Research Article

Formulation and Evaluation of Glyburide Liquisolid Compacts

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ABSTRACT

The intention of present research is to enhance the dissolution rate of water insoluble drugs like Glyburide. It is a poorly soluble drug and the rate of its oral absorption is often controlled by the dissolution rate in the gastrointestinal tract. There are several techniques to enhance the dissolution of poorly soluble drugs, in which the liquisolid compacts is a promising technique. Different formulations were prepared by using different vehicles and carriers and aerosil is used as the coating material. The empirical method as introduced by Spireas and Bolton was applied to calculate the amounts of coating and carrier materials required to prepare glyburide liquisolid tablets. Based upon this method, improved flow characteristics and hardness of the formulation has been achieved by changing the proportion of carrier and coating material ratio. *In vitro* dissolution profiles of the liquisolid formulations were studied and compared with conventional formulation in 0.1N HCl. It was found that liquisolid tablets formulated with PEG 400 and Avicel pH102 produced high dissolution profile and they showed significant higher drug release rates than conventional tablets due to increase in wetting properties and surface of drug available for dissolution. Drug-excipient interaction studies showed that there is no interaction between the drug and excipients. In conclusion, development of glyburide liquisolid tablets is a good approach to enhance the dissolution rate which increases bioavailability.

Keywords: Liquisolid compacts, dissolution rate, glyburide, carrier, coating material

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INTRODUCTION

From the last three decades, the major challenge to pharmaceutical scientists is to enhance the dissolution profile, absorption efficiency and bioavailability of water insoluble drugs. When considering oral administration, drug release from its pharmaceutical form and its dissolution into gastrointestinal fluids generally precedes absorption and systemic availability, an increasing number of newly developed drug candidates in pre-clinical development phases present poor water-solubility characteristics, there is a great need for formulation approaches to overcome this factor [1]. It is estimated that 40% of all newly developed drugs are poorly soluble or in-soluble in water. In addition, up to 50% of orally administered drug compounds suffer from formulation problems related to their low solubility and high lipophilicity [2]. Bioavailabilities of poorly water-soluble drugs are limited by their solubility and dissolution rate [3]. Oral drug delivery is the simplest and easiest way of administering drugs because of the greater stability, smaller bulk, accurate dosage and easy production [4]. Many drugs show incomplete absorption from GIT due to its poor solubility. Bioavailability of BCS-II drugs are limited by their solubility and dissolution rate [5].

The technique of "**liquisolid compacts**" is a new and promising addition towards such a novel aim. The active ingredient in a solid dosage form must undergo dissolution before it is available for absorption from the gastrointestinal tract. The dissolution rate is often the rate determining step in drug

absorption. Several researchers have shown that the liquisolid technique is the most promising method for promoting dissolution rate of poorly water soluble drugs [9, 10]. Liquisolid compacts prepared by using different solvents which dissolves the poorly soluble drug and gives better bioavailability. It has been observed that the drug release superiority of liquisolid tablets are inversely proportional to the aqueous solubility of the contained drug [11]. Liquisolid system is a novel technique developed [12, 13]. Liquid medication can converted into dry looking, non-adherent, free flowing, readily compressible powder by a simple blending with selected powder excipients referred to as the carrier and coating material, such as cellulose, starch, lactose may be used as carriers coating materials[13].

Liquisolids are categorized as, powdered drug solutions, powdered drug suspensions and powdered liquid drugs. First two may be produced from the conversion of drug solutions or drug suspensions and the latter from the formulation of liquid drugs into liquisolid system [14].

Theoretical considerations in powdered solution formulations were flowable liquid-retention potential (Φ value) of a powder. Absorption of a liquid by a powder material occurs when the absorbate molecules diffuse inside the absorbent and are eventually captured and held by the powder particles within their bulk [15].

The flowable liquid-retention potential (Φ value) of a powder material. The Φ value is defined as the maximum weight of liquid, W_{liquid} that can be retained per unit weight of the sorbent, W_{solid}, yielding a mixture with acceptable flowability;

$$\Phi = W_{liquid}/W_{solid} \quad (1)$$

This volume is dependent on the flowable liquid retention potential (Φ) of the carrier material. The remaining liquid, $V_{L,}$ is uniformly distributed and adsorbed onto the internal and external surfaces of the particles, forming a layer of certain thickness, h, thus, mathematically, the volume distribution can be expressed as

$$V = V_{\Phi} + V_L \quad (2)$$

If only a specific volume (V_{Φ}) of liquid is incorporated into the carrier material, the liquid would be absorbed in the interior of the particles without significantly wetting their surface, and consequently, the powder would be dry and free flowing[16].

This portion of the liquid is represented by V_{Φ}, since it depends on the flowable liquid retention potential, Φ, and the quantity, Q, of the carrier material used. Since $W_{solid} = Q$ and $W_{liquid} = V_{\Phi}\rho$, where ρ is the density of the liquid incorporated into the carrier material, Equation (1) can be expressed as

$$\Phi = V_{\Phi}\rho / Q \quad (3)$$

This can be rearranged to give,

$$V_{\Phi} = Q\Phi / \rho \quad (4)$$

In other words the volume V_L must be equal to a volume $V_{\Phi,}$ of the liquid which is a quantity, q, of the coating particles can retain and yet maintain acceptable flowability, therefore Equation (2) can be rewritten as

$$V_L = V_{\Phi} + V_{\varphi} \quad (5)$$

By definition, $V_{\varphi,}$ represents the same characteristics of the coating material as represented by V_{Φ}, for the carrier material in Equation (4). Using the same line of reasoning as was used in deriving Equation (3), it can be concluded that

$$V_{\varphi} = q\varphi / \rho \quad (6)$$

Where φ is the flowable liquid retention potential of the coating material. Thus, $V_{\varphi}$is dependent on the flowable liquid retention potential, φ, and quantity, q, of the coating material [17]. Substituting the values of V_{φ}(Equation 4) and v_{φ} (Equation 6) in Equation 5 we obtain

$$V = (Q\Phi) + (q\varphi) / \rho \quad (7)$$

Equation (7) can be rearranged in terms of Q, the quantity of the carrier material required to retain a specific volume V, of the liquid as

$$Q = (V_{\rho}) - (q\varphi) / \Phi \quad (8)$$

Similarly, Equation (7) can be rearranged in terms of q, the quantity of coating material needed to cover the wet carrier particles effectively, as

$$q = (V\rho) - (Q\Phi) / \varphi \quad (9)$$

Excipient Ratio (R) In some cases, however, the dosage formulation may require a specific ratio of carrier/ coating material in the final powder admixture. This ratio may be termed the excipient ratio, R, and written as

$$R = \frac{\text{Amount of carrier material (Q)}}{\text{Amount of coating material (q)}} \quad (10)$$

For such cases, Equations (7, 8, and 9) can be modified to include the excipient ratio, R. Combining Equations (7, 10), and considering a predetermined quantity, Q, of the carrier material, we obtain

$$V = Q(R\Phi + \varphi) / R\rho \quad (11)$$

Furthermore, solving for Q and considering a predetermined volume V of liquid, Equation (11) will become

$$Q = V\rho R / (R\Phi) + \varphi \quad (12)$$

Accordingly, combining Equations (7, 10) and considering a predetermined quantity, q, of the coating material, one obtains

$$V = q (R\Phi + \varphi) / \rho \quad (13)$$

For a predetermined volume V of drug solution Equation (13) can be solved for q to give

$$q = V\rho / (R\Phi + \varphi) \quad (14)$$

The developed mathematical expressions were shown to such liquisolid formulations of clofibrate could not be compressed into tablets of satisfactory hardness [18, 19]. It has been concluded that this phenomenon occurred due to respective amounts of liquid drug being squeezed out of the liquisolid tablet during compression. For this reason, there is a need for a method of producing on an industrial scale, acceptably flowing and, simultaneously, compressible liquid/powder admixtures of liquid medications. The following applications of liquisolid techniques were [20] enhancement of solubility and dissolution, flowability and compressibility and enhancement of bioavailability [21].

MATERIALS AND METHODS:

The following materials were procured from different sources Glyburide, Avicel PH 101 & 102, Hydroxypropyl methylcellulose, purchased fromMSN Laboratories, Hyderabad, India; PEG 400, Propylene Glycol from CDH, Delhi, India;Starch, Aerosol, magnesim stearate, Talc &Tween 80 from S.D Fine chemicals (P) Ltd, Mumbai, India.

EXPERIMENTAL METHODOLOGY:

Preparation of Glyburide Standard Graph: Accurately weighed amount of 100 mg of Glyb was dissolved in 5 ml of methanol and the volume was made up to 100 ml with methanol this is primary stock solution. From this primary stock solution 10 ml was transferred to another volumetric flask made up to 100 ml with 0.1 N HCl this is secondary stock solution, from this secondary stock solution different concentrations respectively 10mcg/ml, 20mcg/ml, 30mcg/ml, 40mcg/ml, 50 mcg/ml were prepared. The absorbance was measured at 242nm by using a UV-Visible spectrophotometer.

Preformulation Studies: Solubility studies: For the selection of best non volatile solvents solubility studies are used, in this procedure, pure drug was dissolved in different non volatile solvents (propylene glycol, Tween 80 and polyethylene glycol 400) and water. Excess amount of pure drug was adding to the above solvents. From this obtained saturation solution were shaking on the rotary shaker for 48 hours at 25 ^{0}C under constant vibration. After this period the solutions were filtered, diluted with distilled water (at least 1000 times) and analyzed by UV-spectrophotometer at a wavelength of 242 nm. Three determinations were carried out for each sample to calculate the solubility of Glyburide[22].

Calculation of loading factor (L_f): Loading factors were calculated for different carriers, using various solvents. By using L_f = W/Q formula (W: Amount of liquid medication and Q: Amount of carrier material), the drug loading factors were obtained and used for calculating the amount of carrier and coating materials in each formulation. The results showed that if the viscosity of the solvent is higher, lower amounts of carrier and coating materials were needed to produce flowable powder [23].

Pre-Compression Properties

Angle of repose: The angle of repose physical mixtures of liquisolid compacts were determined by fixed funnel method. The accurately weighed physical mixtures of liquisolid compacts were taken in a funnel. The height of the funnel was

adjusted in such a way that the tip of the funnel just touches the apex of the heap of the powder. The powder was allowed to flow through the funnel freely into the surface. The height and diameter of the powder cone was measured and angle of repose was calculated.

Tan θ= h/r

Where, θ is the angle of repose; h is the height in cm; r is the radius in cm

Bulk Density: The loose bulk density and tapped density were determined by using bulk density apparatus. Apparent bulk density was determined by pouring the blend into a graduated cylinder. The bulk volume (V_b) and weight of the powder (M) was determined. The bulk density was calculated using the formula

$$D_b = M/V_b$$

where, M is the mass of powder; V_b is bulk volume of powder

Tapped Density: The measuring cylinder containing a known mass of blend was tapped for a fixed time. The minimum volume (V_t) occupied in the cylinder and the weight (M) of the blend was measured. The tapped density was calculated using the formula

$$D_t = M/V_t$$

Where, M is the mass of powder; V_t is tapped volume of powder

Carr's Index (%): The compressibility index has been proposed as an indirect measure of bulk density, size and shape, surface area, moisture content and cohesiveness of material because all of these can influence the observed compressibility index. The simplest way for measurement of free flow of powder is Carr's Index, a indication of the ease with which a material can be induced to flow is given by Carr's index (CI) which is calculated as follows:

CI (%) = [(Tapped density – Bulk density) / Tapped density] x 100

Preparation of Liquisolid Tablets

Preparation of drug solution: For the preparation of liquisolid compacts of Glyburide, a non-volatile solvent is chosen for dissolving the drug. Liquisolid preparations containing drug and different liquid vehicles to prepare the liquid medication, MCC or Avicel pH 101/102 as carrier and Aerosil as the coating material is selected for the preparation of liquisolid compacts. According to solubility of Glyburide desired quantities of drug and vehicle were accurately weighed in a beaker and then stirred with constantly, until a homogenous drug solution was obtained. Selected amounts (W) of the resultant liquid medication were incorporated into calculated quantities of carrier contained in a mortar; same procedure is repeated for all formulations [24].

The mixing procedure was conducted in three stages. During the first stage, the system was blended at an approximate mixing rate of one rotation/sec for approximately one minute in order to evenly distribute the liquid medication into the powder. In the second mixing stage, calculated quantities of coating material was added to the system and blended for 2 min. the liquid/powder admixture was evenly spread as a uniform layer on the surfaces of the mortar and left standing for approximately 5min to allow the drug solution to be absorbed in interior of the powder particles. In the third stage, the powder was scraped off the mortar surfaces by means of aluminum spatula, then producing the final liquisolid formulation to be compressed.

Evaluation of Liquisolid Tablets [25]

Weight variation: To study the weight variation, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the

drug content uniformity. The percent deviation was calculated using the following formula.

% Deviation = (Individual weight – Average weight / Average weight) × 100

Tablet Hardness: Hardness of tablet is defined as the force applied across the diameter of the tablet in order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. For each formulation, the hardness of 6 tablets was determined using Monsanto hardness tester and the average is calculated and presented with standard deviation.

Disintegration test: Six tablets were taken randomly from each batch and placed in USP disintegration apparatus baskets Apparatus was run for 10 minutes and the basket was lift from the fluid, observe whether all of the tablets have disintegrated.

Friability: It is the measurement of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. Preweighed tablets (20 tablets) were placed in the friabilator. The tablets were rotated at 25 rpm for 4 minutes (100 rotations). At the end of test, the tablets were re weighed, loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = $[(W_1 – W_2) / W_1] \times 100$

Where W_1 = Initial weight of 20 tablets; W_2 = Weight of the 20 tablets after testing

Content of uniformity

i. **Standard Preparation:**About 20 mg of Glyburide was weighed accurately and transferred into a 50 ml volumetric flask. It was dissolved, and then it was suitably diluted and made up to volume with 7.4 pH phosphate buffer and mixed.

ii. **Sample Preparation:** Five tablets were weighed and finely powdered. An accurately weighed portion of the powder equivalent to about 20 mg of Glyb was transferred into a 50 ml volumetric flask and was dissolved in 7.4 pH phosphate buffer. It was sonicated for 30 min and was filtered through 0.45 µ membrane filter. It was then diluted suitably up to the mark.

iii. **Procedure:** The absorbance of both the standard preparation and the sample preparation, after suitable dilutions were measured in a UV-Visible Spectrophotometer at 242 nm using 7.4 pH phosphate buffer. The same procedure was repeated for 3 times.

Calculation: The amount of Glyb present in tablet can be calculated using the formula**:**

$A_t/A_s \times S_w/20 \times 100/S_t \times A_v$

Where,

A_t = Absorbance due to sample preparation;

A_s=Absorbance due to standard preparation.

S_w = Weight of Glyb working standard (mg);

S_t = Weight of Glyb tablet (mg).

A_v = Average weight of tablet (mg).

Dissolution test of Glyburide liquisolid tablets: Drug release from Glyburide liquisolid tablets was determined by using dissolution test United States Pharmacopoeia (USP) type II (paddle).

Dissolution medium : 0.1N HCl; **Volume:** 900 ml; Temperature **:** at $37^0C \pm 0.5^0C$

Speed : 50 rpm.

Procedure: 5ml aliquots of dissolution media were withdrawn each time at suitable time intervals (5, 10, 15, 30, 45, 60 and 120 minutes.) and replaced with fresh medium. After withdrawing, samples were filtered and analyzed after appropriate dilution by using Double beam UV-spectrophotometer. The concentration was calculated using standard calibration curve.

Calculation of dissolution parameter: Cumulative percent drug release was plotted as a function of time and percent drug release in 10 minutes (Q_{10}) was calculated. Initial dissolution rate (IDR) was calculated as percentage dissolved of drug over the first 10 minutes per minute.

Dissolution efficiency (DE) was calculated from the area under the dissolution curve at time t (measured using the trapezoidal rule) and expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time (10). Relative dissolution rate (RDR) is the ratio between amount of drug dissolved from optimized formulation and that dissolved from the conventional formulation at 10 minutes.

Formulation of Glyburide (Glyb) Liquisolid Tablets

Formulation	Glyburide	PG	PEG 400	Tween 80	Avicel PH 101 (mg)	Avicel PH 102 (mg)	Starch (mg)	HPMC (mg)	Aerosil (mg)	Total tablet Weight (mg)
F1	5	5	-	-	320	-	-	-	20	350
F10	5	-	-	5	-	320	-	-	20	350
F11	5	-	-	5	-	-	320	-	20	350
F12	5	-	-	5	-	-	-	320	20	350
F2	5	5	-	-	-	320	-	-	20	350
F3	5	5	-	-	-	-	320	-	20	350
F4	5	5	-	-	-	-	-	320	20	350
F5	5	-	5	-	320	-	-	-	20	350
F6	**5**	**-**	**5**	**-**	**-**	**320**	**-**	**-**	**20**	**350**
F7	5	-	5	-	-	-	320	-	20	350
F8	5	-	5	-	-	-	-	320	20	350
F9	5	-	-	5	320	-	-	-	20	350

RESULTS AND DISCUSSION

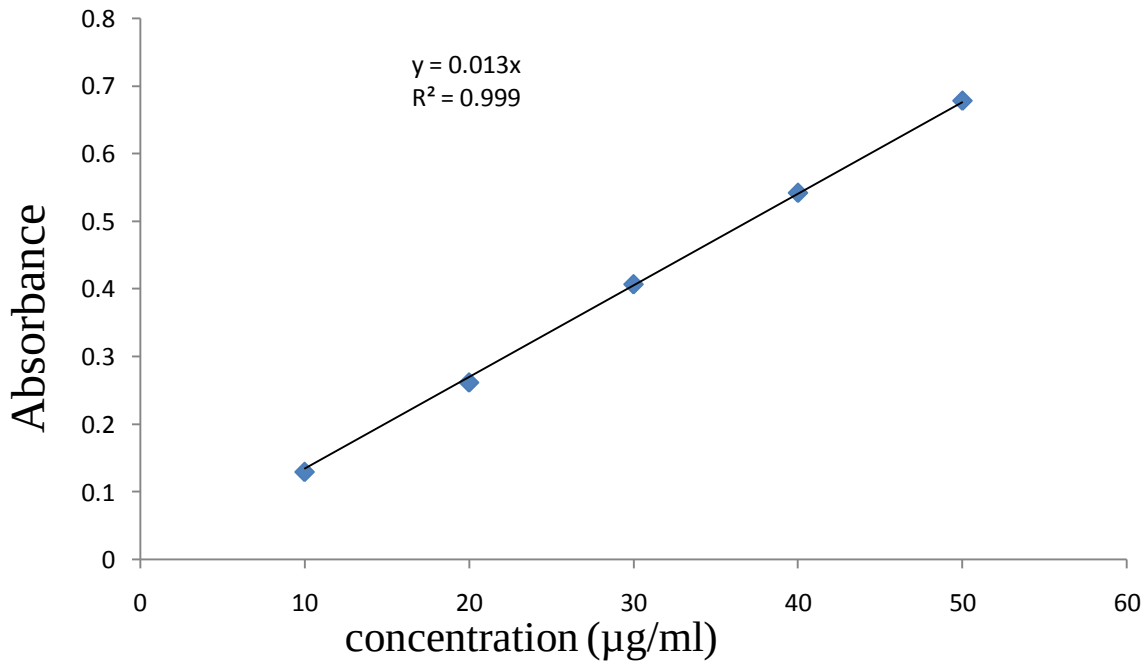

Figure 1: Standard Graph of Glyburide

Table 1: Solubility Studies of Glyburide in non- volatile Solvents

S. No	Solvent	Solubility(µg/ml)
1	PEG 400	84.5
2	PG	45.3
3	Tween-80	28.9
4	Distilled water	12.6

Calculation of loading factor (L_f)

Loading factors were calculated for different carriers, using various co-solvents. By using L_f = W/Q formula (W: Amount of liquid medication and Q: Amount of carrier material), the drug loading factors were obtained and used for calculating the amount of carrier and coating materials in each formulation [26].

Pre compression evaluation studies for Glyburide liquisolid compacts [27]

Powder flow is a complicated matter and is influenced by so many interrelated factors; the factors' list is long and includes physical, mechanical as well as environmental factors [6]. Therefore, in our study, because of the subjective nature of the individual types of measurements as indicators of powder flow, three flow measurement types were employed; the angle of repose, carr's index. The apparent bulk density and tapped bulk density values ranged from 0.324 to 0.337 and 0.382 to 0.414 respectively. The results of angle of repose and compressibility index (%) ranged from 26.72±3.15 to 30.96±1.04 and 11.70 to 20.85 respectively. The results of angle of repose (<40) and compressibility index (<22) indicates fair to passable flow properties of the powder mixture. From these results formulations with Avicel pH102 showed comparatively good flow characteristics (**Table 2**).

Table 2: Evaluation of pre-compression Parameters of Glyburide Formulations

Formulation	Angle of Repose*(^{0})	Bulk Density (g/cc)	Tapped Density (g/cc)	Carr's Index (%)
F1	27.87±1.56	0.324	0.382	15.03
F2	28.52±2.19	0.328	0.414	20.85
F3	31.36±0.79	0.336	0.388	13.23
F4	26.72±3.15	0.333	0.407	18.18
F5	30.22±0.57	0.330	0.412	19.71
F6	26.90±0.70	0.336	0.392	14.43
F7	29.23±2.74	0.324	0.382	15.32
F8	28.95±3.51	0.328	0.389	15.63
F9	30.96±1.04	0.335	0.393	14.73
F10	28.84±3.37	0.337	0.382	11.70
F11	29.59±3.12	0.330	0.382	13.55
F12	27.54±3.76	0.325	0.398	18.40

Data Represents Mean ± SD (n=3)

Post compression evaluation studies for Glyburide liquisolid compacts [28]

In weight variation test, the pharmacopoeial limit for the tablets of not more than 5% of the average weight. The mean hardness of each liquisolid formula was determined and proving that all the liquisolid tablet formulae had acceptable hardness. All the liquisolid tablets had acceptable friability as none of the tested formulation had percentage loss in tablets weights that exceed 1% also, no tablet was cracked, split or broken in either formula. Since all the prepared formulae met the standard friability criteria, they are expected to show acceptable durability and withstand abrasion in handling, packaging and shipment. In general, formulation should be directed at optimizing tablet hardness without applying excessive compression force, while at the same time assuring rapid tablet disintegration and drug dissolution. In other words, tablet should be sufficiently hard to resist breaking during normal

handling and yet soft enough to disintegrate properly after swallowing. The disintegration time for all the liquisolid tablets was found to be 123-150 sec. The drug content uniformity for all the liquisolid formulations was found to be in the limits of 97.20±1.72 to 99.87±1.15 (**Table 3**).

Table 3: Evaluation of post-compression Parameters of Glyburide Formulations

Formulation	Weight variation* (mg)	Hardness† (Kg/cm²)	Friability (%)	Disintegration time‡ (sec)	Drug content‡ (%)
F1	348.15±3.20	3.3±0.86	0.22	140±4	98.60±2.03
F2	349.55±3.36	3.8±0.42	0.18	158±2	99.33±1.34
F3	351.10±3.08	3.3±0.86	0.13	146±4	97.20±1.72
F4	350.80±3.41	3.5±0.28	0.09	142±5	98.48±0.56
F5	349.30±2.49	3.8±0.62	0.22	150±5	97.21±0.16
F6	347.60±3.49	3.7 ±0.52	0.18	123±5	99.50±1.31
F7	348.20±3.04	3.2 ±0.64	0.22	135±5	98.16±0.33
F8	349.55±3.36	3.3±0.86	0.18	152±4	99.32±1.23
F9	352.55±3.43	3.6±0.06	0.13	146±5	98.87±1.46
F10	351.95±3.30	3.0±0.25	0.09	138±4	97.30±2.00
F11	349.23±4.63	3.2±0.31	0.09	143±5	99.87±1.15
F12	350.55±3.36	3.4±0.35	0.18	136±4	99.07±0.55

* All values represent mean ± standard deviation, n=20; † All values represent mean ± standard deviation, n=6; ‡ All values represent mean ± standard deviation, n=3

***In-vitro* release studies** [29]

The cumulative mean percent of Glyburide released from liquisolid compacts containing varying amounts of carrier and coating materials was shown in (**Table 4 and Figure 2 & Figure 3**). This indicates the fast release of drug was observed from above formulations when compared to conventional tablets. From the above formulations F1-F12, formulation F6 was considered as the better formulation, which showed 92.57±0.54% drug release in 10 min where as the conventional tablets showed 23.87±1.13% in 10 min (**Figure 4**). Thus the F6 formulation was considered best among other formulation to produce fast release of the Glyburide from liquisolid tablet. The percent drug release in 10min (Q_{10}) and initial dissolution rate (IDR) for optimized formulations 92.57±0.54, 9.25. This was very much high when compared to conventional tablet 23.87±1.13, 2.38. The DE was found to be 67.52 for F6 formulation where as it is 15.27 for conventional tablets. Overall increase in the dissolution performance of the optimized formulation was 4.5 times compared to conventional tablets could be due to the lesser disintegration time and increased wetting properties and surface area available for drug dissolution (**Table 5**).

Table 4: Dissolution Profiles of Glyburide Formulations

Formulation	Time (min)						
	0	**5**	**10**	**15**	**30**	**45**	**60**
F1	0.0±0.0	32.24±0.31	41.04±1.07	49.54±1.05	55.83±1.0	60.22±1.1	70.87±0.6
F2	0.0±0.0	34.89±1.04	43.26±1.02	55.72±0.52	65.75±0.7	70.65±1.8	75.08±1.1
F3	0.0±0.0	23.36±0.55	34.62±1.06	38.89±1.05	40.33±0.1	41.57±0.3	51.23±0.0
F4	0.0±0.0	18.57±0.32	20.30±0.73	31.23±1.18	38.55±0.2	40.80±0.6	49.62±1.0
F5	0.0±0.0	62.4±1.47	78.32±0.30	96.62±0.61	101±0.89	---	---
F6	**0.0±0.0**	**86.73 ±0.73**	**92.57±0.54**	**99.71±0.63**	**--**	**--**	**--**
F7	0.0±0.0	28.32±0.15	54.76±0.88	58.53±0.34	62.56±0.5	71.84±1.7	74.32±0.4
F8	0.0±0.0	30.61±0.36	48.26±0532	61.48±0.28	72.1±0.22	82.7±0.21	85.4±0.31
F9	0.0±0.0	25.51±0.92	47.08±1.04	67.74±1.28	72.20±1.1	76.82±0.1	81.24±0.7

F10	0.0±0.0	18.62±0.84	29.14±0.21	38.95±0.17	41.27±0.4	48.92±0.8	62.64±0.1
F11	0.0±0.0	12.21±0.37	15.59±0.28	26.57±0.06	31.39±0.3	41.51±0.1	49.92±1.0
F12	0.0±0.0	14.89±0.73	17.75±0.22	28.84±0.34	42.68±0.4	52.43±1.0	71.24±0.4
Conventional	0.0±0.0	18.62±1.21	23.87±1.13	31.45±0.78	39.62±1.29	47.6±0.77	51.23±0.24

Data Represents Mean ± SD (n=3)

Table 5: Dissolution Parameters of Glyb Optimized Formulation (F6) and Conventional Tablet

Formulation	(Q_{10})*	IDR (%/min)	DE	RDR
Optimized (F6)	92.57±0.54	9.25	67.52	2.14
Conventional	23.87±1.13	2.38	15.27	

(Mean ± SD, n=3)

Q_{10}-percent drug release in 10 min, IDR-initial dissolution rate, DE-dissolution efficiency and RDR- relative dissolution rate.

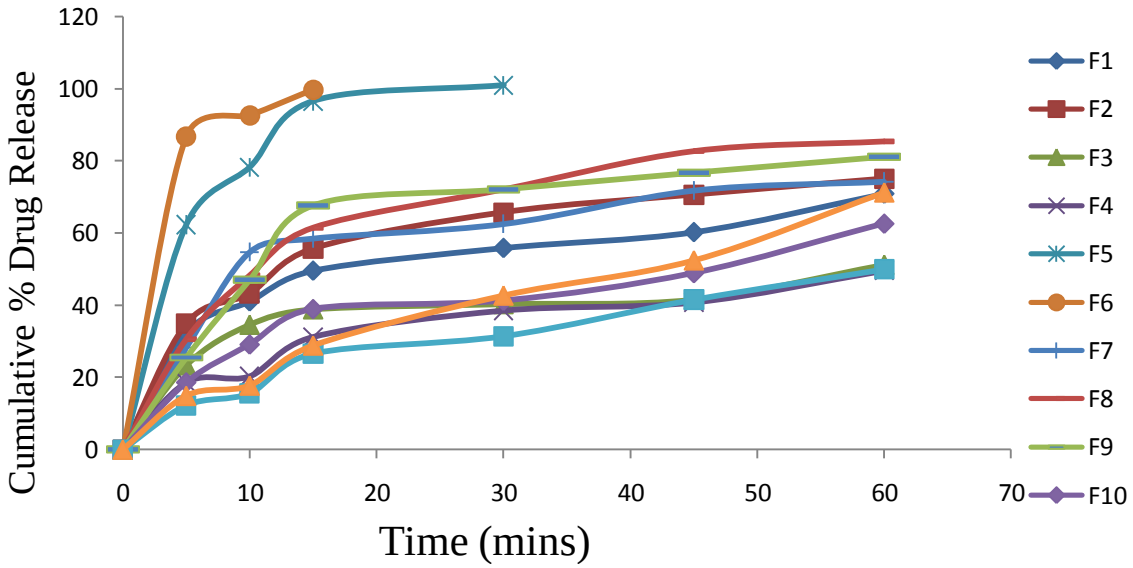

Figure 2: Dissolution Profiles of Liquisolid Formulations

Data Represents Mean ± SD (n=3)

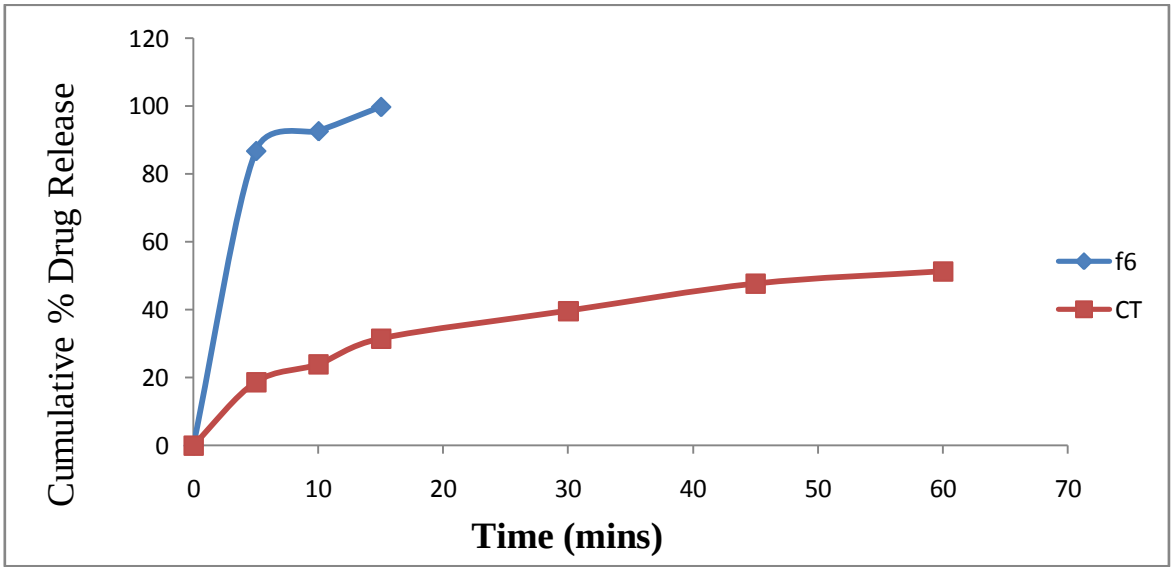

Figure 3: Dissolution Profile of Glyb Optimized Formulation (F6) and Conventional Tablet

Data Represents Mean ± SD (n=3)

The most important observation is that PEG 400 and Avicel PH102 containing formulation had higher drug dissolution rate than the conventional, this could be explained according to the "Noyes Whitney" equation and the diffusion model dissolution theories, the dissolution rate of a drug (D_R) is equal to

D_R= (D/h) S (Cs-C)

where h is the thickness of the stagnant diffusion layer formed by the dissolving liquid around the drug particles, D is the diffusion coefficient of the drug molecules transported through it, S is the surface area of the drug available for dissolution, C is the drug concentration in the bulk of the dissolving medium, and finally Cs is the saturation solubility of the drug in the dissolution medium, and thus it is a constant characteristic property related to the drug and dissolving liquid involved. Since all of dissolution tests for formulations were done at a constant rotational paddle speed (50 rpm) and identical dissolution media, we can safely assume that the thickness of the stagnant diffusion layer (h) and the diffusion coefficient of the drug molecules remain almost identical[30].

CONCLUSION

In the current investigation, Glyburide liquisolid compacts were developed successfully to improve dissolution rate, There by to enhance the bioavailability of Glyburide. From the in-vitro drug release studies the Optimized formulation F6 showed 92.57±0.54% drug release in the 10 min where as the conventional tablets showed 23.87±1.13 in 10 min. Thus the formulation F6 was considered as better formulations among the other formulations to produce fast release of the Glyburide. The percent drug release in 10 min (Q_{10}) and initial dissolution rate (IDR) for optimized formulation was 92.57±0.54, 9.25%/min respectively. These were very much higher compared to conventional tablet (23.87±1.13, 2.38). The improvement in the dissolution characteristics of a drug described in terms of dissolution efficiency (DE) and relative dissolution rate (RDR). The RDR was found to be 2.14for F6. The DE was found to be 67.52 for F6 and it was increased by 4.5 times with optimized liquisolid formulation compared to conventional tablets. The improvement in the dissolution characteristics of liquisolid compacts due to changes the properties of Glyburide particles by simply dispersed the drug particles in a non volatile liquid vehicle, which in turn increase the wetting properties and surface area of drug particles, and hence improve the dissolution profiles and might be oral bioavailability of the drug. The drug-excipients interaction studies showed that there was no interaction between the drug and excipients. In conclusion liquisolid technology was successful in improving the dissolution rate of Glyburide.

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