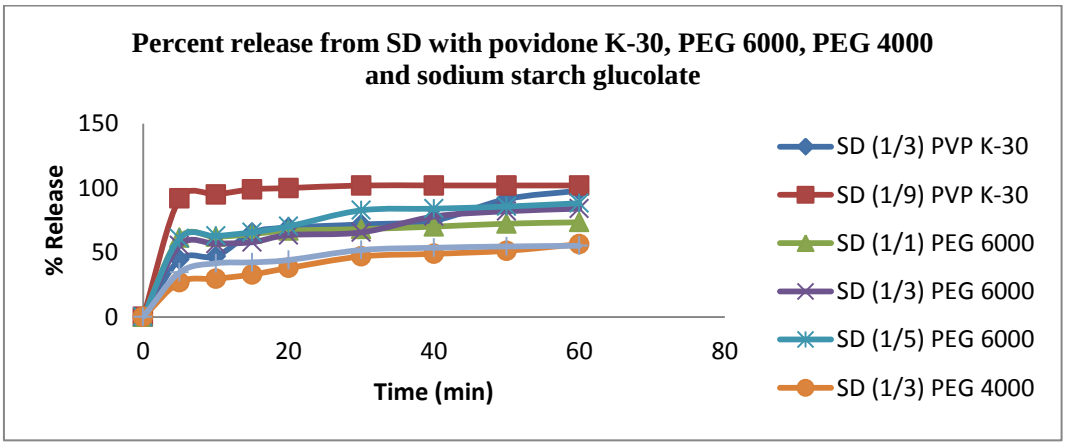

Figure12: Comparison of dissolution profile of solid dispersion (SD) of glimepiride among PEG 6000, PEG 4000, sodium starch glycolate and povidone k-30 in different ratios

Dissolution profile of solid dispersion of glimepiride with ludiflash

Solid dispersion of glimepiride with ludiflash at different ratios 1:1 (SD (1/1) LDF) and 1:3 (SD (1/3) LDF) were used for dissolution study. Drug release from SD 1/1 LDF was found 27 % within 5 min, 30.07 % within 40 min and 32.64 % within an hour. Drug release from SD 1/3 LDF was found 50.02 % within 5 min, 58.99 % within 40 min and 59.13 % within an hour. The above data shows that the dissolution profile of SD (1/3) LDF shows the better result in comparision to the SD (1/1) LDF.

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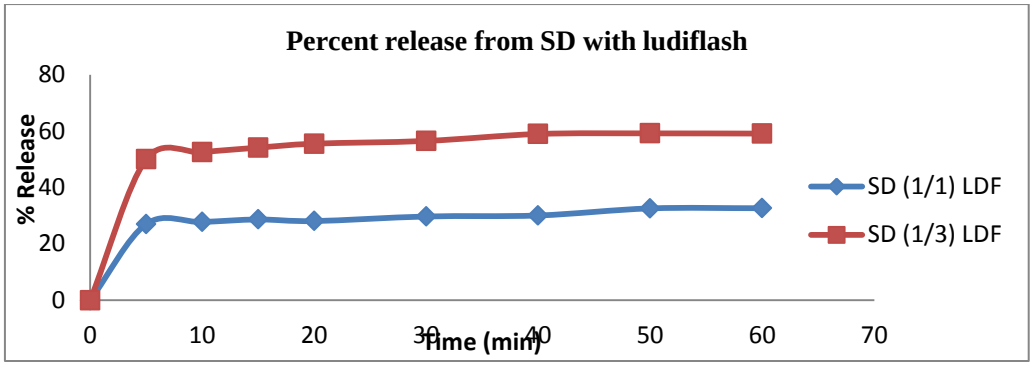

Figure13: Percent release from SD with ludiflash at different ratios

Dissolution profile of solid dispersion of glimepiride with povidone K-30 and Ludiflash

Solid dispersion of glimepiride with povidone k- 30 and ludiflash at ratio 1:9:5 (SD (1/9/5) PVP K-30, LDF) was used for dissolution study. Drug release from SD 1/9/5 PVP K-30 was found 91.26% within 5 min, 95.12 % within 40 min and 97.04% within an hour.

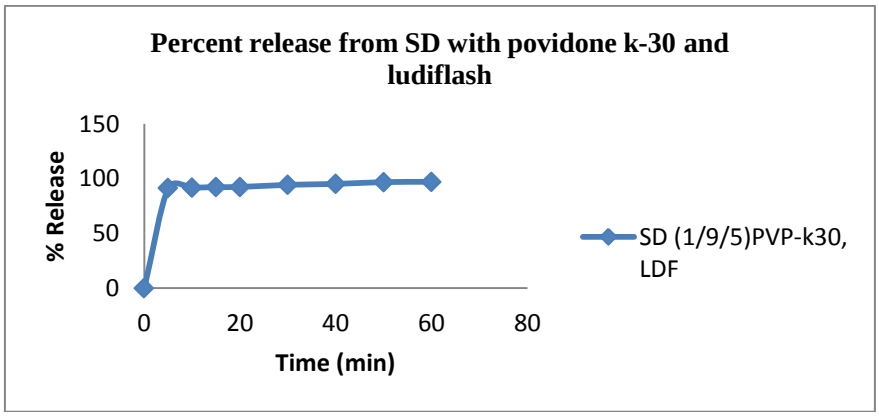

Figure14: Percent release from SD with povidone k-30 and ludiflash

Dissolution profile of solid dispersion of glimepiride with povidone K-30 and lactose

Solid dispersion of glimepiride with povidone k- 30 and lactose at ratio 1:9:5 (SD (1/9/5) PVP K-30, Lactose) was used for dissolution study. Drug release from SD (1/9/5) PVP K-30, Lactose was found 86.02% within 5 min, 95.04 % within 40 min and 101.51% within an hour.

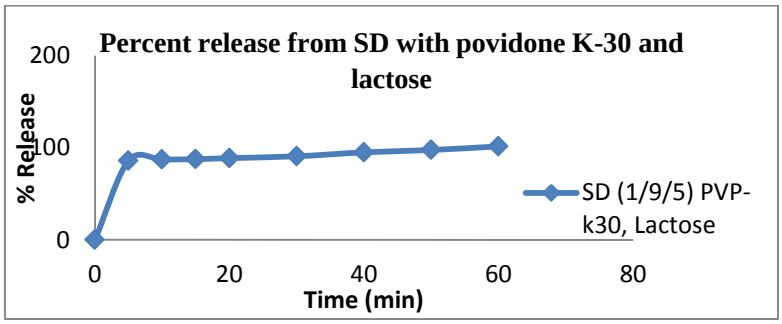

Figure15: Percent release from SD with povidone k-30 and lactose

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Comparision of dissolution profile of solid dispersion (SD) of glimepiride among ludiflash, povidone k-30 and lactose in different ratio

In comparision to the poloxamer 407, povidone K-30, PEG6000, PEG4000 and sodium starch glycolate, we found that solid dispersion prepared from povidone K- 30 gave the best result. So, now we will compare the solid dispersion with povidone K-30 with other polymer like ludiflash, povidone K-30 in combination with lactose and ludiflash. Within solid SD (1/1) LDF and SD(1/3) LDF, SD(1/3) LDF gave the best result. The best result obtained from the each solid dispersion was compared with each other. The release rate was found 50.02% within 5 min and 59.13% within an hour from SD (1/3) LDF, 91.25% within 5 min and 97.04% within an hour from SD (1/9/5) PVP K-30, 86.02% within 5 min and 101.50% within an hour from SD (1/9/5) PVP –K30 lactose and 91.88% within 5 min and 102% within an hour from SD (1/9) PVP k-30. So, from the above data we came to conclude that solid dispersion SD (1/9) PVP K-30 gave the best result in compare to other solid dispersion.

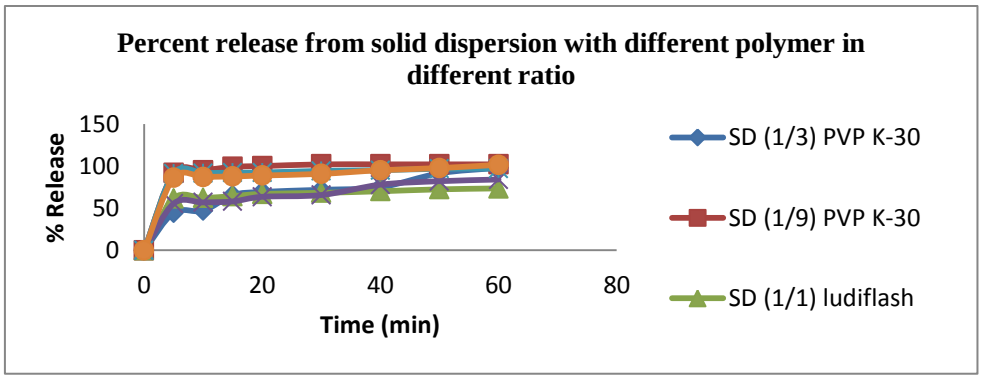

Figure16: Comparison of dissolution profile of solid dispersion (SD) of glimepiride among ludiflash, povidone k-30 and lactose in different ratios

Dissolution profile of immediate release glimepiride tablet prepared from SD powder

Immediate release glimepiride tablets were prepared by using solid dispersion powder. The solid dispersion containing povidone SD (1/9) PVP K-30 was selected for a tablet formulation because it showed the best dissolution result in compare to other polymers. Only one formulation was prepared by using SD (1/9) PVP K-30. The percent release from formulated immediate release tablet is shown in following figure. From this dissolution data it is clear that, around 100% of drug was release within 30 minutes from the formulation.

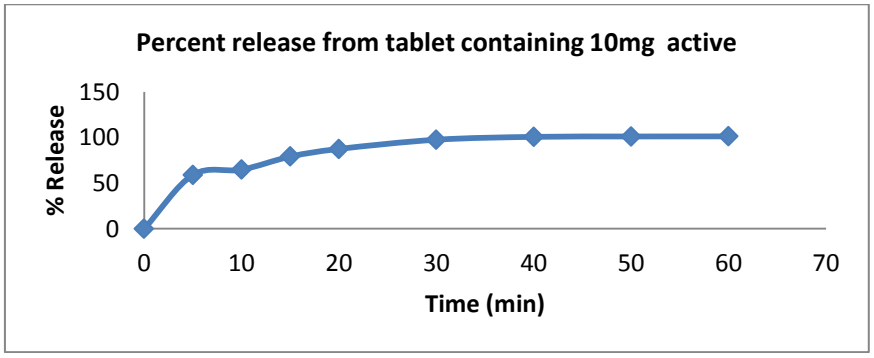

Figure17: Percent drug release from IR tablet

Evaluation of physical properties of IR tablet formulation

In this study thickness, diameter, weight variation, disintegrating test and hardness test of the formulation was measured. Six tablets from the formulation were measure and found that all the test result was within the limit.

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Table5: Evaluation of physical properties of IR tablet formulation

Formulation	Average Weight (mg)	Diameter (mm)	Thickness (mm)	Hardness (N)	Disintegration Time (min)
F-1 (IR)	401.7	13.0 ± 0.05	13.5±0.03	80	8.40

Polymer and glimepiride interaction study Using FT-IR spectroscopy

Fourier Transform Infrared Spectroscopic (FTIR) study was conducted for two samples

a. Pure drug (Glimepiride)
b. Solid dispersion (SD (1/9) PVP K-30)

Fourier Transform Infrared Spectroscopy (FTIR) was used characterize possible interaction between the drugs and the carrier in solid state. The FT-IR spectrum of solid dispersion was compared with the standard spectrum of glimepiride.

FTIR of Glimepiride showed characteristic peaks at 2931.06 (2850 – 3000) (C-H), 1346.22, 1503.46 and 1542.16 (1350 –1550) (N=O), 1219.06 (1220 -1020) (C-N), 1157.94 and 1152.57
(1000 –1300) (C-O) (Figure18).

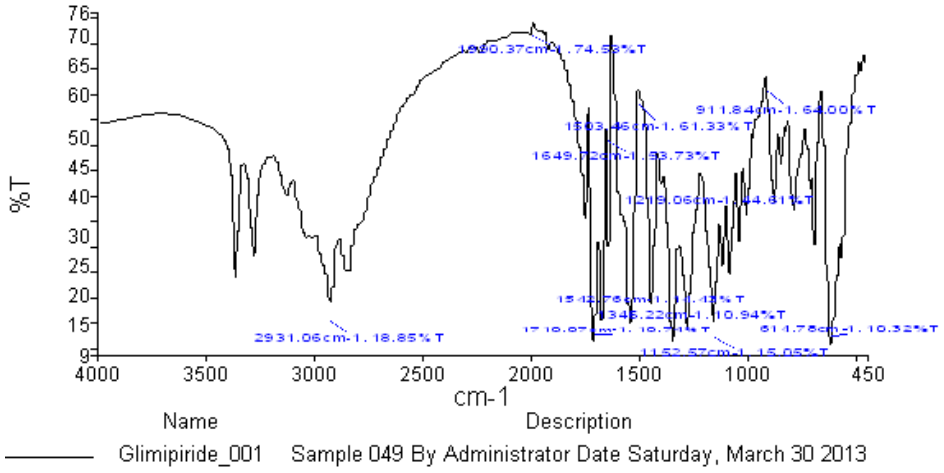

Figure 18: FTIR Spectra of pure drug Glimepiride

FTIR of Solid dispersion showed characteristic peaks at 3445.52 (3300-3500) (N-H), 2924.24 (2850 – 3000) (C-H), 2473.9 (3300 - 2500 (O-H), ~1568.87 (1350 –1550) (N=O), 1288.2 (1000 –1300) (C-O) (Figure19).

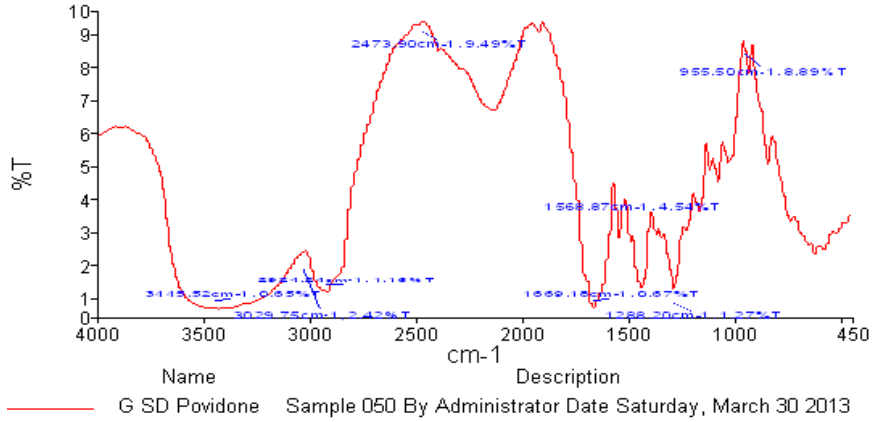

Figure 19: FTIR Spectra of solid dispersion with povidone K-30

From the above shown spectrum we can conclude that the spectrum seen in the pure glimepiride was also found in the case of solid dispersion. The spectrum was at same frequency range but some peaks were shifted to their near values. So we can say that there is no drug carrier interaction in solid dispersion.

XRD study to characterized the SD

The solid state characterization of drug and solid dispersion were investigated using XRD to find out crystallinity nature of glimepiride and SD (1/9) PVP K-30. By this test we can see that pure glimepiride peaks were closer and more in number which indicate the crystalline structure of drug. On the other hand solid dispersion peak were well separated and number of peaks were less, which indicate amorphous like structure.

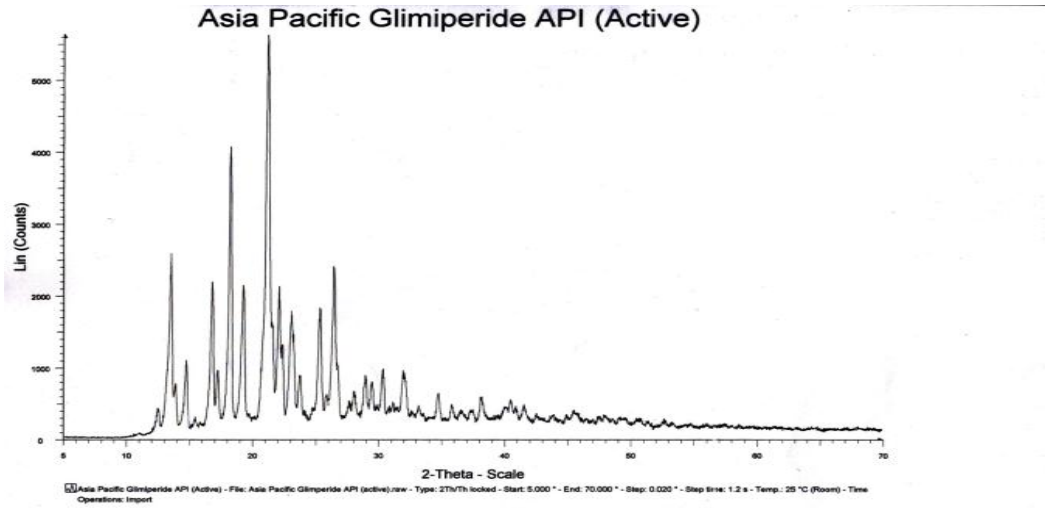

Figure20: X-ray diffraction (XRD) patterns of pure glimepiride

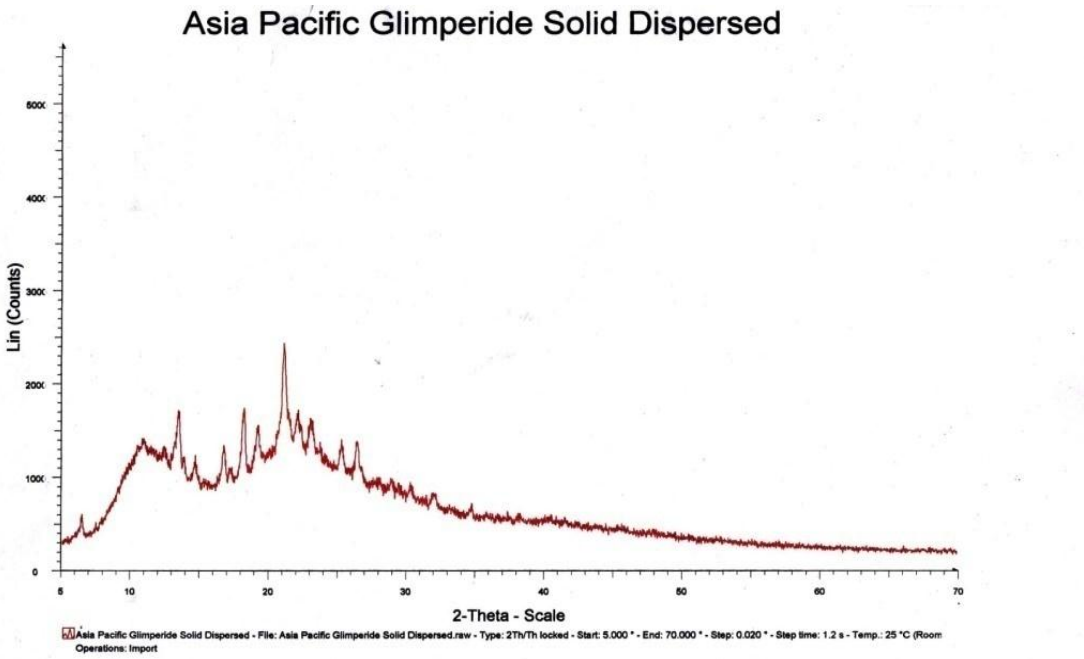

Figure21: X-ray diffraction (XRD) patterns of SD (1/90 PVP K-30 of glimepiride

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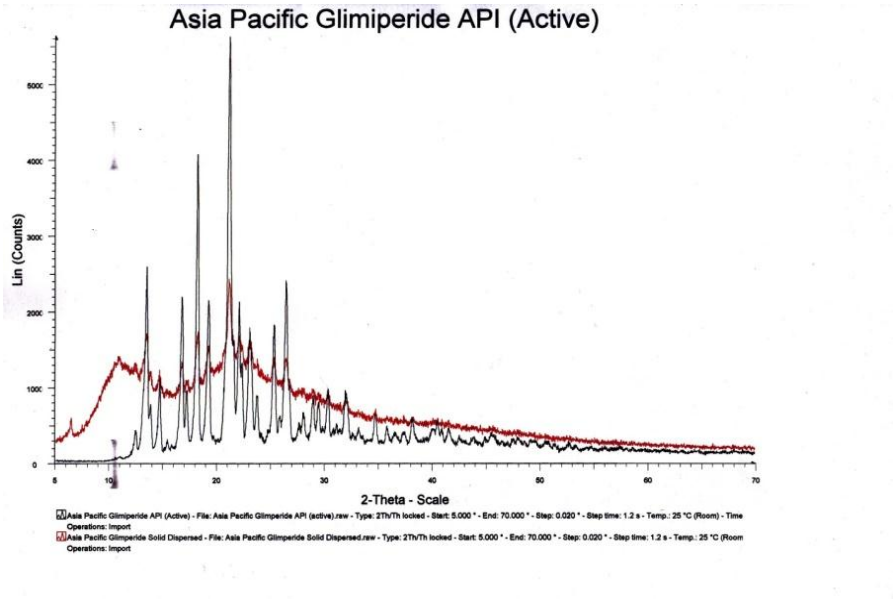

Figure 22: X-ray diffraction (XRD) patterns of pure glimepiride and SD (1/9) PVP K-30

CONCLUSION

This research showed that when glimepiride was dispersed in a suitable water-soluble carriers such as poloxamer 407, povidone K-30, PEG 6000, PEG 4000, sodium starch glycolate, ludiflash and lactose, its dissolution was enhanced compared with pure drugs. In compare to this, all water soluble carrier povidone K-30 gave the best result from both the physical mixture and solid dispersion in 1:9 (drug: polymer) ratio. By in-vitro study, it was clearly proved that preparation of solid dispersion of glimepride with povidone K-30 improved the dissolution rate of glimepiride. The FT-IR spectrooscopic studies showed the absence of any specific chemical interaction between glimepiride and povidone K-30 in solid state. Finally, it can be concluded that glimepiride solid dispersions with povidone K-30 provide a promising way to enhance its solubility and dissolution rate.

Physical and chemical stability of both the drug and the carrier in a solid dispersion are major developmental issues, as exemplified by the recent withdrawal of ritonavir capsules from the market, so future research needs to be directed to address various stability issues. Solid dispersions can improve their stability and performance by increasing drug-polymer solubility, amorphous fraction, particle wettability and particle porosity. Moreover, new, optimized manufacturing techniques that are easily scalable are also coming out of academic and industrial research. Further studies on scale up and validation of the process will be essential.

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