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Development and Validation of Analytical Methods for Simultaneous Spectrophotometric Determination of Pioglitazone and Glimepiride by Derivative Method

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ABSTRACT

A simple, rapid UV-Visible spectrophotometric method for the quantification of Pioglitazone hydrochloride and Glimepiride in bulk drug and tablet formulation was developed and validated.

UV-Visible spectrophotometric methods have been developed for the Derivative Spectrophotometric Method, of Pioglitazone and glimepiride in bulk and pharmaceutical dosage forms. the sampling wavelengths selected are 210 nm and 218 nm over the concentration ranges of 1.5 - 7.5 µg/ml and 0.2-1.0 µg/ml for pioglitazone and glimepiride respectively.

KEYWORDS: *Pioglitazone, Glimepiride, UV-Visible Spectrophotometric, Validation*

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INRODUCTION

Pioglitazone hydrochloride (PIO) is drug of the class thiazolidinedione (TZD) with hypoglycemic (antihyperglycemic, antidiabetic) action to treat diabetes. Chemically it is (±)-5-[p-[2-(5-Ethyl-2-pyridyl) ethoxy] benzyl]-2, 4-thiazolidinedione monohydrochloride. It act by reduces insulin resistance in the liver and peripheral tissues; increases the expense of insulin-dependent glucose; decreases withdrawal of glucose from the liver; reduces quantity of glucose. Glimepiride (GLM) is an antidiabetic drug belonging to a class of medications known as sulfonylureas. Chemically it is 3-ethyl-N,N-bis(3-ethyl-4-methyl-2-oxo-5H-pyrrol-2-yl)-4- methyl-2-oxo-5H-pyrrole-1-carboxamide. The primary mechanism of action of glimepiride in lowering blood glucose appears to be dependent on stimulating the release of insulin from functioning pancreatic beta cells. Both the drugs are official in I.P. 2010.[1] The reported methods are time consuming expensive and relatively complicated. The aim of this study was to develop simple, precise, accurate and convenient method for the simultaneous estimation of PIO and GLM in combined dosage form.

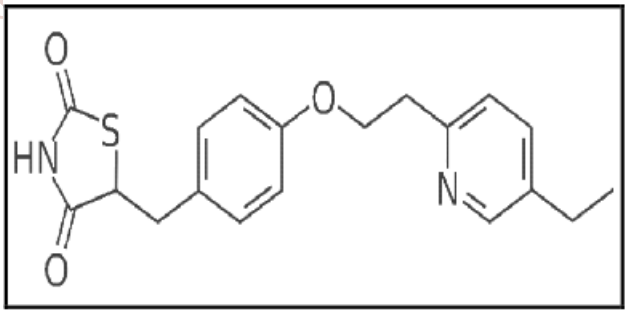

Fig. no. 1 Structure of Pioglitazone

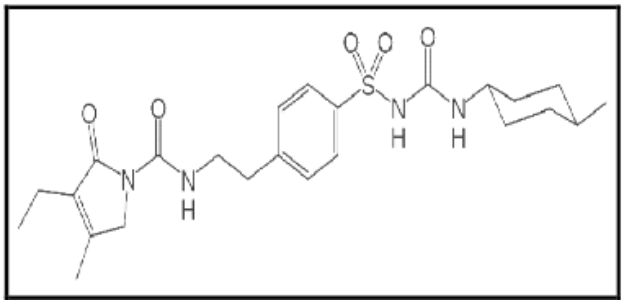

Fig. no. 2 Structure of Glimepiride

MATERIALS AND METHODS

Pioglitazone and glimepiride were obtained as gift samples from Lupin Pharmaceutical pune

MATERIALS AND METHODS:

Table no.1 List of Instruments / equipments

Sr. No.	Instrument / Equipment	Make	Model
1.	UV spectrometry	Shimadzu Corporation	UV-1800 240V
2.	Weighing Balance	Shimadzu Corporation	BL-220H (Electronic balance)

Table no.2 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

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

Simultaneouse spectrophotometric determination of Pioglitazone and Glimepiride by Derivative Method.

Preparation of standard stock solution[5-8]

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 both were diluted with methanol solution.

Selection of sampling wavelengths for analysis[7]

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 for Pioglitazone (210 nm) and Glimepiride (218 nm)

Selection of Analytical Concentration Range and Preparation of Calibration Curves.

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 wavelengthss 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 for (r^2 = 0.998) and 1.50-7.50 µg/ml for Pioglitazone (r^2 = 0.995)

Analysis of powder mixture[8,9]

By using working standard solutions of Pioglitazone and Glimepiride, further dilutions were made to get Pioglitazone and Glimepiride in concentration of 10 µg/ml. The absorbance of this Pioglitazone and Glimepiride mixture was measured at 218 nm by using formula.

Procedure for analysis of tablet formulation[9]

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 Glimipiride 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 first derivative spectra of the resulting solution was recorded, dA/dλ measured at wavelength 218 nm and the concentrations of both drugs were determined using the equation

Procedure for Recovery Studies[10,11]

Recovery studies were carried out by applying the method to drug sample present in tablet dosage form to which known amount of pioglitazone and glimipiride corresponding to 80,100,120% of pioglitazone and Glimipiride 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 Glimipiride standard added was 0.16 mg. In 100 % recovery study the amount of standard added was 0.20 mg of Glimipiride In 120 % recovery study the amount of Glimipiride standard added was 0.24 mg. The mixed sample solutions were analyzed to obtain spectra and absorbance value at 218 nm (λ_{max} of Pioglitazone and Glimipiride respectively) were noted. The concentration of pioglitazone and Glimipiride were calculated from the equation. At each levels of the amount of three determinations were performed and results obtained was compared with expected results.

Formulae for determination of concentration of pioglitazone and glimipiride using Derivative Method

The concentration of drug was then calculated by using following equation.

$$C\ Pio = \frac{d/d\lambda\ [APio/AGlim] - Intercept[C}{Slope}$$

$$C\ Glim = \frac{d/d\lambda\ [Glim/Pio] - Intercept[C}{Slope}$$

$$C_{Pio} \quad = \frac{dA/d\lambda\ (at\ 210\ nm) - 0.0005}{0.0028}$$

$$C_{Glim} = \frac{dA/d\lambda \text{ (at 218 nm)} - 0.225}{0.575}$$

Table No.3 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	0.18	1.48	90	98.66
2.	0.20	1.50	0.19	1.47	95	98
3.	0.20	1.50	0.18	1.48	90	98.66
4.	0.20	1.50	0.19	1.49	95	99.33
5.	0.20	1.50	0.18	1.48	90	98.66

Analysis of tablet formulation[9,10]

The solution was scanned in the range of 200-400 nm against blank to obtain spectra and the first derivative spectra of the resulting solution was recorded, dA/dλ measured at wavelength 218 nm and the concentrations of both drugs were determined using the equation

Table No.4 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	0.19	1.47	95	98
2.	0.20	1.50	0.19	1.48	95	98.66
3.	0.20	1.50	0.18	1.48	90	98.66
4.	0.20	1.50	0.19	1.49	95	99.33
5.	0.20	1.50	0.19	1.48	95	98.66

Table No.5: Statistical analysis of tablet formulation

Component	Mean	Standard Deviation	Co-efficient of Variation	Standard Error
Pioglitazone	94.00	1.236068	1.3787	0.689739
Glimepiride	98.66	0.470234	0.4766	0.308739

Recovery Studies[13-15]

The mixed sample solutions were analyzed to obtain spectra and absorbance value at 218 nm (λ_{max}) of Pioglitazone and Glimipiride respectively) were noted. The concentration of pioglitazone and Glimipiride were calculated from the equation. At each levels of the amount of three determinations were performed and results obtained was compared with expected results.

Table No.6 Recovery studies of Pioglitazone and Glimipiride

Level of % recovery	Preanalysed		Added concentration Ug/ml		Total absorbance ug/ml		Conc.recoverd Ug/ml		Percentage of recovery	
	Pio	Glim	Pio	Glim	Pio 210nm	Glim 218nm	Pio	Glim	Pio	Glim
80	1.50	0.20	1.20	0.16	0.756	0.516	1.15	0.15	95.83	93.75
80	1.50	0.20	1.20	0.16	0.757	0.517	1.17	0.14	97.5	87.5
80	1.50	0.20	1.20	0.16	0.756	0.518	1.18	0.15	98.33	93.75
100	1.50	0.20	1.50	0.20	0.887	0.600	1.43	0.18	95.33	90.00
100	1.50	0.20	1.50	0.20	0.888	0.601	1.44	0.19	96.33	95.00
100	1.50	0.20	1.50	0.20	0.889	0.602	1.43	0.18	95.33	90.00
120	1.50	0.20	1.80	0.24	0.741	0.505	1.72	0.22	95.55	91.66
120	1.50	0.20	1.80	0.24	0.742	0.506	1.76	0.23	96.00	95.83
120	1.50	0.20	1.80	0.24	0.743	0.507	1.78	0.22	95.55	91.66

Table No.7 Statistical analysis of Tablet Formulation

Level of percentage recovery	% Mean Recovery		Standard Deaviation		Co –efficient of variation		Standard Error	
	Pio	Glim	Pio	Glim	Pio	Glim	Pio	Glim
80	97.72	91.66	1.273303	1.608439	1.303011	1.936765	0.128407	0.8995
100	95.66	92.22	0.57735	1.886751	0.604175	1.13028	0.759836	0.69904
120	95.7	93.05	0.259808	1.407551	0.271473	1.587373	0.509714	0.551628

Table No.8 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 ± 0.015275, 1.20	1.20± 0.012190, 0.95
2	1.50	1.42 ± 0.0057, 0.40	1.47 ± 0.0045, 0.32
3	1.80	1.78 ± 0.01, 0.42	1.42 ± 0.01, 0.056

Table No.9 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 ± 0.01211, 9.36	0.14 ± 0.01311, 9.36
2	0.20	0.17 ± 0.01154., 6.79	0.17 ± 0.01142, 6.71
3	0.24	0.24 ± 0.00763, 3.1	0.24 ± 0.0072, 3.01

CONCLUSION:

The developed UV method like derivative method 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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