IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

ENHANCEMENT OF SOLUBILITY AND DISSOLUTION OF GLIPIZIDE BY SOLID DISPERSION USING ROTARY EVAPORATION

Aishwarya T. Jadhav*, Ajit B. Patil, Afaque Raza M. Ansari, Samiksha S. Upadhye.

Department of Pharmaceutics,

D. S. T. S. Mandal's College of Pharmacy, Jule Solapur, Solapur-413003, Maharashtra, India.

ABSRACT:

The objective of the present investigation was to enhance the solubility and dissolution rate of glipizide, a hydrophobic drug, by solid dispersion techniques. In this study, glipizide solid dispersions were prepared using the rotary evaporation by using polyethylene glycol 6000 (PEG 6000) and Poloxamer 188. The drug and polymers were combined in different ratios: 1:1:1, 1:1:2, 1:1:3, 1:2:1, 1:2:2, 1:2:3, 1:3:1, 1:3:2, and 1:3:3. These formulations were investigated for drug content, solubility, and drug release study. FTIR and DSC technique were used to assess the drug-carrier interaction. Based on the FTIR data, there was no chemical interaction observed between the drug and polymers. The X-ray diffraction (XRD) analysis revealed that the crystalline glipizide underwent a transformation into an amorphous state. Solubility of drug and solid dispersions were determined using a phosphate buffer pH 6.8 and distilled water. As compared to pure drug, solid dispersions show the better solubility in both media. The dissolution studies were conducted for a duration of two and a half hours using the USP dissolution apparatus type-I (Basket) in a phosphate buffer solution with a pH of 6.8.

Keywords: Glipizide, PEG 6000, Poloxamer 188, Solid dispersion, Rotary evaporation method.

INTRODUCTION

One of the major current challenges of the pharmaceutical industry is related to strategies that improve the water solubility of drug. Drug release is a crucial and limiting step for oral drug bioavailability, particularly for drug with low gastrointestinal solubility and high permeability. By improving the drug release profile of these drugs, it is possible to enhance their bioavailability and reduce side effects. Solid dispersions are one the most successful strategic approach to improve drug release of poorly soluble drugs. Solid dispersion can be defined as a molecular mixture of poorly water soluble drugs in hydrophilic carriers, which present the drug release profile that is driven by the polymer properties. Additional approaches to enhance the bioavailability of pharmaceuticals with low water solubility include cyclodextrin complexation, co-solvent solubilization, salt formation, and particle size reduction. However, it is important to note that each of these techniques has its own limitations. The drawbacks of previous approaches were overcome by creating solid dispersions of medicines with low bioavailability. Solid dispersion refers to the arrangement of one or more hydrophobic active chemicals within a hydrophilic inert carrier at solid state. This can be accomplished using the fusion technique, the solvent melting method, or the solvent or melting solvent preparation. The enhanced surface area of the solid dispersion results in an accelerated dissolving rate, hence enhancing the bioavailability of the medication with low solubility. This event occurs when the solid dispersion comes into contact with the

aqueous medium, which enables the carrier to dissolve and subsequently release the drug. Sekiguchi and Obi (1961) discovered that the absorption rate and extent of sulfathiazole could be significantly enhanced through solid dispersion. They achieved this by using urea as an inert carrier to generate a eutectic combination with sulfathiazole.

Glipizide is an oral rapid- and short-acting anti-diabetic drug from the sulfonylurea class. It is classified as a second generation sulfonylurea, which means that it undergoes enterohepatic circulation. Second-generation sulfonylureas are both more potent and have shorter half-lives than the first-generation sulfonylureas. It helps to control blood sugar levels. This medication helps your pancreas produce insulin. Glipizide is used together with diet and exercise to treat type II diabetes. It is 100 times more potent than Tolbutamide. As per BP, It Glipizide is practically insoluble in water; because of its poor aqueous solubility (classified as BCS class II drug), conventional Glipizide dosage form show absorption problem, and its dissolutions are considered to be a rate determining step in its absorption from gastrointestinal tract. During high blood glucose level conditions, an antidiabetic drug should show quick and high oral bioavailability, which can be achieved by high aqueous solubility. Many hydrophilic excipients like eudragit E-100, PEG 4000, PEG 6000, urea, Mannitol, PVP and poloxamers can be used to enhance the dissolution of drugs. So, the rationale is to enhance the solubility rate of Glipizide with the use of combination of polymers like PEG 6000 and Poloxamer 188.

MATERIALS AND METHODS

Materials:

Glipizide was gifted by Supra Chemicals, Thane-Belapur Road, Rabale, Navi Mumbai. PEG-6000 was procured from Ozone International Pvt Ltd, Mumbai. Poloxamer was procured from Chemsworth Pvt Ltd, Ambernath (E) and Methanol was procured from Poona chemical laboratory, Pune. All the chemicals mentioned are Analytical grade only.

Method:

Preparation of solid dispersion by rotary evaporation method:

Nine different formulations of Glipizide solid dispersion were prepared using rotary evaporator with two different polymers such as Poloxamer 188 and PEG 6000 in different ratios listed in Table-1

The Polymers (Poloxamer 188 and PEG 6000) and the drug was accurately weighed using a digital weighing balance, this physical mixture was solubilised in a minimum amount of common solvent i.e. methanol in a round bottom flask (RBF) till the mixture dissolved completely. Then the solvent was evaporated using a rotary vaccume flash evaporator equipped with a water bath having a digital temperature controller fitted with RBF was kept at temperature 60°C until the wet mass was obtained. The residue was collected and then kept in a hot air oven at 37°C until the constant weight was achieved. This solid residue was pulverised using a porcelain mortar and pestle. The pulverised powder was passed through sieve No.60 and stored in desiccator for further studies.

Table 1: Composition of solid dispersion containing glipizide, poloxamer 188 and PEG 6000

Sr. NO.	Formulation No.	Composition	Ratio
1.	F1	Drug: Poloxamer 188: PEG 6000	1: 1: 1
2.	F2	Drug: Poloxamer 188: PEG 6000	1: 1: 2
3.	F3	Drug: Poloxamer 188: PEG 6000	1: 1: 3
4.	F4	Drug: Poloxamer 188: PEG 6000	1: 2: 1
5.	F5	Drug: Poloxamer 188: PEG 6000	1: 2: 2
6.	F6	Drug: Poloxamer 188: PEG 6000	1: 2: 3
7.	F7	Drug: Poloxamer 188: PEG 6000	1: 3: 1
8.	F8	Drug: Poloxamer 188: PEG 6000	1: 3: 2
9.	F9	Drug: Poloxamer 188: PEG 6000	1: 3: 3

EVALUATION OF SOLID DISPERSION

1. Percentage Practical Yield:

The percentage yield can be determined by Accurately weighing the initial weight of raw materials and final weight of solid dispersion. The % yield of all the batches was determined by weighing the glipizide solid dispersion after drying.

The % yield was determined using the following formula:

$$Percentage\ Yield = \frac{Mass\ of\ Solid\ Dispersion\ obtained}{Total\ weight\ of\ drug\ and\ polymer} \times 100$$

2. Solubility Study:

Solubility was determined in both water and phosphate buffer solutions with a pH of 6.8 by shake flask method. A conical flask containing 25 ml of distilled water and phosphate buffer pH 6.8 taken and an excess amount of drug and its solid dispersions were added and the solution was shaken for 24 hours at 37±0.5 °C. After that, a 0.45 µm membrane filter was used to filter the dispersion. Following the proper dilution with suitable solvent, the absorbance was then determined by UV Spectrophotometer at 276 nm, and the drug solubility was measured.

3. Estimation of drug content:

The drug concentration of Glipizide solid dispersion was determined by dissolving 10 mg of Glipizide in a 10 ml solution of phosphate buffer (pH 6.8). The solution then passed through 45 µm Whatman filter paper, diluted with an appropriate solvent, and analysed using UV spectrophotometer at a wavelength of 276 nm.

4. In Vitro Dissolution studies:

The dissolution study of Glipizide and its solid dispersion was conducted using the USP rotating basket apparatus (Type I) for a duration of 2 hours and 30 minutes. A hard gelatin capsule was filled with a solid dispersion that is equivalent to 10 mg of glipizide. The dissolution medium used was a phosphate buffer solution (pH of 6.8), with a volume of 900 ml. The dissolution procedure was carried out at a rotational speed of 100 revolutions per minute (rpm) and the temperature was precisely maintained at 37±0.5℃. A 5 ml aliquot was extracted at 5, 10, 15, 30, 45, 60, 120, and 150 minutes, and then replaced with an equal volume of dissolution media to ensure a sink condition. The samples were filtered using Whattman filter paper. Following the dilution of the samples, UV-Visible Spectrophotometry was employed to measure the absorbance of the samples at a wavelength of 276 nm.

5. FTIR (Fourier transform Infrared spectroscopy) :

The infrared spectra (IR) of the samples were performed on Fourier transform infrared spectrophotometer (Perkin Elmer 400 spectrum USA). The pellet of the drug and KBr were prepared on KBr press. The spectra were scanned over number range of 4000 to 400 cm^{-1} at ambient temperature.

6. DSC (Differential scanning calorimetry):

The measurements of DSC were carried out using a differential scanning calorimeter. (Mettler Toledo). The 2–5 mg sample was placed in aluminium pans, subjected to a 10 °C/min temperature scan between 30 °C to 200 °C, and then examined under an inert nitrogen atmosphere.

7. XRD (X ray Diffraction) :

The X-ray diffraction patterns were obtained using the XPERT-PRO diffractometer. The diffractometer was equipped with a Cu Kα filter and operated at a voltage of 45kV and a current of 40mA over a diffraction angle of 2θ.

8. SEM (Scanning electron microscopy):

The morphology of solid dispersions was determined using a scanning electron microscope (SEM) (Jeol model JSM-6610, JAPAN) operated at an accelerating voltage of 3 kV. Samples were prepared by mounting powder on to a brass stub using graphite glue and coated with gold under vacuum before use.

RESULT AND DISCUSSION

Percentage Yield

The percentage yield of SDs ranged between 81.66% to 95.83%. Table 2 shows that the increase in concentration of the polymer leads to increase in manufacturing yield.

Drug Content

The drug content of the prepared solid dispersions ranged from 82.10% to 97.20% (Table 2)

Table 2: % yield and Drug content of solid dispersion of glipizide

Sr. No.	Formulation No.	% Yield (Rotary evaporator)	Drug Content (%) (Rotary Evaporator)
1	F1	81.66	82.10
2	F2	95.00	85.62
3	F3	95.20	94.86
4	F4	90.00	86.15
5	F5	93.00	92.85
6	F6	89.16	96.58
7	F7	87.00	98.36
8	F8	95.83	88.76
9	F9	94.28	97.20

Solubility Studies

Glipizide exhibits low solubility in water. Hydrophilic polymers significantly increased the solubility of glipizide. The solubility increases with increase in polymer ratio. Formulation F7 offers the better solubility than pure drug with a ratio of 1:3:1.

Table 3 : Solubility of solid dispersion of glipizide

Formulation No.	Water (µg/ml)	Phosphate buffer pH 6.8 (µg/ml)
Drug	20.85	30.96
F1	42.03	48.78
F2	44.67	50.60
F3	46.14	54.17
F4	48.85	49.57
F5	47.21	56.46
F6	51.57	68.85
F7	60.12	72.96
F8	54.42	62.35
F9	52.75	57.67

Dissolution Studies

The dissolution test was carried out by using USP-I (Rotating basket). The dissolution conditions include, Dissolution medium (Phosphate buffer pH 6.8), Temperature (370 C ± 0.50 ˚C), Speed of Rotation (50 rpm), Volume of Medium (900 ml). Glipizide containing prepared solid dispersions equivalent to 50 mg of glipizide filled in the capsule and placed in the basket of dissolution medium and the apparatus was run. The 5 ml aliquot was withdrawn at 5, 10, 15, 30, 45, 60, 90, 120 and 150 min12. After withdrawing each sample same amount fresh dissolution medium was replaced so as to maintain sink condition. The samples were filtered through Whatmann filter paper and absorbance was recorded spectroscopically at 276 nm[13]. Table 4 and Fig. 1 shows the in vitro release profile of Glipizide and its prepared batches.

Table 4: Dissolution profile of drug and solid dispersions

Time (min)	Drug (%)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)	F6 (%)	F7 (%)	F8 (%)	F9 (%)
0	0	0	0	0	0	0	0	0	0	0
5	0.64	4.82	15.42	20.89	25.39	27.67	28.92	36.96	32.10	22.62
10	1.92	9.00	20.89	22.17	31.17	31.05	35.35	41.78	38.92	28.10
15	3.85	11.57	22.17	25.39	37.28	36.00	43.39	54.64	45.05	33.12
30	6.42	13.17	26.67	26.67	44.03	37.92	47.57	61.71	52.36	38.88
45	9.64	18.64	31.82	31.82	48.21	41.78	52.07	67.05	60.10	42.10
60	9.96	21.21	33.10	37.28	52.07	47.57	57.21	73.28	68.25	46.76
90	18.32	23.46	34.71	41.14	58.82	52.07	63.05	76.82	74.15	52.45
120	19.60	32.14	38.57	42.10	65.89	63.64	69.20	80.35	76.86	56.57
150	25.07	36	41.14	47.57	69.10	65.89	76.15	85.17	82.35	60.42

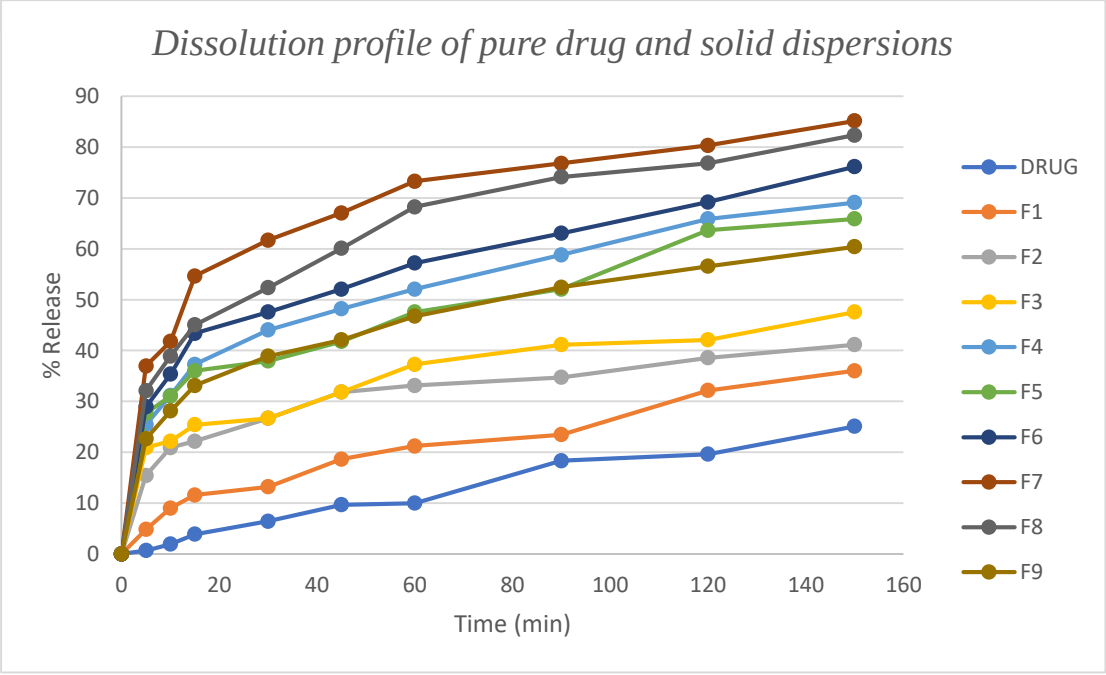

Figure 1: Dissolution profile of drug and solid dispersions

FTIR

The FTIR spectrum of SD were compared to the reference spectrum of Glipizide. FTIR spectrum of Glipizide, poloxamer-188, PEG-6000, mixture of glipizide and Poloxamer 188, glipizide and PEG 6000, physical mixture and solid dispersion are shown in figure 2, 3, 4, 5, 6, 7, and figure 8. The wavenumbers 840, 1688, 1597, 1650, 1444, 1333, 1274, and 1010 cm^{-1} all show prominent peaks that are linked to Glipizide. The MIXTURE OF DRUG AND Poloxamer 188 polymer showed spectral peaks at 842, 1689, 1333, 1280, and 1650 cm-1. However, the mixture of drug and PEG 6000 polymer had clear peaks at 842,1689, 1598, 1444, and 1333 cm^{-1}. The presence of peaks in both the physical mixtures and the optimum batch F7 suggests that there is no interaction between pure Glipizide and the polymers utilized in the manufacturing process of Solid dispersion.

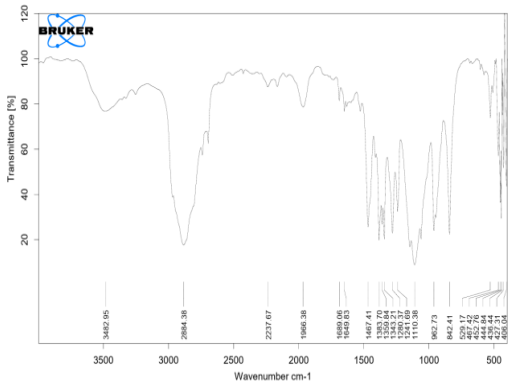

Figure 2: FTIR spectrum of Glipizide

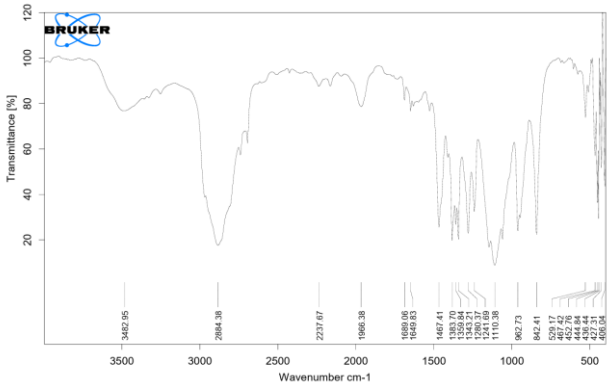

Figure 3: FTIR spectrum of Poloxamer 188

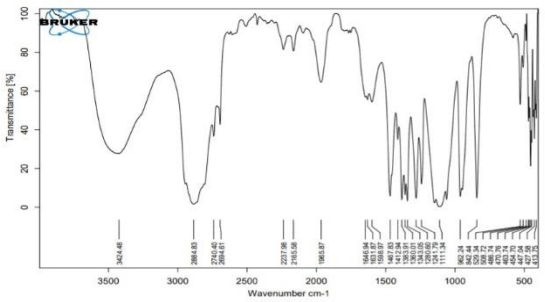

Figure 4: FTIR spectrum of PEG 6000

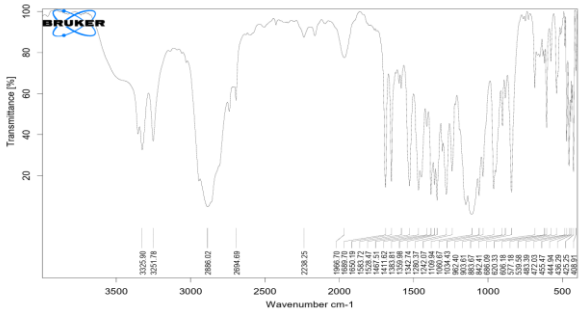

Figure 5: FTIR spectrum of drug and poloxamer 188

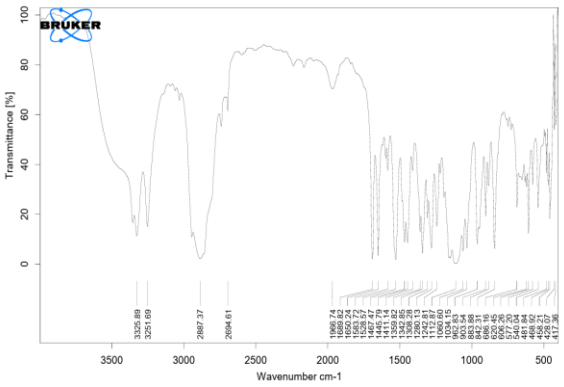

Figure 6: FTIR spectrum of drug and PEG 6000

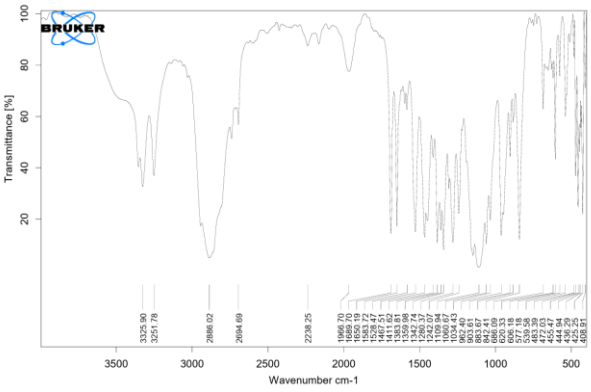

Figure 7: FTIR spectrum of drug Poloxamer 188 and PEG 6000

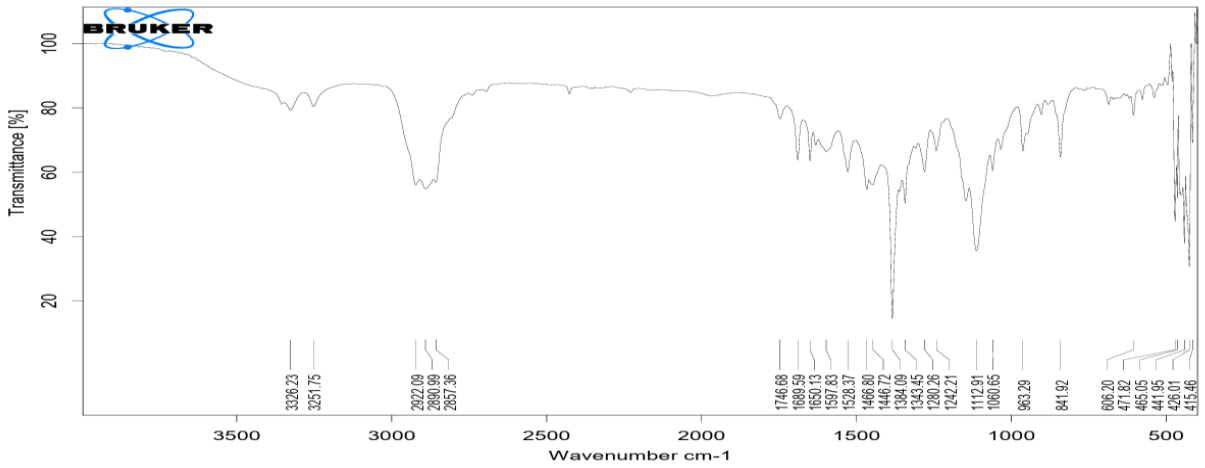

Figure 8: FTIR spectrum of solid dispersion

DSC

DSC thermograms of solid dispersion are shown in Figure 9, Pure glipizide exhibited an endothermic peak at around 219.66 °C, which was consistent with the melting point of glipizide. Conversely, the glipizide peak showed a considerable drop in melting point i. e 57.03°C, indicating that the drug had changed from its crystalline state to an amorphous state.

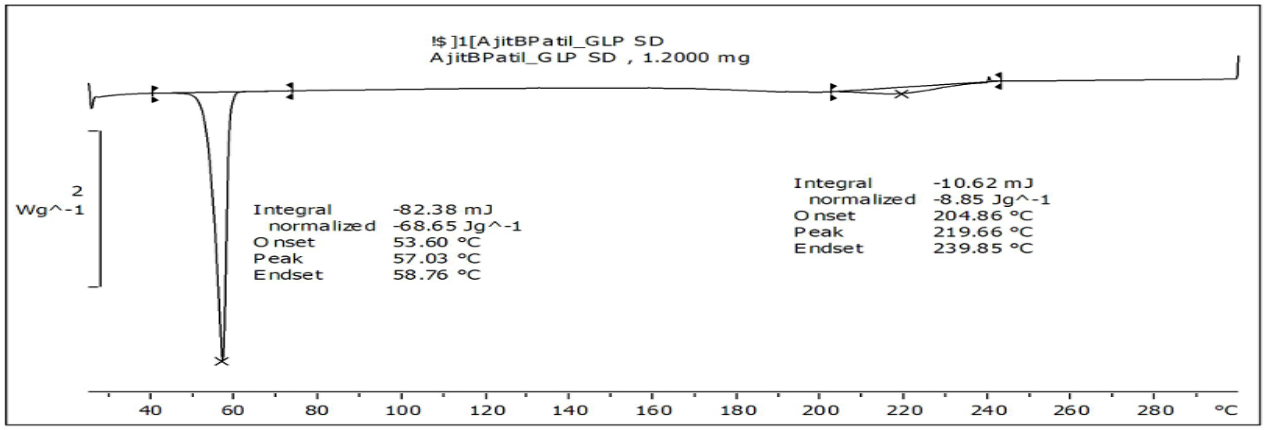

Figure 9: DSC of Solid dispersion

XRD

Prepared dispersion showed changes in the number of peaks or few diffuse peaks were observed in solid dispersion as compared to XRD spectra of drug, which indicate decrease in crystallinity in dispersed glipizide. The decreased drug crystallite size can explain the faster dissolution and increased solubility, which indicates that there is physical interaction between drug and polymers. XRD of solid dispersion showed in fig 10.

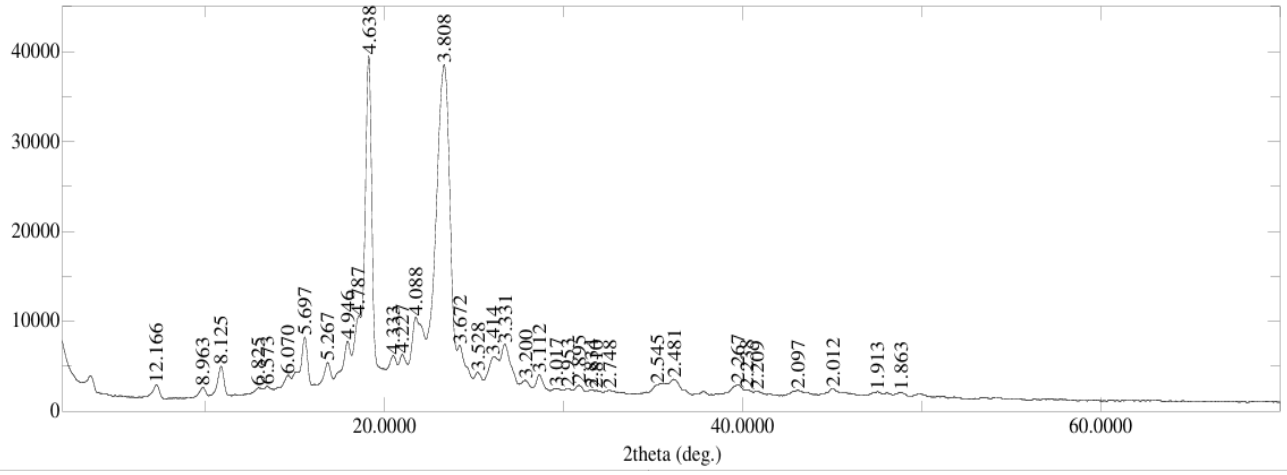

Figure 10: XRD of Solid dispersion

SEM

Based on the scanning electron microscope (SEM) image, it was evident that the size of glipizide particles was considerably decreased after solvent evaporation. The solid dispersion agglomerates were predominantly spherical in shape, with the rest being irregular. The agglomerates had a smooth surface and an average particle size of 2.95 µm. (Fig11)

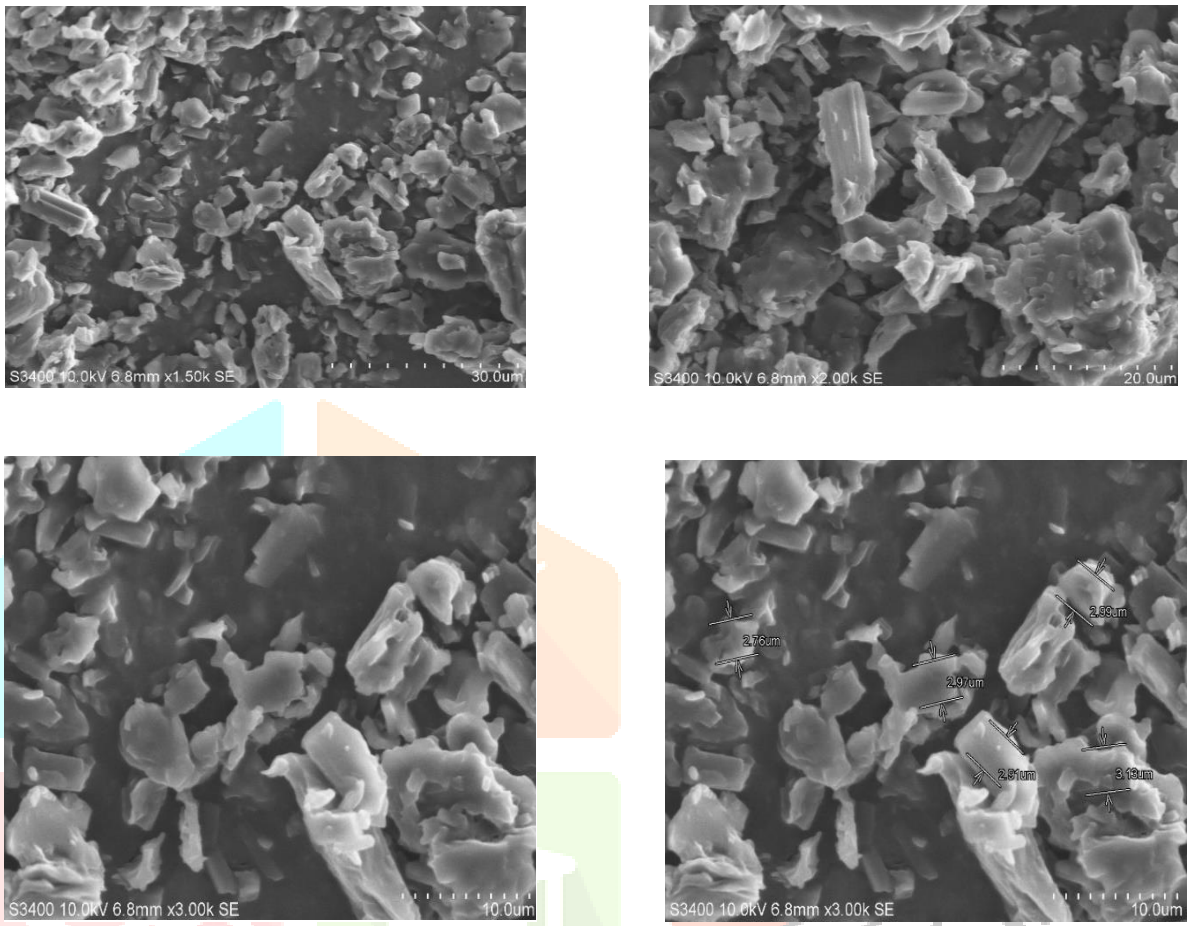

Fig 11: SEM of solid dispersion

CONCLUSION

This study aimed to enhance the solubility and dissolution rate of the Glipizide by using the solid dispersion method using PEG 6000 and poloxamer 188 as polymers. Glipizide's dissolution rate was considerably enhanced by complexation with poloxamer 188 and PEG 6000 due to a variety of mechanisms, including increased drug high degree of porosity and amorphization of the drug. according to FTIR data, it was proved that there are no interactions between drug and polymer and chemical integrity of drug was maintained. The percentage yield of formulation was range of 81.66 % - 93.86%. SEM analysis of solid dispersion showed decrease in crystallinity. DSC studies indicated that drug present in formulation was transformed to amorphous form. Solubility of pure drug i.e. glipizide and its solid dispersion measured by flask shaker method and it indicated increase in solubility observed as compared to pure drug. the dissolution rates of solid dispersion are found higher than those of pure drug. In vitro drug release study for f7 batch found to be 85.17%. the results of the above study show that the research was satisfactory to improve the aqueous solubility and release profile of Glipizide.

AKNOWLEDGEMENT

The author expresses gratitude to Supra Chemicals, Thane-Belapur Road, Rabale, Navi Mumbai, for providing a gift sample of Glipizide. The author expresses gratitude to Ozone International Pvt Ltd, Mumbai, Chemsworth Pvt Ltd, Ambernath (E), and Poona chemical laboratory, Pune for supplying essential chemicals that were crucial for the completion of the current project.

REFERENCES

1. Dharna Allawadi et al. Solid Dispersions: A Review on Drug Delivery System and Solubility Enhancement; International Journal of Pharmaceutical sciences and Research 2013; vol.4 (6): 2094-2105
2. Verma S, Rawat A, Kaul M and Saini S: Solid Dispersion: A Strategy for Solubility Enhancement. International Journal of Pharmacy & Technology 2011; 3(2): 1062-1099.
3. Khater A. S. Hala M. Alkhadi, et al. Lyophilized Amorphous Dispersion of Telmisartan in a Combined Carrier−Alkalizer System: Formulation Development and In Vivo Study, ACS OMEGA 2020, 5, 50, 32466-32480.
4. Shivangi Madhok and Akanksha Madhok: Enhancement of Solubility and Dissolution of Carvedilol by Solid Research and Technology 2015, vol. 5 (2): 81-102.
5. Avinash Hanmant Hosmani, Nikhil Dilip Patil, Arti Achut Pawar, Sandip Mohan Honmane, Yogesh Shripad Thorat: Development and Evaluation of Fenofibrate Surface Solid Dispersion for Improved Solubility and Dissolution Rate; Indian Journal of Pharmaceutical Education and Research. 2024; 58(2):446-452
6. Ankit Gupta, Mahesh Kumar Kataria, Ajay Bilandi: Formulation and Evaluation of Solid Dispersion of Glipizide for Solubility and Dissolution Rate Enhancement; International journal of Pharmaceutics and Drug Analysis 2014; 2(2): 74-87.
7. D. R. Powar, A. V. Desai, V. Y. Rohile, M. V. Bhosale, N. R. Inamdar: Design Development and Optimization of Telmisartan's Ternary Solid Dispersion with Its Formulation; International Research Journal of Pharmacy and Medical Sciences 2022; 6(1): 2581-3277.
8. Bhumika Kumar: Solid Dispersion: A Review: Pharma Tutor 2017; 5(2): 24-29
9. Leila Barghi, Afshin Vekalati and Azin Jahangiri: Stability Enhanced Ternary Solid Dispersion of Glyburide: Effect of Preparation Method on Physicochemical Properties; Advanced Pharmacological and Pharmaceutical Sciences 2023
10. Hasanain Shakir Mahmood: Formulation of Telmisartan Solid Dispersion using Poloxamer 188 and PVP; Scholars Academic Journal of Pharmacy (SAJP) 2017; 6(3): 80-88.
11. Dixit AK., Singh RP: solid dispersion: A Strategy for Improving the Solubility of Poorly Soluble Drugs; IJRPBS 2012; 3(2): 960-966
12. R. Natarajan, G. Komala, TR. Ramcy, Swathi Polineni and S. Mohan: Dissolution Enhancement of Aceclofenac Solid Dispersion Prepared with Hydrophilic Carriers by Solvent Evaporation method; International Journal of Research in Pharmacy and Chemistry 2014, 4(1): 83-89.
13. Punitha.S, Karthikeyan. D, Devi.P and Vedha Hari.B.N, Enhancement of Solubility and Dissolution of Celecoxib by Solid dispersion technique, Journal of Pharmaceutical Sciences and technology Vol.1(2),2009,63-68.
14. A. Abdul Hasan Sathali and V. Selvaraj: Enhancement of Solubility and Dissolution Rate of Racecadotril by Solid Dispersion Methods; Journal of Current Chemical and Pharmaceutical Sciences 2012; 2(3): 209-225.
15. Mahendra Patel, Arpna Indurkhya, Masheer Ahmed Khan: Improvement of Dissolution Rate of Repaglinide by Utilizing Solid Dispersion Technique. Current Research in Pharmaceutical Sciences 2023; 13 (01): 78-82.
16. Mohamed Hassan, J. Dehjhan et al. Comparative Dissolution Study of Glipizide by Solid Dispersion; Journal of Pharmaceutical Sciences and Technology 2010; 2 (9): 293-297.
17. Dehghan M H G et al. Comparative Dissolution Study of Glipizide by Solid dispersion Technique Journal of Pharmaceutical Science and Technology; Volume 2(9),2010: 293-297.
18. Wei-Juan Xu et al. Enhanced Dissolution and Oral Availability of Valsartan Solid Dispersion Prepared by a Freeze-Drying Technique Using Hydrophilic Polymers, Informa healthcare Drug Delivery 2016; 23(1): 41-48.
19. G.V. Betageri et al. Enhancement of Dissolution of Glyburide by Solid Dispersion and Lyophilization Techniques, International Journal of Pharmaceutics 1995; Volume 126, Issues 1–2: 155-160.