Research Article

FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF GLICLAZIDE

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ABSTRACT

Gliclazide is a second generation sulfonyl urea derivative used to treat non insulin dependent diabetes mellitus. The drug has been classified as class-II drug according to biopharmaceutical classification system having low solubility and high permeability. So an attempt was made to enhance the solubility of gliclazide by solid dispersion technique. In this sodium starch glycolate, crospovidone were mixed with the drug in different ratios (1:1, 1:3, 1:5). The optimized solid dispersion was evaluated and formulated in to tablets. The pre and post compression parameters of the tablets were evaluated and compared with the marketed brands. The FTIR & XRD studies revealed that there is no interaction between the drug and excipients used in the formulation.

Keywords: Solid dispersions, Fast dissolving tablets, Gliclazide.

INTRODUCTION

Improving the solubility of the drug was the most important factor that is alarming in the minds of all. Methods such as micronization, salt formation and addition of solvent or surface active agents are some methods to improve the solubility of the poorly water soluble drug. Solid dispersion is one of these methods and involved a dispersion of one or more active ingredient in an inner carrier or matrix in solid state prepared by melting, dissolution in solvent or melting solvent method[1]. Solid dispersion technique has been used for improving the solubility of poorly soluble drugs such as nimesulide[2], ketoprofen[3], tenoxicam[4], nifedipine[5], Nimodipine[6].

Superdisintegrants such as Crospovidone and sodium starch glycolate have widely employed for the preparation of solid dispersion as components of the binary system for various drugs such as Furosemide, tacrolimus, tenoxicam, indomethacin, ibuprofen, nilvadipine.

The present investigation aims to evaluate the potential of the solid dispersion technique for the development of Fast Dissolving tablets of Gliclazide using Crospovidone and sodium starch glycolate as the hydrophilic carrier.

Furthermore, the study undertakes to investigate Kneading as a method for the preparation of such binary system their solid state characterization, by using analytical tools like FTIR, XRD and DSC, and attempts to see the possible mechanism of improved dissolution rate.

MATERIALS AND METHODS

Materials

Gliclazide was obtained as a gift sample from Sun Pharma Limited, Crospovidone and Sodium starch glycolate were obtained from SD Fine chemicals, Bombay. All reagents & solvents used were of analytical grade.

Methods

Preparation of Gliclazide-SSG/CP solid dispersions[7]

A mixture of Gliclazide & SSG/CP (1:1, 1:3 & 1:5 by weight) were wetted with acetone: water (in 1:1 ratio) kneaded thoroughly for about 60min in a glass mortar till the acetone: water mixture gets evaporated. The obtained dispersion is then placed in a desiccator for 24hrs and then the dry dispersion was passed through #100 sieve and is stored in a desiccator till further use. Physical mixtures (PM) were obtained by pulverizing in a glass mortar and carefully mixed accurately in a glass mortar Gliclazide & SSG/CP (1:5 by weight). For convenience, all the prepared dispersions were given a code name, which is summarized in table 1.

Table 1: Composition of solid dispersion samples

S1	Gliclazide:SSG (1:1) Solid dispersions
S2	Gliclazide:SSG (1:3) Solid dispersions
S3	Gliclazide:SSG (1:5) Solid dispersions
S4	Gliclazide:CP (1:1) Solid dispersions
S5	Gliclazide:CP (1:3) Solid dispersions
S6	Gliclazide:CP (1:5) Solid dispersions
P1	Gliclazide:SSG (1:5) Physical mixture
P2	Gliclazide:CP (1:5) Physical mixture
B1	Brand Glicla-40
B2	Brand Reclide-40
D	Pure Drug

Solid state studies

Fourier Transform Infra Red Spectroscopy

FTIR spectra were recorded on samples prepared in KBr disks using Shimadzu. Samples were prepared in KBr disk by means of a hydrostatic pressure at 6-8 tons pressure. The scanning range was 400-4000 cm^{-1}.

Differential scanning calorimetry

It is a thermal method where the energy necessary to establish a zero temperature difference between a substance and reference material is recorded as a function of temperature even when endothermic or exothermic changes occur.

X -Ray Diffraction

When the natural frequency of the electrons in the substance matches with the incident X-ray radiations, the electrons emits electro magnetic radiations in all directions. If the waves undergo constructive interference they should be diffracted from the crystal lattice.

Estimation of Gliclazide[8]

An UV spectrophotometric method based on the measurement of absorbance at 226nm in pH 7.4 phosphate buffer was used in the estimation of Gliclazide. The method obeyed Beer's law in the concentration range of 2-30µg/ml. Low RSD values ensured reproducibility of the method. Thus, the method was found to be suitable for the estimation of Gliclazide content in various products and in the *in-vitro* dissolution studies. The result is shown in fig 1.

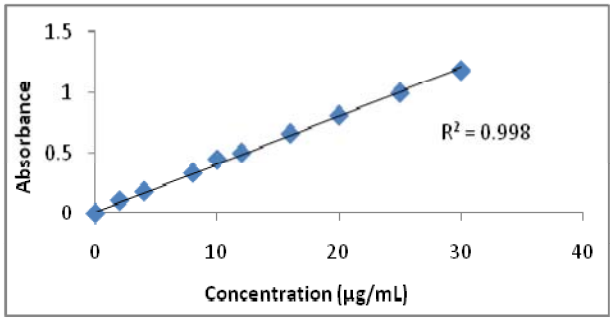

Figure 1: Standard curve of Gliclazide in p^H 7.4 phosphate buffer.

Dissolution rate studies

The dissolution was studied using USP apparatus II taking 900ml of dissolution medium, pH 7.4 phosphate buffer for one hour. The rotational speed of the paddle was set at 50rpm at 37±0.5°C. The 5ml of aliquots was withdrawn at predetermined time interval by maintaining sink condition. The samples were analyzed for drug content using a double beam UV spectrophotometer (Analytical) at 226nm. Results are shown in table 3 & 4, fig 2 & 3.

Table 2: Formulae for Fast dissolving tablets of Gliclazide with solid dispersions by direct compression method

Ingredients	F1	F2	F3	F4
S1	80mg	80mg	-	-
S4	-	-	80mg	80mg
MCC	152.5mg	-	152.5mg	-
Lactose	-	152.5mg	-	152.5mg
Mannitol	12.5mg	12.5mg	12.5mg	12.5mg
Magnesium stearate	2.5mg	2.5mg	2.5mg	2.5mg
Talc	2.5mg	2.5mg	2.5mg	2.5mg

Table 3: Dissolution Profiles of solid dispersions in p^H 7.4 Phosphate buffer

Time (min)	Cumulative % Drug Dissolved				
	S1	S2	S3	P1	D
5	91.81±1.01	98.04±0.11	87.82±0.13	34.59±0.93	0
10	102.01±0.13	98.04±0.58	91.25±0.95	41.25±0.48	10.57±0.77
20	101.67±0.56	101.0±0.91	95.02±0.78	42.99±0.19	19.78±0.37
30	98.79±0.49	100.32±1.01	94.26±0.79	52.79±0.63	30.11±0.93
45	98.63±0.69	100.32±0.35	95.77±1.17	63.35±0.17	45.59±0.18
60	99.29±1.12	100.32±0.51	91.25±0.95	76.18±0.49	52.68±0.83

Table 4: Dissolution Profiles of solid dispersions in p^H 7.4 Phosphate buffer

Time (min)	Cumulative % Drug Dissolved				
	S4	S5	S6	P2	D
5	97.28±0.27	94.26±0.61	99.55±0.19	24.39±0.79	0
10	101.43±0.89	103.55±1.16	97.34±0.87	39.89±0.19	10.57±0.77
20	99.55±0.61	101.85±1.07	98.85±0.29	41.25±0.48	19.78±0.37
30	98.79±0.94	100.98±0.58	97.33±0.64	49.02±0.87	30.11±0.93
45	97.74±1.06	100.98±0.48	92.62±0.35	55.81±0.58	45.59±0.18
60	98.5±0.73	99.56±0.83	94.12±1.03	64.11±0.49	52.68±0.83

Table 5: Evaluation of Physical characteristics of Gliclazide tablets

Parameter	F1	F2	F3	F4
Avg.wt(mg)±SD (n=20)	250±0.2	250±0.32	250±0.24	250±0.36
Hardness(Kg/cm^2) (n=3)	4±0.12	4±0.34	3±0.22	4±0.25
Friability (%) (n=10)	0.19	0.21	0.17	0.20

Table 6: Evaluation of Gliclazide Orodispersible tablets

Parameter	F1	F2	F3	F4
In-vitro Disintegration time (sec) (n=6)	22	14	18	11
Drug content (%) (n=3)	92±0.26	100.34±0.45	101±0.35	100.67±0.27
Wetting time (sec) (n=3)	19	17	15	12
Water absorption ratio (mg) (n=3)	0.52	0.35	0.49	0.21

Table 7: Dissolution profiles of Orodispersible tablets of Gliclazide in p^H 7.4 phosphate buffer

Time (min)	Cumulative % drug release			
	F1	F3	B1	B2
5	74.65±0.79	64.01±1.01	33.97±0.29	38.85±0.11
10	80.32±0.58	88.62±1.18	49.95±0.69	57.99±0.38
20	82.58±0.81	89.93±0.78	74.68±0.16	74.67±0.97
30	85.97±0.97	89.75±0.67	77.69±0.98	87.88±0.29
45	88.24±0.11	87.48±0.72	85.22±0.93	91.98±0.65
60	90.03±1.17	90.45±0.91	96.54±0.91	95.12±0.19

Table 8: Dissolution profiles of Orodispersible tablets of Gliclazide in p^H 7.4 phosphate buffer

Time (min)	Cumulative % drug release			
	F2	F4	B1	B2
5	100.31±0.29	99.18±0.42	33.97±0.29	38.85±0.11
10	98.52±1.09	96.45±0.11	49.95±0.69	57.99±0.38
20	95.01±1.11	95.67±0.19	74.68±0.16	74.67±0.97
30	96.65±1.01	94.18±0.27	77.69±0.98	87.88±0.29
45	94.09±0.98	94.09±0.54	85.22±0.93	91.98±0.65
60	94.09±0.98	94.09±0.73	96.54±0.91	95.12±0.19

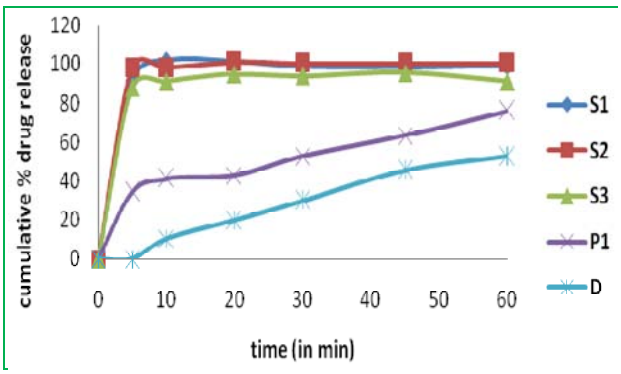

Figure 2: Dissolution Profiles of solid dispersions S1, S2, S3 in comparison with pure drug & Physical Mixture (P1) in p^H 7.4 Phosphate buffer.

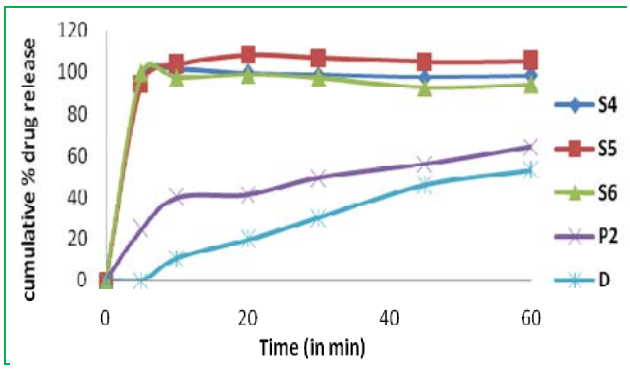

Figure 3: Dissolution Profiles of solid dispersions S4, S5, S6 in comparison with pure drug & Physical Mixture (P2) in P^H 7.4 Phosphate buffer.

Tablet preparation & characterization

Tablets containing equivalent of 40mg of Gliclazide were compressed using single punch Cadmach machine. All the formulations are reported in table 2. Prepared tablets were evaluated for hardness (3-4 Kg/cm^2), friability (0.17-0.21), weight variation and drug content (92-101). Results were shown in table 5 & 6. *In-vitro* dissolution studies of prepared tablets F1, F2, F3 & F4 and 2 commercial tablets of Gliclazide (containing 40mg) Glicla-40 and Reclide-40, respectively, were carried using 900ml of P^H 7.4 phosphate buffer as the dissolution media. Results were shown in table 7 & 8, fig 4 & 5.

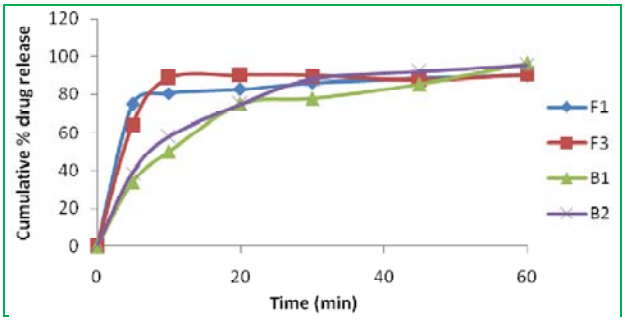

Figure 4: Dissolution profiles of Formulations (F1, F3) in comparison with Brands (B1, B2) in p^H 7.4 phosphate buffer

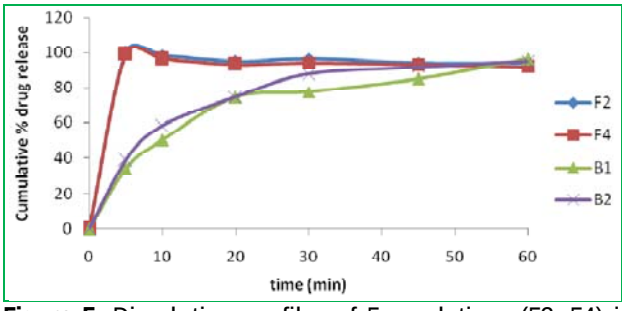

Figure 5: Dissolution profiles of Formulations (F2, F4) in comparison with Brands (B1, B2) in p^H 7.4 phosphate buffer

RESULTS AND DISCUSSION

The objective of the present study was to improve the solubility of Gliclazide and formulate it into an orally disintegrating tablet. In the present study SSG & CP are employed in the preparation of solid dispersions as they act as *hydrophilic carriers*, thereby enhancing the solubility of the drug. As physical mixtures that are prepared at high ratios hasn't shown good dissolution profile, solid dispersion technique was employed.

Totally, six solid dispersions are prepared (S1, S2, S3, S4, S5, and S6) with varying drug: excipient ratios. For the prepared dispersions drug content (table no. 6) and *in-vitro* dissolution studies (table no. 3 & 4, Fig no 2 & 3) were performed. All the prepared dispersions showed satisfactory drug release and *in-vitro* dissolution result. S1 and S4 were selected for further study as the excipient concentrations employed in both the cases was low (table no 1).

Totally, four different ODT (F1,F2,F3,F4) of Gliclazide were formulated using S2 and S4. Out of the prepared four formulations, F1 & F3 showed lower dissolution profiles (table no. 7 & fig. 4) this might be because of the retardant action shown by the diluent MCC. Whereas, formulations F2 & F4, showed a better result (table no 8 & fig. 5). The result was compared with the brands B1 & B2. Formulations F2 & F4 fulfilled all the specifications prescribed for orally disintegrating tablets of Gliclazide.

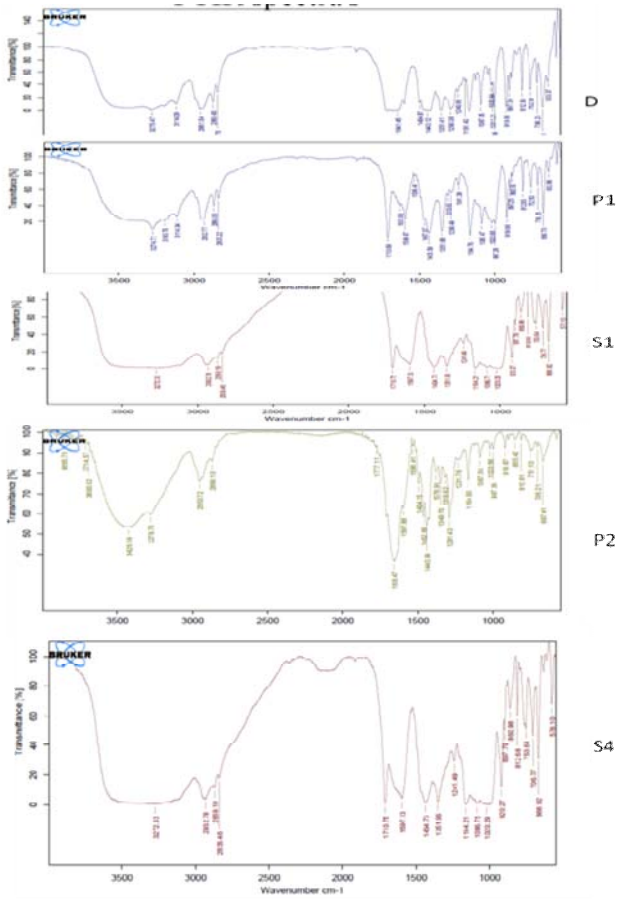

Figure 6: FTIR Spectra of the samples

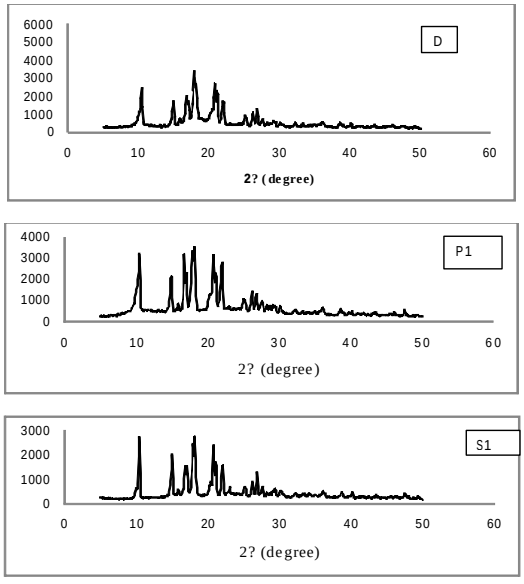

Figure 7: X-ray Diffractograms of the samples.

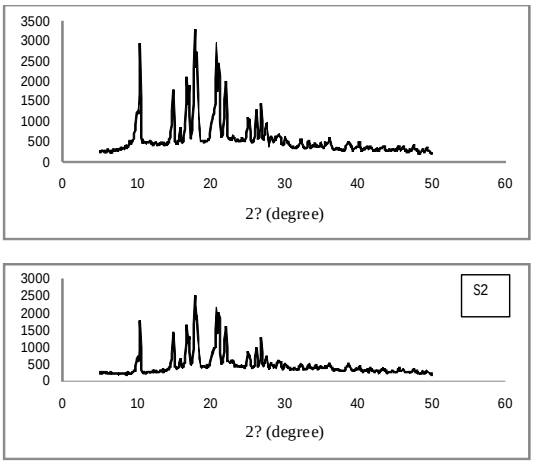

Figure 8: X- ray Diffractograms of the samples.

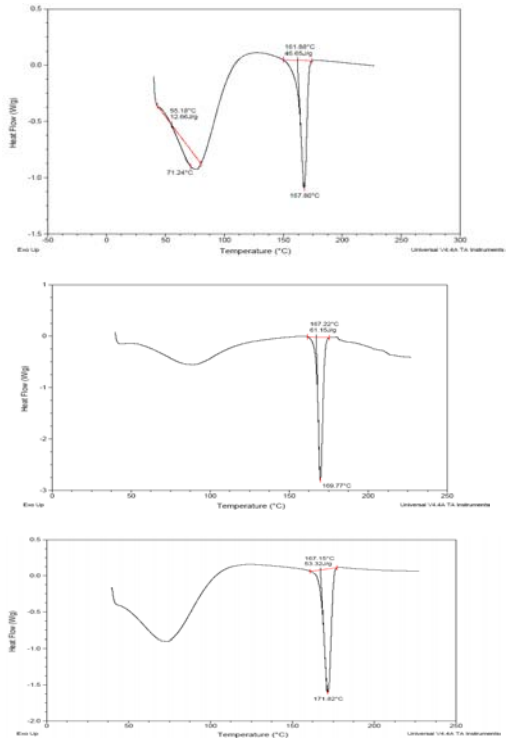

Figure 9: DSC Thermograms of the samples.

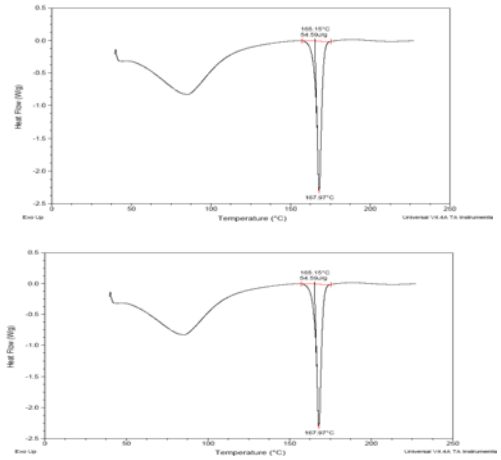

Figure 10: DSC thermograms of the samples.

CONCLUSION

The optimized formulations were F2 & F4. The study shows that the dissolution rate of Gliclazide can be enhanced to a great extent by solid dispersion technique using Kneading method. Hence, Gliclazide-CP, Gliclazide-SSG systems can be considered for formulations of ODT of Gliclazide.

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REFERENCES

1. Chiou WL, Riegelman S. Pharmaceutical applications of solid dispersion systems. J Pharm Sci. 60:1971; 1281-1302.
2. Md.Nehal Siddiqui, Garima Garg, Pramod Kumar Sharma, Fast dissolving tablets: preparation, characterization and evaluation: an overview, International Journal of Pharmaceutical Sciences Review and Research, 4:2, 2010, 87-96.
3. Babu GV, Kumar NR, Himasankar K, Seshasayana A, Murthy KV. Nimesulide-modified gum karaya solid mixtures: Preparation, characterization and formulation development. Drug Dev Ind Pharm. 29:2003; 855-864.
4. Rogers JA, Anderson AJ. Physical characteristics and dissolution profiles of ketoprofen-urea solid dispersions. Pharm Acta Helv. 57:1982; 276-281.
5. El-Gazayerly ON. Characterization and evaluation of tenoxicam coprecipitates. Drug Dev Ind Pharm. 26:2000; 925-930.
6. Vippagunta SR, Maul KA, Tallavajhala S, Grant DJW. Solidstate characterization of nifedipine solid dispersions. Int J Pharm. 236:2002; 111-123.
7. Murali Mohan Babu GV, Prasad CHDS, Ramana Murthy KV. Evaluation of modified gum karaya as carrier for the dissolution enhancement of poorly water soluble drug nimodipine. Int J Pharm. 234:2002; 1-17.
8. Ganesh chaulang. Preparation & Characterization of solid dispersion tablets of Furosemide with crosspovidone. Research J. Pharm and Tech 1(14): Oct-Dec. 2008,386.
9. Instrumental methods of chemical analysis Gurdeep R.Chatwal Sham K. A and 2.306-2.705.

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