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Formulation and Evaluation of Glibenclamide by Solid Dispersion Method using Compritol 888 ATO as a Carrier

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Abstract

Glibenclamide is an antidiabetic drug that is poorly soluble, to enhance its rate of dissolution, it is formulated into solid dispersions using various polymers by solvent evaporation method. The present study aims to enhance the dissolution of poorly soluble drug Glibenclamide by solid dispersion technique using solvent evaporation method with various carriers such as Compritol 888 ATO, PEG 6000, at ratios (1:1,1:2 and 1:3) and to study the effects of carriers on the dissolution of the drug. The solid dispersions characterized by FTIR showed no possible interactions between drug and carriers, XRD results showed conversion of crystallinity of drug to its amorphous form. The *in vitro* results showed a significant enhancement in the dissolution rate of all solid dispersion prepared by solvent evaporation method when compared with the pure drug itself (39.82%). Among the two polymers, Compritol 888 ATO and PEG6000 the formulation SD9 containing Compritol 888 ATO as a carrier at 1:3 ratio showed the highest rate of dissolution (99.17%), thus the concentration of carriers used in this study played an important role in enhancing dissolution. This study concludes that Glibenclamide's dissolution rate can be significantly increased using Compritol 888 ATO and PEG6000 as polymers by solvent evaporation and lyophilization method, from which Compritol 888 was chosen as the best polymer for enhancing *in-vitro* dissolution rate of poorly soluble drug Glibenclamide.

Keywords: Glibenclamide, Fast Dissolving Tablets, Synthetic polymer, Compritol 888 ATO, Antidiabetic

Introduction

Glibenclamide (5-chloro-N-[2-[4] ethyl] [1-(cyclohexylcarbamoylsulfamoyl) two-methoxybenzamide), is an anti-diabetic drug, which inhibits the ATP-sensitive potassium channels, which when not inhibited, causes depolarization and insulin secretion. However, despite its therapeutic efficiency, glibenclamide is poorly soluble, since the absorption of glibenclamide is extremely poor. This limits the use of oral formulations for glibenclamide.

The oral route is the most prevalent and quite mostly used delivery route because of advantages like convenience, ease of administration, and patient compliance. However, complications seen in oral medications encompass poor bioavailability of drugs, or in other words, three aspects that are specific to disintegration, penetrability, and solubility (1). If the solubility of the drug is less than desirable, necessary action should be taken to improve its solubility. Hence, estimation of drug and excipient solubility is very crucial in pre-

formulation studies (2).

In cases of decreased or limited solubility of a drug or compound, certain techniques are employed pharmaceutically to enhance their solubility. Most formulation strategies would be chemical (derivatization, pH changes, salt formation, complexation, etc) or physical changes (nanosuspension, micronization, crystal habit alteration, eutectic mixtures, etc) to the drug or compound. In this study, we employed the solid dispersion technique, which increases the bioavailability of the low soluble compounds. A rate-limiting step in increasing the bioavailability is the dissolution rate. Nowadays, the prevalent efficient process to improve the dissolution rate is using a solid dispersion method. However, this is reliant on the optimization of the carrier plus solution. Also, one more method that is beneficial for increasing the dissolution rate is by adding super-disintegrants, such as Croscarmellose sodium, crospovidone, and sodium starch glycolate (3).

Solid dispersions can be characterized using several techniques. In this study, we employed the solvent evaporation method under the solid dispersion technique, with FTIR and XRD as the tools for characterization. Due to certain strong hydrophilic characteristics, synthetic polymers like Compritol 888 ATO and PEG6000 have been used as hydrophilic matrices for this study. The principal benefit of this process is no thermal decomposition of drugs and carriers due to the comparatively fewer temperatures needed to evaporate the organic solvents. The major advantages of this method are particle size reduction, elevated wettability, and drug porosity while converting a less soluble crystalline form to a more soluble amorphous form (4,5).

To the best of our knowledge, the use of the solid dispersion technique to increase the dissolution of glibenclamide has not been studied yet. Hence, this study aims to develop the Solid dispersions of glibenclamide in Compritol 888 ATO and PEG6000 by using the solvent evaporation and lyophilization method and characterize the obtained complexes. Additionally, the dissolution profiles of glibenclamide alone and as solid dispersions were investigated.

Materials and Methods

All the chemicals were bought from licensed suppliers. The binder solubilizer PEG 6000 was obtained from the Stem chem enterprises, Chennai. The binder microcrystalline cellulose was bought from the R. R. Scientific Suppliers, Chennai. The sweetener and diluent mannitol was bought from the Sisco Research Laboratories. The surfactant and emulsifying agent Compritol 888 ATO was supplied by the Gattefosse. All other chemicals obtained were of analytical grade. Automated Tablet Friabilator and Dissolution Tester USP were of Lab Indian make. Digital weighing balance is of Schimadzu make, while tablet hardness tester was Monsanto hardness tester. The Duralab disintegration tester, Antech sonicator, and Industrial and Laboratory Tools Corporation's Hot Air Oven were used.

Preparation of buffers: (6)

Preparation of dissolution media (phosphate buffer pH 6.8):

Placed 50 ml of potassium hydrogen phthalate solution and added 22.4 ml of 0.2M sodium hydroxide solution in 200 ml volumetric flask and then made up with water.

Preparation of potassium hydrogen phosphate solution:

In 1000 mL of water, dissolved 27.218 g potassium dihydrogen phosphate.

Preparation of 0.1M NaOH:

Dissolved 8g of sodium hydroxide pellets in 1000 ml of water.

Calibration Curve and λ_{max} Determination: (7)
Standard stock solution of Glibenclamide in simulated gastric fluid (pH 1.2):

In the form of a stock solution (1000 µg/ml), glibenclamide (50 mg) was carefully weighed and dissolved with 50 ml of chloroform to 1 ml, final volume to 100 ml with 0.1 N HCl per 100 ml (100 µg/ml) of volumetric fibre. Applying a concentration of 10 mg/ml, 20 mg/ml, 30 mg/ml, 40 ml/ml, and 50 µg/ml, the working normal solution was properly diluted. The solutions were then scanned and determined by 241 nm UV-spectrometry. The normal absorption of 2 µg/ml and 4 µg/ml, 6 µg/ml, and 8 µg/ml were taken.

Standard stock solution of Glibenclamide in simulated intestinal fluid (pH 6.8):

Glibenclamide (50 mg) was reliably weighed and dissolved to form a stock solution in 50 ml chloroform (1000 µg/ml) with a 1 ml final volume of up to 100 ml of pH 6.8 phosphate buffer in 100 ml (100 µg/ml). Diluted to 10 g/ml, 20 g/ml, 30 g/mL, 40 g/mL and 50 g/ml this job standard solution was used. The solutions were then scanned and determined by 241 nm UV-spectrometry. The normal absorption of 2 µg/mL and 4 µg/mL, 6 µg/mL and 8 µg/mL was then taken.

Determination of λmax:

The resultant solutions were scanned in the range of 229nm using UV spectrophotometer.

Preparation of Glibenclamide solid dispersion by Solvent Evaporation Method:

Preparation of solid dispersion of Glinenclamide by solvent evaporation method involves two stages. The first stage was the preparation of a solution consisting of both the hydrophobic drug and the hydrophilic polymer. In the second stage, solvent evaporation and solid dispersion formation were followed. Methanol was used to dissolve both the hydrophobic drug and the hydrophilic polymer. The hydrophilic polymers used were Compritol 888 ATO and PEG6000.

Drug + Compritol 888 ATO: (8)

Both the drug and polymer were dissolved in chloroform. During the entire experimental process, the drug–polymer ratio was maintained in a range of 1:1, 1:2 and 1:3. In three different round bottom flasks containing 300mg of Glibenclamide, the drug was dissolved in 20 ml of methanol separately and stirred for 1 hour. Then 300mg, 900mg, and 1500mg of polymer (Compritol 888 ATO) were introduced in the above round bottom flask respectively. These mixtures were evaporated using a rotary vacuum evaporator for 30 min at 50℃ ± 2℃. The resulting powder was pulverised, filtered through an 80 mesh sieve, and deposited in a desiccator at about 25 °C. Table 1 depicts the composition of Glibenclamide and Compritol 888 ATO.

Table 1. Composition of Solid dispersion of Glibenclamide using Compritol 888 ATO prepared by Solvent Evaporation Method

Amount of Substance added in mg	**SD1**	**SD2**	**SD3**
	1:1	**1:3**	**1:5**
Drug [mg]	5	5	5
C888 [mg]	5	10	15
Total [mg]	10	15	20

Drug + PEG6000: (9)

Both the drug and polymer were dissolved in chloroform. During the entire experimental process, the drug – polymer ratio was maintained in a range of 1:1, 1:2 and 1:3. In three different round bottom flasks containing 300mg of Glibenclamide, the drug was dissolved in 20 ml of methanol separately and stirred for 1 hour. Then 300mg, 900mg, and1500mg of polymer (Poloxamer188) were introduced in the above round bottom flask respectively. These mixtures were evaporated using a rotary vacuum evaporator for 30 min at 50℃ ± 2℃. The resulting powder would be

pulverised, filtered through an 80 mesh sieve, and deposited in a desiccator at about 25 °C.

Table 2: Composition of Solid dispersion of Glibenclamide using PEG6000 prepared by Solvent Evaporation Method

Amount of Substance added in mg	**SD4**	**SD5**	**SD6**
	1:1	**1:3**	**1:5**
Drug [mg]	5	5	5
PEG6000 [mg]	5	10	15
Total (mg)	10	15	20

Pre-formulation studies:

Drug-excipient compatibility tests:

X-ray diffraction analysis: (10)

X-ray diffraction experiment was carried out using Scintag X-Ray Diffractometer with Cu-K radiation through Ni screen, at 40 kV and 30 mA. Diffraction patterns for pure drug Glibenclamide, Compritol 888 ATO, Polyethylene glycol 6000 and Solid dispersions was carried out.

Fourier transformed infrared spectroscopy: (11)

The test samples were dispersed in potassium bromate powder and analysed. FTIR spectra were utilized to study compatibility between the drug and polymer. The position of FTIR bands of important functional groups of drugs were identified.

Percentage yield: (12)

The percentage yield of all solid dispersions is determined to see which polymer is best when we have prepared the solid dispersion using different ratios of polymer and have to get the respective amount of product. The raw material, amount of drug, either Compritol 888 ATO or PEG 6000 and other process parameters which are going to determine the effects of the percentage yield during the preparation of solid dispersion. The percentage yield was composed by weighing the solid dispersion loaded with drug and calculated the percentage yield against the weight of raw materials. i.e., weight of polymers and drug used. The formula to calculate the percentage yield is given below,

Drug content for the solid dispersion: (13)

$$\text{Percentage Yield} = \frac{\text{Solid dispersion equivalent to 20 mg of Weight of the solid dispersion}}{\text{Weight of the drug and polymer}} \times 100$$

Glibenclamide was taken in a 100 ml standard flask, taken separately from SD1 to SD9 and dissolved with 2 ml of chloroform completely then made up to 100 ml of phosphate buffer pH 6.8. Once dissolved completely, filtered the solution using Whattman filter paper. 1 ml stock solution was pipetted out and diluted using phosphate buffer up to 100 ml for the solid dispersion formulation SD1, SD4, SD7, SD9 gives the final concentration of 2 µg/ml. the solid dispersion SD2, SD5, SD8, gives the final concentration of 8 µg/ml. the solid dispersion SD3, SD6, SD9, gives the final concentration of 12 µg/ml. Drug content was determined by UV spectrophotometry from the absorbance obtained at 241 nm for the pH6.8 phosphate buffer. The drug content was calculated from the absorbance obtained with the help of the calibration curve and the drug content percentage using the formulae.

$$\text{Drug content} = \frac{Sample\ Absorbance}{Standard\ Absorbance} Std.\ Conc.$$

$$\%\ \text{Drug content} = \frac{Drug\ content}{Theoritical\ value} \times 100$$

Preparation and evaluation of glibenclamide fast-dissolving tablets (fdts):

Preparation: (14)

The solid dispersion formulation which showed highest drug release was formulated into tablets using various proportions of super-disintegrants. The SDs equivalent to 50 mg of glibenclamide was used to prepare FDT, and the formulation of tablets is given in the Table 3. Mixing of excipients and the drug or its equivalent solid dispersions was performed. Compression of tablets was performed using Cadmach 16 station rotary punch tablet machine. Figure 1 shows the prepared Glibenclamide FDTs.

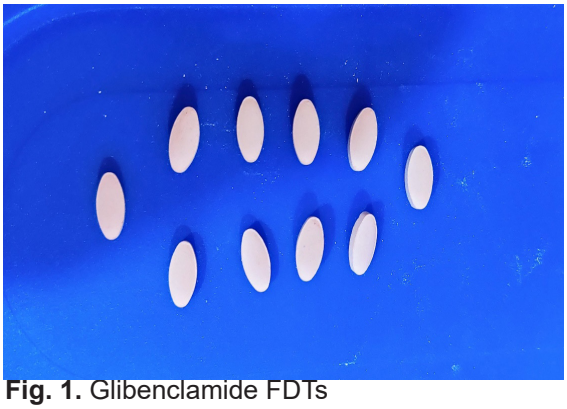

Fig. 1. Glibenclamide FDTs

Evaluation: (15)

Uniformity of weight:

Randomly selected and weighed twenty tablets, then compared the individual weight of tablets with average weight. The allowed percentage deviation for tablets weighing 500 mg is ± 5%. The formulated tablets pass the USP test if not more than two tablets are outside the limit and no tablet differs by more than twice the limit.

Table No 3. Formula for the preparation of fast dissolving tablets of Glibenclamide

S.No	Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	Glibenclamide + Mixture		20	20	20	20	20	20	20	20
2.	Croscarmellose sodium	15	10	20						
3.	crospovidone				15	5	10			
4.	Sodium starch glycolate							20	15	10
5.	Aspartane	10	10	10	10	10	10	10	10	10
6.	Megnasium.stearate	02	02	02	02	02	02	02	20	20
7.	Aerosil	03	03	03	03	03	03	03	03	03
8.	Methyl cellulose	03	03	03	03	03	03	03	03	03
9.	MCC	37	37	37	37	37	37	37	37	37
10.	Mannitol	60	65	55	60	70	65	55	60	65
	Total weight (mg)	150	150	150	150	150	150	150	150	150

Hardness:

Randomly selected the tablets of all formulations, then the tablet was placed vertically in the equipment to determine the hardness. Force was applied to break the tablet into two parts. Noted the reading on the scale and expressed it in kg/cm^2 units.

Tablet friability:

Friability test was determined by the Roche friabilator. Selected 20 tablets, then subjected it to 100 revolutions. The speed was adjusted to 25 rotations per min and rotated for 4 min. The tablets were wiped with a clean cloth and weighed again. The friability was calculated as the percentage loss which should not exceed 1%. The formula for calculating is as follows

Percentage friability = Initial weight – final weight / initial weight × 100

Drug content for the fdts:

It was analysed by means of selecting ten tablets and each tablet had undergone determination of drug content. The tablets complied the test if the content of each of at least nine tablets were in the range of 85-115% of the labelled amount of the drug. The tenth tablet should not contain <75% or >125% of the labelled content. If these conditions were not met the remaining 20 tablets were to be analysed individually and all of them should be within the limit.

Disintegration test:

Based on the capillary action, the disintegration process happens by the water uptake, so the superdisintegrants swells up to break down the tablet. In this process, 6 tablets were placed individually in each glass tube and a disc was placed over it. Using 0.1N HCl as a media and maintaining the temperature at 37ºC ± 2ºC, noted down the complete disintegration time of every tablet, until no visible portion of the sample leftover was seen in the apparatus.

In vitro drug release study:

The release rate of a Glibenclamide fast dissolving tablets was determined using USP XXIV dissolution testing apparatus II. The *invitro* dissolution test was performed using 900 ml of 0.1N HCl at (37 ± 0.5ºC) in 50 rpm. Aliquot of dissolution medium was withdrawn at regular time intervals, and the same volume of pre-warmed fresh dissolution medium was replaced. The samples were filtered, and the amount of drug released was determined by Shimadzu-UV spectrophotometer at 229nm.

Results and Discussion

Calibration curve and λmax determination: Curve in simulated gastric fluid at ph 1.2:

Table 4 and Figure 2 depict the results obtained.

Table 4. Standard curve Absorbance value

S.No	Concentration (µg/ml)	Absorbance
1.	2	0.258
2.	4	0.527
3.	6	0.683
4.	8	0.937
5.	10	1.119

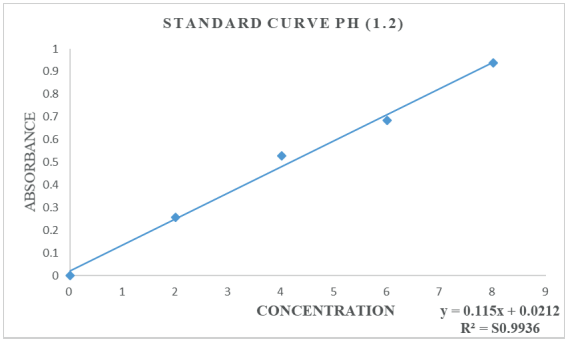

Fig. 2. Standard Curve at pH 1.2

Curve in simulated gastric fluid at pH 6.8:

Table 5 and Figure 3 depict the results obtained.

Table 5. Standard curve absorbance value

S.No	Concentration (µg/ml)	Absorbance
1.	2	0.015
2.	4	0.031
3.	6	0.059
4.	8	0.074
5.	10	0.092

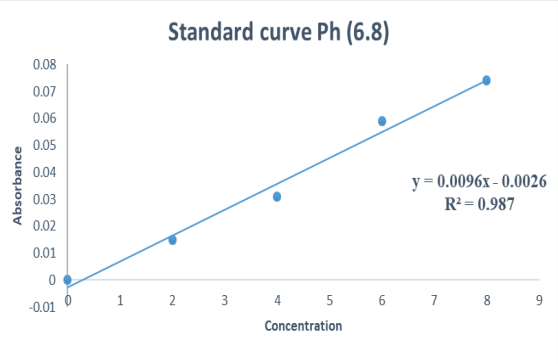

Fig. 3. Standard Curve at pH 6.8

Determination of λmax:

Scanning of λ_{max} for pure drug Glibenclamide (10 µg/ml) was carried out in the range of 220 – 350 nm in pH 1.2 and pH 6.8 and it was found to be 229nm. Figures 4 and 5 depict the results.\

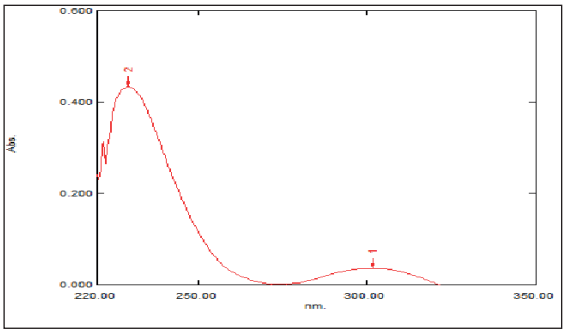

Fig. 4. λmax for glibenclamide in pH 1.2

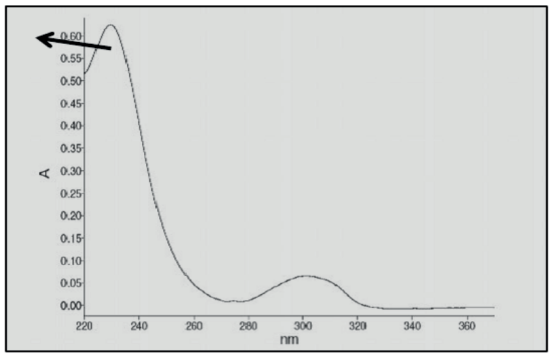

Fig. 5. λmax for glibenclamide in pH 6.8

Pre formulation studies:

Drug-excipient compatibility tests:
X-ray diffraction analysis:

In pure drug form glibenclamide is crystalline in nature, in various physical mixtures the crystallinity decreases and amorphous characteristics increases. Figures 6, 7, and 8 depict the powder XRD results for Drug + Compritol 888 ATO (1:2 and 1:3); and for Drug + PEG 6000 (1:3). The test powder X ray diffraction could provide the further verification of drug crystal conversion. The bulk drug and Compritol 888 ATO 1:3 have shown a sharp and more intense diffraction peak at 2θ values of 5.35, 11.32, 18.81, 20.15., which are more consistent with the characteristic peaks of the crystalline form.

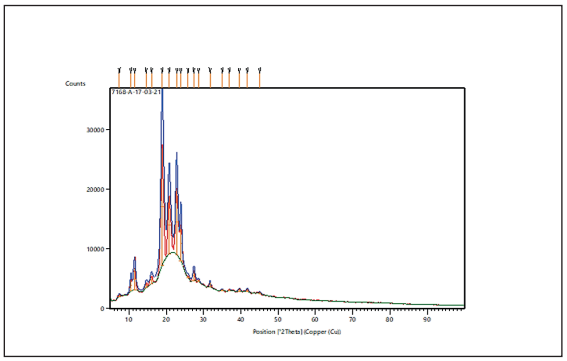

Fig. 6. XRD of Drug + Compritol 888 ATO (1:2)

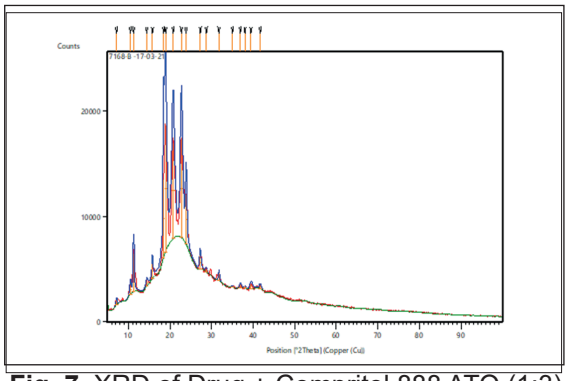

Fig. 7. XRD of Drug + Compritol 888 ATO (1:3)

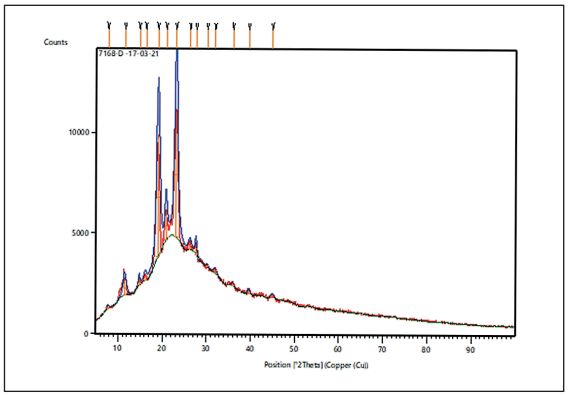

Fig. 8. XRD of Drug + PEG 6000 (1:3)

FTIR:

Figures 9, 10, 11, and 12 depict the FTIR results.

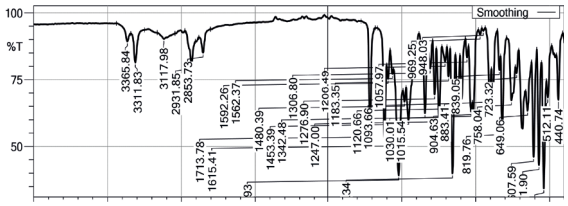

Fig. 9. FTIR spectroscopy of pure Glibenclamide

The FTIR spectra was obtained for the pure drug of Glibenclamide is shown in Figure 9. The pure drug Glibenclamide has exhibited the characteristic peak at the frequency of 2931 cm $^{-1}$, which implies the C–H stretching, 1615 cm $^{-1}$, which implies the – C=O Stretching(amides), 1592 cm $^{-1}$, which implies the – N–H bending (deformation), 1453 cm $^{-1}$, which implies the – deformation in CH_2S

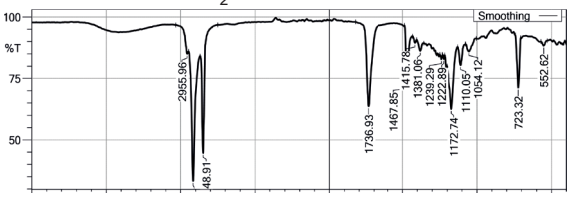

Fig. 10. FTIR spectroscopy of pure Compritol 888 ATO

The FTIR spectra was obtained for the Compritol 888 ATO as shown in figure 10. The Compritol 888 ATO has exhibited the characteristic peak at the frequency of 2848.91 cm $^{-1}$, which implies the methylene C-H asymmetrical /symmetrical, 1736.93. cm $^{-1}$, which implies the carbonyl compound - Aldehyde, 1467.85 cm $^{-1}$, which implies the methylene – C–H bending, 1110.05 cm $^{-1}$, which implies the skeletal C-C-Vibrations.

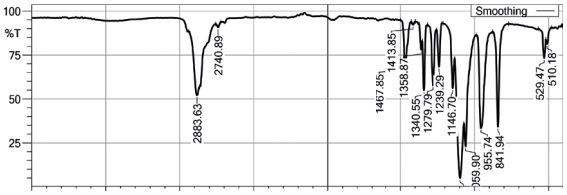

Fig. 11. FTIR spectroscopy of pure PEG 6000

The spectrum of PEG 6000 shows important function groups at 2883.63 cm $^{-1}$ (C –H stretching), 1340.55 cm $^{-1}$ (C –O groups), 1146.70 (C –H bending), 2740.89 (C –OH).

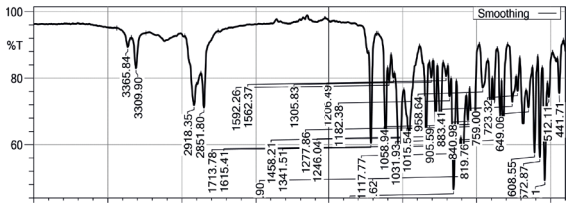

Fig. 12. FTIR spectroscopy of Drug and Polymers

The FTIR spectrum of the drug and Polymers exhibited the same peaks in the frequency of 2851.80cm $^{-1}$, which implies the –

C–F stretching, 1246.04 cm $^{-1}$, 1277.86 cm $^{-1}$, 1058.94cm $^{-1}$, which are represents the – C– N Stretching, – C–H bending, – C=O stretching accordingly. It was compatible with drug and polymer.

Percentage yield:

The percentage yield of the six Glibenclamide solid dispersion from SD1 to SD6 was calculated. The results are given in Table 6 and Figure 13. From the solvent evaporation method, the SD3 (1:3) & SD6 (1:3) has the highest yield of the product after solid dispersion formulated. Among the two polymers such as Compritol 888 ATO and PEG 6000, it is concluded that from the yield, the PEG6000, (1:3) ratio prepared by solid dispersion was the best polymer. When compared with these two polymers Compritol 888 ATO gives more yield of the solid dispersion in lyophilisation method.

Table 6. Percentage Yield of SD1 - SD6

Formula code	Percentage Yield (%)
Solid dispersion prepared by Solvent Evaporation Method	
Drug + compritol 188 ato	
SD1	97.11
SD2	98.22
SD3	99.05
Drug + PEG 6000	
SD4	97.99
SD5	98.81
SD6	99.25

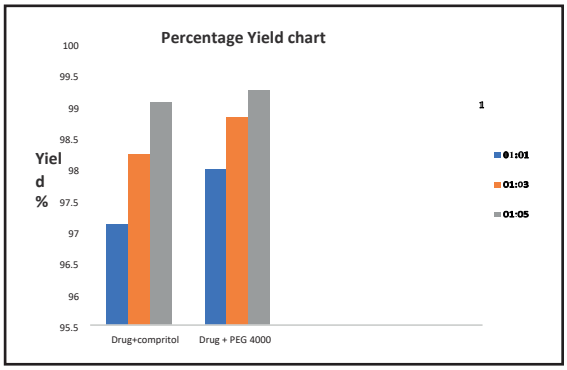

Fig. 13. Percentage Yield of SD1 - SD6

Drug content and solubility:

The drug content was determined and calculated by UV spectrophotometry at 229 nm for all the prepared solid dispersion (SD1 to SD6). Solid dispersion was taken equivalent to 20 mg of the drug. Table 7 and Figure 14 depict the results pictorially.

Table 7. Drug Content & Solubility for Solid dispersion

S.No	Formula code	Percentage of drug content (%)	Drug in mg	Solubility (mg/mL)
	Solid dispersion prepared by Solvent Evaporation Method			
				Drug + Compritol
1.	SD1	87.25	17.45	1.12
2.	SD2	92.82	18.56	2.98
3.	SD3	95.17	19.03	3.33
				Drug + PEG 6000
4.	SD4	92.20	18.44	2.02
5.	SD5	96.53	19.30	3.33
6.	SD6	98.86	19.77	4.11

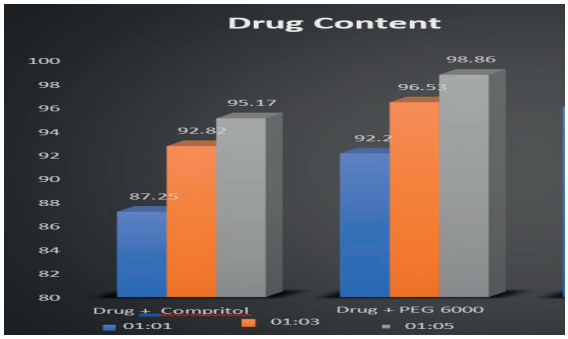

Fig. 14. Drug Content & Solubility for Solid dispersion

Evaluation of compressed tablets:

Weight variation test:

The results obtained from weight variation test as shown in Table 8, depicts that the average weight of all tablets are having variation within the limit of ± 7.5 from the total weight of each tablet in formulation. The results indicated that the formulated tablets are uniform in weight.

Table 8. Evaluation of Compressed Tablets

Formulations	Weight Variation (mg)	Hardness Test (kg/cm²)	Friability (%)	Drug Content (%)	Disintegration Time (Sec)
F1	393.33 ± 7.5	3	95	94	60
F2	391.5 ± 7.5	3	95.7	97.5	60
F3	388.9 ± 7.5	3	96.2	102	103
F4	387.66 ± 7.5	3	96.8	107.33	96
F5	390.33 ± 7.5	3	97.3	101	98
F6	391.63 ± 7.5	3	97.9	99.8	89

Hardness test:

The formulated tablets are having the hardness in the range of 3. kg/cm^2. The results as shown in Table 8, show the resistance of prepared tablets to abrasion, capping breakage during storage and transportation.

Friability test:

The results of the friability test as shown in Table 8, showed the weight loss in all the prepared tablets were less than one percentage. Hence the prepared tablet passes the friability test.

Drug content:

The formulated Glibenclamide tablet passes the drug content assay. The results of all tablet batches showed average percentage drug content is 90 to 110 % as per USP, as shown in Table 8.

Disintegration test:

The disintegration test showed that when the proportion of super-disintegrants used in the formulation increased, which decreases the disintegration time of the tablets, as shown in Table 8. This signified that the increasing level of super disintegrants was found to have a positive impact in disintegration time of Glibenclamide fast dissolving tablet

In vitro dissolution pro ile:

Table 9 and Figure 15 depict the in vitro dissolution profile of SD1 to SD3; while Table 10 and Figure 16 depict that of SD4 to SD6. Tables 11, 12, and 13 tabulate the dissolution values of F1-F3, F4-F6, and F7-F9 respectively; while Figures 17, 18, and 19 pictorially represent the same.

Table 9. Cumulative drug release from pure drug and SDs of Compritol 888 ATO

Time in min	Pure drug	SD1	SD2	SD3
0	0	0	0	0
5	3.51	11.25	14.27	15.95
10	5.48	15.13	16.10	22.92
15	6.20	18.91	24.58	26.88
20	9.85	22.23	26.91	30.29
25	10.11	25.21	30.60	34.11
30	14.91	27.78	34.80	39.82

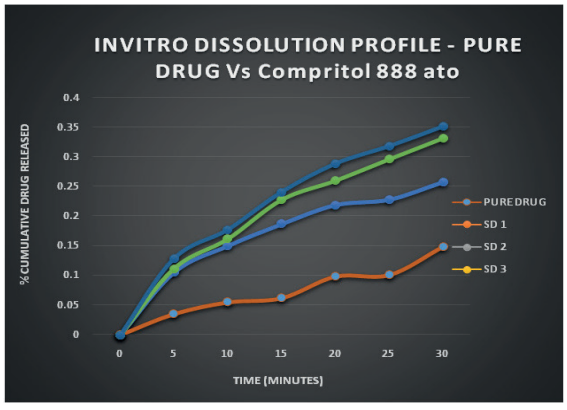

Fig. 15. Cumulative drug release from pure drug and SDs of Compritol 888 ATO

Table 10. Cumulative drug release of pure drug and SDs of PEG 6000

Time in mins	Pure drug	SD 4 1:1	SD 5 1:2	SD 6 1:3
0	0	0	0	0
10	3.51	10.60	11.2	12.86
20	5.48	15.07	16.2	17.75
30	6.20	18.77	22.81	24.12
40	9.85	21.98	26.04	28.9
50	10.11	22.9	29.67	31.87
60	14.91	25.88	33.22	35.20

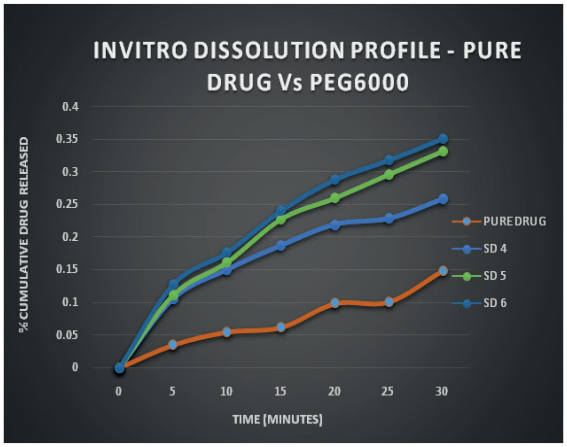

Fig. 16. Cumulative drug release from pure drug and SDs of PEG 6000

Table 11. Dissolution profile of croscarmellose as a super disintergrants

Time in mins	F1	F2	F3
0	0	0	0
5	42.3	**52.4**	61.8
10	48.5	63.2	70.4
20	57.1	72.3	76.8
30	62.3	79.9	81.3
40	71.5	81.5	89.7
50	79.5	86.5	94.3
60	**89.7**	**94.2**	**98.8**

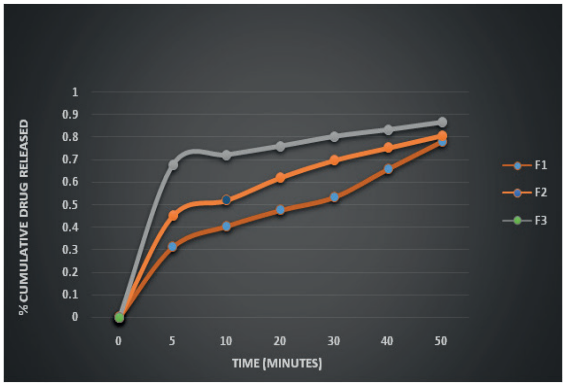

Fig. 17. Dissolution profile of croscarmellose as a super disintegrants

Table 12. Dissolution profile of crosspovidone as a super disintegrants

Time in mins	F4	F5	F6
0	0	0	0
5	35.2	52.7	65.1
10	43.2	63.7	72.6
20	47.7	77.8	86.3
30	56.3	83.1	96.5
40	66.7	94.2	98.2
50	73.4	95.5	98.9
60	**91.2**	**96.8**	**99.6**

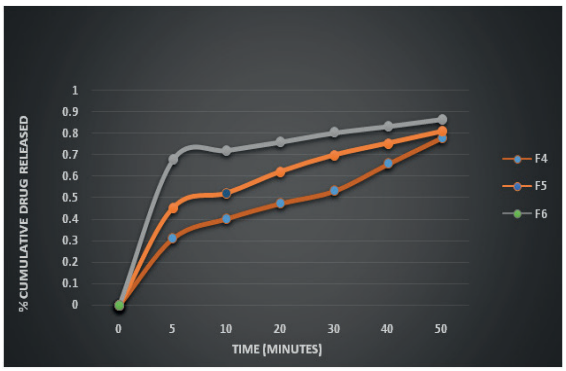

Fig. 18. Dissolution profile of crosspovidone as a super disintegrants

Table 13. Dissolution profile of sodium starch glycolate as a super disintegrants

Time in min	F7	F8	F9
0	0	0	0
5	31.3	45.5	68.1
10	40.5	52.3	72.4
20	47.6	62.4	76.3
30	53.4	70.1	80.6
40	66	75.6	83.6
50	78.2	81.1	86.9
60	**82.3**	**83.5**	**89.7**

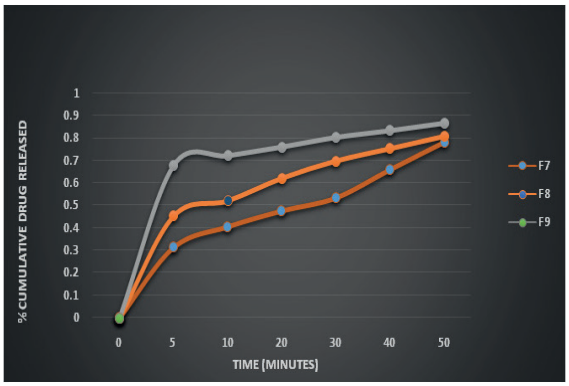

Fig. 19. Dissolution profile of sodium starch glycolate as a super disintegran

Conclusion

Glibenclamide is widely used drug anti-diabetic, but nausea, heartburn, weight gain and bloating are some of the side effects. Medications-induced hypoglycaemia is also a common occurrence. It is a BCS class II drug which has high permeability and low solubility which leads to poor bioavailability. In order to enhance the rate of dissolution of the drug Glibenclamide is formulated into SDs by solvent evaporation method using different carriers.

In the present study solvent evaporation method is used for preparing Glibenclamide solid dispersion using Compritol 888 ATO, PEG6000 at different ratios 1:1, 1:2 and 1:3 ratios. The solid dispersions of Glibenclamide are characterized by FTIR, no possible interactions are found between drug and carriers, XRD results proved conversion of crystallinity of drug to its amorphous form by reduction in peaks in the solid dispersions.

The results from invitro dissolution showed significant increase in dissolution of all the Glibenclamide solid dispersions which is prepared by solvent evaporation method, then that of pure drug itself. Among the two polymers Compritol 888 ATO, PEG 6000, formulation SD3 containing Compritol 888 ATO as a carrier at 1:3 ratio showed highest rate of dissolution (39.82%). The concentration of carriers used in this study played important role in enhancement of dissolution. The *invitro* dissolution rate was enhanced by enhancing proportions of carriers in the SDs and order of rank for dissolution of Glibenclamide from various carriers are Compritol 888 ATO> PEG6000.

Thus from various studies conducted and from results and discussions, the *invitro* dissolution of Glibenclamide can be significantly increased using Compritol 888 ATO, PEG6000 as polymers by solvent evaporation method, from which Compritol 888 ATO was chosen as best polymer for enhancing invitro dissolution rate of poorly soluble drug Glibenclamide. Among the three super disintegrants croscarmellose Na, crosspovidone and sodium starch glycolate, formulation F6 containing Crosspovidone as a super disintegrant showed highest rate of dissolution (99.6). The concentration of carriers used in this study played important role in enhancement of dissolution. The significance of results obtained provides a convenient and useful way for regulating the release of poorly soluble drug Glibenclamide from solid dispersion by selection of appropriate polymer.

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Conflict of interests

There is no conflict of interests.

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