ISSN:0976-0172

Dr.K.Ashok, JBio sci Tech, Vol 11(3),2023,08-20

Journal of Bioscience And Technology
www.jbstonline.com

Boosted Anti-Diabetic Agent Yield via Improved Growth of Penicillium Strains Ceutres

Dr.K.Ashok[1], T Malyadri[2], M Vamshi Krishna[3], I. Devi[4]

1. Professor , Department of pharmaceutics , QIS College of pharmacy , Ongole , A.P

2.Assistant Professor , Department of pharmaceutics , QIS College of pharmacy , Ongole , A.P

3.Associate Professor , Department of pharm chemistry , QIS College of pharmacy , Ongole , A.P

4.Assistant Professor , Department of pharmaceutics , QIS College of pharmacy , Ongole , A.P

ABSTRACT:
The study's goal is to prepare and describe the bilayer Type 2 diabetes, Glibenclamide, PioglitazoneHCl, tablets that mix Glibenclamide, an asulphonylurea, and PioglitazoneHCl, A thiazolidinedione bilayer tablet for improving glycaemic management in people with Type 2 diabete

- Corresponding Author
  Ashok
  ashok@gmail.com

Introduction

Several nations, both developed and developing, are now considering the use of combination therapy to treat a number of conditions and illnesses that call for long-term treatments, such as hypertension, diabetes, and cardiovascular diseases. Numerous medications may be combined into a single dose form thanks to bilayer tablet technology. Bilayer tablets made of different polymers enable the manipulation of multiple drug delivery methods for one or more drugs. For example, the drug can be delivered to the GIT via targeted drug delivery using the pH development of the polymers, or it can be released in a bolus and then at a controlled rate. 1, 2. The World Health Organization (WHO) defines diabetes mellitus as a long-term metabolic condition marked by high blood glucose levels that eventually damages the heart, blood vessels, eyes, kidneys, and nerves. T2DM, which accounts for more than 90% of cases of diabetes mellitus, is characterized by tissue insulin resistance (IR), insufficient compensatory insulin secretory response, and insufficient insulin secretion by pancreatic islet β-cells. 3. The foundation of DM2 therapy is the combination of an insulin sensitizer and an insulin secretagogue medication to address metabolic issues and control persistent hyperglycemia. Two medications, pioglitazone and glibenclamide, have been used extensively for this. Glibenclamide is a member of the second-generation sulfonylurea family and works primarily by increasing the pancreatic production of insulin. Pioglitazone is a member of the thiazolidinediones family of oral antidiabetics, often known as glitazones 4. By focusing on distinct glucose regulation mechanisms, combining these medications might improve glycemic control. Compared to monotherapy, the combination may enable lower dosages of each medication, possibly lowering the risk of adverse effects. Both are low-bioavailability BCS class II medications. Solubility may be improved in bilayer tablets by utilizing polymers in the SR layer and superdisintegrants in the IR layer. Combining immediate and sustained release methods enables a rapid release followed by a prolonged release, which keeps blood medication levels constant, lessens glucose swings, and enhances glycemic control. Thus, an effort was undertaken to create a bilayer tablet containing pioglitazone HCl and glibenclamide. RESOURCES AND METHODS: Resources: Pioglitazone HCl from Sain Medicaments Pvt Ltd and Glibenclamide were gift samples from Sri Krishna Pharmaceutical. Further excipients include Magnesium Stearate (SDFCL, S.D Fine-CHEM Ltd.), Micro-Crystalline, Cellulose, and Cros-Povidone. Mannitol and Lactose (Lab Tech Corporation), Sodium Starch Glycolate (Otto Kemi), HPMCK4 (Otto), HPMCK100 (INRChem), and Talc (Mylochem). Studies Prior to Formulation: Organoleptic Characteristics: Using descriptive language, the drug's color, smell, and look were assessed. Melting Point: The capillary tube technique was used to ascertain the melting points of both medications. Both drug samples were put into capillary tubes and heated until they melted completely. Both the starting and ending temperatures were noted. Solubility: Ten milligrams of

ISSN:0976-0172

Journal of Bioscience And Technology
www.jbstonline.com

glibenclamide were suspended in ten milliliters of various solvents and then left in a shaker for twenty-four hours. After that, a UV-visible spectrophotometer was used to record the absorbance. For the other medication, the identical process was carried out. Standard Graph Construction of Pioglitazone HCl with Glibenclamide: Glibenclamide's standard graph in phosphate buffer (6.8 pH buffer) was created by combining solutions with doses ranging from 2 to 12 µg/ml. As shown in Fig. 1, the absorbance of solutions was measured using a UV spectrophotometer set to an absorption maximum of 300 nm. As seen in Fig. 2, the calibration curve for the second medication, pioglitazone HCl, was created in 0.1 N HCl using amounts ranging from 2 to 12 µg/ml. At 227 nm, the solutions were scanned.

FTIR Spectroscopy: A 1:100 mixture of KBR and the medication samples Glibenclamide and Pioglitazone HCl were used. Diets were used to compress the mixture into a disk. After inserting the disk into the spectrophotometer, the spectrum was captured. The spectra was then recorded after a sample of Glibenclamide was combined with an excipient like Cross-povidone and a sample of Pioglitazone HCl was combined with HPMC K-100M and compressed. As shown in Fig. 7, FTIR analysis was also carried out for the improved formulation, and the IR spectra showed no discernible alterations.

DSC Analysis: The DSC operator is used in the analysis to ascertain the thermal behavior of the medicines. For about fifteen minutes, the sample bilayer tablet was cooked steadily in aluminum pans with flat bottoms. Both glibenclamide and pioglitazone HCl display thermal characteristics in line with their known melting points, according to the DSC data shown in Fig. 8. The DSC curves of the two medications showed no interaction, and the formulation remained unchanged.

Pre-Compression Parameter Evaluation: Angle of Pose: The funnel technique was used to calculate the angle of repose. A cone-shaped heap was created when the powder was dumped from a certain height via a funnel onto a level surface. To get the angle, the height and radius of the heap were computed. The formula $\tan\theta=h/r$ may be used to determine the angle of repose. where r is the powder cone's radius and h is its relative height. Bulk Density: A predetermined amount of powder was carefully leveled without compacting after being put into a measuring cylinder. Use the following formula to get the bulk density, expressed in gm/ml gm/cc: Density of Bulk = Bulk Mass/Bulk The volume

Tapped Density: Twenty taps were performed on the powdered grains in a measuring cylinder. After tapping the powder, the mass of the first and last levels was recorded. Mass/FinaltappedVolume = Tappeddensity

Granule Compressibility: Carr's index and Hausner's ratio were used to calculate the compressibility index. Index of Carr's = TD-BDX100/BD TD/BD is Hausner's ratio. Development of Formulations:

TABLE 1: MEDIATERELEASE COMPOSITION Glibenclamide and Pioglitazone HCl Blend Preparation Using the Wet Granulation Method: • Transfer the drugs and excipients to a new mortar and pestle after carefully weighing them in accordance with the quantities indicated in the table. In order to create starch mucilage, distilled water and starch are combined, heated on a water bath until the starch gelatinizes and forms mucilage, and then the starch mucilage is added to the mixture and properly mixed. • Next, add a little bit of amaranth for glibenclamide and turmeric for pioglitazone HCl stir till a moist dough forms. A sieve such as #12 should be used to filter this mixture. Dry the granules in a hot air oven set to 60 degrees Celsius for 10 to 15 minutes. #22 mesh was used to	FG1	FG2	FG3	FG4	FG5	FG6	FG7	FG8

filter the dry grains. Add the talc and magnesium stearate to the blender along with all of the sifting grains, and mix for two minutes. Then, add as much flavoring agent as needed. The composition of immediate-release and sustained-release tablets is shown in Tables 1 and 2.Ingredients								
Glibenclamide	10	10	10	10	10	10	10	10
Cros-Povidone	-	-	-	-	3	6	9	12
SodiumStarchGlycolate	3	6	9	12	-	-	-	-
MicroCrystallineCellulose	15	30	45	60	15	30	45	60
Lactose	116	98	80	62	116	98	80	62
StarchMucilage	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
Magnesiumstearate	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

TABLE2:COMPOSITIONOFSUSTAINEDRELEASE

Ingredients	FP1	FP2	FP3	FP4	FP5	FP6	FP7	FP8
PioglitazoneHCl	45	45	45	45	45	45	45	45
HPMCK100	-	-	-	-	10	20	30	40
HPMC K14	10	20	30	40	-	-	-	-
Lactose	188	178	168	158	188	178	168	158
StarchMucilage	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
Magnesiumstearate	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

Bilayer Tablet Preparation: First, wet granulation was used to create mixes of immediate release and sustained release tablets utilizing starch mucilage as a binding agent. Formulations of instant release optimum layer were chosen based on dissolving behavior. Eight continuous release layer formulations with ideal hardness (6–8 kg/cm2) were compacted with optimized instant release to create bilayer tablets. 9mm punches were used for compression. As seen in Table 3, the 400 mg tablet's total weight included 150 mg of glibenclamide in the immediate release layer and 250 mg of pioglitazone HCl in the sustained release layer. Bilayer tablets were prepared, and their in-vitro dissolving outcomes and different post-compression parameters were assessed and adjusted.

TABLE3:FINALOPTIMIZEDFORMULATIONOFBILAYERTABLET

S.no.	MaterialName	Quantity(mg)	MaterialName	Quantity(mg)
1	Glibenclamide	10mg	PioglitazoneHCl	45
2	Cros-Povidone	6	HPMCK100	40
3	SSG	--	HPMC K4	-
4	MCC	30	StarchMucilage	2.5
5	StarchMucilage	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

ISSN:0976-0172

Journal of Bioscience And Technology
www.jbstonline.com

Assessment of Post-Compression Factors: Weight Variance: To calculate the weight variance, twenty pills were weighed individually. The pills' average weight and individual weights are contrasted. The sample mean and percentage variation were calculated using pill weight. When pills weigh between 85 and 250 mg± 7.5% and more than 250 mg± 5%, the IP limit for weight fluctuation % Individual weight minus average weight divided by average weight times 100 is the deviation. Hardness: The hardness was measured using a Monsanto hardness tester. To assess hardness, six pills were taken and put between the jaws of the hardness tester. Friability was assessed by weighing ten pills and rotating them in a Roche Friabilator set at 25 rpm for five minutes. Following dusting, the mass of all the tablets that remained was measured, and the percentage of friability was observed. %Friability = initial weight x 100/final weight Thickness: The thickness and diameter of the formulation experiments were measured using a Vernier Calliper. Ten tablets were taken from each batch in order to calculate the average crushing strength or tablet hardness. Drug Release Studies in Vitro: To conduct in vitro drug release experiments, the USP dissolving test equipment (Type 2) was used. The pH was 1.2 for the first two hours and 6.8 for the remaining six hours when the dissolving experiments were carried out using 900ml of dissolution medium that had been agitated at 50 rpm and 37.5°C. Aliquots were often taken out and swapped out for fresh media. Following filtering, the drug content of each sample was investigated. It was found that the F8 batch of instant release exhibited better regulated release while the F6 batch exhibited quicker disintegration. Kinetic Evaluation of Data on Dissolution: In order to explore the mechanism of drug release from the tablets, the release data were evaluated using the zero-order, first-order, Higuchi, and Korsmeyer equations, which are often used to characterize the drug release behavior from polymeric systems.Research on Stability: Charged and packaged at room temperature (65±5% RH and 30 + 2 deg * C) was formulation batch F2. The tablets were evaluated for assay and dissolving profile testing at 0, 1, 2, and 3 months. As shown in Table 20, the results of the stability investigation revealed no appreciable variations in the dosage or rate of dissolution. The drug's content and rate of dissolution did not significantly alter after three months.

RESULTSAND DISCUSSION
Pre-formulationStudies:

TABLE4:ORGANOLEPTICPROPERTIES

S.no.	Parameter	Glibenclamide	PioglitazoneHCl
1	Color	White	OffWhite
2	Odour	Characteristic	No odour
3	Appearance	Amorphous	Amorphous
4	Taste	Tasteless	Unpleasanttaste

TABLE5:SOLUBILITYOFGLIBENCLAMIDEINDIFFERENTSOLVENTS

Solvents	Solubility(mg/ml)
Methanol	0.152±0.03
0.2MNaOH	0.178±0.02
0.1NHCl	0.139±0.02
PhosphatebufferpH7.4	0.167±0.02
Water	0.206±0.02

TABLE6:SOLUBILITYOFDRUGINPIOGLITAZONEHCL

Solvents	Solubility(mg/ml)
Ethanol	0.138±0.02
Methanol	0.152±0.02
Acetone	0.157±0.01
0.1HCl	0.416±0.02
PhosphatebufferpH6.8	0.398±0.02
Water	0.013±0.02

TABLE7:MELTINGPOINTOFDRUGGLIBENCLAMIDEANDPIOGLITAZONEHCL

Drug	ReferenceRange	ObservedRange
Glibenclamide	173-175 ºC	175-177 ºC
PioglitazoneHCl	193-194 ºC	193-195 ºC

Preparation ofStandardCurveof Glibenclamide:

TABLE8:STANDARDCALIBRATIONCURVEOFGLIBENCLAMIDEIN6.8PHPHOSPHATEBUFFER

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

Standarddeviationn=3

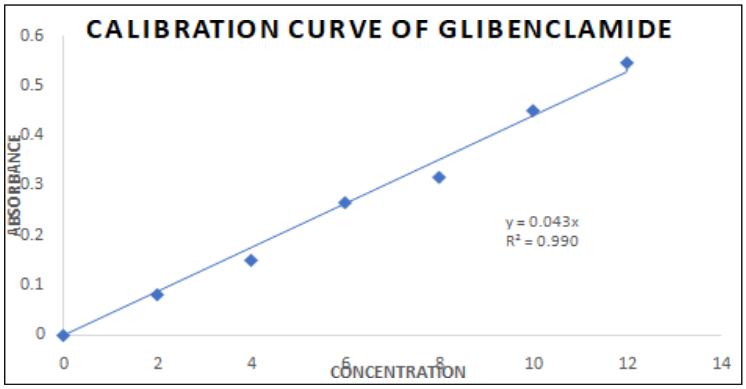


FIG.1:CALIBRATIONCURVEFORGLIBENCLAMIDEINPHOSPHATEBUFFERPH6.8

PreparationofStandardCalibrationCurveofPioglitazoneHCl:

TABLE9:CALIBRATIONPLOTOFPIOGLITAZONEHCLIN0.1 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

Standarddeviationn=3

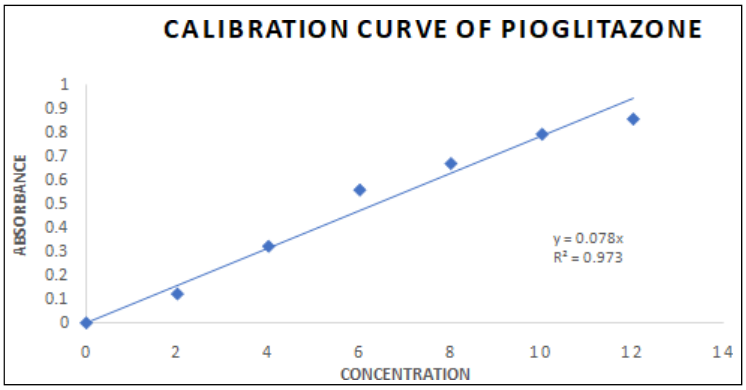


FIG.2:STANDARDGRAPHOFPIOGLITAZONEHCLIN0.1 HCL

FTIRAnalysis:

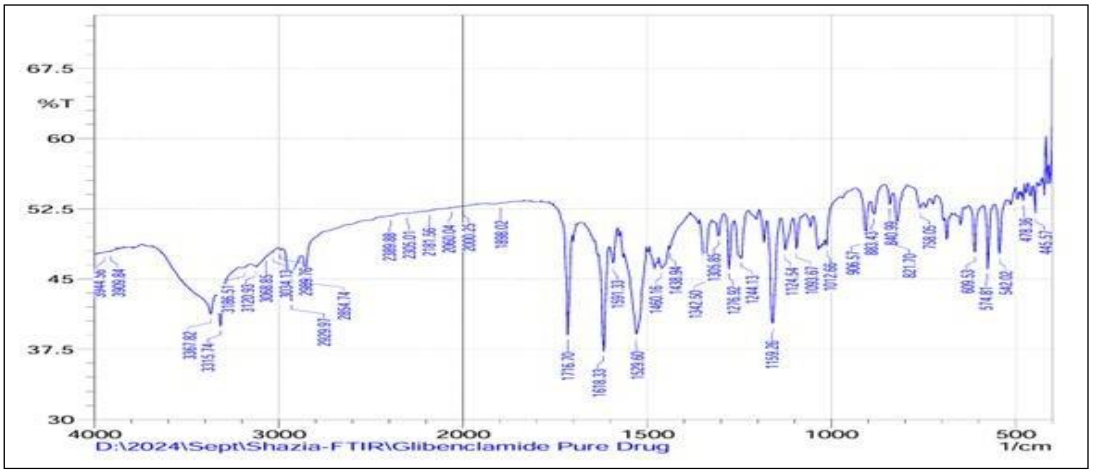


FIG.3:FTIRSPECTRAOFGLIBENCLAMIDEPUREDRUG

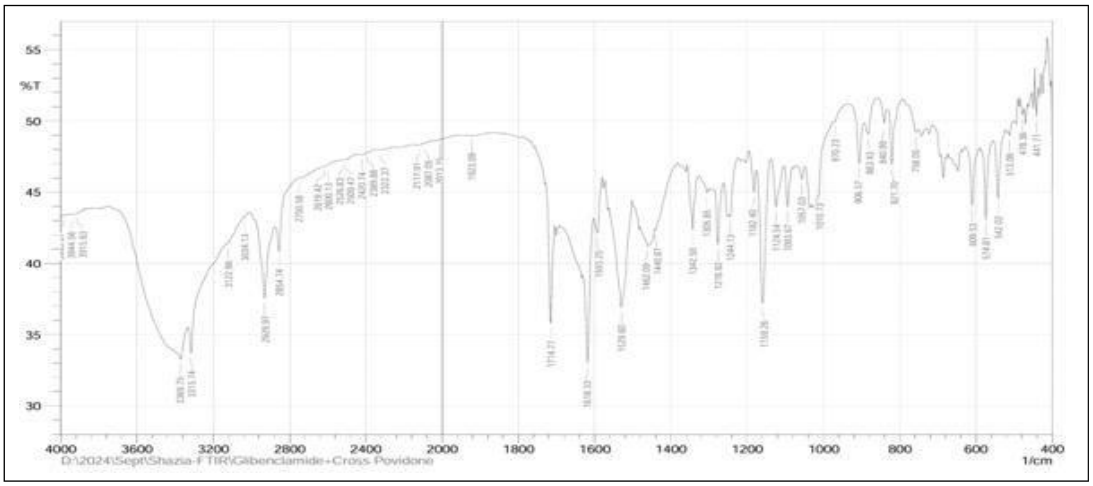


FIG.4:FTIRSPECTRAOFGLIBENCLAMIDEWITHCROSS-POVIDONE

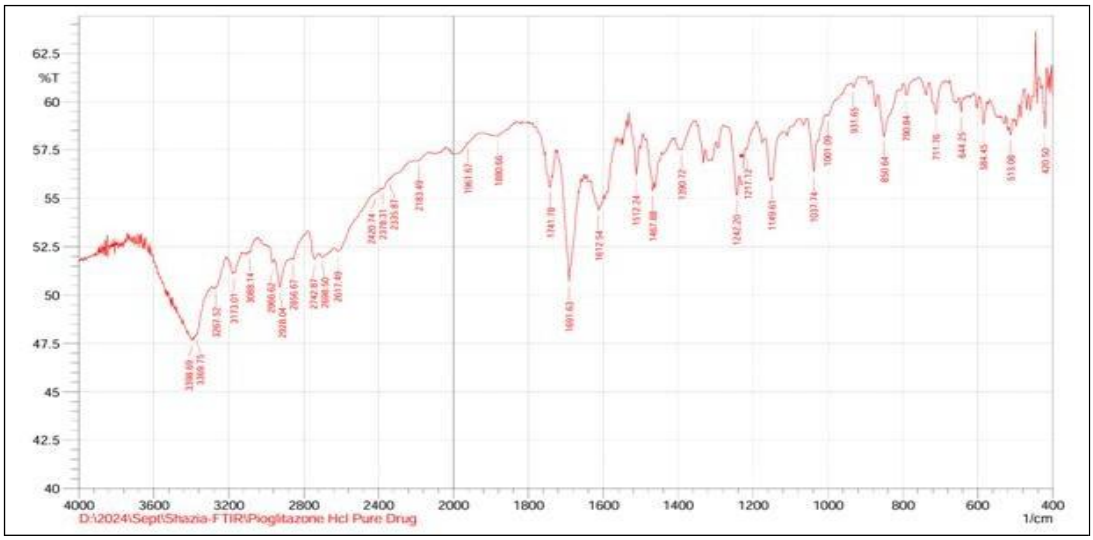


FIG.5:FTIRSPECTRAOFPUREPIOGLITAZONEHCL

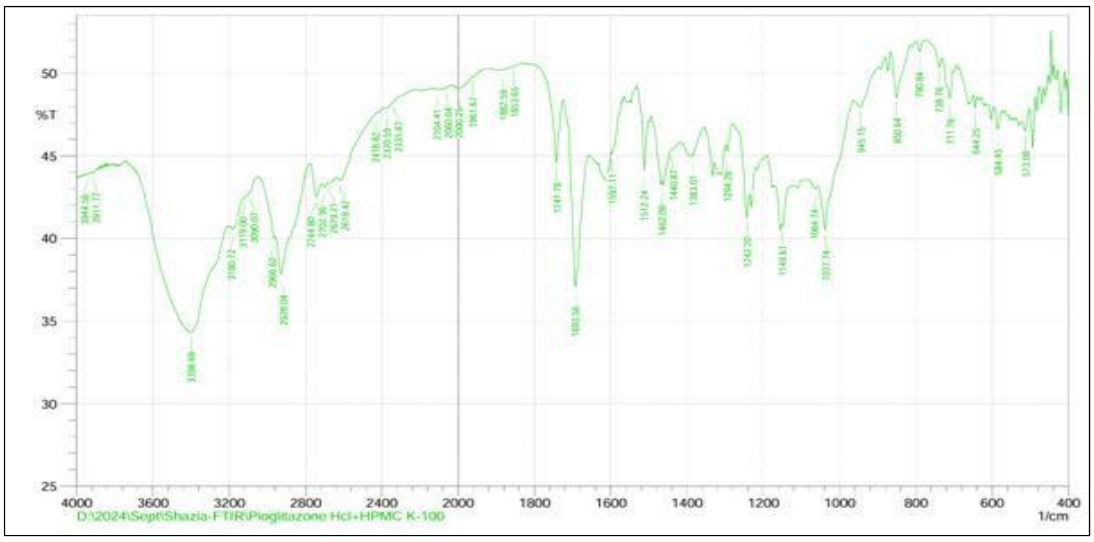


FIG.6:FTIRSPECTRAOFPIOGLITAZONEHCLWITHHPMCK-100

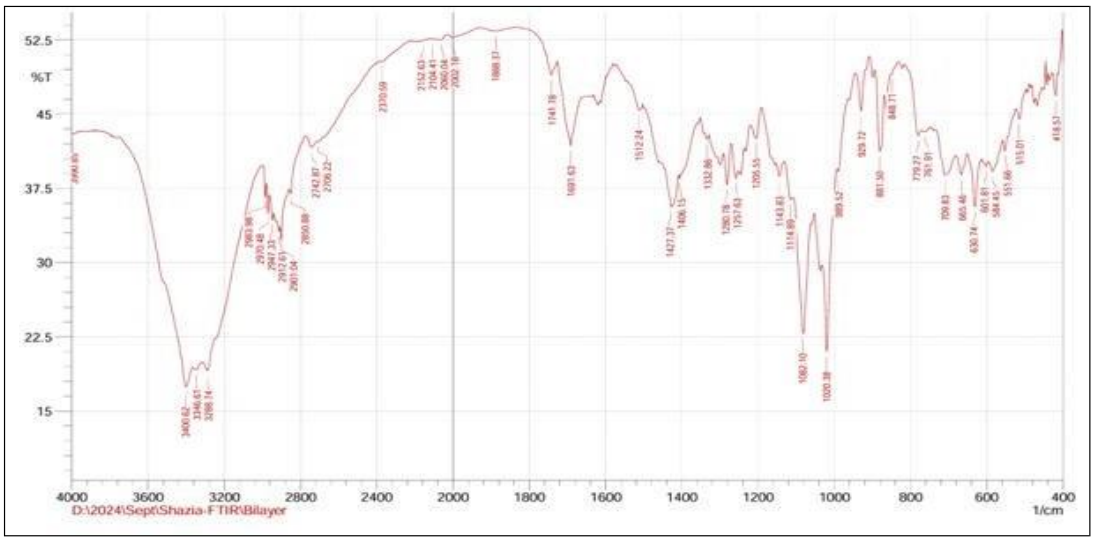


FIG.7:FTIRSPECTRAOFBILAYERTABLET

DSCStudy forBilayerTablet:

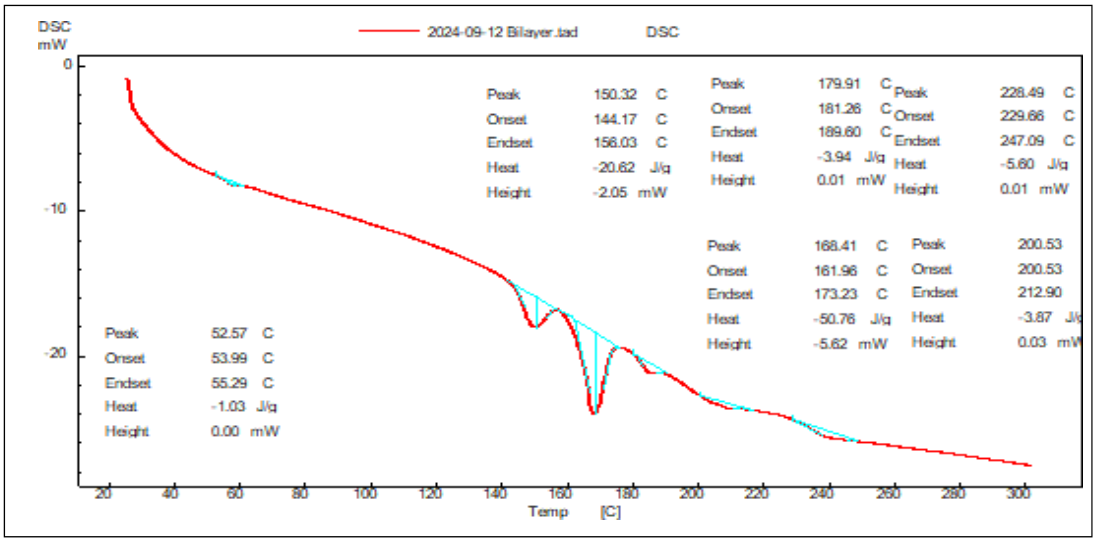


FIG.8:DSCSPECTRAOFOPTIMIZEDFORMULATION

TABLE10:PRE-COMPRESSIONEVALUATIONFORIMMEDIATERELEASEFORMULATIONS

S.no.	Formulation	Angle of repose(°)	BulkDensity (g/mL)	TappedDensity (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

TABLE11:PRE-COMPRESSIONEVALUATIONFORSUSTAINEDRELEASEFORMULATIONS

S.no.	Formulation	Angle of Repose(°)	BulkDensity (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

TABLE12:POST-COMPRESSIONEVALUATIONOFIMMEDIATELAYER

S.no.	Formulation	Hardness (kg/cm2)	Thickness (mm)	Weight Variation(mg)	Friability(%)	Drugcontent (%)
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

TABLE13:POST-COMPRESSIONEVALUATIONOFSUSTAINEDLAYER

S.no.	Formulation	Hardness (kg/cm2)	Thickness (mm)	Weight Variation(mg)	Friability(%)	Drugcontent (%)
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

TABLE14:RESULTSOFDISINTEGRATIONTIMEFORIMMEDIATERELEASELAYEROFGLIBENCLAMIDE

Formulation	DisintegrationTime
FG1	1min50sec
FG2	1min56sec
FG3	1min44sec
FG4	1min34sec
FG5	1min42sec
FG6	1min27sec
FG7	1min38sec
FG8	1min41sec

*In-vitro*DissolutionStudyofGlibenclamide&PioglitazoneBilayer Tablets:

TABLE15:*IN-VITRO*DISSOLUTIONSTUDYOFGLIBENCLAMIDE

Timeinminutes	CumulativePercentageRelease							
	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

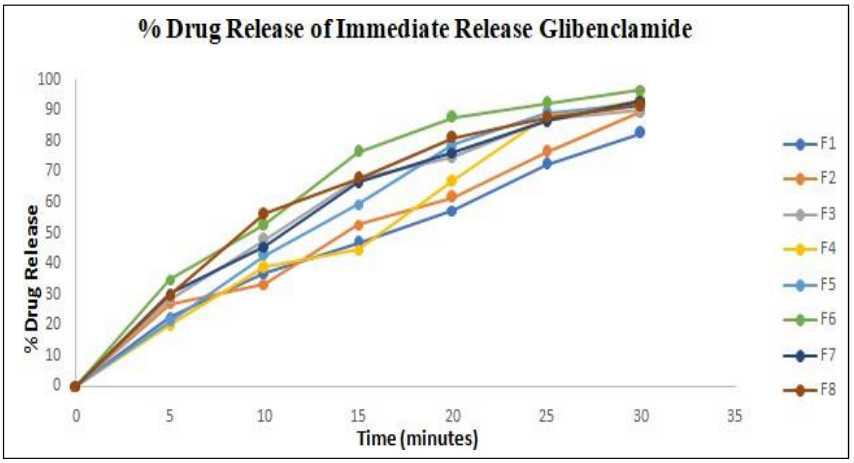


FIG.9:DISSOLUTIONGRAPHFORFORMULATIONSFG1-FG8 TABLE 16:

IN-VITRO DISSOLUTION STUDY OF PIOGLITAZONE HCL

Time(InHrs.)	%CumulativeDrugRelease							
	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

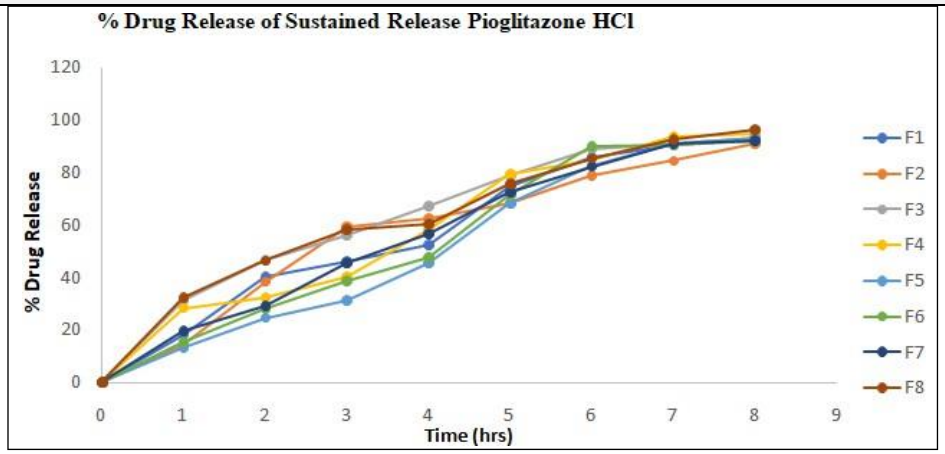


FIG.10:DISSOLUTIONGRAPHFORFORMULATIONSFP1-FP8

Drug Release Profile in Vitro for the Optimal Formulation: The F6 formulation for rapid release and the F8 formulation for continuous release are two of the formulations that use HPMCK100 as a binder and Crospovidone as a super-disintegrant. Table 17 shows the dissolution findings, while Fig. 11 shows the cumulative percentage release.

TABLE17:DISSOLUTIONRESULTOFBI-LAYEREDTABLETGLIBENCLAMIDEANDPIOGLITAZONEHCL

Time(Hour)	PercentDrugRelease	
	Glibenclamide(Immediaterelease)	PioglitazoneHCl(Sustainedrelease)
0thHr	0	0
0.5thHr	64.55	-----
1thHr		68.3
2thHr		71.4
4thHr		78.6
6thHr		84.5
8thHr		89.6
10thHr		90.2
12thHr		94.6

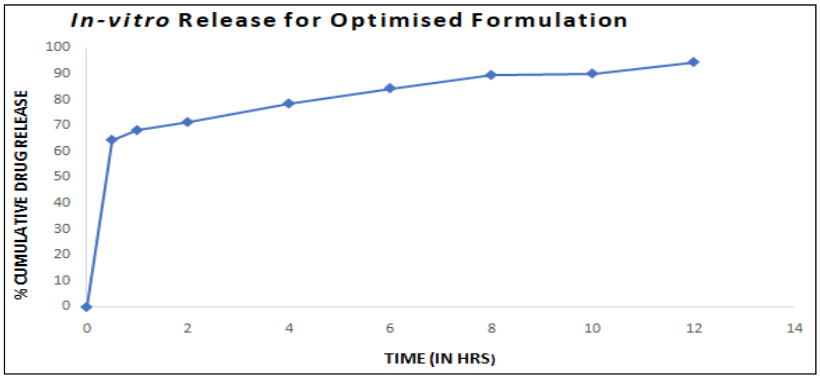


FIG.11:CUMULATIVEPERCENTAGEDRUGRELEASEOFBI-LAYEREDTABLETGLIBENCLAMIDEAND PIOGLITAZONE HCL

TABLE18:COMPARISONOFCUMULATIVEPERCENTAGEDRUGRELEASEWITHTHATOFTHE MARKETED PRODUCT

S.no.	Time(hrs)	Bilayertablet	MarketedProduct
Dissolutionmedium6.8pHphosphatebuffer			
1	0	0	0
2	0.5	64.55	31
3	1	67.13	45
0.1NHCL			
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

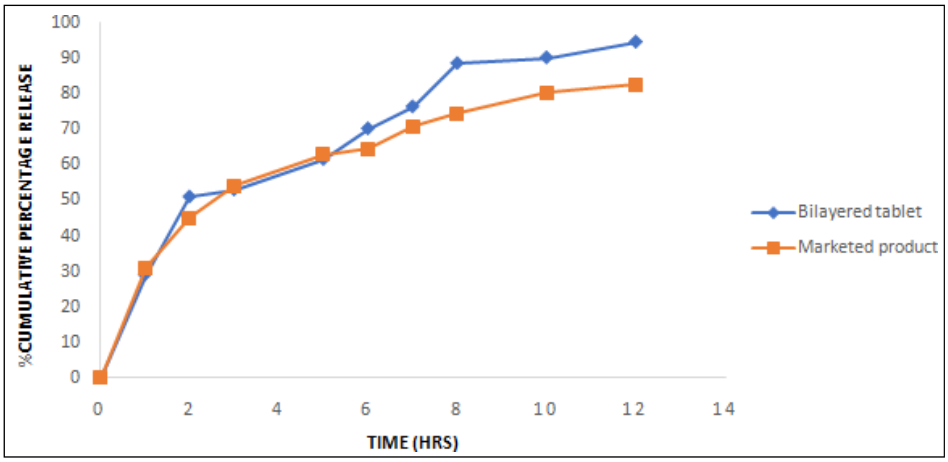
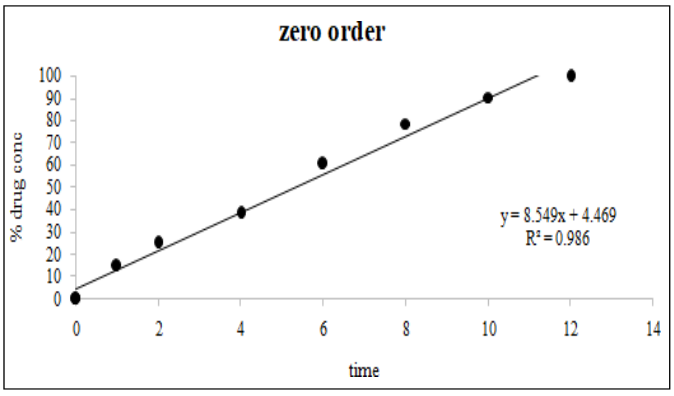


FIG. 12: COMPARISON OF CUMULATIVE PERCENTAGE DRUG RELEASE WITH THAT OF THE MARKETED PRODUCT

DrugReleaseKineticAnalysisofSustainedReleaseLayerofBilayer Tablet:

TABLE19:RELEASEKINETICSOFOPTIMIZEDBILAYERTABLETS

Parameters	ZeroOrder	Firstorder	Higuchi	Pappas
	%CDRVsT	Log%CVsT	%CDRVs √T	LogCVsLogT
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



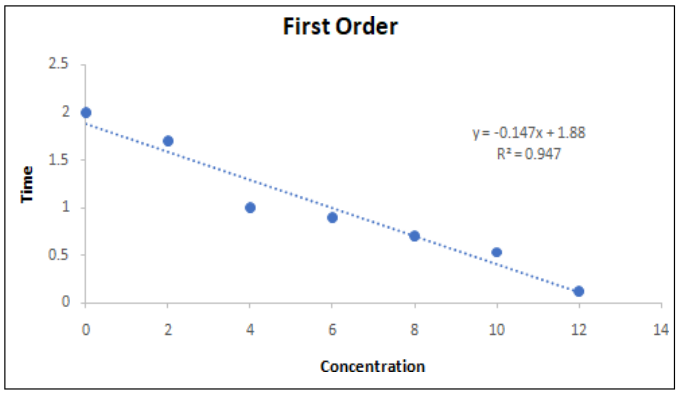


FIG.13:ZEROORDERPLOT

FIG.14:FIRSTORDERGRAPH

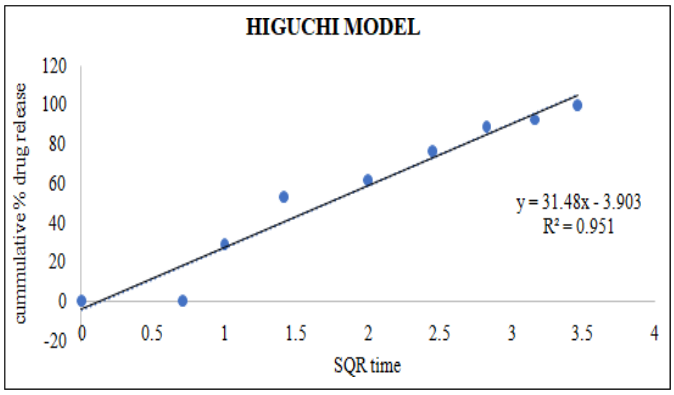


FIG.15:HIGUCHIPLOT

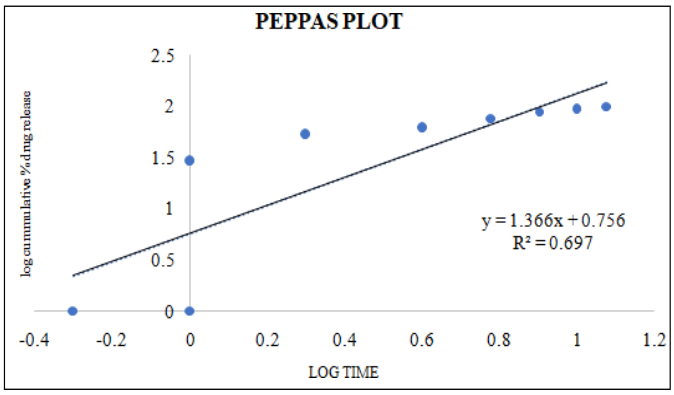


FIG.16:REPRESENTINGPEPPASPLOT

Stability Studies:

TABLE20:PERCENTAGEDRUGCONTENTIN0AND3MONTHS

Parameter	Storagecondition			
	Initialrelease	Roomtemperature40±2ºCand65±5%*RH		
	0months	1months	2months	3months
%DrugContent	99.8±0.25	99.8±0.26	99.8±0.27	99.8±0.27

The sulphonyl urea family, which includes glibenclamide, is essential for the management of Type II diabetes. Pioglitazone belongs to the thiazolidinedione family and raises insulin sensitivity. Glycemic control may be enhanced by combining these drugs in the proper dose form. The polymers and excipients, together with the pure drug, were shown to be compatible when evaluated using FTIR and DSC investigations. The standard calibration curves for Glibenclamide and Pioglitazone HCl in 6.8 pH phosphate buffer and 0.1N HCI, respectively, showed a significant association.

The permeability and bioavailability were enhanced by creating eight formulations (IR&SR) using various polymers at varied concentrations. Glibenclamide (10 mg) and pioglitazone HCl (45 mg) were successfully combined in a 400 mg tablet using the wet granulation procedure. The resultant bilayer pill included HPMC K100 M 40 mg (F8) in sustained release and Cross-povidone 6 mg (F6) in instant release. In in-vitro dissolving testing, the enhanced recipe worked better than the commercial version, releasing 94.6% of the medication in 12 hours. According to Higuchi's kinetics and zero order, the formulation had regression values of 8.0638 and 31.479, respectively. Finally, further evaluations were conducted on the enhanced tablet's thickness, hardness, friability, and CDR %. According to ICH guidelines, stability study data showed no appreciable variations in drug content or dissolution rates over a three-month period. his constant assistance, wise counsel, and motivation throughout our research. Most significantly, without my parents' love and patience, who have supported and encouraged me throughout my endeavor, none of this would have been possible.

REFERENCES:

1. Akhtar M, Jamshaid M, Zaman M and Mirza AZ: Bilayer tablets: A developing novel drug delivery system. Journal of Drug Delivery Science and Technology 2020; 60: 102079.
2. Farida Nizami and Yogendra Malviya: Recent advancement and challenges in bilayer tablet technology: anoverview.CurrentResearchinPharmaceuticalSciences 2021; 11 (04): 91-97
3. Unai Galicia-Garcia, Asier Benito-Vicente, Shifa Jebari, Asier Larrea-Sebal, Haziq Siddiqi, KepaB. Uribe, Helena Ostolazaand César Martín: Pathophysiology of Type 2 Diabetes Mellitus. Int J Mol Sci 2020; 21: 6275.
4. Camila Pires Mendes, Barbara Graziela Postal, Marisa JAdna Silva Frederico, Rui Goncalves Marques Elias, Veronica Aiceles de Medeiros Pinto, Cristiane da Fonte Ramos,PatríciaDevantierNeuenfeldt,RicardoJose Nunes and Fatima Regina Mena Barreto Silva: Synthesis of a novelglibenclamide-pioglitazonehybridcompoundandits effects on glucose homeostasis in normal and insulin-resistant rats. BioorganicChemistry2021; 114:105157:1-
5. Sachin Atre, Sona Deshmukh and Manjusha Kulkarni: Prevalence oftype 2 diabetes mellitus

ISSN:0976-0172

Journal of Bioscience And Technology
www.jbstonline.com

(T2DM) in India: A systematic review (1994-2018) Diabetes & Metabolic Syndrome: Clinical Research & Reviews Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2020; 14.

6. Xueqin Xie, ChangchunWu, YuduoHao, TianyuWang, Yuhe Yang, Peiling Cai, Yang Zhang, Jian Huang, Kejun Deng,DanYanandHaoLin:Benefitsandriskofdrug combinationtherapyfordiabetesmellitusanditscomplications:acomprehensivereview.Frontiersin endocrinology2023;https://doi.org/10.3389/fendo.2023.13 01093.
7. Poojashree Verma, Deepika Bairagi, Aswin Somkuwar, Mukesh Mehra and Mahavir Chhajed Formulation and Evaluation of Transdermal Patch of Glibenclamide International Journal of Pharmacy & Life Sciences 2020; 11(7): 6724-6737.
8. Annapureddi Indira Revathi, Duggi Venkatesh and Santhoshi P: Formulation and evaluation of bilayer tablets of diabetis drugs. World Journal of Pharmaceutical Research 2022; 8(9): 336-399.

Rakshita Chaudhari Rahul Wagh, June Milind Wagh and Valmik Wagh: Formulation and evaluation of glibenclamide oral dispersible tablet by solid dispersion technique. International Journal of PharmaceuticalSciences and Research 2023; 14 (6): 406-415.

9. Doaa Alshora, Mohamed IbrahimA, Nouf Alanazi, Malak Alowyid and Zainab Ali Alnakhl: Formulation of glibenclamide proniosomes for oral administration: pharmaceutical and pharmacodynamics evaluation. Saudi Pharmaceutical Journal 2023; 31: 101830.
10. Safiullah Khan, Asadullah Madni, Muhammad Abdur Rahim A, Hassan Shah and Abdul Jabar: Enhanced *in- vitro* release and permeability of glibenclamide by proliposomes:development,characterizationand histopathological evaluation. Journal of Drug Delivery Science and Technology 2021; 63.
11. Ashwini Arun Zanke, Santosh Ghule and Sachin Jain: Development and evaluate nanoparticles of poorly soluble anti-diabetic drug (pioglitazone) loaded tablets latin. American Journal of Pharmacy 2023; 42(10): 703-718.
12. Kavitha Ganesan, Muhammad Burhan Majeed Rana and Senan Sultan: Oral Hypoglycemic medications 2023; https://pubmed.ncbi.nlm.nih.gov/29494008/.
13. Sandesh Kumar, Yograj Mahajan, Vishal Gupta, Harish Kumar and Singh Kumar Abhishek: Formulation and evaluation of bilayer anti diabetic tablets. International Journal of Novel Research and Development 2023; 8(10) ISSN: 2456.