Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

ENHANCEMENT OF DISSOLUTION RATE OF GLIBENCLAMIDE USING LIQUISOLID TECHNIQUE

N. Arun Kumar[1*], Lincy Varghese[1], S. Ramesh[2], L.H. Thameemul Ansari[2], K. Sathesh Kumar[2]

[1*]Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore-641048, Tamil Nadu, India.
[2]Department of Pharmaceutics, Sri Ramachandra University, Porur, Chennai-600116, Tamil Nadu, India.

ABSTRACT

The purpose of this study was to improve the dissolution rate of a poorly soluble drug, glibenclamide using Liquisolid technique. Different LS compacts were prepared using a mathematical model to calculate the required quantities of powder and liquid ingredients to produce acceptably flowable and compressible admixture. Propylene glycol was selected as the solvent. Avicel pH 102, Aerosil 200 and cross carmellose sodium were used as carrier, coating material and disintegrant respectively for preparing the tablets. The formulations were then evaluated for their flow properties such as bulk density, tapped density, compressibility index, angle of repose and Hausner's ratio. DSC and XRPD analysis were performed to know whether there is any interaction between drug and excipients and also to study the changes in drug crystallinity. The dissolution studies revealed that all the formulations have higher drug release rates than that of marketed and conventional tablets. The DSC and XRPD results showed that there is no interaction between the drug and excipients and also confirmed the existence of the drug in the solubilised form, which is proved by the absence of endothermic peak in DSC and reduction in the intensity of XRPD peaks. Among the different formulations prepared, LS-3 with a Lf value of 0.270 and R value of 30, was chosen as the best formulation based on its higher percentage release (91.35%). The study has produced encouraging results and it was concluded that Liquisolid technology can be used as an efficient method in improving the solubility and dissolution characteristics of poorly soluble drugs.

KEYWORDS

Glibenclamide, Liquisolid, Liquid load factor, Excipient ratio and Carrier and Coating material.

Author for Correspondence:
Arun Kumar N,
Department of Pharmaceutics, KMCH College of Pharmacy, Coimbatore, Tamil Nadu, India.

Email: mmcarun@gmail.com

INTRODUCTION

Aqueous solubility of any therapeutically active substance is a key property as it governs dissolution, absorption and thus the *in vivo* efficacy. Poorly water soluble compounds have solubility and dissolution related bioavailability problems. The dissolution rate is directly proportional to the solubility of drugs. Drugs with low aqueous

solubility have low dissolution rates and hence suffer from oral bioavailability problems. The poor solubility and poor dissolution rate of poorly water soluble drugs in the aqueous gastro intestinal fluids often cause insufficient bioavailability.

Nearly 40%[1] of the new chemical entities currently being discovered are poorly water soluble drugs. Thus, there is a greater need to develop a composition, which provides enhanced solubility of the poorly soluble drugs and increases its dissolution rate and thus improves its bioavailability to provide a formulation with reduced dose and better therapeutic efficacy and as a result overcomes the drawbacks presented by the prior art.

There are various techniques available to improve the solubility of poorly soluble drugs like particle size reduction, solid dispersion, solubilization by surfactants, complexation etc. Liquisolid technique is a new and promising method to enhance the dissolution rate of poorly soluble drug. With the liquisolid technology, a liquid may be transformed into a free flowing, readily compressible and apparently dry powder by simple physical blending with selected excipients named the carrier and coating material. The liquid portion, which can be a liquid drug, a drug suspension or a drug solution in suitable non-volatile liquid vehicles, is incorporated into the porous carrier material. Once the carrier is saturated with liquid, a liquid layer is formed on the particle surface which is instantly adsorbed by the fine coating particles. Thus, an apparently dry, free flowing, and compressible powder is obtained[2].

Glibenclamide is an antidiabetic drug which belongs to the class sulfonyl ureas. It is poorly water soluble and hence have less oral bioavailability[3]. Thus by using this technique the dissolution rate can be increased and consequently improve oral bioavailability.

MATERIALS AND METHODS

Materials

Glibenclamide (Capplin point, Pondicherry), Propylene Glycol (Nice chemicals pvt .ltd, Kerala), Micro crystalline cellulose (Mitutiyo, India), Aerosil (FMC Biopolymer, Ireland), sodium starch glycolate (Ascot pharmachem Pvt Ltd, Gujarat), croscarmellose sodium (DME Fonterra Excipients, USA), Magnesium stearate (Parag Fine Organics, Mumbai), Talc (CP Kelco US Inc. USA).

Solubility studies

Solubility studies of glibenclamide were carried out in water, Propylene Glycol, Polyethylene Glycol 400, and Tween 20. Saturated solutions were prepared by adding excess drug to the vehicles and shaking on the shaker for 48 h at 25 ± 0.5°C under constant vibration. After this period the solutions were filtered, diluted and analyzed by UV-spectrophotometer at 227 nm.

Formulation of liquisolid system

Calculated quantities of Glibenclamide and propylene glycol was accurately weighed and mixed thoroughly in a mortar to produce the drug solution. Quantities of carrier and coating materials required were calculated based on 'R' value and were added into the drug solution and mixed thoroughly. Mixing process is carried out in three steps. During first stage powder was blended for approximately one minute so that the liquid medication will equally distribute in the powder. In second stage, mixture was evenly spread as a uniform layer on the surfaces of mortar and left standing for approximately 5 min to allow drug solution to be absorbed in the interior of powder particles[4]. In third stage, powder was scraped off the mortar surfaces by means of aluminum spatula and then blended with 5% super disintegrant (CCS), 2% magnesium stearate and 1 % talc for another 30 seconds in a similar to first stage. This gives final formulation of liquisolid tablets. A total of 12 formulations were made using four different concentrations of drug (5,10,15 and 20% w/w) at three different R values i.e 10, 20 and 30. The composition of all liquisolid formulations is listed in Table No.1.

Evaluation of flowability and compressibility of liquisolid powder

The flowability of the liquisolid powder, was calculated by measuring the angle of repose[5]. Determination of bulk and tap densities of the powder was used to calculate both the Hausner's ratio and the Carr's index[6]. Compatibility studies

were performed by taking the IR spectra. The powders were compressed into tablets.

Evaluation of Tablets

Compressed tablets were then evaluated for hardness, friability, weight variation, content uniformity as per the standard IP procedure.

***In vitro*-Dissolution studies**

The Glibenclamide release from different formulations was determined using a USP XXIII paddle apparatus 2 under sink condition. The dissolution medium was 900 ml phosphate buffer (pH 7.4) at 37 ± 0.2 °C; paddle speed 50 rpm, to simulate *in vivo* conditions. All experiments were done in triplicate and average values were taken. The formulation prepared was subjected to dissolution tests for 1 hr. Sample (10 ml) was withdrawn at predetermined time intervals, filtered through Whatmann filter paper and replaced by an equal volume of dissolution medium. Drug content in the dissolution sample was determined by UV spectrophotometer at 227nm.

Differential scanning calorimetry (DSC)

DSC (Q20 V24.2) was performed to assess thermotropic properties and thermal behaviors of Glibenclamide and of liquisolid system prepared. Samples (3-5mg) were placed in aluminum pans and lids at constant heating range of 10 °C/min, covering temperature range 30 to 300 °C. Nitrogen was used as purge gas through DSC cell[7].

X-ray powder diffraction analysis (XRPD)

Crystallinity of the drug and the samples was determined using the XRD-6000 diffract meter with copper target. The conditions were 40 kV voltages 30 mA current. The samples were loaded on to the diffractometer and scanned over a range of 2θ values form 10 to 80 ^{0} at a scan rate of 10.00 ^{0} /min[8].

Stability studies

The prepared formulations which showed best *in vitro* results was selected and kept for stability testing for 90 days. The tablets were kept at 40± 2°C/ 75%±5%RH in a stability chamber and samples were withdrawn at initial, 30th , 60th and 90th day and evaluated for drug content, disintegration, dissolution study.

RESULTS AND DISCUSSION

Solubility studies

The solubility of Glibenclamide in different solvents were studied to select the suitable solvent to be used in the formulation. Glibenclamide showed a maximum solubility of 2.7407%w/w in propylene glycol (PG) followed by 1.837%w/w in Tween 80 and 0.5919%w/w in PEG 400. Maximum solubility of the drug is needed for preparing liquisolid compacts, as higher the solubility, the more the drug will be dissolved in the vehicle prior to the adsorption onto the carrier particles. As Propylene glycol showed greater solubility of the drug than the other two solvents, it was selected as the suitable solvent for preparing Glibenclamide liquisolid compacts in this study.

Application of new mathematical model for design of liquisolid system

The liquisolid technique as suggested by Spireas *et al*[9], states that the drug dissolved in a liquid vehicle is incorporated into carrier and coating materials having porous structure and closely matted fibres in its interior, is a phenomenon of both adsorption and absorption. Coating materials like Aerosil PH 102 have high adsorptive capacity and greater surface area and thus gives the liquisolid systems the desirable flow and compaction properties.

To calculate the required quantities of carrier and coating materials, the flowable liquid-retention potentials (Φ values) of the powder materials were used. Spireas *et al*[9] has given a mathematical model equation for Avicel PH 102 and Aerosil 200 in propylene glycol according to values of Phi (Φ) which is given below.

$$Lf = 0.16 + 3.31\ (1 / R) \quad \text{..... 1}$$

where 0.16 is the Φ value for Avicel PH 102 and 3.31 for Aerosil 200. Based on this equation, Liquid Load factor (Lf) was calculated by using different R values for all the formulations[10].

The quantity of carrier material (Q) required and the quantity of coating material (q) was calculated by using the following equation:

Amount of carrier material required (Q) = W/Lf 2

Amount of coating material required (q) = Q/R 3

where, W is the weight of the liquid medication, Lf is the liquid load factor, R is the coating and carrier material ratio. The formulation table according the above calculations is shown in Table No.2.

Evaluation of flowability and compressibility of liquisolid powder

Powders with angles of repose greater than 50° have unsatisfactory flow properties, whereas minimum angles close to 25° correspond to very good flow properties [11]. Table No.2 revealed that. All the tested liquisolid systems had a satisfactory flow according to the obtained results of measuring the angle of repose for each liquisolid system. The range was from 30.13 to 37.78˚.

The mean densities of liquisolid powders were found to be from 0.285 to 0.419 g/cm^3 for bulk density and from 0.385 to 0.511 g/cm^3 for tapped density. Hausner ratio and Carr's index were calculated from the density values. Compressibility is indirectly related to the relative flow rate, cohesiveness, and particle size of a powder. A compressible material will be less flowable, and powders with compressibility values greater than 20-21 % have been found to exhibit poor flow properties[12]. The results revealed that LS-9, LS-10, LS-11 and LS-12 had Hausner ratio of 1.16, 1.19, 1.16 and 1.18, respectively, which were less than 1.2 and is an indication for good flowability and the rest formulae had low flowability because it had Hausner ratio more than 1.2. Formulae LS 3 and LS 5 in addition to LS- 9 to LS-12 had Carr's index values of less than 21% which supports the fact that these formulations have good flow and compaction properties.

Evaluation of tablet

The mean hardness of the tablets ranged from 3.5 -5 kg/cm^2 and the values were shown in Table No.3. LS-6 showed the best result of friability test regarding to the loss of weight (0.006 %), while LS-5 had the largest weight loss (0.015%). It was found that the mean of the disintegration times for all the investigated tablets were less than 16 minutes, which meets the Pharmacopoeial requirements. All the investigated liquisolid tablets complied with the pharmacopoeial requirements with regard to their content uniformity, which was found to lie within the range of 96.12 to 101.2 %.

Compatibility studies

The IR spectrum obtained after the analysis is shown in Figure No.1,2. The IR spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. All the characteristic peaks of Glibenclamide were also found in the spectrum formulations. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the excipients.

Differential scanning calorimetry (DSC)

DSC studies were carried out to determine the interaction between drug and excipients in prepared liquisolid formulation and also to detect changes in the drug crystallinity. DSC thermograms of Glibenclamide and final liquisolid formulation system were represented in Figure No.3 and 4. The DSC thermogram of pure glibenclamide (Figure No.3) gave a sharp characteristic peak at temperature range 177.12°C corresponding to its melting temperature (Tm). This shows that Glibenclamide used was in pure form. The DSC thermogram of liquisolid system (Figure No.4) does not feature a sharp characteristic peak of Glibenclamide at 177.12°C which ensures the formation of drug solution in liquisolid formulation and thus confirms that the drug was molecularly dispersed in liquisolid system. Also there is a broad peak at 86.85˚C which corresponds to the evaporation of water associated with Avicel PH102 particles.

X-ray powder diffraction (XRPD)

Polymorphic changes in the drug are important since they might affect the dissolution rate and in turn bioavailability. So, it was necessary to study the polymorphic changes of Glibenclamide in liquisolid compacts. Figure No.5 and 6 shows the XRPD of pure drug and the liquisolid system Glibenclamide has sharp peaks at 18.84, 20.85, 19.40 and 22.94 at 2θ. Avicel PH 102 has a sharp diffraction peak at 24.29 at 2θ while the liquisolid powder had a sharp diffraction peak at 22.37 at 2θ which is evidence that Avicel PH 102 remains in its crystalline state. The

absence of characteristic peaks of Glibenclamide in the liquisolid system shows the conversion of drug to an amorphous or solubilized form. The absence of crystallinity in the liquisolid system is due to the solubilization of drug in the liquid vehicle.

***In vitro* dissolution study**

Cumulative release of 12 formulations conventional and marketed tablets are shown in Table No.4. Liquisolid compacts displayed more distinct *in-vitro* release characteristics than the conventional and marketed drug. Among all, LS-3 showed higher release rate (91.35%) at the end of the 60th min. Conventional tablet and marketed tablet showed only 35.73% and 33.22% cumulative release. From Figure No.7 it was confirmed that at 10 min LS-3 had the highest drug release 57.73% compared with 15.75% for the conventional tablet. Since the liquisolid compacts contain a solution of the drug in non-volatile vehicle used for preparation of the liquisolid compacts, the drug surface available for dissolution is tremendously increased. In essence, after disintegration, the liquisolid primary particles suspended in the dissolving medium contain the drug in a molecularly dispersed state, whereas the directly compressed compacts are merely exposed micronized drug particles. Therefore, in the case of liquisolid compacts, the surface area of drug available for dissolution is much greater than that of the directly compressed compacts.

According to Noyes and Whitney, the drug dissolution rate (DR) is directly proportional not only to the concentration gradient (Cs-C) of the drug in the stagnant diffusion layer, but also to its surface area (S) available for dissolution[13]. Moreover, since all dissolution tests for both Glibenclamide preparations were carried out at a constant rotational paddle speed (50 r/min) and identical dissolving media, it is assumed that the thickness (h) of the stagnant diffusion layer and the diffusion coefficient (D) of the drug molecules transported through it remain almost identical under each set of dissolution conditions. Therefore, the significantly increased surface area of the molecularly dispersed Glibenclamide in the liquisolid compacts may be principally responsible for their higher dissolution rates. The consistent and higher dissolution rate displayed by liquisolid compacts will improve the absorption of drug from the GI tract[14].

This can be explained by the dissolved drug in the liquid medication as follows:

$$FM=C_L/C_D \quad \text{..... 4}$$

where FM is the fraction of molecularly dispersed or dissolved drug in liquid medication of the prepared liquisolid formulation, C_L is the saturation solubility of Glibenclamide in the liquid vehicle and C_D is the drug concentration in the liquid medication. According to Spireas et al, FM value cannot exceed unity[15]. The saturation solubility of Glibencamide in PG is 2.7407%w/w (Table No.2), by applying Eq. (4), it can be calculated that 52.4% of the drug was solubilised in LS-3, 27.40% of Glibenclamide was solubilised in LS-6, 18.27% of Glibenclamide was solubilised in LS-9 and 13.703%w/w of Glibenclamide in LS-12. The higher the drug concentration in a liquisolid formulation, the lower will be the amount of drug solubilised in the liquid vehicle. Apparently, LS-3 which has 52.41% of drug available in solubilised form promote higher dissolution rate than LS-6, LS-9 and LS-12. It was proven that FM is directly proportional to the drug dissolution rate. The FM values of such liquisolid formulations were listed in Table No.1. Another explanation for this phenomenon is that high concentration of the drug could precipitate within the silica (Aerosil) pores; thus, drug dissolution rate would be reduced. The potential of Glibenclamide to precipitate within the silica pores is depending on the solubility of the drug in the solvent, the degree of saturation of the drug solution or the interactions between drug and excipients.

Effect of powder excipient ratio (R) on drug release

From the obtained results, it was clear that there exists a relationship between the powder excipient ratio and the *invitro* release of Glibenclamide from liquisolid tablets. The powder excipient ratio was directly proportional to the *in vitro* release i.e., when the powder excipient ratio increased, the release will increase. This finding was confirmed from the following results. Formulae LS-1, LS-2, and LS-3

were having R value 10, 20, 30, and the cumulative percent released were 85.97, 88.62, and 91.35%, respectively. Also, formulae LS-4, LS-5, and LS-6 were having R value equal to 10, 20, 30, and the cumulative percent released of them were 77.47, 80.34, and 83.68%, respectively. This may be attributed to the high microcrystalline cellulose content where Avicel PH 102 functions as a swellable disintegrant. In addition, the highly hydrophilic characteristic of microcrystalline cellulose could increase the wetting of Glibenclamide and enhance its dissolution.

Stability studies

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, and to establish a re-test period for the drug substance or a shelf life for the drug product and recommended storage conditions. Here the tablets were loaded at accelerated condition at $40^0C \pm 2^0C$/75% RH±5%RH in a stability chamber. Samples were withdrawn at initial, 30, 60, and 90 days and evaluated for drug content, dissolution and disintegration time. The result showed that storage at 40 ºC had no effect on the drug content, disintegration time and dissolution time. This indicates that the technology is a promising technique to enhance the release rate without having any physical stability issues.

Table No.1: Formulation chart

S.No	Formulation	Drug conc (%w/w)	R	Lf	Q	q	Fm
1	LS-1	5	10	0.491	213.85	21.38	0.54814
2	LS-2		20	0.325	323.07	16.15	0.54814
3	LS-3		30	0.270	388.88	12.96	0.54814
4	LS-4	10	10	0.491	224.03	22.40	0.27407
5	LS-5		20	0.325	338.46	16.92	0.27407
6	LS-6		30	0.270	407.407	13.58	0.27407
7	LS-7	15	10	0.491	234.21	23.42	0.1827
8	LS-8		20	0.325	353.84	17.69	0.1827
9	LS-9		30	0.270	425.93	14.19	0.1827
10	LS-10	20	10	0.491	244.39	24.43	0.13703
11	LS-11		20	0.325	369.23	18.46	0.13703
12	LS-12		30	0.270	444.44	14.81	0.13703

R - Excipient ratio, Q - weight of carrier, q - weight of coating material, Fm - fraction of molecularly dispersed drug.

Table No.2: Post Compression Parameters

S.No	Formulations	Angle of repose	Densities (g/cm^3)		Hausners ratio	Carr's index
			BULK	TAP		
1	LS-1	36.53	0.298	0.385	1.29	22.5
2	LS-2	34.21	0.312	0.403	1.31	22.6
3	LS-3	34.13	0.364	0.453	1.24	19.6
4	LS-4	32.59	0.285	0.425	1.49	32.9
5	LS-5	34.95	0.416	0.511	1.22	18.6
6	LS-6	33.68	0.321	0.496	1.54	35.2
7	LS-7	37.78	0.357	0.473	1.32	24.52
8	LS-8	35.17	0.364	0.463	1.27	21.38
9	LS-9	36.62	0.419	0.490	1.16	14.48
10	LS-10	33.47	0.395	0.473	1.19	16.4
11	LS-11	33.18	0.412	0.482	1.16	14.52
12	LS-12	30.13	0.407	0.483	1.18	15.73
13	CT	32.65	0.423	0.471	1.11	10.19

Table No.3: Precompression Parameter

S.No	Formulations	Average Weight (mg)	Hardness (kg/cm^2)	Friability (%)	Disintegration time (min)	Content uniformity (%)
1	LS-1	253±3	4	0.007	3.20	96.5
2	LS-2	251±9	4.5	0.009	1.50	96.7
3	LS-3	250±5	5	0.013	1.46	99.3
4	LS-4	248±1	3.5	0.015	3.45	98.6
5	LS-5	246±2	5	0.008	2.45	99.7
6	LS-6	253±4	5	0.006	2.10	97.3
7	LS-7	250±1	3.5	0.019	4.21	101.2
8	LS-8	249±5	4	0.007	4.57	98.5
9	LS-9	250±2	5	0.014	5.32	99.1
10	LS-10	250±6	3	0.017	12.30	96.12
11	LS-11	254±4	4	0.006	9.40	96.6
12	LS-12	255±2	5	0.008	7.25	98.7
13	CT	250±1	3.5	0.015	20.10	97.2
14	MT	10±5	4	0.009	18.15	96.9

LS-Liquisolid tablet, CT- Conventional tablet, MT- Marketed tablet

Table No.4: Percentage of drug release from liquisolid tablets, conventional and marketed tablets

S.No	Formulation	Time (hrs)					
		10	**20**	**30**	**40**	**50**	**60**
1	LS-1	48.56	59.73	65.19	72.32	81.92	85.97
2	LS-2	52.92	61.43	67.66	76.96	83.64	88.62
3	LS-3	57.73	65.94	69.17	78.53	86.72	91.35
4	LS-4	25.96	37.52	48.39	59.38	70.37	77.47
5	LS-5	27.12	40.35	51.55	69.75	78.41	80.34
6	LS-6	29.19	42.72	55.69	71.33	80.53	83.68
7	LS-7	20.79	32.13	40.59	54.24	63.95	71.84
8	LS-8	21.98	35.63	43.74	56.19	67.33	74.57
9	LS-9	25.96	39.52	48.42	59.37	70.69	76.38
10	LS-10	12.13	27.95	32.31	41.82	53.73	65.31
11	LS-11	10.31	29.33	37.53	42.29	57.54	67.95
12	LS-12	14.73	32.64	41.30	48.73	60.14	69.77
13	**Pure Drug**	15.75	27.50	31.91	33.32	35.20	35.73
14	**Marketed**	17.52	26.06	27.21	30.28	31.14	33.22

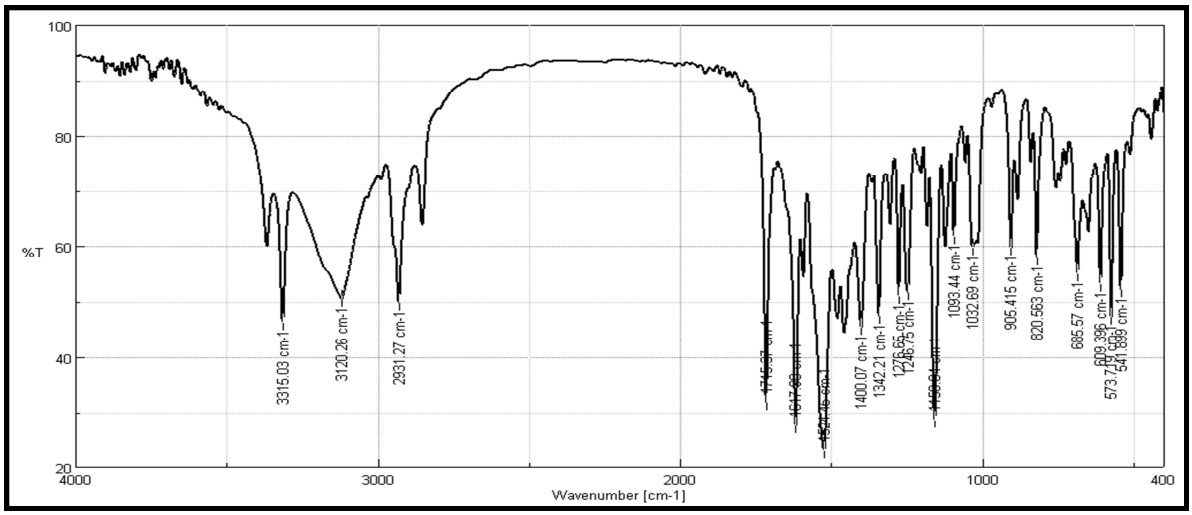

Figure No.1: IR of Glibenclamide

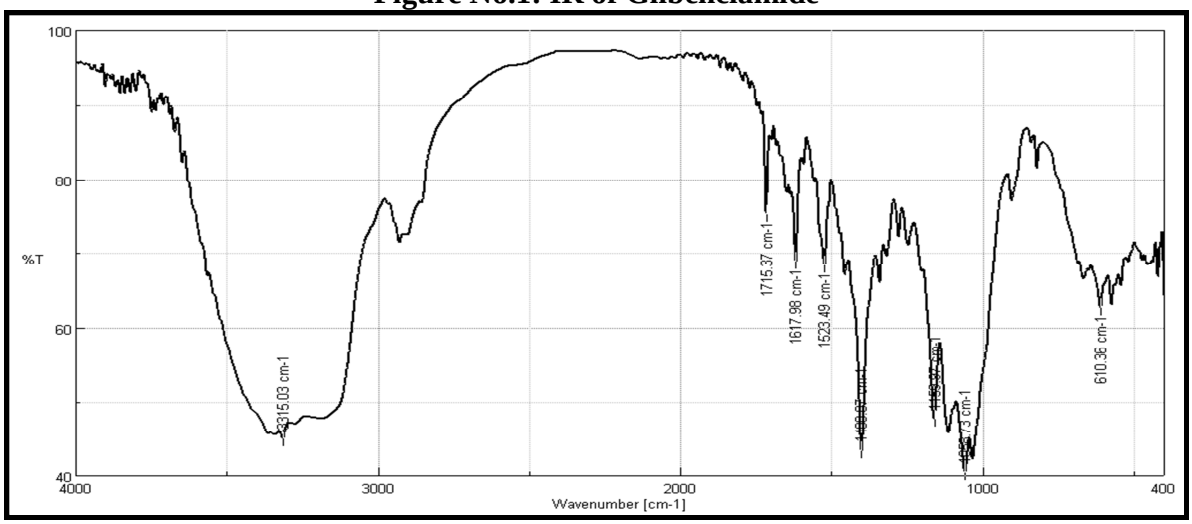

Figure No.2: IR of Liquisolid Formulation

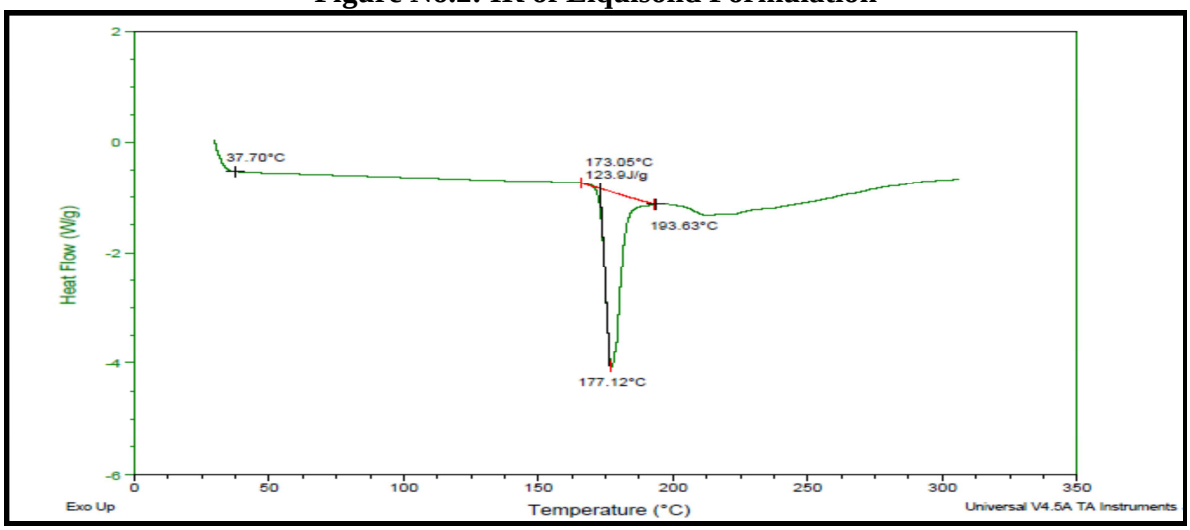

Figure No.3: DSC of Glibenclamide

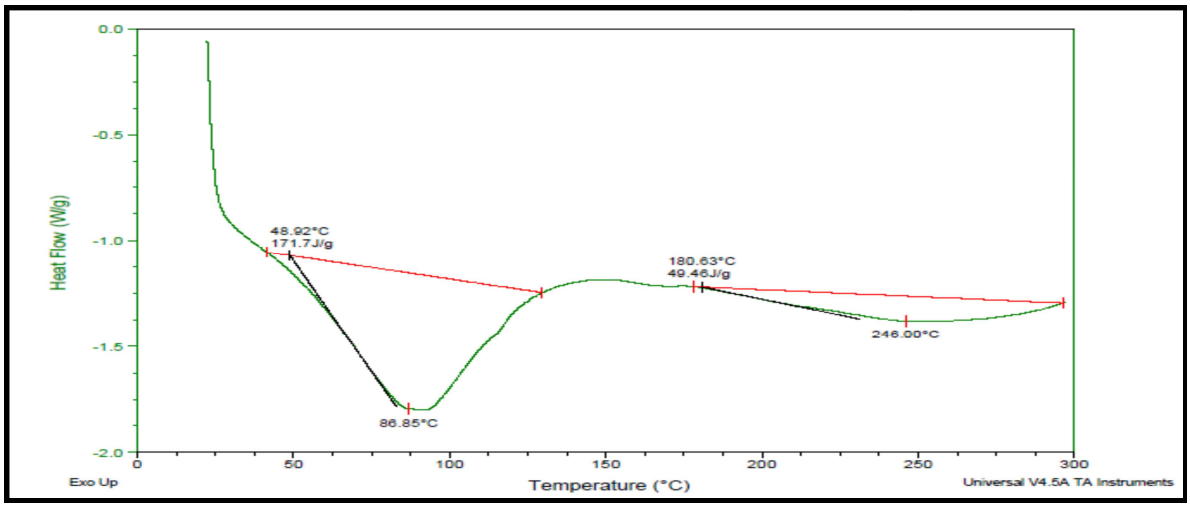

Figure No.4: DSC of Liquisolid System

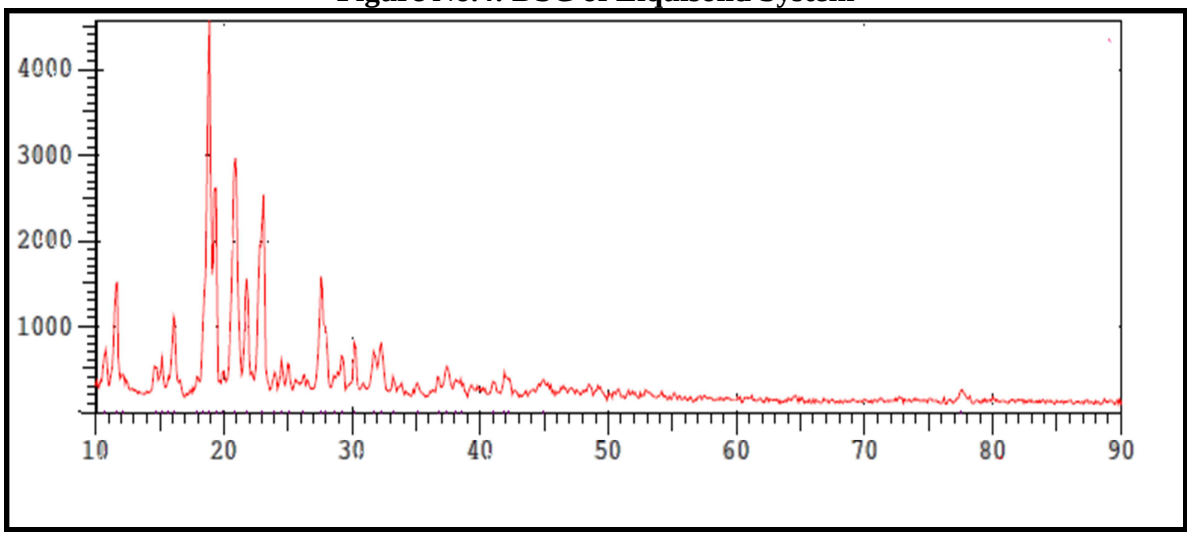

Figure No.5: X-RAY diffractogram of Glibenclamide

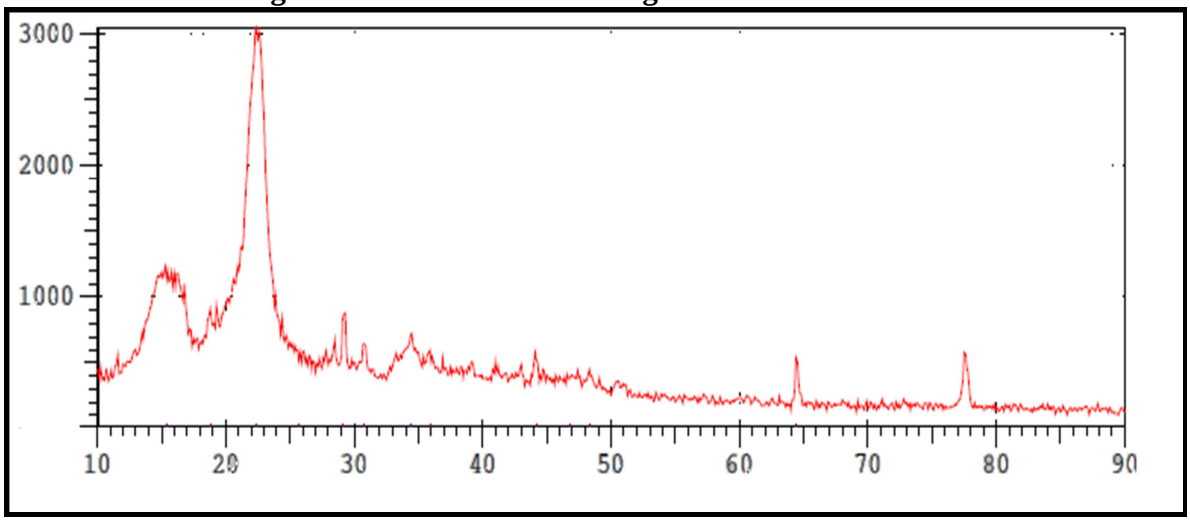

Figure No.6: X-RAY diffractogram of Liquisolid system

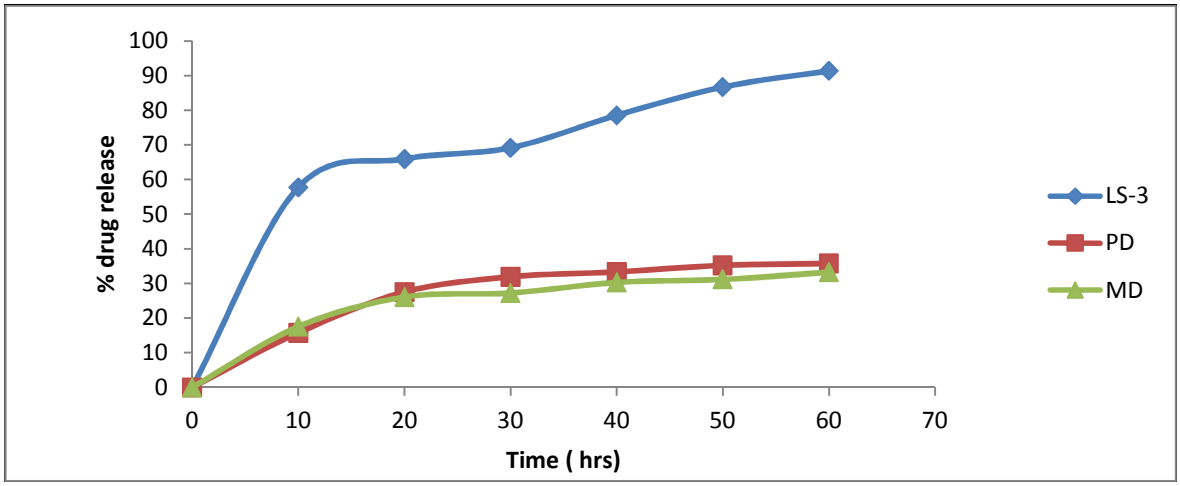

Figure No.7: Dissolution profile of best formulation (LS-3) conventional and marketed tablet

CONCLUSION

Solubility is one of the major factors which affect the *in vivo* performance of the drug. Hence, in this study, liquisolid technique was chosen to enhance the dissolution properties of Glibenclamide. The Glibenclamide liquisolid compacts were prepared by using propylene glycol as the non-volatile liquid vehicle. Avicel PH 102 and Aerosil 200 were used as the carrier and coating material, respectively. The flow properties of Glibenclamide liquisolid compacts showed an acceptable flowability. The hardness, friability, weight variation and disintegration tests were within acceptable limit. The *in vitro* dissolution study confirmed enhanced drug release from liquisolid compacts compared with conventional and marketed tablet. XRPD studies showed complete inhibition of crystallinity in the Glibenclamide liquisolid compacts suggesting that the drug has been transformed into amorphous form having more solubility than the parent drug. The DSC study also supported the findings of XRPD analysis and confirmed the absence of any interaction between the drug and excipients used in the preparation of Glibenclamide liquisolid compacts. The liquisolid tablets having drug concentration of 5%w/w (LS-3) with Lf value of 0.270 and R value of 30, was chosen as best formulation among the twelve batches, in terms of faster disintegration time, superior dissolution profile and acceptable tablet properties.

ACKNOWLEDGEMENT

We are thankful to Managing Director of Capplin point, Pondicherry for Providing Glibenclamide, Avicel PH 102 and Aerosil 200.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

REFERENCES

1. Yadav V B, Yadav A V. enhancement of solubility and dissolution rate of BCS class II pharmaceuticals by nonaquious granulation technique, *IJPRD*, 1, 2008, 1-12.
2. Nagabandi V K, Ramarao T, Jayaveera K N. Liquisolid compacts A novel approach to enhance bioavailability of poorly soluble drugs, *IJPBS*, 1, 2011, 89-102.
3. Remington. The science and practice of pharmacy, 21st edition, *Wolters Kluwer Health, New Delhi*, 1454.
4. Kulkarni A S, Aloorkar N H, Mane M S. Liquisolid System A Review, *Int Jour Pharm Sci*, 3, 2010, 795-802.
5. Yadav V B. Improvement of solubility and dissolution of indomethacin by liquisolid and compaction granulation technique, *JPSR*, 1, 2009, 44-51.
6. Herbert A Lieberman, Leon Lachman, Joseph B Schwartz. Pharmaceutical dosage forms Tablets, 2nd edition, Vol.1, 99.

7. Arunkumar N, Deccarman M, Rani C. Preparation and solid state characterization of Atorvastatin Nanoparticles, *IJP*, 1, 2010, 39-43.
8. Patel T B, Patel L D. Formulation and characterization of solid dispersions containing glibenclamide, *Int J Pharmacy Pharm*, 2, 2010, 138-141.
9. Spireas S. Liquisolid system and methods of preparing same, U.S. Patent 6423339B1, 2002.
10. Spireas S, Wang T, Grover R. Effect of powder substrate on the dissolution properties of Methchlorothiazide liquisolid compacts, *Drug Dev Ind Pharm*, 25, 1999, 163-168.
11. Martin A, Bustamante P, Chun A H C. "Physical Pharmacy Physical Chemical Principles in the Pharmaceutical Sciences" *4th Ed, Martin A. (ed.), Lea and Febiger, Philadelphi,* 1993, 284-323.
12. Carr R L. Powder density equations, *Chem Eng*, 72, 1965, 163-168.
13. Fahmy R H, Kassem M A. Enhancement of famotidine dissolution rate through liquisolid tablets formulation in vitro and in vivo evaluation, *Eur J Pharm Biopharm*, 69, 2008, 993-1003.
14. Javadzadeh Y, Siahi M R, Asnaashari N, Nokhodchi A. Liquisolid technique as a tool for enhancement of poorly water-soluble drugs and evaluation of their physicochemical properties, *Acta Pharm*, 57, 2007, 99-109.
15. Spireas S, Sadu S, Grover R. *In vitro* release evaluation of hydrocortisone liquisolid tablets, *J Pharm Sci*, 87, 1998, 867-872.

Please cite this article in press as: N. Arun Kumar *et al.* Enhancement of Dissolution Rate of Glibenclamide using Liquisolid Technique, *International Journal of Research in Pharmaceutical and Nano Sciences*, 4(4), 2015, 206 - 216.