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Simultaneous Spectrophotometric Determination of Pioglitazone and Glimepiride in Bulk and Pharmaceutical Dosage Form by Using Area under Curve Method

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Abstract

Glimepiride and Pioglitazone in combination are available as tablet dosage forms in the ratio of 2: 15. A simple, reproducible and efficient spectrophotometric method has been developed for the simultaneous estimation of Glimepiride and Pioglitazone in bulk and tablet dosage forms. The proposed method is based on the area under curve. This mixture was analyzed for getting the spectra from 200-400 nm for Pioglitazone and Glimepiride mixture. After getting the AUC at 222-232 nm and 230-240 nm, the concentration of Pioglitazone and Glimepiride were calculated by putting the values of absorbance of mixture in formula. The method was validated statistically according the ICH guidelines. The recovery studies confirmed the accuracy of the proposed methods.

Key-words: Pioglitazone, Glimepiride, area under curve method, U-V spectrophotometric method

Introduction

Diabetes Mellitus commonly referred to as diabetes is a group of metabolic diseases in which there are high blood sugar levels over a prolonged period.[1,2]

Anti-diabetics such as sulfonylurea and thiazolidinedione derivatives are commonly prescribed hypoglycemic drugs for non-insulin dependent type II diabetes mellitus.

Pioglitazone hydrochloride, (±)-5-{4-[2-(5-ethyl-2-pyridyl) ethyl]benzyl}-2,4-thiazolidinedione hydrochloride salt is a member of thizolidinedione class, which exerts its glucose-lowering effect by binding to peroxisome proliferator-activated receptors gamma. (PPARγ), thus increasing the receptor sensitivity to insulin.

Glimepiride, 1-H-pyroll-1-carboxamide-3-ethyl-2,5-dihydro-4-methyl-N-[2-[4-[[[[(4-methylsiklohexyl) amino] carbonyl] amino] sulfonyl] [phenyl] ethyl]-2-oxo-trans, is a member of sulfonylurea drugs, which can increase the secretion of insulin by functioning islet β -cells. In the past few decades, several generations of sulfonylurea drugs have been developed for common use such as glimepiride. [3, 4]

This generation of hypoglycemic drugs is much more potent hence are effective at much lower dosages. Several analytical methods have been reported for the determination of pioglitazone and Glimepiride in bulk and

pharmaceutical dosage form. Even though various methods were reported in the literature for estimation of glimepiride and pioglitazone individually or in combination with other drugs no method had been reported for simultaneous estimation of these two drugs using Multiwavelength spectroscopy method in bulk drug and pharmaceutical dosage forms.[5,6]

Aim and objective of the present work was to develop & validate UV-Spectrophotometric methods for the simultaneous estimation of Pioglitazone and Glimepiride in combined dosage form by area under curve method.

Materials and Methods

List of Instruments / equipments

Sr. No.	Instrument / Equipment	Make	Model
1.	UV spectrometry	Shimadzu Corporation	UV-1800 240V
2.	Weighing Balance	Shimadzu Corporation	BL-22OH (Electronic balance)

Apparatus and Glass wares

Sr. No.	Glass wares	Make
1.	Volumetric flasks (25 ml)	BOROSIL, INDIA
2.	Beaker	BOROSIL, INDIA
3.	Measuring Cylinder (250 ml, 1000 ml, 2000 ml)	BOROSIL, INDIA

List of Drugs

Sr. No.	Name of drug	Supplied By	Quantity
1.	Pioglitazone	Lupine Pharmaceuticals	2.0 gm
2.	Glimepiride	Lupine Pharmaceuticals	2.0 gm

Marketed Formulation Available

Brand Name: PIOGLAR-G

Manufactured by: RANBAXY

Labeled claim: Pioglitazone – 15 mg

Glimepiride – 2 mg

Reagents and Chemicals

All reagents and chemicals used were of AR analytical grade.

- Methanol

Selection of sampling wavelength for analysis and preparation of standard calibration curves:

1) Solvents Used:

Methanol AR grade.

2) Drugs used: Pioglitazone, Glimepiride.

3) Preparation of standard stock solution:

The standard stock solutions of Pioglitazone and Glimepiride were prepared by dissolving separately 10 mg of drug each in 100 ml methanol. Aliquots of working stock solutions of Pioglitazone and Glimepiride were diluted with methanol solution.

4) Selection of sampling wavelengths for analysis:

Appropriate dilutions were made with methanol to give concentration of 10 µg/ml. Further the solution was scanned in UV range from 200-400 nm and the spectrum was recorded.

From the spectrum, wavelengths chosen were 222-232 nm and 230-240 nm for Pioglitazone and Glimepiride respectively. The selected two wavelengths were utilized for the measurement of absorbance of each drug and further analysis was done.

5) Selection of analytical concentration range

From working standard solution of Glimepiride 0.02, 0.04, 0.06, 0.08 and 0.10 ml were pipette out and each was diluted to 10 ml to get the concentrations 0.20, 0.40, 0.60, 0.80 and 1.0 µg/ml. Similarly, from working standard solution of Pioglitazone 1.5, 3, 4.5, 6, and 7.5 ml were pipette out and each was diluted to 10 ml to get the concentrations 1.50, 30, 4.50, 60, and 7.50 µg/ml. The absorbance of each of this solution was measured at selected wavelengths and plotted against concentration. The concentration range over which the drug obeyed

Beer's law was chosen. The range was found to be 0.20 - 1.0 µg/ml for Glimepiride (r^2 = 0.998) and 1.50-7.50 µg/ml for Pioglitazone (r^2 = 0.995).

Result and Discussion

Figure No.1 Calibration curve of Pioglitazone

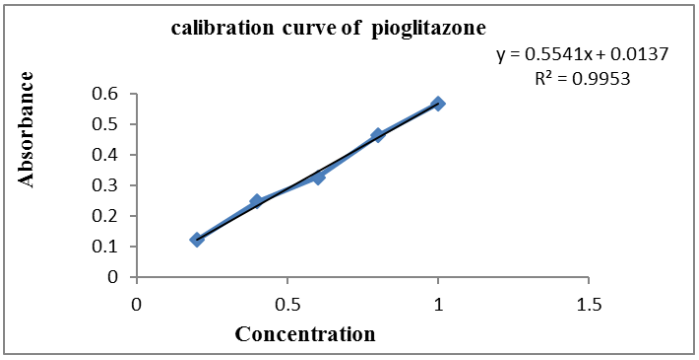


Figure No.2 Calibration curve of Glimepiride

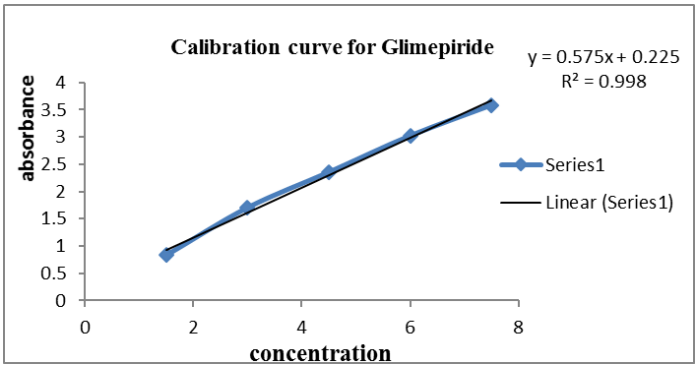
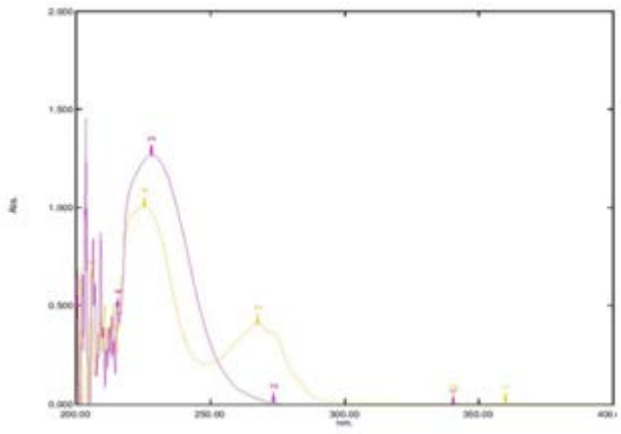


Figure No.3 Overlain spectra of Pioglitazone and Glimepiride



Analysis of powder mixture:

Powder mixture of Pioglitazone and Glimepiride having composition 1mg/ml was made in methanol and 10 ml of this solution diluted to 100 ml with this mixture was analyzed for getting the spectra from 200-400 nm. For Pioglitazone and Glimepiride mixture. After getting the AUC at 222-232 nm and 230-240 nm, the concentration of Pioglitazone and Glimepiride were calculated by putting the values of absorbance of mixture in the formula.

Table No.1 Data of powder mixture Analysis

Sr.No.	Amount present in (µg/ml)		Amount found in (µg/ml)		Amount found in %	
	Glim	Pio	Glim	Pio	Glim	Pio
1	0.20	1.50	0.182	1.50	90.12	98.33
2	0.20	1.50	0.197	1.47	98.50	98.00
3	0.20	1.50	0.195	1.49	97.90	99.33
4	0.20	1.50	0.196	1.48	98.34	98.66
5	0.20	1.50	0.195	1.49	97.90	99.33

Procedure for analysis of tablet formulation

Twenty tablets were weighed accurately and powdered. Powder equivalent to 50 mg Pioglitazone was weighed and transferred to 50 ml volumetric flask; in the same flask 50 mg of pure Glimepiride drug was added and dissolved in methanol by shaking the flask for 10 minutes. The solution was scanned in the range of 200-400 nm against blank to obtain spectra and the AUC is recorded using wavelength range from 222-232 nm and 230-240 nm for Pioglitazone and Glimepiride respectively.

Table No.2 Analysis of Tablet Formulation

Sr. No.	Label Claim (µg/ml)		Amount Found (µg/ml)		% of Label Claim	
	Glim	Pio	Glim	Pio	Glim	Pio
1.	0.20	1.50	0.197	1.47	98.50	98.00
2.	0.20	1.50	0.195	1.49	97.90	99.33
3.	0.20	1.50	0.196	1.48	98.34	98.66
4.	0.20	1.50	0.195	1.49	97.90	99.33
5.	0.20	1.50	0.196	1.48	98.09	98.66

Table:3 Statistical analysis of tablet formulation

Component	Mean	S.D.	%RSD	S.E.
Pioglitazone	98.146	0.267	0.272	0.231
Glimepiride	98.796	0.556	0.5637	0.333

Procedure for Recovery Studies

Recovery studies were carried out by applying the method to drug sample present in tablet dosage form to which known amount of Pio and Glim corresponding to 80,100,120% Pioglitazone and 80,100,120% of Glimepiride was added (standard addition method). In 80% recovery study amount of standard added was 1.20 mg of pioglitazone. In 100 % recovery study the amount of standard added was 1.50 mg of pioglitazone. In 120 % recovery study the amount of pioglitazone standard added was 1.80 mg. In 80% recovery study the amount of glimepiride standard added was 0.16 mg. In 100 % recovery study the amount of standard added was 0.20 mg of Glimepiride In 120 % recovery study the amount of Glimepiride standard added was 0.24 mg The mixed sample solutions were analyzed to obtain spectra and the AUC is recorded in the wavelength range from 222-232 nm and 230-240 nm. The concentration of Pioglitazone and Glimepiride were calculated from the equation. At each level of the amount of three determinations were performed and results obtained.

Table:4 Recovery studies of Pioglitazone and Glimepiride

Level of % reco.	Total Absorbance ug/ml		Conc. recoverd Ug/ml		% of recovery	
	Pio 222-232 nm	Glim 230-240 nm	Pio	Glim	Pio	Glim
80	0.756	0.516	1.16	0.13	96.66	81.25
80	0.757	0.517	1.17	0.14	97.5	87.5
80	0.756	0.518	1.18	0.15	98.33	93.75
100	0.887	0.600	1.43	0.18	95.33	90.00
100	0.888	0.601	1.48	0.19	98.66	95.00
100	0.889	0.602	1.43	0.18	95.33	90.00
120	0.741	0.505	1.72	0.19	95.55	79.16
120	0.742	0.506	1.76	0.23	96.00	95.83
120	0.743	0.507	1.78	0.22	95.55	91.66

Table: 5 Statistical validation of Tablet Formulation

Level Of % Reco.	% Mean Recovery		S.D.		% RSD		S.E.	
	Pio	Glim	Pio	Glim	Pio	Glim	Pio	Glim
80	97.72	91.66	1.27	3.60	1.30	3.93	0.12	0.88
100	95.66	92.22	0.57	2.88	0.60	3.13	0.74	0.64
120	95.7	93.05	0.25	2.40	0.27	2.58	0.50	0.55

Procedure for precision study

Precision of the method was studied as intra-day and inter-day precision. Intra-day precision was determined by analyzing the 0.2, 0.6, 1.0 µg/ml of Glimepiride and 1.20, 1.50, 1.80 µg/ml of Pioglitazone for three times in same day. Inter-day precision was determined by analyzing the same concentration of the solution daily for three days.

Table: 6 Precision studies for Pioglitazone

Sr. No.	Conc. µg/ml	Measured area (µg/ml) ± S.D, RSD (%)	
		Repeatability (n=2)	Intermediate Precision (n=2)
1	1.20	1.27 ± 0.0152, 1.20	1.27± 0.01219, 0.95
2	1.50	1.42 ± 0.005, 0.40	1.42 ± 0.0045, 0.32
3	1.80	1.78 ± 0.01, 0.42	1.78 ± 0.01, 0.056

Table: 7 Precision studies for Glimepiride

Sr. No.	Conc. µg/ml	Measured area (µg/ml) ± S.D, RSD (%)	
		Repeatability (n=2)	Intermediate Precision (n=2)
1	0.16	0.14 ± 0.013, 9.36	0.14 ± 0.0131, 9.36
2	0.20	0.17 ± 0.011., 6.79	0.17 ± 0.0114, 6.71
3	0.24	0.24 ± 0.007, 76.38	0.24 ± 0.007, 3.01

Conclusion

The developed UV methods like area under curve are precise, specific, and accurate. Statistical analysis proves that these methods are suitable for the analysis of Pioglitazone and Glimepiride in bulk and pharmaceutical formulation without any interference from the excipient.

These methods have been found to be better than previously reported methods, because of use of less, economical and readily available solvent like methanol.

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