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Research Article

Formulation and Evaluation of Gliclazide Solid Dispersions Incorporated Tablets for Controlled Drug Release

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ABSTRACT

The current study deals with the formulation and evaluation of gliclazide solid dispersion (GSD) with HP β Cyclodextrin to enhance solubility and incorporate into tablet formulation for the controlled release of gliclazide. Gliclazide solid dispersion (SD) prepared using varying ratios of HP β Cyclodextrin and evaluated. The optimized SD formulation was incorporated into tablet by using hydroxypropyl cellulose, HPMC K 100M. The drug dissolution from tablet formulation analyzed and characterize. The formulation SD3 comprising of drug and polymer in 1:3 ratio displayed 43-fold increase in solubility when compared to pure drug. The formulation SD13 displayed a maximum yield of 98.96% and maximum drug content of 99%, optimal for tablet formulation. Fourier transform infrared spectroscopy (FTIR) studies revealed that there is no incompatibility between drug and polymers found. XRD studies revealed that the optimized solid dispersion formulation was found to be in an amorphous state. Around 15 formulations of controlled release tablet blends evaluated for micrometric properties show that all the formulations posses' good flow properties. Formulation F15 with maximum drug content of 99.99% and drug release of 99.96 % over 16h was chosen optimal and characterized. The release kinetics suggest that drug release followed zero-order and release from tablets was anomalous non- fickian diffusion super case II transport. The results show that combination of solid dispersion and application of hydrophilic and hydrophobic polymers in matrix formation can facilitate better dissolution and absorption profile with greater patient compliance.

Introduction

The solid dispersion (SD) technique was applied to augment the dissolution and bioavailability of scarcely water-soluble drugs by dispersing them into water-soluble carriers. The use of SD formulations and water insoluble and water-swellable polymer in developing controlled release formulations is of great interest in the recent past. The controlled-release formulations are designed to achieve a therapeutically effective concentration of drug for extended time periods. They can also be cost-effective, possess higher efficacy, and reduce adverse effects.[1] In the majority of cases, these formulations release initial large amounts of drugs known as 'burst release.' Burst release lead to high initial drug concentration and reduce the effective lifetime of the delivery system among various approaches for controlled drug release, the matrices prepared in insoluble polymers using SD technique is proved to be effective. The controlled release SD formulations can bypass the risk of burst release as the drug is homogeneously dispersed in the SD formulation. The drug release is also controlled by matrix that comprises of hydrophilic or hydrophobic polymeric excipients.[2,3]

Gliclazide is an antihyperglycemic agent employed for the treatment of type -2 diabetics (T2D). It belongs to the oral hypoglycemics class used in controlling blood sugar in people suffering with T2D. Gliclazide raises the insulin released by pancreas, thus helping body to use insulin

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more resourcefully. It belongs to BCS class II that has lower solubility and higher permeability. It is insoluble in water and has a higher permeability of log P = 2.6. Gliclazide posses slower GI absorption rates that originate from poor drug dissolution and poor drug permeability in GI track.[4-6] Even though the drug displays 96% protein binding capacity, its deprived water solubility makes it difficult to attain the required therapeutic effect.

Many studies have been reported in the literature for the preparation of a controlled release system using solid dispersion technique.[7-12] The current paper deals with incorporating gliclazide SD into a controlled release matrix for enhanced solubility and continuous drug release.

Materials and Methods

The drug gliclazide procured from Zhejiang Jiuzhou Pharmaceutical co. Ltd., China. The hydroxypropyl cellulose purchased from Ashland, Colloidal silicon dioxide from Evonik industries limited, HB β-Cyclodextrin purchased from Cydex pharmaceuticals, microcrystalline cellulose (Avicel PH 101) purchased from FMC International Health and Nutrition, polyvinylpyrrolidone (povidone K-30) from BASF, and magnesium stearate from Nitika Pharmaceutical Specialties Pvt. Ltd.

Preliminary Solubility Studies

Solubility studies were performed according to the Higuchi and Connors method. An excess amount of drug was placed into 50 mL flask containing different carriers' concentrations, i.e., (1:1,1:2,1:3) in distilled water. All flasks were closed with a stopper and covered with cellophane membrane to avoid solvent loss. The flasks were kept in the incubator shaker for 72 hours. After 72 hours the content of each flask was then filtered through Whatman filter paper. The filtrate was diluted and assayed spectrophotometrically for Gliclazide content at 230 nm[13] (Table 1).

Preparation of Gliclazide Solid Dispersions

In this method, accurately weighed quantities of HP β cyclodextrin in the stated proportions were carefully transferred into boiling test tubes and dissolved in acetone. To these solutions, accurately weighed quantities of gliclazide were added and allowed to dissolve. The solution was transferred to a Petri dish, the solvent was allowed to evaporate at room temperature, and dispersions were dried at room temperature for 1-hour, and then dried at 65°C for 6 hours in a hot air oven. The mass obtained in each case was crushed, pulverized, and sifted through 100 mesh (Table 2).[14]

Evaluation of Gliclazide SD

Solubility Studies

Solubility studies were carried out by preparing suspensions of SD and agitating for 48 hours, followed by filtration. The filtrate was estimated for gliclazide at 230 nm.[13]

Percentage Practical Yield (PPY) Estimation

The PPY of GSD was determined as follows

Percent yield = (weight of prepared solid dispersion/ weight of drug + carriers) × 10.[15]

% Drug content determination

Weighed amount of SD equal to 10 mg transferred into 10mL standard flasks and made to 10 mL with methanol. The drug content estimated spectrophotometrically at 230 nm against suitable blank using UV-visible spectrophotometer (T60 PG Instruments).[16]

In vitro Dissolution of Gliclazide Solid Dispersions

The dissolution of gliclazide from SDs prepared was investigated in 900 mL phosphate buffer of pH 6.8 using USP apparatus type II (paddle type) dissolution test apparatus with a stirring speed of 50 RPM at 37 ± 0.5°C.

Table 1: Phase solubility studies

Polymer	*Drug: Polymer ratio*	*Solubility(mg/mL)*
Pure drug		0.07 ± 0.87
Xanthan gum	1:01	0.8 ± 1.75
Xanthan gum	1:02	0.84 ± 1.24
Xanthan gum	1:03	0.92 ± 0.89
Hupu gum	1:01	0.85 ± 1.27
Hupu gum	1:02	0.94 ± 1.94
Hupu gum	1:03	1.04 ± 0.37
Methyl cellulose	1:01	0.84 ± 1.83
Methyl cellulose	1:02	0.95 ± 1.88
Methyl cellulose	1:03	1.03 ± 1.26
HP β Cyclodextrin	1:01	0.84 ± 1.14
HP β Cyclodextrin	1:02	0.94 ± 1.85
HP β Cyclodextrin	1:03	1.16 ± 1.62
Povidone	1:01	0.632 ± 1.51
Povidone	1:02	0.84 ± 1.47
Povidone	1:03	1.01 ± 1.52
HPC	1:01	0.448 ± 1.89
HPC	1:02	0.52 ± 1.72
HPC	1:03	0.62 ± 1.26
Captisol	1:01	0.79 ± 1.26
Captisol	1:02	0.85 ± 1.15
Captisol	1:03	0.94 ± 0.63

Table 2: Preparation of gliclazide SD

Formulation code	*Gliclazide (mg)*	*HP β Cyclodextrin (mg)*	*Acetone (mg)*
SD1	10	10	80
SD2	10	20	70
SD3	10	30	60

Table 3: Formulation table of gliclazide controlled release tablets

Code	*Gliclazide+HP β Cyclodextrin complex (mg)*	*Avicel PH 101 (mg)*	*Klucel EXF (mg)*	*HPMC K100M (mg)*	*Povidone K-30 (mg)*	*Purified Water*	*silicon dioxide (mg)*	*Magnesium Stearate (mg)*	*Tablet weight in mg*
F1	120	111	5	4	5	Qs	3	2	250
F2	120	107	5	8	5	Qs	3	2	250
F3	120	103	5	12	5	Qs	3	2	250
F4	120	94	10	16	5	Qs	3	2	250
F5	120	90	10	20	5	Qs	3	2	250
F6	120	86	10	24	5	Qs	3	2	250
F7	120	77	15	28	5	Qs	3	2	250
F8	120	73	15	32	5	Qs	3	2	250
F9	120	69	15	36	5	Qs	3	2	250
F10	120	60	20	40	5	Qs	3	2	250
F11	120	56	20	44	5	Qs	3	2	250
F12	120	52	20	48	5	Qs	3	2	250
F13	120	43	25	52	5	Qs	3	2	250
F14	120	39	25	56	5	Qs	3	2	250
F15	120	34	25	60	5	Qs	3	2	250

5 mL aliquots of dissolution medium were drawn at an interval of 5 minutes and filtered through 0.45 µm filter. The equal volume withdrawn from the dissolution medium was replaced. The collected sample solution is suitably diluted and assayed at 230 nm and the drug release was compared with the pure drug.[17,18]

Stability Studies

The gliclazide SD was subjected to stability study for 3 months as per ICH guidelines. Samples were withdrawn after 1st, 2nd, and 3rd and analyzed for % drug content and drug release.

Characterization of Gliclazide SD

The dispersions are further characterized for Fourier transforms infrared spectroscopic analysis using Shimadzu FTIR 8400S spectrophotometer,[19] X-ray diffractometer (XRD) using (Shimadzu, Japan).[20] and Differential scanning calorimetry studies using Mettler DSC 30S, Mettler Toledo India Pvt. Ltd.[21].

Formulation of Gliclazide SD Incorporated Controlled Release Tablets

Pre-compression Parameters

The lubricated blend was evaluated for angle of repose, Carr's index bulk and tapped density, Hausner's ratio[22] as per the referred procedures.

Preparation of Gliclazide SD Controlled Release Tablets

The gliclazide SD controlled-release tablets were prepared by wet granulation method (Table 3).[23] Gliclazide SD equivalent to 40mg of gliclazide in weight was chosen for formulation. In this hydroxypropyl cellulose, HPMC K100 M was used as rate controlling polymers. Microcrystalline cellulose was used as diluent; colloidal silicon dioxide was used as a glidant with magnesium stearate used as a lubricant.

Table 4: Solubility studies of gliclazide solid dispersions (SD1-SD3)

Gliclazide solid dispersion	*Solubility (mg/ml)*
Pure drug	0.07 ± 0.87
SD1	2.68 ± 0.29
SD2	2.82 ± 0.20
SD3	3.01 ± 0.16

Accurate quantity of the gliclazide, microcrystalline cellulose, hydroxypropyl cellulose (klucel EXF), hydroxypropyl methylcellulose (HPMC K-100M), colloidal silicon dioxide, magnesium stearate were weighed and sieved through #40 separately. The mixture was then granulated with purified water, in which povidone is dissolved. The wet mass died in a hot air oven, and then it is lubricated with colloidal silicon dioxide, and magnesium stearate and the lubricated blend is compressed into tablets.

Evaluation of Gliclazide SD Incorporated Controlled Release Tablets

Physical Properties

Average weight, hardness, thickness, weight variation, friability were recorded as per the referred procedures.[24,25]

In-vitro Drug Dissolution

The dissolution study of all tablets conducted using dissolution testing USP apparatus II (paddle method) using 900 mL phosphate buffer (pH 6.8) at 37 ± 0.5ºC and at 50

rpm, aliquots of dissolution medium was withdrawn at an interval of 5 minutes and filtered through 0.45 µm filter. The equal volume withdrawn from the dissolution medium was replaced. The collected sample solution is suitably diluted and assayed against suitable blank using UV-visible spectrophotometer (T60 PG Instruments) (Bezerra 2018) at 243 nm and the drug release was compared with the pure drug.[18]

Drug Release Kinetics Gliclazide SD Incorporated Controlled Release Tablets

To describe the kinetics of the drug release from gliclazide SD incorporated controlled-release tablets, mathematical models such as zero-order, first-order and Higuchi, models were used. The selecting was based on basis of the goodness-or fittest.

Stability Studies Gliclazide SD Incorporated Controlled Release Tablets

Prepared tablets were placed under controlled temperature environment inside a stability chamber (Thermo Lab, India) with relative humidity of 75% ± 5% RH and temperature of 40°C ± 2°C for accelerated stability studies as mentioned in ICH guidelines. Samples were removed after 1, 2, and 3 months and evaluated.

Characterization of Gliclazide SD Incorporated Controlled Release Tablets

The optimized tablet formulation was analyzed for FTIR[19,20] as per the referred methods.

Results

Preliminary Solubility Studies of Gliclazide

The pure gliclazide exhibits maximum solubility in 6.8 pH phosphate buffer (1.68 mg/mL). The solubility of gliclazide and HP β Cyclodextrin physical mixture show that 1:3 ratio of the mixture exhibited higher solubility (1.12 mg/mL), which was almost 16-fold increase than that of pure drug (Fig. 1).

Preparation of Gliclazide SD

The gliclazide SDs prepared by solvent evaporation method using varying amounts of polymers. The solubility of gliclazide SD comprising HP β cyclodextrin (SD3) exhibited greater solubility of 3.01 ± 0.16 mg/mL, which was an almost 43-fold increase when compared to pure drug solubility (Table 4 and Fig. 2).

Percentage Practical Yield (PPY) and Drug Content of Gliclazide SD

The PPY for all gliclazide SD's found to be within 90.61 ± 0.21% - 98.96 ± 0.25 %. A maximum yield of 98.96 ± 0.25% was observed for formulation SD13 (Table 5).

The drug content in all gliclazide SD's lie within 90.66 ± 0.20–99.45 ± 0.30% with SD13 exhibiting maximum drug content (Table 5).

In vitro Drug Dissolution Studies of Gliclazide SD

A significant increase in drug dissolution rate is observed in all the formulated SDs of gliclazide in comparison to pure drug. The formulation SD3 exhibiting the highest dissolution rate of 99.74 ± 5.39% (Fig. 3). Hence 1:3 ratio of gliclazide and HP β Cyclodextrin solid dispersion (SD3) was further chosen for characterization.

Stability Study of Gliclazide SD

Optimized formulation (SD3) was studied for stability for 90 days at accelerated conditions as per International Council for Harmonisation (ICH) guidelines. The formulation SD3 found stable during 3 months period. Results indicate that optimized formulation (SD3) is stable with no variations in its physical properties (Table 6).

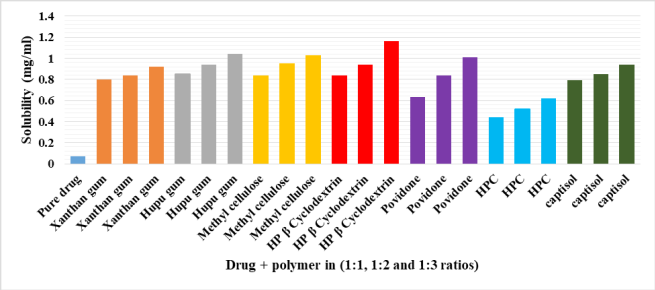

Fig. 1: Solubility of gliclazide pure drug + polymer in 1:1, 1:2 and 1:3 ratios

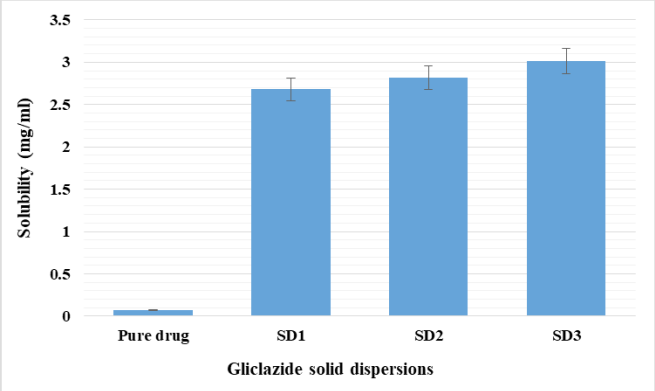

Fig. 2: Solubility of gliclazide pure drug and gliclazide solid dispersions (SD1-SD3)

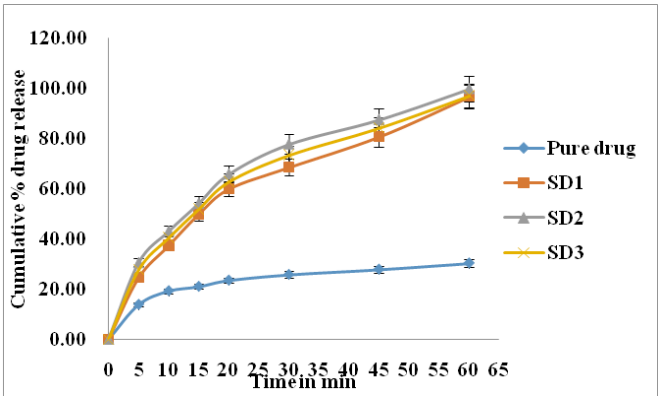

Fig. 3: In vitro drug dissolution of pure gliclazide and SD1-SD3

Characterization of gliclazide SD

FTIR Studies

The FTIR spectrum of pure gliclazide display most prominent bands for-secondary amine N-H bending at 1492.2cm^{-1}, the absorption band was observed at = CH stretching at 3116.4 cm^{-1}, Acyclic ketone carbonyl (C=O) stretching at 1688.3 cm^{-1}, the asymmetric and symmetric stretching were observed at SO_2NH stretching at 1239.8 cm^{-1}, sulphonyl S=O stretching at 1099.2cm^{-1}. (Fig. 4)

The spectra were compared for confirmation of common peaks. Similar peaks were observed and showed no disposition/disappearance in the spectra of gliclazide SD (Fig. 5), suggesting that drug and recipients were compatible.

Table 5: PPY and % drug content for gliclazide SD

S.No	*Gliclazide SDs*	*% Practical yield*	*Drug content(%)*
1	SD1	94.98 ± 0.21	95.63 ± 0.26
2	SD2	95.44 ± 0.23	96.18 ± 0.25
3	SD3	98.61 ± 0.21	99.33 ± 0.26

Above parameters are communicated as Average ± Standard Deviation; (n = 3)

Table 6: Stability studies of SD3

Retest Time for Optimized formulation SD3	*Drug content (%)*	*In-vitro drug release profile (%)*
0 days	99.33 ± 0.26	99.82 ± 1.41
30 days	98.56 ± 0.78	99.21 ± 1.78
60 days	98.03 ± 1.37	98.43 ± 0.75
90 days	97.65 ± 0.85	97.86 ± 0.47

X-ray diffraction studies

The X-ray diffraction pattern of gliclazide pure drug and gliclazide-HP β Cyclodextrin solid dispersion are shown in Figs. 6 and 7. The XRD pattern of gliclazide showed crystalline morph characterized by numerous peaks which were recorded at 2θ values of 11.47°, 14.56°, 18.32°, 19.03°, 23.12°, 26.36°, 27.30°, 27.80° and 30.73. The presence of

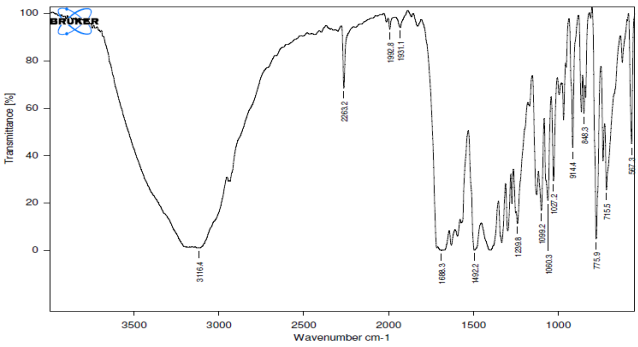

Fig. 4: FTIR of gliclazide

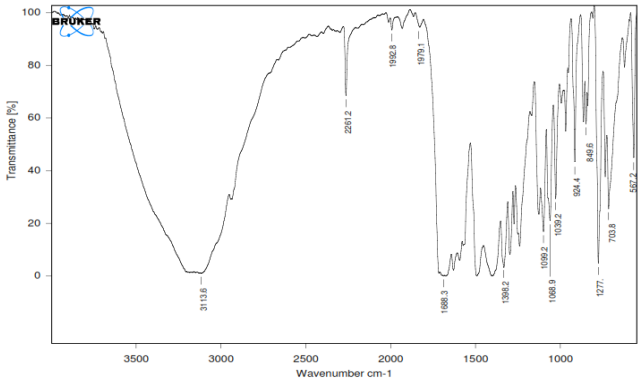

Fig. 5: FTIR of gliclazide and HP β Cyclodextrin solid dispersion

Table 7: Micrometric properties of gliclazide controlled release tablets lubricated blend

Formulation	*Bulk density (g/ml)*	*Tapped density (g/ml)*	*Carr's index*	*Hausner's Ratio*	*Angle of repose(°)*
F1	0.518 ± 0.48	0.608 ± 0.39	14.8 ± 0.57	1.17 ± 0.59	28.43 ± 0.23
F2	0.482 ± 0.28	0.554 ± 0.86	13 ± 0.12	1.15 ± 0.79	28.54 ± 0.59
F3	0.445 ± 0.72	0.512 ± 0.31	13.09 ± 0.36	1.15 ± 0.87	28.62 ± 0.62
F4	0.452 ± 0.52	0.528 ± 0.97	14.39 ± 0.31	1.17 ± 0.36	28.75 ± 0.47
F5	0.505 ± 0.86	0.589 ± 0.56	14.26 ± 0.33	1.17 ± 0.50	27.17 ± 0.49
F6	0.452 ± 0.45	0.52 ± 0.591	13.24 ± 0.78	1.15 ± 0.98	27.32 ± 0.64
F7	0.457 ± 0.25	0.534 ± 0.45	14.42 ± 0.52	1.17 ± 0.37	27.54 ± 0.86
F8	0.517 ± 0.54	0.593 ± 0.94	12.82 ± 0.72	1.15 ± 0.89	27.22 ± 0.26
F9	0.475 ± 0.62	0.555 ± 0.72	12.41 ± 0.63	1.17 ± 0.82	26.83 ± 0.71
F10	0.458 ± 0.74	0.522 ± 0.11	12.26 ± 0.25	1.14 ± 0.65	26.74 ± 0.31
F11	0.47 ± 0.47	0.53 ± 0.18	11.32 ± 0.59	1.13 ± 0.57	26.62 ± 0.29
F12	0.507 ± 0.41	0.567 ± 0.12	11.65 ± 0.58	1.14 ± 0.40	26.56 ± 0.38
F13	0.487 ± 0.39	0.58 ± 0.22	10.34 ± 0.40	1.16 ± 0.61	26.43 ± 0.57
F14	0.517 ± 0.48	0.587 ± 0.32	9.09 ± 0.23	1.17 ± 0.59	26.3 ± 0.77
F15	0.512 ± 0.43	0.591 ± 0.83	8.37 ± 0.90	1.15 ± 0.38	24.85 ± 0.82

Above parameters are communicated as Average ± Standard Deviation; (n=3)

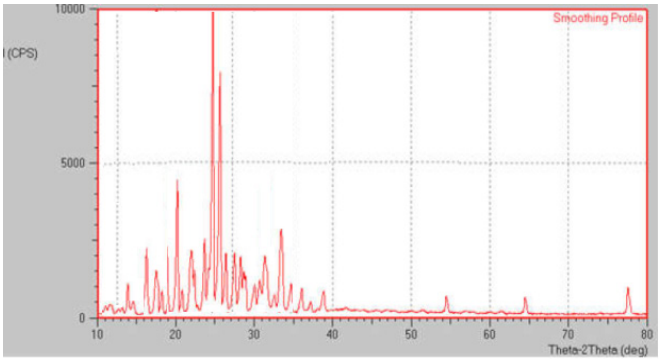

Fig. 6: XRD of gliclazide

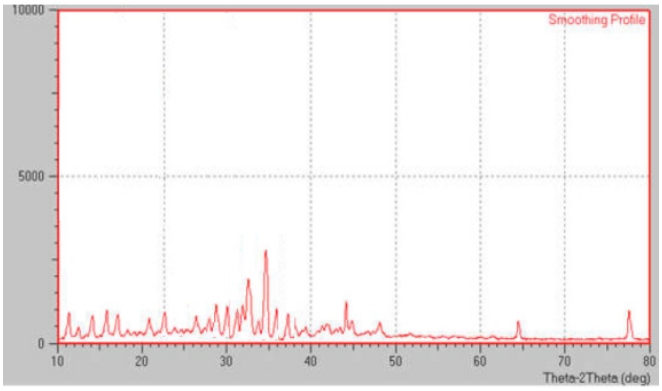

Fig. 7: XRD of optimized gliclazide and HP β Cyclodextrin solid dispersion (SD3)

abundant distinct peaks in the diffraction spectrum of pure gliclazide indicates crystalline form. The absence of diffraction peak in the spectrum of gliclazide solid dispersion indicates that the formulation is amorphous in nature, which attributes to the higher dissolution of these formulations.

Differential Scanning Calorimetry studies (DSC)

The DSC trace of pure gliclazide showed an endothermic peak at 170.59°C (Fig. 8), the thermograms of the gliclazide solid dispersion (172.29°C) (Fig. 9) did not show any significant or drastic shift in the endothermic peak, indicating there was no physical change of the drug in solid dispersion and tablet formulation.

Preparation of Gliclazide SD Incorporated Controlled Release Tablets

Gliclazide controlled-release tablets were round in shape, white in color with a smooth appearance.

Evaluation of Gliclazide SD Incorporated Controlled Release Tablets

The bulk densities of F1 toF15 were measured and ranged between 0.445 ± 0.72g/cc^3 to 0.518 ± 0.48g/cc^3. The tapped density ranged from 0.512 ± 0.31g/cc^3 to 0.608 ± 0.39g/cc^3. Angle of repose of F1-F15 was found to be good, and F15 was found to be with a value of 24.85 ± 0.82^0 having excellent flow property.

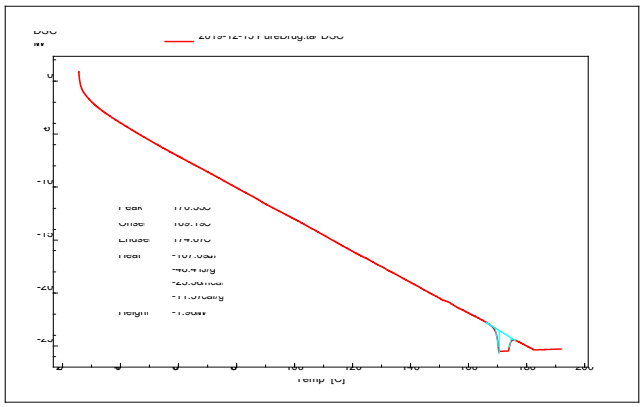

Fig. 8: DSC of gliclazide

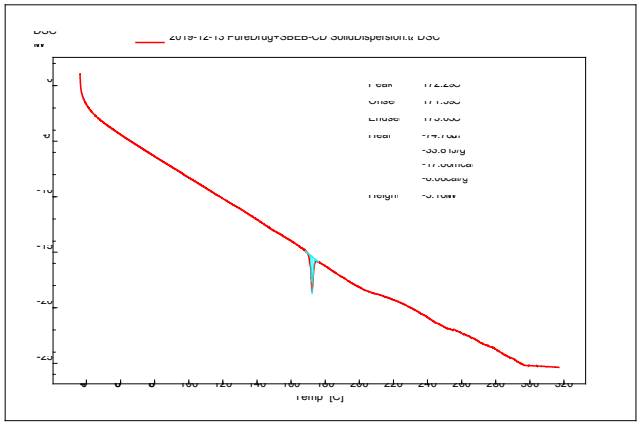

Fig. 9: DSC of gliclazide and HP β Cyclodextrin solid dispersion

The compressibility index ranged from 8 to 15%. These findings show that all the formulation blends exhibited good flow properties (Table 7).

Physical Evaluation of Gliclazide SD Incorporated Controlled Release Tablets

The results of the physical properties of gliclazide controlled-release tablets are shown in Table 8.

The results of the physical tests of the prepared blends were within limits (Table 8).

The weight variation of all the formulations is within limits. The hardness of formulations F1 to F15 ranged between 9.0 to 11.0 kg/cm^2. The thickness of all tablet formulations is uniform with values ranging between 3.3-3.5 mm. The friability value ranged between 0.13-0.22. The drug content of all formulation varied between 96.1-99.99%, with highest value exhibited by F15 formulation.

In vitro Drug Dissolution Study

Due to the high viscosity of rate-controlling polymers (HPMC K 100 M and klucel EXF) used in the formulation, sustained release of gliclazide was achieved. Formulation F15 containing a higher amount of rate-controlling polymers exhibited highest drug release of 99.96% up to 16 hours, whereas the marketed product released 98.12%

up to 12 hours. Hence out of all formulation, F15 is selected as the best-optimized formulation and further studied for its characterization (Figs. 10, 11).

The drug release results of F15 is closer to unity in the case of zero-order plot, i.e., 0.9993, indicating that the drug release follows a zero-order mechanism. Further, the n = 1.3558 for Korsmeyer-Peppa's plots suggest that the drug dissolution from tablet was anomalous non- Fickian diffusion super case II transport.

From the results of preformulation study, post-compression parameters, in vitro dissolution profile, and release order kinetics, formulation F15 was chosen best formulation among all the other formulations.

Stability Study of Gliclazide SD Incorporated Controlled Release Tablets

Optimized formulation (F15) was subjected to stability study for 90 days at accelerated as per ICH guidelines.

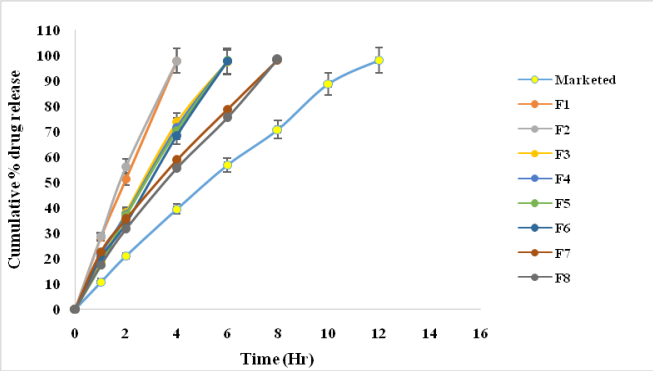

Fig. 10: %e drug release of gliclazide tablet formulation (F1 to F8) and marketed product
Above parameters are communicated as Average ± Standard Deviation; (n=3)

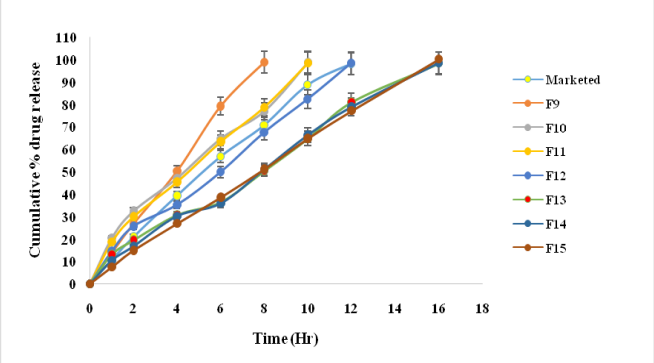

Fig. 11: Percentage drug release of gliclazide tablet formulations F9 to F15 and marketed product
Above parameters are communicated as Average ± Standard Deviation; (n=3)

Table 8: Physical properties of gliclazide SD incorporated controlled release tablets

Parameters	*Average Weight (in mg)*	*Thickness (in mm)*	*Hardness (in KP)*	*Friability (%)*	*Drug content (%)*
F1	248.35 ± 2.5	3.4 ± 0.07	9.8 ± 0.15	0.16 ± 0.09	96.8 ± 0.34
F2	249.50 ± 4.9	3.42 ± 0.15	9.7 ± 0.59	0.13 ± 0.04	96.1 ± 0.23
F3	248.20 ± 5.6	3.4 ± 0.11	9.7 ± 1.04	0.18 ± 0.11	96.49 ± 0.67
F4	248.77 ± 6.1	3.35 ± 0.17	10.1 ± 0.92	0.2 ± 0.05	97.4 ± 0.59
F5	249.15 ± 5.4	3.38 ± 0.08	9.8 ± 1.01	0.21 ± 0.09	97.2 ± 0.68
F6	250.2 ± 3.9	3.4 ± 0.05	9.9 ± 0.74	0.22 ± 0.10	97.83 ± 0.24
F7	249.8 ± 6.3	3.45 ± 0.11	10.1 ± 1.05	0.14 ± 0.02	98.11 ± 0.92
F8	248 ± 2.3	3.35 ± 0.09	10 ± 0.36	0.15 ± 0.08	97.99 ± 0.62
F9	248.8 ± 5.1	3.37 ± 0.14	9.7 ± 0.78	0.19 ± 0.03	98.23 ± 0.41
F10	249 ± 4.2	3.41 ± 0.11	10 ± 1.05	0.16 ± 0.9	98.4 ± 0.93
F11	249.8 ± 2.9	3.4 ± 0.06	9.4 ± 0.91	0.14 ± 0.11	98.88 ± 0.72
F12	248.2 ± 3.03	3.36 ± 0.17	9.6 ± 0.45	0.16 ± 0.34	98.9 ± 0.46
F13	250.2 ± 3.7	3.36 ± 0.76	9.8 ± 0.16	0.16 ± 0.08	99.03 ± 0.26
F14	249.2 ± 1.54	3.36 ± 0.23	10.1 ± 0.56	0.15 ± 0.03	99.32 ± 0.54
F15	250.2 ± 2.19	3.35 ± 0.20	10.5 ± 0.18	0.14 ± 0.10	99.99 ± 0.25

Above parameters are communicated as average ± standard deviation; (n = 3)

Table 9: Stability studies of F15 stored at 40 ± 2^0C /75 ± 5% RH

Retest Time for Optimized formulation F15	*Drug content (%)*	*In-vitro drug release profile (%)*	*Hardness (kg/cm^2)*
0 days	99.99 ± 0.25	99.96 ± 1.83	10.5 ± 0.18
30 days	99.56 ± 1.47	99.05 ± 1.42	10.5 ± 0.85
60 days	98.45 ± 1.64	98.81 ± 0.51	10.5 ± 0.26
90 days	97.87 ± 1.07	98.08 ± 0.87	10.5 ± 0.38

Above parameters are communicated as average ± standard deviation; (n=3)

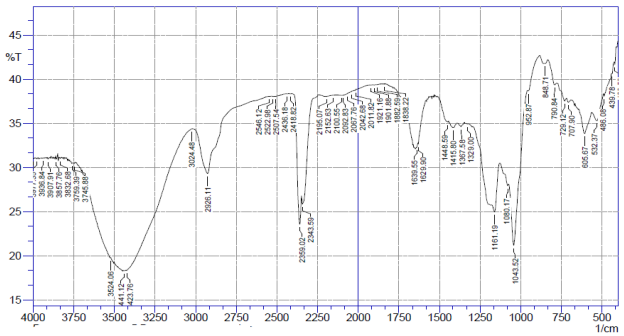

Fig. 12: FTIR of gliclazide controlled release tablets

The optimized formulation was stable during 3 months period. Results indicate that optimized formulation (F15) is stable with no variations in its physical properties (Table 9).

Characterization of gliclazide SD incorporated controlled release tablets

FTIR Studies

FTIR spectrophotometric method was developed to establish the compatibility of gliclazide pure drug and gliclazide-HP β Cyclodextrin solid dispersion and gliclazide controlled-release tablets. Fig. 4 represents the FTIR spectrum of pure gliclazide. The spectra were compared for confirmation of common peaks. Similar peaks were observed and showed no disposition/disappearance in the spectra of gliclazide controlled-release tablets (Fig. 12), indicating that drug and recipients were compatible.

Discussion

In the current research, the SD tablets of gliclazide were formulated using hydrophilic polymer and hydrophobic polymer for controlled drug release. The gliclazide SD prepared using HP β Cyclodextrin (1:3) and evaluated for percentage yield, drug content, and drug release. The formulation SD3 with higher values of drug content and drug release of 99% was chosen optimally for incorporating into tablet formulation by wet granulation technique. The controlled release tablet blend was initially evaluated for pre-compression parameters, and results show that formulation F15 exhibited excellent flow properties. The post-compression parameters were also found within an acceptable limit. The drug release of F15 was found to be 99% extended over a period of 16 hours while the marketed formulation release about 98% of drug in 12 hours. The drug excipient compatibility study for FTIR and DSC shows that the combination is compatible. The results conclude that this formulation system is one of the potential techniques for the controlled release of gliclazide, enhancing drug absorption and reducing side effects. This technique also helps in the reduction of dosage frequency with increased patient compliance.

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