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IMPROVEMENT IN MICROMERITIC PROPERTIES AND DISSOLUTION RATE OF GLIMEPIRIDE

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ABSTRACT

Glimepiride is a third generation hypoglycemic therapeutic agent prescribed for the treatment of non-insulin dependent diabetes mellitus. It is relatively insoluble in water, with poor gastro intestinal dissolution, slow absorption rate and low bioavailability. The objective of the present research is to improve the micromeritic properties, solubility and dissolution rate of glimepride by solid dispersion technique. The solid dispersions were prepared by solvent evaporation method using hydrophilic carriers like PEG6000, PEG10000 and gelucire 44/14. Phase solubility studies showed negative ΔG_{tr}^{0} values for all the 3 carriers at various concentrations (0-5% w/v), indicating the spontaneous nature of solubilization. FT-IR and DSC studies revealed that glimepride is compatible with carriers used in this study. Kawakita analysis revealed reduced cohesiveness and improved flowability for solid dispersions. In vitro dissolution study showed maximum dissolution of 75% in 30 min for gelucire 44/14 based solid dispersion with 1:5 ratio of drug to carrier (F9). Q_{30} values for formulation F9 showed nearly 10 fold increase in dissolution rate compared to glimepride. The mean dissolution time for solid dispersion F9 decreased from 33 min to 18 min. Hence solid dispersion F9 was selected as the optimized formulation to improve micromeiritc properties, solubility and dissolution rate of glimepiride.

KEYWORDS: phase solubility, kawakita analysis, solvent evaporation method, mean dissolution time.

INTRODUCTION

Glimepiride is a third generation hypoglycemic therapeutic agent prescribed for the treatment of non-insulin dependent diabetes mellitus.[1] Literature review suggests that the drug shows more potential benefits over currently available sulfonylureas such as low dose, quick onset of action, longer duration of action and lower insulin C-peptide level.[2] Glimepiride is a white crystalline powder, relatively insoluble in water with dissociation constant value of pKa = 6.2. Glimepiride exhibits poor GI absorption rate and inter individual variations in its bioavailability due to its poor water solubility.[3] Several approaches have been reported for enhancement of solubility and dissolution of poorly soluble drugs include increasing the particle surface area available for dissolution by milling.[4] improving the wettability with surfactants or doped crystals.[5] decreasing crystallinity by preparing a solid dispersion (SD)[6], use of inclusion compounds such as cyclodextrin derivatives.[7] use of polymorphic forms or solvated compounds.[8] and use of salt forms.

Polyethylene glycols (PEGs) with molecular weights of 1,500-20,000 and various hydrophilic grades of gelucire are among the several carriers which have been employed in preparing solid dispersions. PEGs are widely used due to their low melting point, low toxicity, wide drug compatibility and hydrophilicity.[9] Solubility of PEGs in water is generally good, but it decreases with increase in their molecular weight.[10] PEGs have the ability to solubilize poorly water soluble compounds by improving their wettability.[11] The SDs of drugs with PEG 6000 may be useful to solve various problems such as stability, solubility, dissolution and bioavailability.[12] Many researchers reported SD using Gelucire (polyglycolized glyceride) by fusion and solvent evaporation techniques.[13-14] Gelucire is a varying mixture of mono, di and triglycerides with polyethylene glycol esters of fatty acids. They are inert, semisolid and waxy amphiphilic excipients. A low hydrophilic–lipophilic balance (HLB) value in Gelucire decreases the dissolution rate whereas a high HLB value enhances the dissolution rate. The low HLB compounds are composed of partial glycerides while those with HLB values above 10 are mixtures of partial saturated glycerides and polyethylene glycol (PEG) esters. Gelucire 44/14 is a semisolid excipient with an HLB value of 14 and melting point of 44 ^{0}C. Its hydrophilic property makes it a good choice for use as a carrier in preparation of solid dispersions by fusion and solvent evaporation method.[15] The objective

of this research is to prepare and characterize solid dispersions of glimepiride in PEG6000, PEG10000 and Gelucire 44/14 by solvent evaporation method to improve micromeritic properties, solubility and dissolution rate.

MATERIALS AND METHODS

Glimepiride was a gratis sample from Aurobindo Pharma Ltd, Hyderabad. Gelucire 44/14 was a gift sample from Gattefosse India Ltd, Mumbai. PEG6000 and PEG10000 were procured from Fine chemicals, Mumbai. Acetone was purchased from Loba Chemie, India. All other chemicals and reagents used were of analytical grade.

Phase solubility study

Phase solubility studies were performed as per method described by Higuchi.[16] An excess amount of powdered glimepiride was placed in a screw-cap glass vial to which 20 mL of distilled water containing various concentrations (0, 0.5, 1, 2, 3, 4 and 5% w/v) of carriers vis-à-vis PEG6000, PEG10000 and gelucire 44/14 (Table 1). The samples were shaken at 37 ± 0.5 °C for 72 h on a Remi mini rotary shaker-12R-DX. After 72 h of shaking, the samples were filtered through a 0.45 µm membrane filter (Auroco, Thailand). The filtrate was diluted suitably and analyzed in an UV-Visible spectrophotometer UV-1800 (Shimadzu, Japan). The relationship between concentration of carrier and concentration of glimepiride are shown in figure 1.

The value of the apparent stability constant, Ks for glimepride-PEG6000, glimepride-PEG10000 and glimepride-gelucire 44/14 combinations was computed from the phase-solubility profiles, as described by

$$Ks = {Slope}/{Intercept\,(1 - Slope)} \quad (1)$$

The Gibb's free energy of transfer (ΔG_{tr}^{0}) of glimepiride from distilled water to solutions of carrier was calculated by using formula:

$$\Delta G_{tr}^{0} = -2.303RT\left\{log\frac{S_0}{S_s}\right\} \quad (2)$$

Where S_0/S_s is the ratio of the molar solubility of glimepiride in distilled water of PEG6000, PEG10000 and gelucire 44/14 to that in the same medium.

FT-IR spectroscopy study

Solid dispersions of Glimepiride-carriers (1:1) interactions were assessed by FT-IR spectroscopy (IR-Affinity-1, Shimadzu, Japan). FT-IR spectra of pure drug glimepiride and its 1:1 solid dispersions with PEG6000, PEG10000 and gelucire 44/14 were recorded on IR using potassium bromide (KBr) discs. The instrument was operated under dry air purge and the scans were collected at a scanning speed of 2 mm/sec with resolution of 4 cm^{-1} over the region 4000-400 cm^{-1}. The FT-IR spectra are shown in figure-2 and table 2.

Differential scanning calorimetry (DSC) study

The DSC measurements were performed on a DSC with thermal analyzer (DSC-60, Shimadzu, Japan). All the accurately weighed samples (about 2 mg) were placed in sealed aluminum pans before heating under nitrogen flow (20 mL/min) at a scanning rate of 10 °C/min from 25 to 175°C. An empty aluminum pan was used as reference. DSC measurements were performed for glimepiride and its 1:1 solid dispersions with PEG6000, Peg10000 and gelucire 44/14 to study drug carrier interaction. The results are shown in figure.3.

Preparation of solid dispersion (SD) of glimepiride by solvent evaporation method

The SDs of glimepiride with different hydrophilic carriers such as PEG6000, PEG10000 and Gelucire 44/14 containing three different weight ratios (1:1, 1:3, 1:5) were prepared by solvent evaporation method. In solvent evaporation method, to a solution of glimepiride in acetone, an appropriate amount of carrier was added. The solvent was evaporated under reduced pressure at 40^{o}C by using rotary evaporator (RV 10 Digital V, IKA, Germany) and the resulting residue was dried. The mixture was stored overnight in a desiccator. The dried mixture was powdered in a mortar, sieved through a 40-mesh screen, and stored in a screw-cap vial at room temperature until further use. The composition of solid dispersion is shown in Table 3.

Evaluation

Percentage Yield and Drug Content

Percentage practical yield was calculated to know about percent yield or efficiency of any method, thus it helps in selection of appropriate method of production. Solid dispersions of were collected and weighed to determine practical yield (PY). The results are shown in table.4.

Drug content of solid dispersions was determined by weighing an amount equivalent to 10 mg of glimepiride for each formulation and mixed in phosphate buffer pH 7.4, sonicated for 10 min, filtered, diluted with same solvent and analyzed for drug content. The results are presented in table 4.

Solubility measurement of solid dispersions

Solubility of glimepiride and its solid dispersions was determined. [17] An excess amount of glimepiride and solid dispersions were added to 20 mL of freshly prepared distilled water in clean vials with continuous shaking on a Remi mini rotary shaker-12R-DX at 25 ± 0.5 °C for 24 h to achieve equilibrium. The filtered solutions were suitably diluted and analyzed spectrophotometrically. The results are shown in Table 4.

Flowability and Compressibility Measurement

Glimepiride, and solid dispersions were characterized for flow and compressibility by measuring Compressibility index (%), Hausner's ratio (H.R) and angle of repose (Ɵ).[18] The results are shown in Table 5.

The Hausner's ratio is a number that is correlated to the flowability of powder. The Hausner's ratio is determined by following formula.

$$Hausner's\ Ratio = \frac{Tapped\ Density}{Bulk\ Density} \quad (3)$$

Compressibility index (CI) was determined according to the formula

$$C.I = \frac{(Tapped\ Density - Bulk\ Density)}{Tapped\ Density} \times 100 \quad (4)$$

Angle of repose was determined by allowing the pure drug powder of glimepiride and solid dispersions to flow through a funnel (with a 10 mm orifice diameter) and measuring the angle between the horizontal and the slope of the heap of solid dispersions. The radius (r) and height (H) of the pile were measured. Then the angle of repose (θ) was calculated using following formula.

$$\theta = tan^{-1}\ {}^{h}/_{r} \quad (5)$$

Kawakita analysis

Pure drug glimepiride and solid dispersions were compressed using a hydraulic pellet press KP (Kimaya Engineers, India). Compression loads used were 10, 20, 30, 40 and 50 kg/cm^2 with dwell time of 2 sec. The dimensions (thickness, volume and diameter) of compacts were

determined at each compression pressure. Kawakita equation describes the relationship between the volume reduction of a powder column and the applied pressure. [19] The Kawakita equation is written as,

$$P/C = (1/ab) + (P/a) \quad (6)$$

Where C is the degree of volume reduction = $(V_o - V)/V_o$, V_0 is initial volume, V is volume of tablet under the applied pressure P, an intercept at the P/C axis, extrapolated from the linear region of the plot, gives a value for 1/ab. The constants 'a' gives an indication of maximum volume reduction available and is considered to describe the compressibility of the powder, while 'b' is considered to describe an inclination towards volume reduction. The results are shown in table 5.

In-vitro dissolution test

The release of glimepiride from PEG6000, PEG10000 and gelucire 44/14 based solid dispersions were determined using USP paddle type Dissolution Tester at 50 rpm. Dissolution was examined using 900 mL of simulated intestinal fluid (SIF) without enzyme. The temperature was maintained at 37 ± 0.2°C. Samples each containing 5 mL were withdrawn at 10, 20, 30, 40, 50 and 60 min intervals, filtered through a Whatman filter of 0.45 µm and replaced with an equal amount of fresh dissolution medium to maintain sink condition. Samples were then suitably diluted and analyzed spectrophotometrically at 226 nm. The dissolution studies were conducted in triplicate. The profiles are shown in figures 4-6. The dissolution profiles were evaluated for amount of drug released in initial 30 min (Q_{30} min) and T_{50} i.e. time taken for dissolution of 50% of glimepiride.

Dissolution Efficiency

The percent dissolution efficiency (% DE) was computed to compare the relative performance of various formulations. The % DE of a pharmaceutical dosage form is defined as the area under the dissolution curve up to a certain time, t, expressed as a percentage of the area of the rectangle described by 100% dissolution at the same time.[20] The % DE can be calculated from the following equation

$$\% DE = \frac{\int_0^t Y dt}{Y_{100} t} \quad (7)$$

Where, Y is the percent drug dissolved at time t.

Mean Dissolution Time

To understand the extent of glimepiride dissolution rate enhancement from its solid dispersions, the dissolution data were used to calculate the mean dissolution time (MDT). The MDT can be calculated by using following equation.

$$MDT_{in\ vitro} = \frac{\sum_{i=1}^{n} T_{mid}\,\Delta M}{\sum_{i=1}^{n} \Delta M} \quad (8)$$

Where, i is the dissolution sample number, n is the number of dissolution sampling times, T_{mid} is the midpoint between times T_i and T_{i-1} and ΔM is the amount of glimepiride dissolved between times T_i and T_{i-1}.

All the above mentioned dissolution related parameters like Q_{30}, T_{50}, DE_{30}, MDT are summarized in table 6.

RESULTS AND DISCUSSION

Phase solubility study

The solubility of glimepiride in water at 25°C is 0.035 mg/mL therefore it can be considered as a poorly water soluble drug. The phase solubility data for glimepiride with all the 3 carriers PEG6000, PEG10000 and gelucire 44/14 are presented in table 4. From this table, it can be seen that the apparent solubility of glimepiride increased with increase in the concentration of all the 3 carriers. At the highest carrier concentration (5% w/v), the solubility increased approximately 10-fold, 17 fold and 28 fold for PEG6000, PEG10000 and gelucire 44/14 respectively at 25°C. An indication of the process of transfer of glimepiride from pure water to aqueous solution of carriers was obtained from the values of Gibbs free energy change (Patel RP, 2008). The obtained values of ΔG_{tr}° are shown in Table 1. The ΔG_{tr}° values show whether the reaction condition is favorable or unfavorable for drug solubilization in the aqueous carrier solution. Negative ΔG_{tr}° values indicate favorable conditions. ΔG_{tr}° values were all negative for all the 3 carriers PEG6000, PEG10000 and gelucire 44/14 at various concentrations, indicating the spontaneous nature of glimepiride solubilization, and decreased with an increase in carrier concentration, demonstrating that the reaction became more favorable as the concentration of carrier increased. These values also indicated that the extent of improvement in solubility was more with gelucire 44/14 as compared with both grades of PEG i.e. PEG6000 and PEG10000. The phase solubility plot for all the 3 carriers showed A_L type solubility curve, signify that complex is formed between drug and carriers (Figure 1).

Table 1: Effect of Concentration of carriers (PEG6000, PEG10000 and Gelucire 44/14) on Gibbs free energy.

Concentration of carrier (% w/v)	Solubility (mg/mL)			ΔG_{tr}° (J/mol)*		
	PEG 6000	PEG 10000	Gelucire 44/14	PEG 6000	PEG 10000	Gelucire 44/14
0	0.035	0.356	0.352	0	0	0
0.5	0.16	0.24	0.37	-2.435	-4.217	-.8.751
1	0.2	0.28	0.54	-3.598	-6.341	-10.324
2	0.24	0.32	0.61	-6.367	-8.234	-11.387
3	0.29	0.46	0.72	-7.267	-10.502	-14.214
4	0.33	0.51	0.86	-9.128	-11. 343	-16.398
5	0.37	0.59	0.97	-10.456	-14.236	-19.435

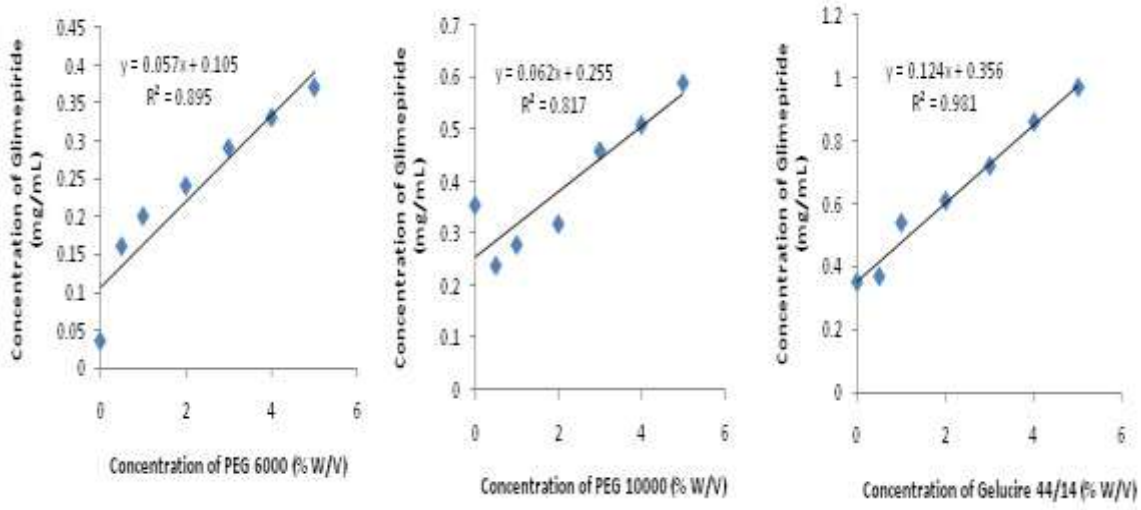

Fig. 1: Phase solubility of Glimepiride in PEG6000 (1A), PEG10000 (1B) and Gelucire 44/14 (1C) in the concentration range of 0 to 5% w/v.

Fourier Transform Infrared (FT-IR) Spectroscopy

FT-IR spectrum of glimepiride (Figure 2A) is characterized by the absorption of carbonyl (C=O) group at 1707.66 cm^{-1}. It also contains NH group as it showed absorption band at 3388.07 and 3288.04 cm^{-1}. The sulphonyl group bands are located at 1346.07 and 1152.26 cm^{-1} for pure glimepiride. The absorption band at 1275.68 cm^{-1} corresponds to C-N stretching vibrations. The band at 1543.74 cm^{-1} indicated the presence of C=C. The absorption band for C-H was found at 2931 cm^{-1}. All the peaks were retained in all solid dispersions with PEG6000 (Figure 2B), PEG10000 (figure 2C) and gelucire 44/14 (Figure 2D). The results of FT-IR spectroscopy are summarized in Table 2.

Table 2: FT-IR data of Glimepiride and its solid dispersions.

Functional groups	Glimepiride	SD of Glimepiride: PEG6000 (1:1)	SD of Glimepiride: PEG10000 (1:1)	SD of Glimepiride: Gelucire 44/14 (1:1)
NH group	3388.07 and 3288.04	3389.03 and 3288.04	3369.03 and 3288.04	3387.03 and 3288.01
C-H	2931	2885.95	2884.02	2932
Carbonyl (C=O)	1707.66	1707.66	1707.66	1706.41
C=C	1543.74	1543.74	1543.70	1544.32
Sulphonyl group	1346.07	1342.21	1345.11	1347.09
C-N stretching vibrations	1275.68	1279.54	1278.57	1274.65

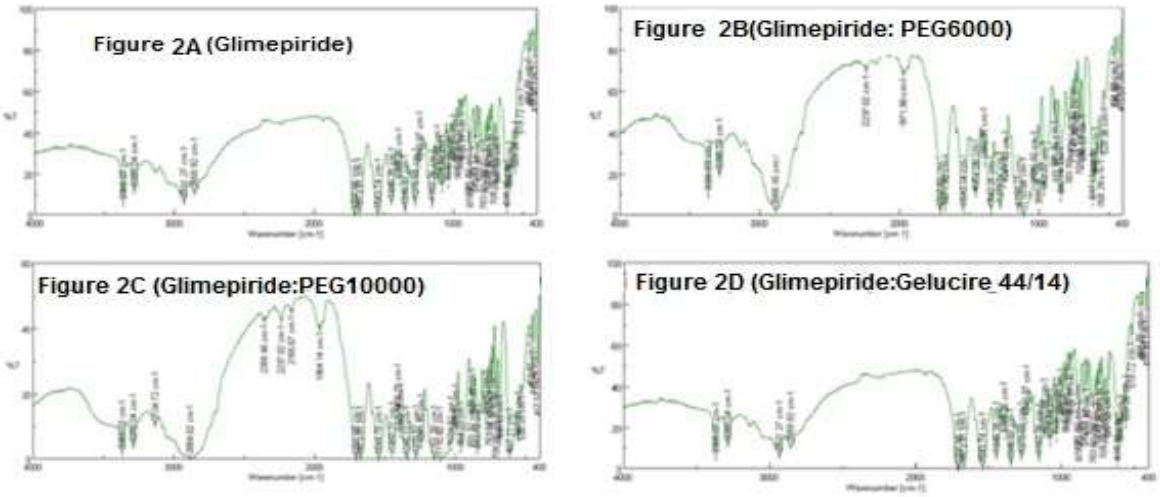

Fig. 2: FT-IR spectra of glimepiride (2A) and its solid dispersion (1:1) with PEG6000 (2B), PEG10000 (2C) and Gelucire 44/14 (2D).

Differential Scanning Calorimetry

DSC enables the quantitative detection of all processes in which energy is required or produced (i.e., endothermic or exothermic phase transformations). The thermal behavior of glimepiride and its solid dispersion with PEG6000, PEG10000 and gelucire 44/14 was studied by DSC. The DSC thermogram of pure glimepiride is shown in figure 3A. The glimepiride showed a sharp melting peak at 210^0C releaving that it is a pure and crystalline drug substance. The DSC thermogram of soild dispersion with all the 3 carriers showed a sharp peak at 54^0C, 62^0C and 45^0C for PEG6000, PEG10000 and gelucire 44/14 respectively (Figure 3B to 3D). Solid dispersions exhibited a single endothermic peak for carrier whereas all solid dispersions corresponding to the fusion of the carrier no peak was present associated to the melting of the drug. We can hypothesize that during the scanning of the temperature the solid drug (when present) dissolves into the molten carrier starting from the melting of the

carrier (around 45^0C) and is no more present in its undissolved form inside the systems, when the melting temperature of glimepiride is reached. [21] Hence there is no interaction between the carriers and glimepiride used in the present research.

In order to achieve improved solubility and dissolution rate, solid dispersions were prepared by solvent evaporation method using PEG6000, PEG10000 and gelucire 44/14 in various drug to carrier ratios such as 1:1. 1:3 and 1:5. The compositions of solid dispersions are shown in Table 3.

Table 3: Composition of solid dispersions of Glimepiride by solvent evaporation method.

Formulation Code	Glimepiride	PEG 6000	PEG10000	Gelucire 44/14	Acetone (mL)
1	1	1	-	-	5
F2	1	3	-	-	5
F3	1	5	-	-	5
F4	1	-	1	-	5
F5	1	-	3	-	5
F6	1	-	5	-	5
F7	1	-	-	1	5
F8	1	-	-	3	5
F9	1	-	-	5	5

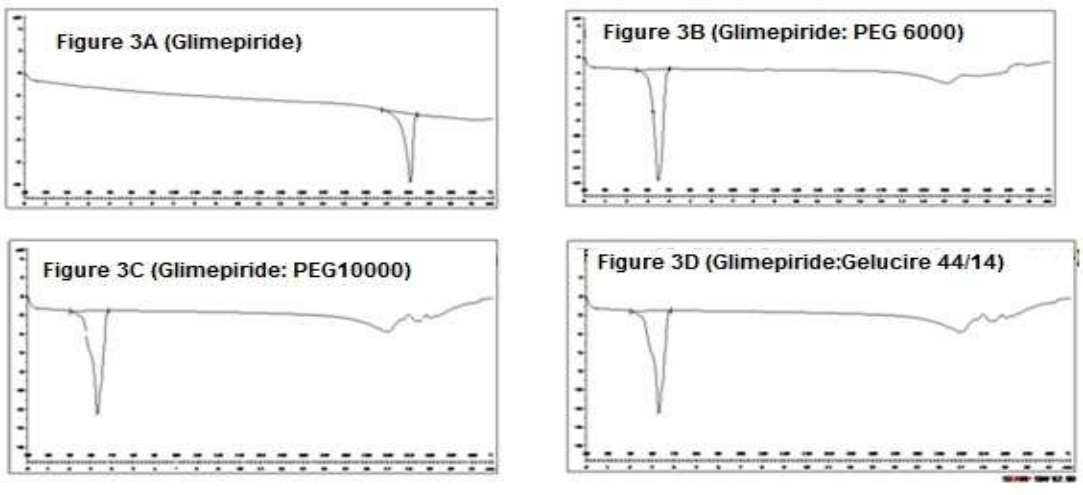

Fig. 3: DSC thermograms of glimepiride (3A) and its solid dispersions (1:1) with PEG6000 (3B), PEG10000 (3C) and Gelucire 44/14 (3D).

Practical Yield and Drug Content

The practical yield and drug content of solid dispersions are shown in table 4. It was observed that more than 95% practical yield observed for solid dispersions by solvent evaporation

method. The major advantage of solid dispersion method in comparision to fusion method is its yield. The loss of drug substance was very minimum; this method also has the potential of manufacturing at commercial scale. Drug content was high for all the formulation indicating uniform mixing of drug with carriers.

Solubility Study

Solubility of pure drug glimepiride and its solid dispersions with various carriers were determined and presented in Table 4. As the proportion of hydrophilic carrier increased solubility of glimepiride also increased in solid dispersions. PEG6000, PEG10000 and gelucire 44/14 based solid dispersions showed 3, 4 and 6 times improvement in solubility respectively with the highest ratio of drug to carrier (1:5). The improved solubility of glimepiride in solid dispersions can be explained by the improved wettability of the glimepiride particles in aqueous solution from all the 3 carriers.[22]

Table 4: Practical yield, Drug content and solubility of solid dispersions.

Formulations	Practical Yield (%)*	Drug Content (%)*	Solubility* (µg/mL)
Glimepiride	-	-	35 ± 2
F1	97.4 ± 2.5	98.7 ± 0.5	57 ± 8
F2	96.5 ± 2.1	97.8 ± 1.3	68 ± 6
F3	98.5 ± 2.5	98.7 ± 2.1	97 ± 8
F4	99.4 ± 1.2	97.6 ± 1.4	87 ± 8
F5	97.5 ± 1.8	99.5 ± 0.9	118 ± 6
F6	98.6 ± 3.2	99.4 ± 1.7	145 ± 8
F7	97.5 ± 1.5	97.5 ± 1.2	123 ± 4
F8	98.3 ± 2.4	98.6 ± 0.4	165 ± 12
F9	98.9 ± 1.5	98.3 ± 1.7	167 ± 11

***Mean** ± SD, n = 6, - Not required to determine.

Micromeritic Properties

Flowability and compressibility

The values of angle of repose, Carr's index (C.I) and Hausner's ratio (H.R) for drug powder glimepiride reveals that it is a poorly flowable drug. All the formulations showed significant improvement in flowability and compressibility suggesting their suitability for tablet formulation.[23] The flowability and compressibility data are shown in Table 5. These powder formulations could be processed into a capsule or tablet dosage form.

Table 5: Micromeritic properties of Glimepiride and its solid dispersions.

Formulations	Angle of repose (^{0})*	Compressibility Index (%)*	Hausner's ratio*	Kawakita Parameters	
				a	1/b
Glimepiride	44 ± 3	32 ± 1.5	1.42 ± 0.4	0.314	12.45
F1	24 ± 3	17 ± 1	1.22 ± 0.2	0.023	8.34
F2	26 ± 2	19 ± 2	1.31 ±0.3	0.034	7.65
F3	25 ± 3	18 ± 2	1.24 ±0.2	0.021	8.23
F4	24 ± 2	19 ± 1	1.23 ±0.1	o.o43	8.76
F5	25 ± 3	19 ± 2	1.25 ± 0.3	0.032	9.56
F6	26 ± 2	18 ± 3	1.24 ±0.4	0.029	7.87
F7	21 ± 1	20 ± 2	1.26 ±0.5	0.056	9.32
F8	24 ± 2	18 ± 1	1.26 ±0.4	0.048	8.11
F9	22 ± 3	17 ± 3	1.21 ±0.3	0.013	8.23

*Mean ± SD, n = 6.

Kawakita Analysis

Lower the value of 'a' better is the flowability of formulation. Solid dispersions showed lower values of 'a' compared to glimepiride pure drug indicating better flowability of solid dispersions for all carriers. Similarly lower the value of '1/b' lesser is the cohesive nature of formulation (Table 5). Lower value of '1/b' for solid dispersions compared to glimepiride indicates that solid dispersions are less cohesive due to dense nature of particles. Generally dense particles are less cohesive to enhance flowability.[24]

In vitro Dissolution Study

In case of PEG6000, PEG10000 and gelucire 44/14 based solid dispersions prepared by solvent evaporation method showed improvement in dissolution rate with increase in the ratio of drug to carriers from 1:1 to 1:5. In case of PEG6000 based solid dispersions (F1 to F3), Formulation F3 showed maximum of 35% dissolution in 30 min of dissolution study. In case of PEG10000 based solid dispersions (F4 to F6), Formulation F6 showed maximum of 57% dissolution in 30 min of dissolution study. In case of Gelucire 44/14 based solid dispersions (F7 to F9), Formulation F9 showed maximum of 76% dissolution in 30 min of dissolution study. Among the 3 carriers used in the above solvent evaporation method, gelucire 44/14 exhibited highest dissolution enhancement potential (figure 4-6) i.e. more than 75% in 30 min.

The dissolution data solid dispersions were also subjected to evaluation of parameters like Q_{30}, T_{50}, DE_{30}, MDT and Hixson Crowell cube root constant. Q_{30} value for the pure drug glimepiride was 8% i.e. only 8% of drug dissolved in 30 min but gelucire 44/14 based solid

dispersion (F9) showed nearly 77% drug dissolution. Solid dispersion (F9) exhibited nearly 10 time improvement in dissolution. T_{50} value for pure drug and PEG 6000 based solid dispersion (F1) could not be determined as 50% of drug was not dissolved during 1 h of dissolution study. Lowest time of 15 min was observed for solid dispersion (F9) to dissolve 50% of drug. Solid dispersion (F9) showed nearly 9 times improvement in dissolution efficiency at 30 min. Lowest mean dissolution time of 18 min was observed for F9. Hence formulation F9 was selected as the best optimized formulation Table-6.

Table 6: Dissolution related parameters for glimepiride and its solid dispersions.

Formulations	Q_{30}	T_{50} (min)	% DE_{30}	MDT (min)
Glimepiride	8	*	8.7	33.17
F1	20.31	*	22.61	29.16
F2	31.23	55	34.97	28.51
F3	35.53	42	38.16	26.90
F4	31.32	48	33.23	28.54
F5	55.34	26	58.72	21.79
F6	52.34	22	55.38	22.43
F7	40.62	35	43.21	24.76
F8	64.89	22	68.21	19.56
F9	76.65	15	78.31	18.54

*50 % of drug was not dissolved within 1 h of dissolution study; % DE_{30} is the percent dissolution efficiency at 30 min, Q_{30} Percent of drug dissolved in 30 min.

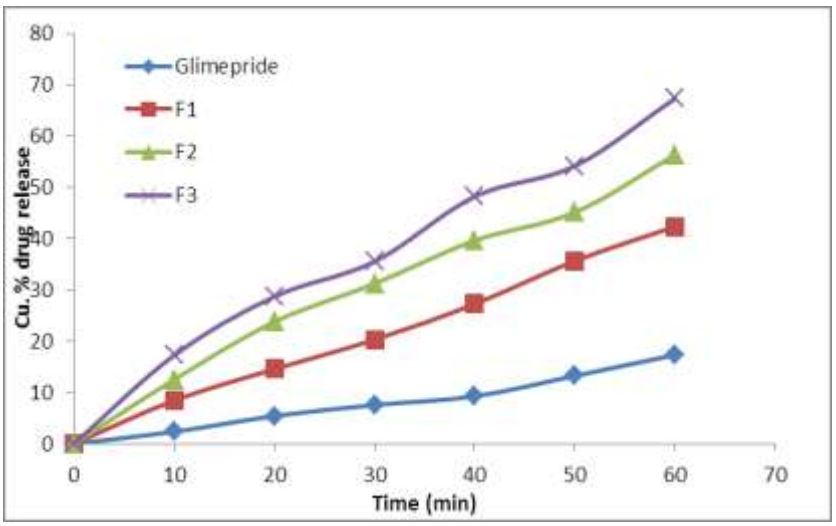

Fig. 4: Dissolution profile of PEG6000 based solid dispersions.

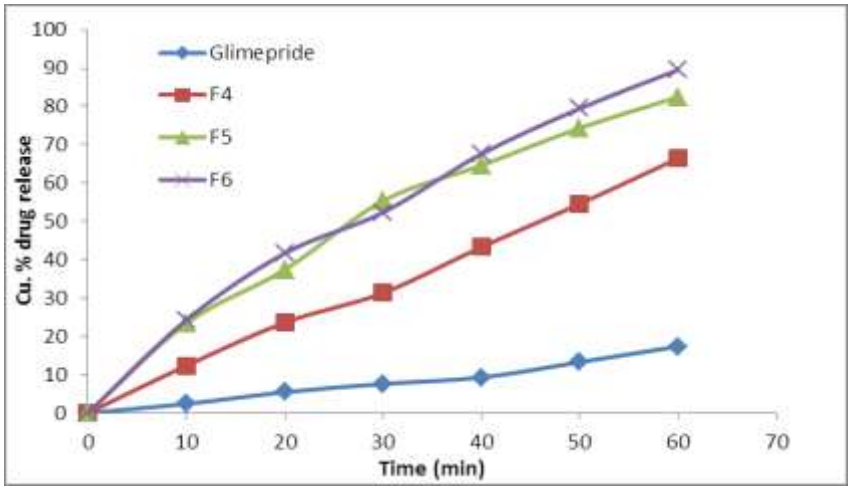

Fig 5: Dissolution profile of PEG10000 based solid dispersions.

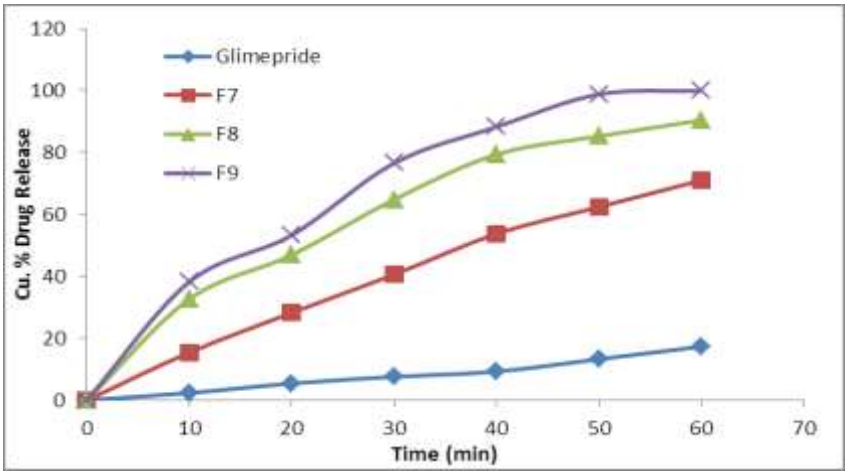

Fig. 6: Dissolution profile of Gelucire 44/14 based solid dispersions.

CONCLUSION

Hence from the above research work, it may be concluded that PEG6000, PEG10000 and gelucire 44/14 can be used to enhance micromeritic properties, solubility and dissolution rate of poorly soluble drug glimepiride by solvent evaporation method. All the formulations showed improved flowability as reveled from kawakita analysis. Gelucire 44/14 showed higher solubility and dissolution rate enhancement potential. The solid dispersion formulation (F9) showed more than 75% drug release in 30 min. These powder formulations can be compressed into tablet, filled into capsule or filled into a sachet.

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