IJPSR (2025), Volume 16, Issue 5 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 21 December 2024; received in revised form, 16 January 2025; accepted, 28 January 2025; published 01 May 2025

DEVELOPMENT AND *IN-VITRO* ASSESSMENT OF A BILAYER TABLET FOR GLIBENCLAMIDE AND PIOGLITAZONE HCL: A NOVEL APPROACH TO DIABETES MANAGEMENT

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Keywords:

Glibenclamide, Pioglitazone HCl, Type 2 diabetes, Bilayer tablet

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ABSTRACT: The research study aims to prepare and characterize bilayer tablets that combine Glibenclamide, a sulphonyl urea and Pioglitazone HCl, a thiazolidinedione for enhancing glycaemic control in Type 2 Diabetes. The bilayer design incorporates an immediate-release layer of Glibenclamide for rapid onset of action and a sustained-release layer of Pioglitazone HCl to maintain prolonged therapeutic levels. Using wet granulation process, a 400 mg bilayer tablet was prepared. Eight formulations of the immediate and sustained release layers were prepared using different quantities of Crospovidone and sodium starch glycolate, as well as different viscosity grades of HPMC K4 M and HPMC K100M polymers. The FTIR spectra confirmed that the medication and polymers do not interact chemically. DSC analysis was conducted for an optimized formulation, and no incompatibility was discovered. According to dissolution rate studies of bilayer tablets it was observed that the bilayer tablet showed 94.6% while the marketed tablet showed 82.5% release over a 12-hour period. The optimized formulation of drug release data demonstrated the best fit into zero-order kinetics and the Higuchi model of kinetics. According to ICH criteria, stability study data showed no appreciable variations in drug content or dissolution rates over three months. Thus, a novel bilayer tablet formulation of Glibenclamide and Pioglitazone HCl was successfully developed by combining both immediate and sustained release layers.

INTRODUCTION: Today, several countries, including the developing and the developed ones, have started to consider using combination therapy for treating several diseases and ailments that require long-term therapies like diabetes, cardiovascular diseases, and hypertension. Bilayer tablet technology enables the incorporation of many drugs into a single dosage form.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.16(5).1360-72

This article can be accessed online on www.ijpsr.com

DOI link: https://doi.org/10.13040/IJPSR.0975-8232.16(5).1360-72

The formuallow of bilayer tablets from various polymers allows manipulation of more than one type of drug delivery for one or more drugs, *i.e.*, the drug may be released in a bolus and then at a controlled rate, or it may be delivered to the GIT *via* targeted drug delivery using the polymers' pH development [1, 2].

According to the World Health Organization (WHO) diabetes mellitus is a chronic, metabolic disease characterized by elevated levels of blood glucose, which leads over time to damage to the heart, vasculature, eyes, kidneys and nerves. Over 90% of diabetes mellitus cases are T2DM, a condition marked by deficient insulin secretion by pancreatic islet β-cells, tissue insulin resistance

(IR) and an inadequate compensatory insulin secretory response [3]. The basis of the treatment of DM2 is to associate an insulin secretagogue drug with an insulin sensitizer to correct metabolic problems and regulate chronic hyperglycemia. For this, two drugs have been widely used, glibenclamide and pioglitazone, respectively. Glibenclamide belongs to the class of second-generation sulfonylureas; its main mechanism of action is to increase the secretion of insulin by the pancreas. Pioglitazone belongs to the class of oral antidiabetics, thiazolidinediones, also called glitazones [4]. Combining these drugs can provide better glycemic control by targeting different pathways in glucose regulation. The combination may allow for lower doses of each drug compared tomonotherapy, potentially reducing the risk of side effects. Both are BCS class II drugs with low bioavailability. By employing super disintegrants in the IR layer and using polymers in the SR layer in Bilayer tablet, solubility can be enhanced. Combining immediate and sustained release mechanisms allows for a quick release and thereafter prolong release that maintains steady drug levels in blood, reducing fluctuations on glucose levels and thereby improving glycemic control. Therefore, an attempt was made to formulate bilayer tablet of Glibenclamide and Pioglitazone HCl.

MATERIALS AND METHODS:

Materials: Glibenclamide was a gift sample from Sri Krishna Pharmaceutical and Pioglitazone HCl from Sain Medicaments Pvt Ltd. And excipients Micro-Crystalline Cellulose Cros-Povidone, Starch, Magnesium Stearate (SDFCL, S.D FINE-CHEM Ltd) Sodium Starch Glycolate (Otto Kemi) Mannitol and Lactose (Lab Tech Corporation) HPMC K4(Otto) HPMC K100(INR Chem) and Talc (Mylochem).

Pre -Formulation Studies:

Organoleptic Properties: The colour, odour and appearance of the drug was evaluated using descriptive terminology.

Melting Point: The melting point of both drugs was determined using capillary tube method. The samples of both drugs were filled in capillary tube and heated until the drug sample completely melts. The initial and the final temperature was recorded.

Solubility: 10mg of glibenclamide was suspended in 10ml of different solvents then was kept in shaker for 24 hrs. Then the absorbance was recorded using UV-Visible spectrophotometer. The same procedure was repeated for the other drug.

Construction of Standard Graph Construction of Glibenclamide and Pioglitazone HCl: The standard graph of Glibenclamide in phosphate buffer (6.8 pH buffer) was constructed by making the concentrations of 2-12 µg/ml solutions. The absorbance of solutions was examined under UV-spectrophotometer at an absorption maximum of 300 nm as shown in **Fig. 1.** For the other drug Pioglitazone HCl the calibration curve was formulated in 0.1 N HCl by making proportions ranging from 2-12 µg/ml as shown in **Fig. 2.** The solutions were scanned at 227nm.

FTIR Spectroscopy: The sample of two drugs Glibenclamide and Pioglitazone HCl were mixed with KBR in ratio of 1:100. The mixture was compressed to form a disc using dies. The disc was placed in the spectrophotometer and the spectrum was recorded. Then sample of Glibenclamide was mixed with excipient such as Cross-povidone and sample of Pioglitazone HCl was mixed with HPMC K-100M and compressed then the spectrum was recorded. FTIR analysis for the optimized formulation was also performed as shown in **Fig. 7** and no significant changes were observed in the IR spectra.

DSC Analysis: The Analysis is done to determine thermal behavior of drugs by using DSC operator. The sample bilayer tablet was placed in flat-bottomed aluminum pans and heated at a constant rate for about 15 min. The DSC results as shown in **Fig. 8** indicate that both glibenclamide and pioglitazone HCl exhibit thermal behaviors consistent with their known melting points. No interaction was observed in the DSC curves of both drugs where no change was observed in the formulation.

Evaluation of Pre-Compression Parameters:

Angle of Repose: The angle of repose was determined by the funnel method. The powder was poured from a certain height through funnel into flat surface allowing it to form cone-shaped heap. The height and radius of heap were calculated to

know the angle. The angle of repose can be calculated by using formula

$$\text{Tan } \theta = h/r$$

Where h is the relatively height; r is radius of the powder cone.

Bulk Density: A known quantity of poured was poured into measuring cylinder then carefully level the powder without compacting. Calculate bulk density, in gm per ml gm/cc, by the formula:

Bulk density = Bulk Mass/ Bulk Volume

Tapped Density: The powdered granules were taken in measuring cylinder and was tapped for 20 times. The mass of initial level of powder and final level was noted after tapping the powder.

Tapped density = Mass /Final tapped Volume

Compressibility of Granules: The compressibility index was determined by Carr's index and Hausner's ratio.

Carr's Index = TD-BD X 100 /BD

Hausner's ratio = TD/BD

Formulation Development:

Preparation of Glibenclamide and Pioglitazone HCl Blend by Wet Granulation Method:

- Weigh the medications and excipients precisely according to the amounts listed in the table, then transfer them to a different mortar pestle.
- Starch mucilage is made by combining starch with distilled water, heating the mixture on a water bath until the starch gelatinizes and produces mucilage, and then adding the starch mucilage to the blend and mixing it thoroughly.
- Now, until a wet dough forms, add a small amount of amaranth for glibenclamide and turmeric for pioglitazone HCl mix. This mixture should be run through a sieve like #12. For 10 to 15 minutes, dry the granules in a hot air oven set at 60 degrees Celsius. The dry granules were run through #22 mesh. After transferring all of the sifted granules to the blender, add the talc and magnesium stearate and stir for two minutes. Next, add the necessary amount of flavouring agent. The **Table 1** and **2** illustrate composition of immediate release and Sustained release tablets.

TABLE 1: COMPOSITION OF IMMEDIATE RELEASE

Ingredients	FG1	FG2	FG3	FG4	FG5	FG6	FG7	FG8
Glibenclamide	10	10	10	10	10	10	10	10
Cros-Povidone	-	-	-	-	3	6	9	12
Sodium Starch Glycolate	3	6	9	12	-	-	-	-
Micro Crystalline Cellulose	15	30	45	60	15	30	45	60
Lactose	116	98	80	62	116	98	80	62
Starch Mucilage	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Amaranth	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2
Total weight	150	150	150	150	150	150	150	150

TABLE 2: COMPOSITION OF SUSTAINED RELEASE

Ingredients	FP1	FP2	FP3	FP4	FP5	FP6	FP7	FP8
Pioglitazone HCl	45	45	45	45	45	45	45	45
HPMC K100	-	-	-	-	10	20	30	40
HPMC K14	10	20	30	40	-	-	-	-
Lactose	188	178	168	158	188	178	168	158
Starch Mucilage	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Turmeric	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Magnesium stearate	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2
Total weight	250	250	250	250	250	250	250	250

Preparation of Bilayer Tablet: Firstly, blends of immediate release and sustained release tablets were prepared by wet granulation method by using starch mucilage as binding agent. Based on dissolution behaviour, formulations of immediate release optimized layer were selected. Optimized immediate release were compressed with eight formulations of sustained release layer with optimum hardness 6-8 kg/cm^2 to form bilayer tablets. Compression was done using 9mm punches. The total weight of tablet was 400mg containing 150 mg of glibenclamide in immediate release layer and 250 mg of pioglitazone HCl in sustained release layer as shown in **Table 3.** Prepared bilayer tablets were optimized and evaluated for various post compression parameters and *in-vitro* dissolution results.

TABLE 3: FINAL OPTIMIZED FORMULATION OF BILAYER TABLET

S. no.	Material Name	Quantity(mg)	Material Name	Quantity (mg)
1	Glibenclamide	10mg	Pioglitazone HCl	45
2	Cros-Povidone	6	HPMC K100	40
3	SSG	--	HPMC K4	-
4	MCC	30	Starch Mucilage	2.5
5	Starch Mucilage	1.5	Mg. Stearate	2
6	Mannitol	98	Lactose	158
7	Amaranth	0.5	Talc	2
8	Mg. Stearate	2	Curcumin	0.5
9	Talc	2		
	Total weight	150mg	Total weight	250mg

Evaluation of Post -Compression Parameters:

Weight Variation: Twenty tablets were weighed separately to determine the weight variance. The average weight of the tablets is compared to their individual weights. And tablet weight was analysed for sample mean and percent deviation. The IP limit for weight variationin case of tablets weighing 85 -250 mg± 7.5 % and more than 250mg ± 5%

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

Hardness: A Monsanto hardness tester was used to measure the hardness. Six tablets were taken and placed between the hardness tester's jaws to measure hardness.

Friability: The test was determined by weighing 10 tablets and placing them in Roche Friabilator which was rotated for 5 min at 25 rpm. After dusting the mass of total remaining tablets was noted and percent friability was recorded.

% Friability = Initial weight – final weight x 100 /Initial weight

Thickness: A Vernier Calliper was used to measure the formulation trials' thickness and diameter. To determine the average tablet hardness or crushing strength, ten tablets were sampled from each batch.

***In-vitro* Drug Release Studies:** *In-vitro* drug release tests were performed using the USP dissolving test apparatus (Type 2). The dissolution tests were conducted using a pH approach in 900ml of dissolution media that was agitated at 50 rpm and 37.5°C, meaning that the pH was 1.2 for the first two hours and 6.8 for the next six.

On a regular basis, aliquots were removed and replaced with new media. After the samples were filtered, each one's drug content was examined. It was observed that F6 batch of immediate release showed faster dissolution and F8 batch showed better controlled release.

Kinetic Analysis of Dissolution Data: The release data were analyzed using the zero-order, first-order, Higuchi equation, and Korsmeyer equation, which is commonly employed to describe the drug release behavior from polymeric systems, to investigate the mechanism of drug release from the tablets.

Stability Studies: Formulation batch F2 was charged and packed at room temperature (65±5% RH and 30 + 2 deg * C). At 0, 1,2 and 3 months, the tablets were assessed for assay and dissolution profile testing. The findings of the stability analysis showed no discernible differences in the amount of medication or the rate of dissolution as shown in **Table 20.** After three months, there was no significant changes in drug content and dissolution rate.

RESULTS AND DISCUSSION

Pre-formulation Studies:

TABLE 4: ORGANOLEPTIC PROPERTIES

S. no.	Parameter	Glibenclamide	Pioglitazone HCl
1	Color	White	Off White
2	Odour	Characteristic	No odour
3	Appearance	Amorphous	Amorphous
4	Taste	Tasteless	Unpleasant taste

TABLE 5: SOLUBILITY OF GLIBENCLAMIDE IN DIFFERENT SOLVENTS

Solvents	Solubility(mg/ml)
Methanol	0.152±0.03
0.2 M NaOH	0.178±0.02
0.1 N HCl	0.139±0.02
Phosphate buffer pH 7.4	0.167±0.02
Water	0.206±0.02

TABLE 6: SOLUBILITY OF DRUG IN PIOGLITAZONE HCL

Solvents	Solubility (mg/ml)
Ethanol	0.138±0.02
Methanol	0.152±0.02
Acetone	0.157±0.01
0.1 HCl	0.416±0.02
Phosphate buffer pH 6.8	0.398±0.02
Water	0.013±0.02

TABLE 7: MELTING POINT OF DRUG GLIBENCLAMIDE AND PIOGLITAZONE HCL

Drug	Reference Range	Observed Range
Glibenclamide	173-175 ºC	175-177 ºC
Pioglitazone HCl	193-194 ºC	193-195 ºC

Preparation of Standard Curve of Glibenclamide:

TABLE 8: STANDARD CALIBRATION CURVE OF GLIBENCLAMIDE IN 6.8PH PHOSPHATE BUFFER

Concentration	Absorbance
0	0
2	0.82±0.04
4	0.151±0.082
6	0.267±0.051
8	0.318±0.067
10	0.452±0.074
12	0.545±0.078

Standard deviation n=3

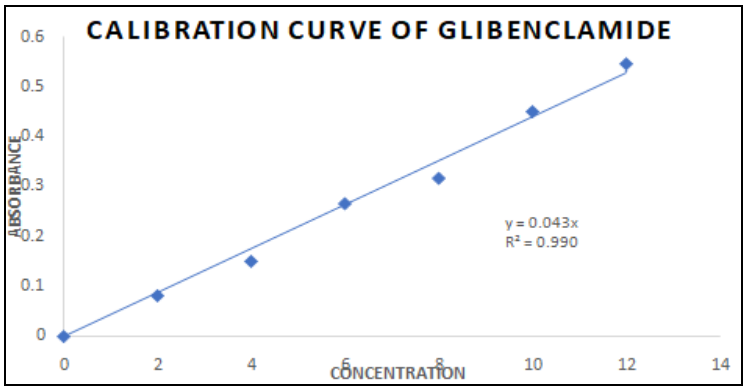

FIG. 1: CALIBRATION CURVE FOR GLIBENCLAMIDE IN PHOSPHATE BUFFER PH 6.8

Preparation of Standard Calibration Curve of Pioglitazone HCl:

TABLE 9: CALIBRATION PLOT OF PIOGLITAZONE HCL IN 0.1 HCL

Concentration	Absorbance
0	0
10	0.123±0.015
20	0.324±0.026
30	0.562±0.031
40	0.674±0.052
50	0.798±0.047
60	0.862±0.056

Standard deviation n=3

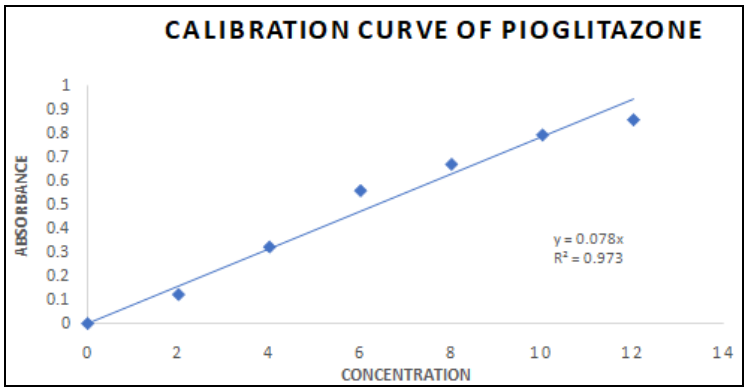

FIG. 2: STANDARD GRAPH OF PIOGLITAZONE HCL IN 0.1 HCL

FTIR Analysis:

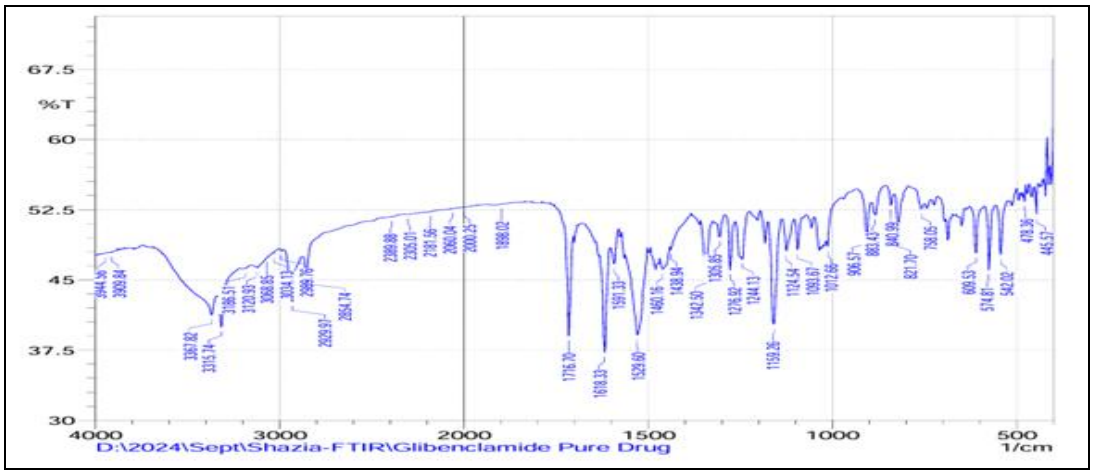

FIG. 3: FTIR SPECTRA OF GLIBENCLAMIDE PURE DRUG

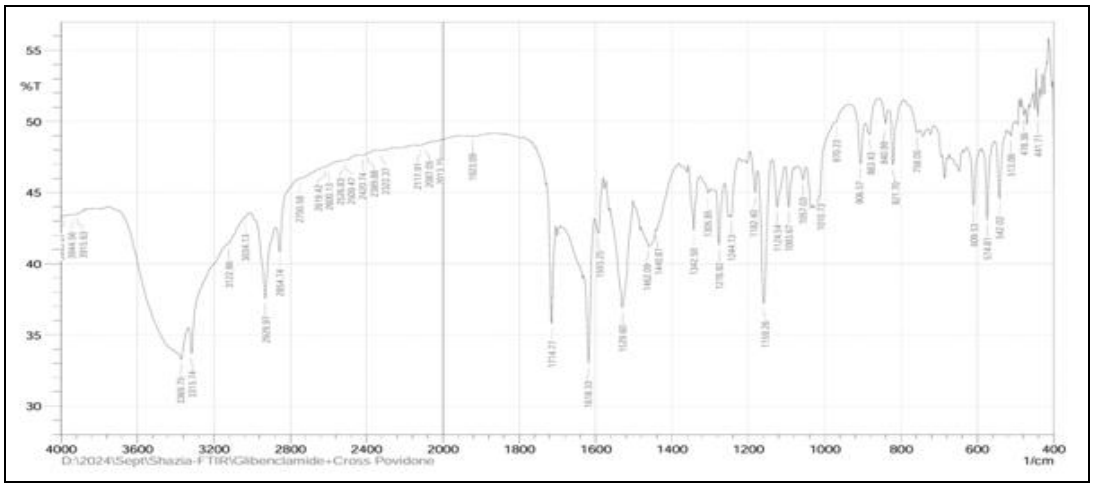

FIG. 4: FTIR SPECTRA OF GLIBENCLAMIDE WITH CROSS-POVIDONE

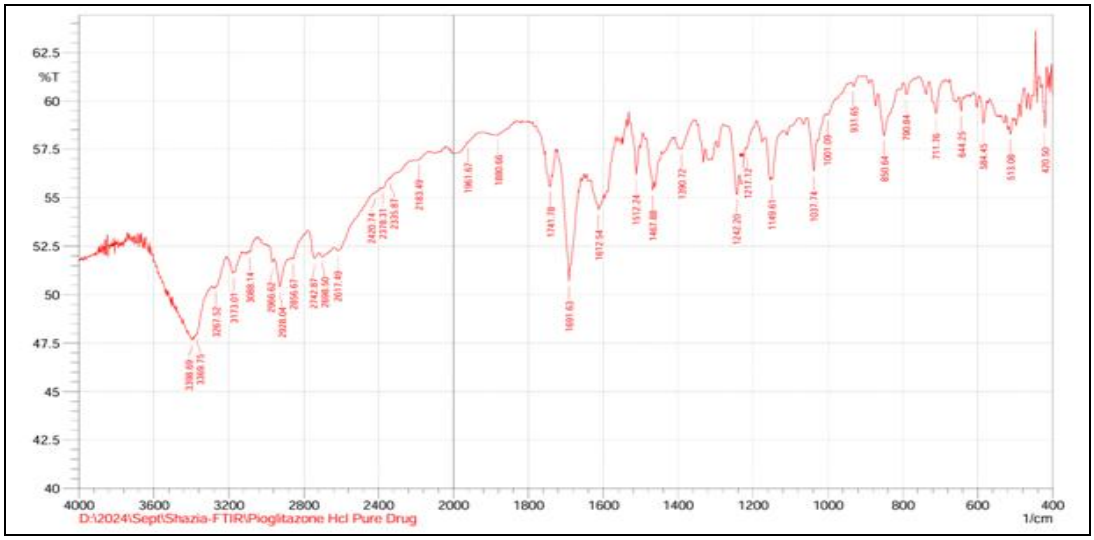

FIG. 5: FTIR SPECTRA OF PURE PIOGLITAZONE HCL

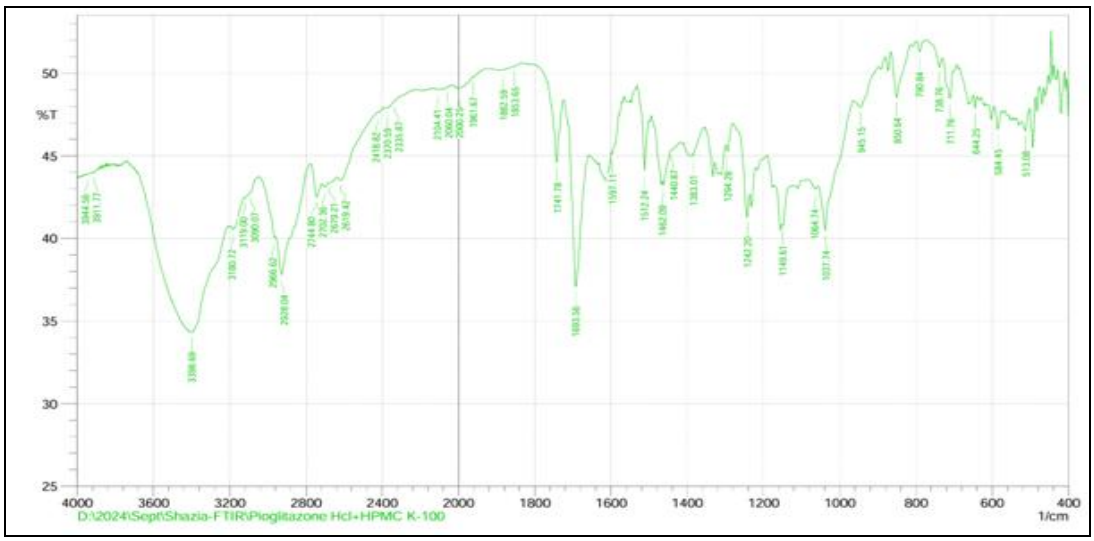

FIG. 6: FTIR SPECTRA OF PIOGLITAZONE HCL WITH HPMC K-100

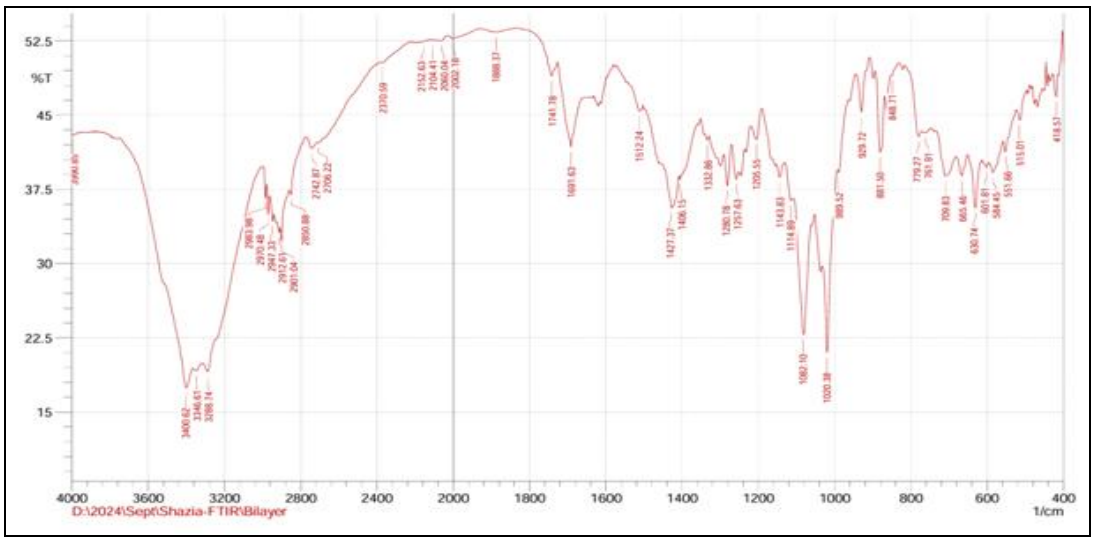

FIG. 7: FTIR SPECTRA OF BILAYER TABLET

DSC Study for Bilayer Tablet:

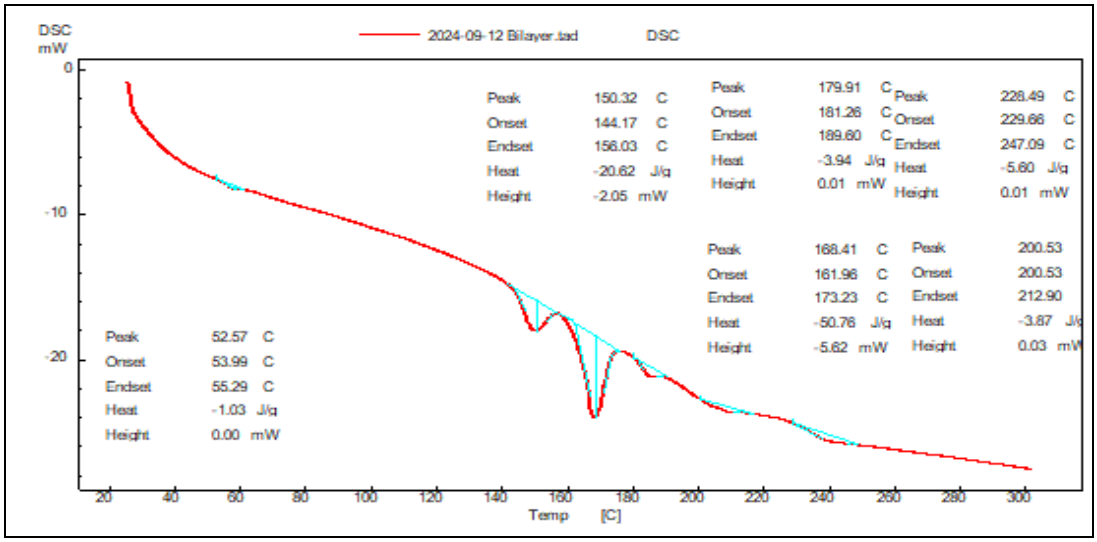

FIG. 8: DSC SPECTRA OF OPTIMIZED FORMULATION

TABLE 10: PRE- COMPRESSION EVALUATION FOR IMMEDIATE RELEASE FORMULATIONS

S. no.	Formulation	Angle of repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's ratio	Flow property
1	FG1	26	0.416±0.2	0.458±0.1	10.09±0.5	1.10±0.3	Excellent
2	FG2	24.5	0.516±0.1	0.516±0.22	5.03±0.3	1.05±0.4	Excellent
3	FG3	25	0.527±0.3	0.527±0.32	19.6±0.4	1.13±0.8	Good
4	FG4	26.5	0.553±0.5	0.553±0.2	11.8±0.8	1.4±0.15	Good
5	FG5	25.5	0.579±0.7	0.579±0.5	5.7±0.11	1.06±0.2	Excellent
6	FG6	24	0.608±0.1	0.608±0.8	20.5±0.15	1.2±0.18	Good
7	FG7	28	0.569±0.7	0.569±0.1	22.6±0.12	1.3±0.16	Good
8	FG8	25.6	0.442±0.8	0.442±0.9	7.8±0.11	1.7±0.1	Excellent

TABLE 11: PRE-COMPRESSION EVALUATION FOR SUSTAINED RELEASE FORMULATIONS

S. no.	Formulation	Angle of Repose (°)	Bulk Density (g/mL)	Tapped Density (g/mL)	Carr's Index (%)	Hausner's ratio	Flow property
1	FP1	27.5	0.50±0.12	0.57±0.12	14.00±0.1	1.14±0.3	Good
2	FP2	25	0.49±0.16	0.54±0.16	10.2±0.2	1.10±0.12	Excellent
3	FP3	26.4	0.56±0.22	0.64±0.18	14.28±0.4	1.14±0.4	Good
4	FP4	30	0.45±0.13	0.56±0.19	24.44±0.3	1.18±0.21	Good
5	FP5	28	0.48±0.11	0.54±0.21	11.1±0.8	1.25±0.3	Good
6	FP6	26	0.42±0.32	0.46±0.32	20.05±0.6	1.24±0.1	Good
7	FP7	24.5	0.45±0.1	0.49±0.42	9.18±0.2	1.10±0.5	Excellent
8	FP8	27	0.51±0.36	0.845±0.36	14.1±0.8	1.14±0.2	Good

TABLE 12: POST -COMPRESSION EVALUATION OF IMMEDIATE LAYER

S. no.	Formulation	Hardness (kg/cm2)	Thickness (mm)	Weight Variation (mg)	Friability (%)	Drug content (%)
1	FG1	4.3±0.2	2.42±0.05	148±5	0.31±0.1	92±0.32
2	FG2	4.6±0.1	2.45±0.06	149±3	0.32±0.2	98±0.26
3	FG3	4.5±0.3	2.50±0.08	150±3	0.33±0.11	98±0.25
4	FG4	4.4±0.3	2.53±0.05	152±4	0.36±0.21	96±0.32
5	FG5	4.5±0.1	2.56±0.03	149±5	0.34±0.15	97±0.28
6	FG6	4.6±0.2	2.48±0.07	148±2	0.35±0.12	99±0.27
7	FG7	4.6±0.3	2.47±0.08	148±5	0.36±0.13	99±0.15
8	FG8	4.5±0.2	2.55±0.06	149±6	0.33±0.22	98±0.45

TABLE 13: POST-COMPRESSION EVALUATION OF SUSTAINED LAYER

S. no.	Formulation	Hardness (kg/cm2)	Thickness (mm)	Weight Variation (mg)	Friability (%)	Drug content (%)
1	FP1	7.2±0.52	3.86±0.22	252±1.48	0.74±0.1	98±0.32
2	FP2	7.3±0.46	3.91±0.25	249±1.62	0.65±0.13	99±0.25

3	FP3	7.8±0.45	3.95±0.18	252±1.64	0.68±0.2	96±0.46
4	FP4	7.6±0.42	3.92±0.26	250±0.68	0.56±0.4	98±0.53
5	FP5	7.6±0.30	3.88±0.88	255±0.89	0.78±0.6	97±0.34
6	FP6	7.5±0.44	3.89±0.89	253±1.64	0.65±0.5	96±0.44
7	FP7	7.4±0.55	3.93±0.56	252±1.82	0.59±0.3	97±0.55
8	FP8	7.3±0.60	3.96±0.62	248±1.93	0.62±0.7	98±0.65

TABLE 14: RESULTS OF DISINTEGRATION TIME FOR IMMEDIATE RELEASE LAYER OF GLIBENCLAMIDE

Formulation	Disintegration Time
FG1	1 min 50 sec
FG2	1 min 56 sec
FG3	1 min 44 sec
FG4	1 min 34 sec
FG5	1 min 42 sec
FG6	1 min 27 sec
FG7	1 min 38 sec
FG8	1 min 41 sec

In -vitro Dissolution Study of Glibenclamide & Pioglitazone Bilayer Tablets:

TABLE 15: *IN-VITRO* DISSOLUTION STUDY OF GLIBENCLAMIDE

Time in minutes	Cumulative Percentage Release							
	FG1	FG2	FG3	FG4	FG5	FG6	FG7	FG8
0	0	0	0	0	0	0	0	0
5	22.5	26.7	28.4	19.8	21.3	34.8	30.2	29.7
10	36.9	33.3	47.8	38.8	42.7	52.6	45.6	56.2
15	46.7	52.8	67.7	44.5	59.4	76.6	66.4	67.8
20	57.3	61.7	74.6	66.9	78.8	87.8	76.3	81.2
25	72.4	76.6	87.19	87.9	89.2	92.4	86.4	87.6
30	82.6	89.5	90.14	93.3	92.4	96.8	93.2	91.5

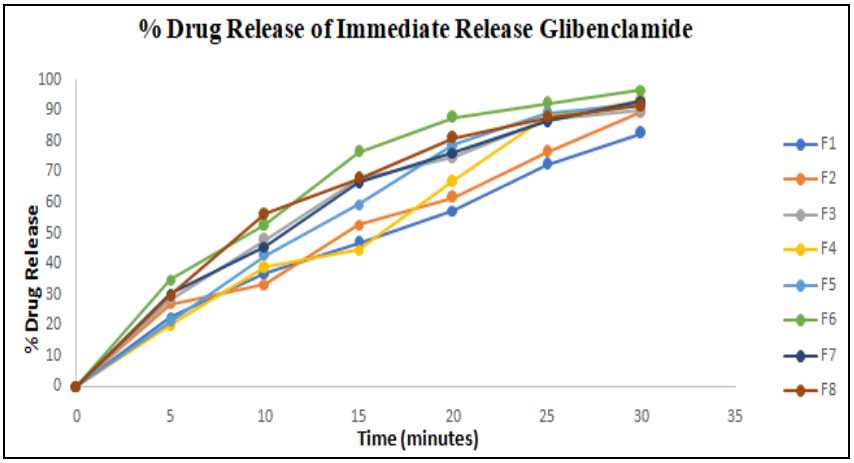

FIG. 9: DISSOLUTION GRAPH FOR FORMULATIONS FG1-FG8

TABLE 16: *IN-VITRO* DISSOLUTION STUDY OF PIOGLITAZONE HCL

Time (In Hrs.)	% Cumulative Drug Release							
	FP1	FP2	FP3	FP4	FP5	FP6	FP7	FP8
0	0	0	0	0	0	0	0	0
1	18.2	14.3	31.2	28.2	13.4	15.2	19.58	32.5
2	40.2	38.4	46.8	32.2	24.6	28.2	29.2	46.4
3	45.9	59.5	56.1	40.2	31.2	38.7	45.7	58.2
4	52.4	62.4	67.4	58.2	45.6	47.6	56.8	60.2
5	74.6	68.2	78.9	79.2	68.4	71.2	72.7	75.6
6	85.3	78.9	89.1	89.1	82.5	89.2	82.3	85.4
7	90.2	84.5	91.2	91.2	91.2	90.4	91.2	92.6
8	92.4	91.1	93.3	93.3	93.2	91.9	92.2	96.3

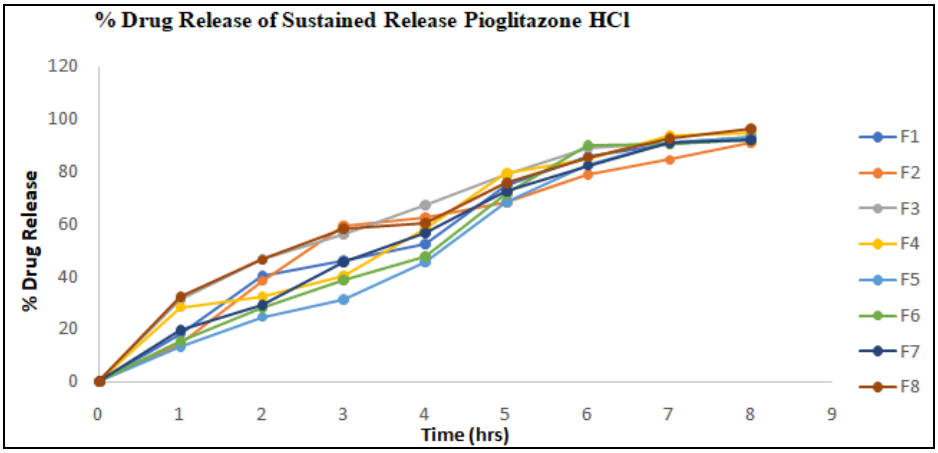

FIG. 10: DISSOLUTION GRAPH FOR FORMULATIONS FP1-FP8

***In-vitro* Drug Release Profile for the Optimized Formulation:** Among the formulations are the F6 formulation for quick release and the F8formulation for continuous release, both of which comprise Crospovidone as a super-disintegrant and HPMC K100 as binder. The results of dissolution are depicted in **Table 17** and the cumulative percentage release is shown in **Fig. 11.**

TABLE 17: DISSOLUTION RESULT OF BI-LAYERED TABLET GLIBENCLAMIDE AND PIOGLITAZONE HCL

Time (Hour)	Percent Drug Release	
	Glibenclamide (Immediate release)	Pioglitazone HCl (Sustained release)
0th Hr	0	0
0.5th Hr	64.55	-----
1th Hr		68.3
2th Hr		71.4
4th Hr		78.6
6th Hr		84.5
8th Hr		89.6
10th Hr		90.2
12th Hr		94.6

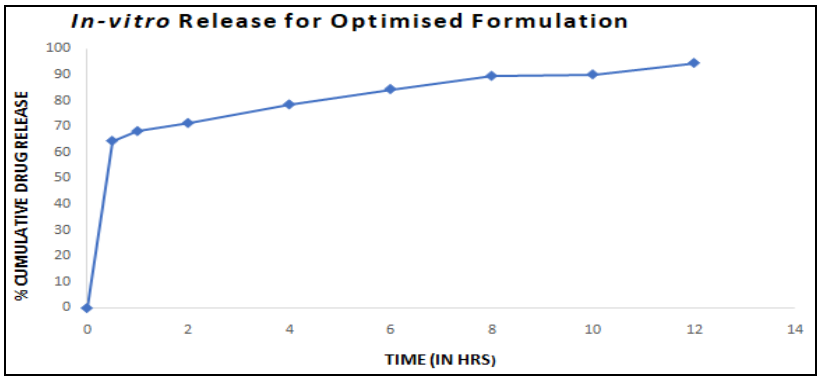

FIG. 11: CUMULATIVE PERCENTAGE DRUG RELEASE OF BI-LAYERED TABLET GLIBENCLAMIDE AND PIOGLITAZONE HCL

TABLE 18: COMPARISON OF CUMULATIVE PERCENTAGE DRUG RELEASE WITH THAT OF THE MARKETED PRODUCT

S. no.	Time (hrs)	Bilayer tablet	Marketed Product
Dissolution medium 6.8pH phosphate buffer			
1	0	0	0
2	0.5	64.55	31
3	1	67.13	45
0.1N HCL			
4	2	53	54
5	4	61.6	62.8

6	5	70.2	64.3
7	6	76.4	70.8
8	8	88.6	74.5
9	10	90.2	80.1
10	12	94.6	82.5

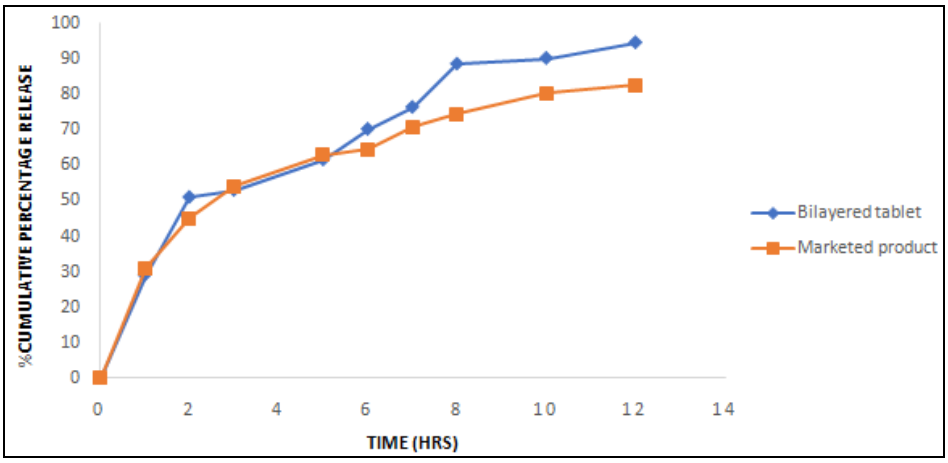

FIG. 12: COMPARISON OF CUMULATIVE PERCENTAGE DRUG RELEASE WITH THAT OF THE MARKETED PRODUCT

Drug Release Kinetic Analysis of Sustained Release Layer of Bilayer Tablet:

TABLE 19: RELEASE KINETICS OF OPTIMIZED BILAYER TABLETS

Parameters	Zero Order	First order	Higuchi	Pappas
	% CDR Vs T	Log % C Vs T	% CDR Vs √T	Log C Vs Log T
Slope	8.0638	0.1346	31.4798	1.3664
Intercept	16.673	0.7684	3.9036	0.7568
R^2	0.8567	0.5211	0.9511	0.6979

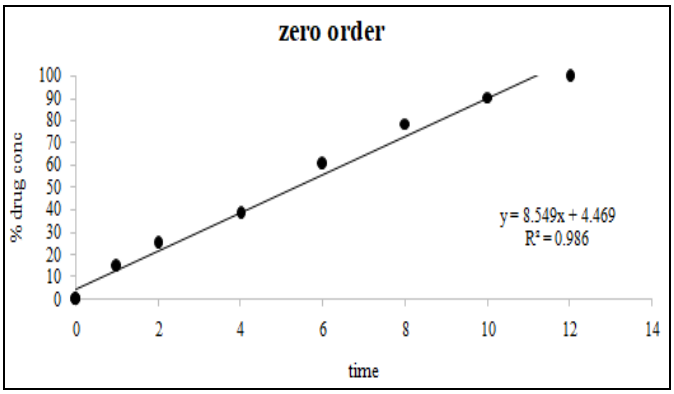

FIG. 13: ZERO ORDER PLOT

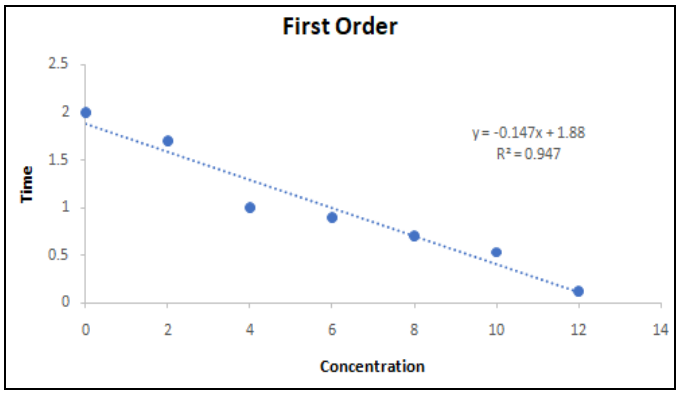

FIG. 14: FIRST ORDER GRAPH

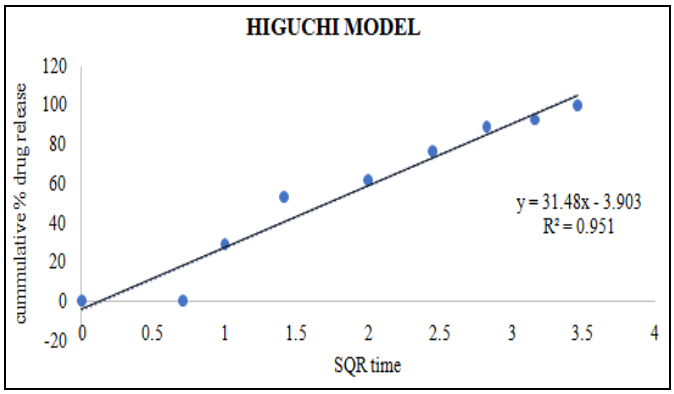

FIG. 15: HIGUCHI PLOT

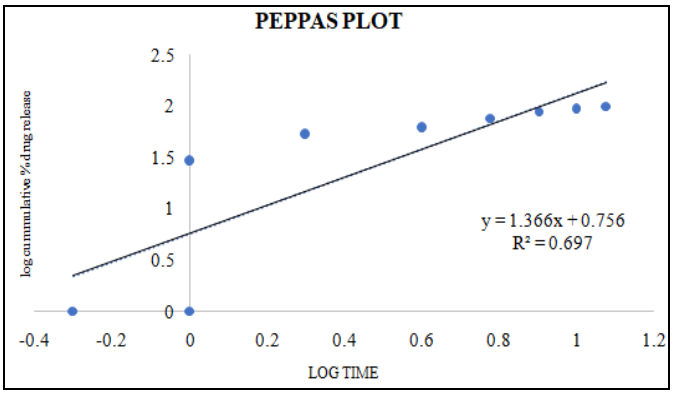

FIG. 16: REPRESENTING PEPPAS PLOT

Stability Studies:

TABLE 20: PERCENTAGE DRUG CONTENT IN 0 AND 3 MONTHS

Parameter	Storage condition			
	Initial release	Room temperature 40±2ºC and 65±5% *RH		
	0 months	1 months	2 months	3 months
% Drug Content	99.8±0.25	99.8±0.26	99.8±0.27	99.8±0.27

CONCLUSION: Glibenclamide is a member of the sulphonyl urea family, which is crucial for the treatment of Type II diabetes. Pioglitazone increases insulin sensitivity and is a member of the thiazolidinedione class. By combining these medications in an ideal dosage form, glycaemic control may be improved. When assessed utilizing FTIR and DSC studies, the polymers and excipients as well as the pure medication were determined to be compatible. There was a strong correlation between the standard calibration curves for Glibenclamide and Pioglitazone HCl in 6.8 pH phosphate buffer and 0.1N HCI, respectively.

Eight formulations (IR&SR) with different polymers at varying concentrations were created in order to improve the permeability and bioavailability. Using the wet granulation process, a 400 mg tablet containing glibenclamide (10 mg) and pioglitazone HCl (45 mg) was successfully made. Cross-povidone 6 mg (F6) and HPMC K100 M 40 mg (F8) in immediate and sustained release, respectively, made up the resulting bilayer tablet. With a 94.6% drug release in 12 hours, the improved recipe outperformed the commercial product in in-vitro dissolution tests. With regression values of 8.0638 and 31.479, respectively, the formulation adhered to zero order and Higuchi's kinetics. Lastly, the improved tablet's thickness, hardness, friability, and CDR percentage were assessed further. Data from stability studies revealed no discernible changes in drug content or dissolution rates over a three-month period, in accordance with ICH requirements.

ACKNOWLEGMENTS: I am immensely gratefully too Almighty for his blessings throughout the research work. I express my profound sense of gratitude to our esteemed Principal, Dr. Syed Abdul Azeez Bash for providing me with the necessary samples and laboratory facilities to carry out the research work. I would also like to express my sincere gratitude to Dr. S. M. Shahidullah, my research supervisor, for his unwavering support, insightful suggestions, and encouragement throughout this study. Most importantly, none of this would have been possible without the love and patience of my parents who have aided and encouraged me throughout this Endeavour.

CONFLICT OF INTEREST: We declare that we have no conflict of interest.

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How to cite this article:
Shahidullah SM and Nazneen SS: "Development and *in-vitro* assessment of a bilayer tablet for glibenclamide and pioglitazone HCl: a novel approach to diabetes management". Int J Pharm Sci & Res 2025; 16(5): 1360-72. doi: 10.13040/IJPSR.0975-8232.16(5).1360-72.