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Research Article

ENHANCEMENT OF DISSOLUTION RATE OF GLIBENCLAMIDE BY SOLID DISPERSION TECHNOLOGY

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ABSTRACT

The aim of the study is to prepare solid dispersion of Glibenclamide using different carriers such as PEG 6000, Polyvinyl pyrolidine (PVP) and Poloxamers in different ratios (1:1, 1:2, 1:3, 1:4 and 1:5) by Solvent Evaporation method. Drug carrier interactions were analysed by X-ray diffraction and Infra-Red Spectroscopy. Dissolution studies using the USP paddle method were performed for all solid dispersions. All solid dispersions showed increased dissolution rate as compared to pure Glibenclamide and PVP was found to be better than PEG and Poloxamer. The tablets were formulated using solid dispersion of Glibenclamide containing PVP as carrier. The tablets containing solid dispersion exhibited better dissolution profile than commercial tablets. Thus solid dispersion technique can be successfully used for improvement of dissolution of Glibenclamide.

Key words: Glibenclamide, PVP, Poloxamer, PEG, Solid dispersion

INTRODUCTION

In lowering blood glucose level, Glibenclamide appears to be dependent on stimulating the insulin release from pancreatic β-cells and by increasing the sensitivity of peripheral tissue to insulin. High affinity receptors for Glibenclamide are present on the K_{ATP} channels in β-cells of plasma membranes and the binding of drug parallels their potency in stimulating insulin release[1,2].

Glibenclamide, which is a poorly water-soluble drug shows poor solubility or poor wetability which leads to decrease in bio-availability.[3] Solid dispersion is one of the unique approaches, to increase the solubility, dissolution and absortion of poorly soluble drugs.[4,5] In SD technique dissolution rate can be improved by increasing the surface area and there by reducing the particle size.[6] The present work aims to evaluate the potential of the solid dispersion technique for the development of fast dissolving tablets of Glibenclamide using PVP, PEG_{6000} and Poloxamer as hydrophilic carrier.

MATERIALS AND METHODS

MATERIALS

Glibenclamide-Gift sample from Micro labs, Hosur. Poloxamer $_{407}$ - SD Fine- Chem Ltd, Mumbai. Polyethyleneglycol $_{4000}$ - Sisco Research Laboratories Pvt Ltd. Poly vinyl Pyrrolidone (PVP K_{30})- SD Fine-Chem Ltd, Mumbai. All reagents and solvents used were of analytical grade.

METHODS

Preparation of solid dispersion by solvent evaporation method

Solid dispersions of Glibenclamide with carriers at 1:1, 1:2, 1:3, 1:4, and 1:5, weight ratios were prepared by the solvent evaporation method.[7]

In the present study, 15 formulations of solid dispersions of Glibenclamide were formulated by using various carriers such as Poloxamer, PEG 4000,[8] and Poly Vinyl Pyrrolidine.[9] The carrier was dissolved in required amount of solvent mixture of chloroform[10] which is taken in a conical flask to get a clear completely soluble polymer solution with the help of magnetic stirrer. Weighed amount of Glibenclamide was added to this solution carefully with constant stirring. Stirring was continued until the drug is completely incorporated in solvent. Then the solvent was removed by evaporation at 40º C under vacuum. The mass obtained was dried, crushed, pulverized and seived through mesh no: 60.

Solid state studies

Estimation of drug content

The uniform distribution of Glibenclamide in SD system was confirmed by estimating the drug content in SD system by using JASCO V-530 UV visible spectrophotometer[11,12].

Drug Carrier interaction studies

The drug carrier interactions were studied by TLC method and IR spectral analysis[13].

1. TLC

A silica gel- G coated thin glass plates were used for the determination of RF values of Glibenclamide pure sample and SD systems. Chloroform , ethyl acetate and 25% ammonium hydroxide were used as mobile phase and it is detected by UV light method.

2. Fourier transform infrared (FTIR) spectroscopy

IR spectra of glibenclamide and its solid dispersions are identical. The principle IR absorption peaks of glibenclamide solid dispersions were observed and found to be identical with the spectra of glibenclamide pure drug. Thus, from the spectra it was understood that there was no interaction between glibenclamide and the carriers used in the preparation of solid dispersions.

3. X-ray powder diffractometry

The crystalline nature of Glibenclamide was studied for pure drug and for solid dispersions by using x'pert proanalytical diffractometer.

In vitro release studies of pure drug and solid dispersion:

In vitro dissolution of pure drug, physical mixture and SD of drug with PVP, PEG -4000 , Poloxamer were carried out on USP XXII type II dissolution test apparatus using 900 ml of 7.4 pH Phosphate buffer as a medium at 37 ± 1º C temperature with stirring rate of 50 rpm. The samples were analyzed for the drug content at 240 nm using Shimadzu UV- 1700 spectrophotometer[14,15].

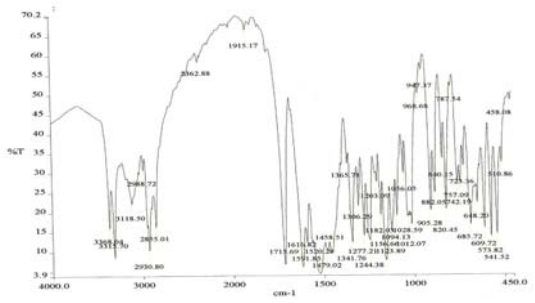

Fig. 1: IR spectrum of pure Glibenclamide

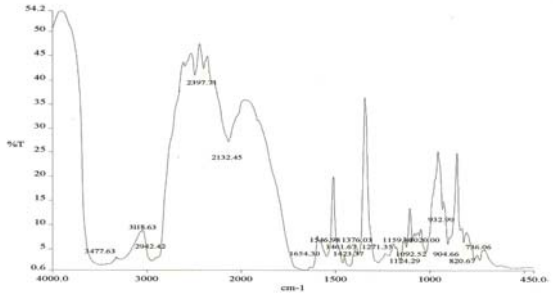

Fig. 2: Spectrum of solid dispersion of Glibenclamide & PVP K-30

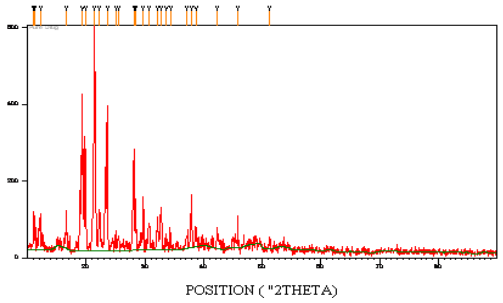

Fig. 3: X-ray diffraction of pure Glibenclamide

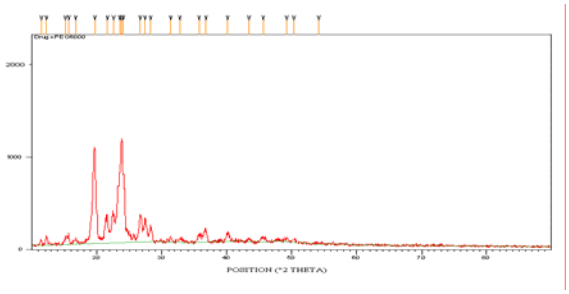

Fig. 4: X-ray diffraction of solid dispersion of Glibenclamide & PEG 6000

RESULTS AND DISCUSSIONS

The TLC and IR spectra of pure drug, physical mixtures and solid dispersions shows no interaction between Glibenclamide with various carriers and X- ray diffraction studies revealed that crystalline nature of Glibenclamide in pure form was reduced to amorphous form in the dispersions.

In this study solid dispersions prepared using various hydrophilic carriers enhanced the solubility of the Glibenclamide to varying degree. Results of dissolution studies showed rapid and fast dissolution of Glibenclamide from all solid dispersions when compared with pure drug and physical mixture. Among the 15 formulations of Glibenclamide solid dispersions with different carriers, the formulation of Glibenclamide with PVP in the ratio of 10:90 (F 3_E) showed the highest dissolution rate.

All solid dispersions showed increased dissolution rate as compared to pure Glibenclamide and PVP was found better than PEG and Poloxamer.

Preparation and characterization of tablets

Glibenclamide solid dispersions in PVP and in PEG4000 at a drug carrier ratio of 10:90 were formulated into tablets. The tablets containing 7.5mg of Glibenclamide were prepared by direct compression method as per the formula given in the table. The prepared tablets were stored in screw capped glass bottles. The prepared tablets were evaluated for drug release characteristics.

Table 1: Percentage release of Glibenclamide from various solid dispersions

Time in min	Percentage Release of Glibenclamide from														
	Glibenclamide : Poloxamer SD					Glibenclamide:PEG_{4000} SD					Glibenclamide:PVP SD				
	90:10	75:25	50:50	25:75	10:90	90:10	75:25	50:50	25:75	10:90	90:10	75:25	50:50	25:75	10:90
10	2.25	3.37	5.62	9	4.5	4.5	4.5	18.0	13.5	18	5.6	11.25	11.2	36	12.3
20	11.25	11.25	11.25	11.25	15.11	20.25	18.0	20.2	40.5	24.0	22.5	13.5	15.75	54	47.2
30	18.0	18.0	22.5	18.0	36.0	22.5	22.5	27.0	49.5	45.0	27.0	27.0	49.5	56.2	74.0
40	20.25	31.5	32.6	33.75	56.0	24.0	24.0	47.2	58.5	69.75	29.2	29.25	69.5	57.3	90
60	24.0	36.0	63.0	97.5	72.0	33.75	33.75	51.7	72.0	78.75	33.7	36.0	76.5	69.7	96
90	29.45	45.0	76.0	83.2	85.5	47.25	47.25	67.5	85.5	94.5	45	49.5	85.5	81.0	100

Table 2: Composition of polymer mixing ratios and binary solid dispersions

Sl.no	Ingredients	Formulations (mg)		
		F I	F II	F III
1	Glibenclamide	7.5	-	-
2	Glibenclamide-PVP SD(10:90)	-	75	-
3	Glibenclamide-PEG4000 SD(10:90)	-	-	75
4	Lactose	25	25	25
5	Micro crystalline cellulose	157.5	90	90
6	Talc	5	5	5
7	Magnesium stearate	5	5	5

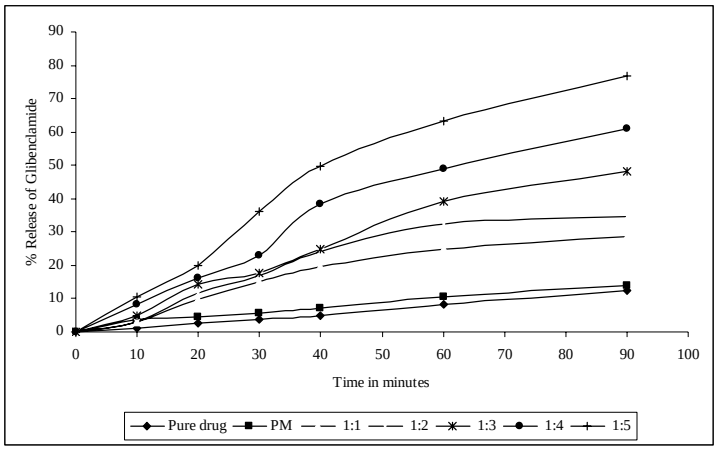

Fig. 5: Dissolution of GLIBENCLAMIDE from PEG 4000 solid dispersion of different drug:carrier ratios

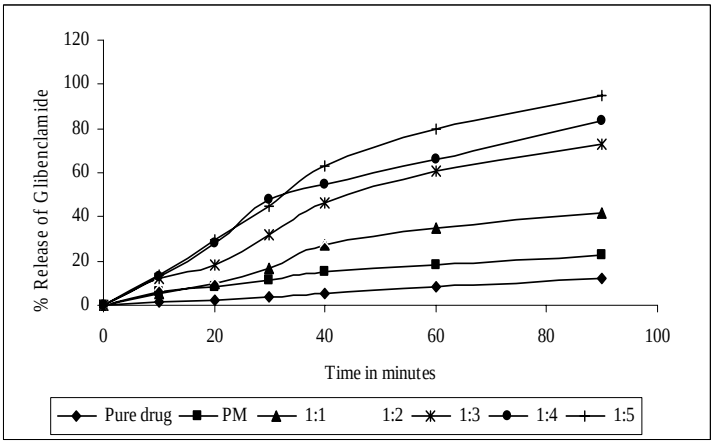

Fig. 6: Dissolution of GLIBENCLAMIDE from PEG 6000 solid dispersion of different drug:carrier ratios

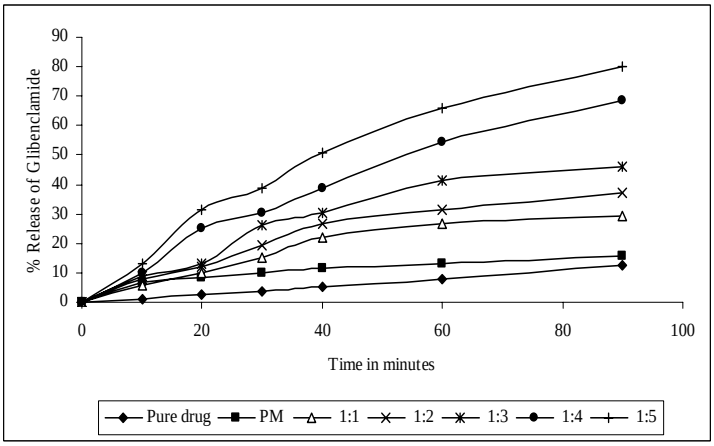

Fig. 7: Dissolution of Glibenclamide from PVP K-30 solid dispersion of different drug: carrier ratios

Physical characterization of tablets

The diameter, friability, thickness, and weight of formulated tablets are described in table. To be acceptable by USP standards, the weight variation tolerance for uncoated tablets must be 7.5% or less. It was found that weight variation for the formulated tablets were less than 7.5%. the friability obtained (<1%) confirmed the suitability of direct compression technology. Good uniformity in drug content was found among different batches of tablets.

Dissolution studies of tablets

Dissolution of glibenclamide from various tablets were studied in USP dissolution rate apparatus (Lab India, DISSO 2000).

Table 3: Dissolution of Glibenclamide from tablet formulations

Time in min	Percentage Glibenclamide dissolved (%)			
	FI	FII	FIII	Marketed tab
10	7.5	33.7	45.0	22.5
20	18.0	49.5	68.0	45.6
30	18.0	65.0	91.0	57.5
40	20.25	73.5	97.5	65.3
60	24.0	89.5	100	78.2
90	33.7	95.0	100	89.9

CONCLUSION

Solid dispersions of Glibenclamide prepared with PVP by the solvent evaporation method resulted in greater increase in drug dissolution. As demonstrated by X-ray diffraction a decreased crystallinity of Glibenclamide and the surface morphology of the polymeric particles explained this improved dissolution rate. Tablets containing those SD particles had drug dissolution profiles that were better than those of conventional tablets without PVP. Moreover, flow properties of the granules as well as the disintegration analysis technological parameters of the tablets indicated that PVP is a suitable excipient for the development of Glibenclamide fast release tablets.

REFERENCES

1. Martindale, Kathlean Parafitt editor, 32nd edition, 1999, 31-32.
2. Satoskar RS, Bhandarkar SJ, Pharmacology and pharmacotherapeutics, 17th edition, 155, 166.
3. Serajuddin A. Solid dispersion of poorly water soluble drugs:early promises, subsequent problems and recent breakthroughs. Int J Pharm Sci 1999;88:1058-1066.
4. Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion system. J Pharm Sci 1971;60:1281-1302.
5. Craig DQM. The mechanisms of drug release from solid dispersions in water soluble polymers. Int J Pharm 2002;231:131-144.
6. Van den Mooter G, Augustijns P, Blaton N, Kinget R. Physicochemical charaterization of solid dispersions of temazepam with polyethylene glycol 6000 and PVP K30. Int J Pharm 1998;164:67-80.
7. Ali A,Sharma SN. Preparation and evaluation of solid dispersions of Ibuprofen. Indian J Pharm Sci 1991;53:233-236.
8. Patil et al. Improvement in dissolution efficiency of poorly soluble naproxen. The Eastern pharmacist 2001;521:107-109.
9. Sethia S, Squillante E. Solid dispersion of carbamazepine in PVPK30 by conventional solvent evaporation and supercritical methods. Int J Pharm 2004;272:1-10.
10. Chowdary KPR, Hymavathi R. Enhancement of dissolution rate of Glibenclamide. J Pharm Sci 2001;63:150-154.
11. Bassam M. tashtoush, Zubaida S.al-quashi. In Vitro and In Vivo evaluation of Glibenclamide in solid dispersion systems. Drug development and industial pharmacy 2004;30:601-607.
12. Ilse weuts, Dieter kempen. Physicocheemical properties and stability of solid dispersions of loperamide. Eur J Pharm & Biopharm 2005;59:119-126.
13. Martina Maria Smikalla et al. Influence OF Povidone k17 on the storage and stability of solid dispersions of Nimodipine. Eur J Pharm & Biopharm 2007;66:106-112.
14. Alazar N.Ghebremeskel, Chandra vemavarapu. Surfactants as plasticizers in preparing solid dispersions. Int J Pharm 2007;328:119-129.
15. Nora Anne Urbanetz et al. Dissolution properties and physico chemical characterization of solid dispersions of Nimodipine. Eur J Pharm & Biopharm 2005;59:107-118.