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Development and Validation for the Simultaneous Estimation of Pioglitazone Hydrochloride and Glimipride in Mixed Dosage Form by UV-Spectrophotometric Method

Rajini Talla*, K.Veena, M. Akiful haque, D.Sireesha, B.Vasudha, S. Harshini
Department of Pharmaceutical analysis and Quality assurance, Anurag group of institutions (Formerly lalitha college of pharmacy) Hyderabad, Telangana, India.

ABSTRACT

A Simple, precise, accurate and economical spectrophotometric method was developed and validated for simultaneous estimation of Pioglitazone hydrochloride (PIO) and Glimipride(GLM) in combined dosage form. In simultaneous equation method, Pioglitazone hydrochloride (PIO) and Glimipride (GLM) were quantified using their absorptivity values at selected wavelengths, viz., 267nm and 227nm respectively. The linearity range was found to be 5-50µg/ml for Pioglitazone hydrochloride (PIO) and 5-50µg/ml Glimipride(GLM).The accuracy and reproducibility of the proposed method was statistically validated by recovery studies. The simultaneous equation method permits simple, rapid and direct determination of Pioglitazone Hydrochloride (PIO) and Glimipride (GLM) in commercially available combined dosage form without previous separations and analysis.

Keywords: Pioglitazone Hydrochloride (PIO) and Glimipride (GLM), Simultaneous equation Method.

*Corresponding Author Email: rajini.talla796@gmail.com
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INTRODUCTION

Pioglitazone Hydrochloride (PIO) is a thiazolidinedione derivative. Chemically, it is 5-({4-[2-(5-ethylpyridin-2-yl)ethoxy]phenyl}methyl)-1,3-thiazolidine-2,4-dione. It is used for the treatment of diabetes mellitus type 2 (previously known as non-insulin-dependent diabetes mellitus, NIDDm) in monotherapy and in combination with a sulfonylurea, metformin, or insulin and Glimipride.[9]

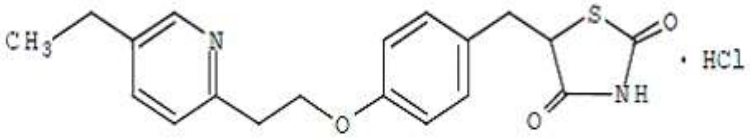

Figure 1: Structure of Pioglitazone Hydrochloride

Glimepiride is a sulfonylurea derivative chemically 3-ethyl-2,5-dihydro-4-methyl-N[2-[4-s(trans-4-methyl cyclohexyl) amino] carbonyl]amino] sulfonyl] phenyl]ethyl]-2-oxo-1Hpyrrole-1-carboxamide1, widely used in patient with type 2 diabetic mellitus.[10]

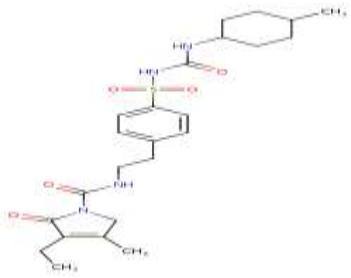

Figure 2: Structure of Glimipride

Both the drugs are marketed as combined dose tablet formulation in the ratio of 15:2mg PIO: GLM. Literature survey revealed that there is no method reported for the simultaneous estimation of these drugs, some methods for estimation of individual drugs or with other drugs UV-spectrophotometry[3-8], RP-HPLC[9] are available. Hence present study aim to developing a precise, linear, simple, rapid, validated and cost effective. UV- spectrophotometry method for the simultaneous estimation of these drugs in mixed dosage forms.

MATERIALS AND METHOD

Instruments used

SHIMADZU double beam UV/Visible Spectrophotometer model UV 1800s was employed with a spectral band width of 1nm and a wavelength accuracy of 0.3 nm (with automatic wavelength correction with a pair of 1cm matched quartz cells). SHIMADZU Electronic balance model AX 200 and Ultra Sonicator (Fast clean) model 2k811056 were also used during the analysis.

Materials

Analytically pure samples of Pioglitazone Hydrochloride and Glimipride were obtained as gift samples from Comprime labs Hyderabad. Tablets of brand "Pioglar-G" having combination of Pioglitazone Hydrochloride (15mg) and Glimipride (2mg) manufactured by Ranbaxy pharmaceutical laboratories was purchased from pharmacy.

METHOD

Selection of solvent and wavelength

The UV spectra of Pioglitazone Hydrochloride and Glimipride in different solvents like water, methanol, and ethanol were recorded. These two drugs showed good absorbance when dissolved in methanol at wavelengths 267 nm and 227 nm were selected as the λ_{max} of Pioglitazone Hydrochloride and Glimipride respectively. The normal overlain spectra of Pioglitazone Hydrochloride and Glimipride was shown in the figure 3.

Preparation of standard solutions

Pioglitazone Hydrochloride and Glimipride (10mg each) were separately weighed and transferred to a 10 ml volumetric flask and both the drugs were dissolved in methanol to get a solution of 1000µg/ml. 100 µg/ml standard solutions were prepared by diluting 1ml of standard solution (1000 µg/ml) to 10ml with methanol.

Preparation of working standard solutions

The working standard solutions of 5-50 µg/ml for Pioglitazone Hydrochloride and Glimipride were prepared by diluting 0.5 ml, 1ml, 1.5ml, 2ml up to 5ml of 100 µg/ml of standard solution of Pioglitazone Hydrochloride and Glimipride to 10ml with methanol. The absorptivity values were determined at the two selected wavelengths. The concentration of two drugs in the mixture was calculated using the following equation

$$C_{PIO=}A_2ay_1\text{-}A_1ay_2/ax_2ay_1\text{-}ax_1ay_2$$

$$C_{GLM=}A_1ax_2\text{-}A_2ax_1/ax_2ay_1\text{-}ax_1ay_2$$

Where $C_{PIO,}$ C_{GLM} are the concentrations of Pioglitazone Hydrochloride and Glimipride in mixture and in sample solutions. $A_{1,}$ A_2 are the absorbance's of sample at 267nm and 227nm respectively, $ax_{1,}ax_2$ are the absorptivity values of Pioglitazone Hydrochloride at 267 nm, $ay_{1,}ay_2$ are the absorptivity of Glimipride at 227nm.

RESULTS AND DISCUSSION

Method Validation

The analytical method was validated with respect to parameters such as linearity, precision,

accuracy, limit of detection (LOD), limit of quantification (LOQ).

Linearity and Range

Linearity was established by least squares linear regression analysis of the calibration curve. The calibration curves were linear over the concentration range of 5-50 µg/ml for Pioglitazone Hydrochloride, 5-50µg/ml for Glimipride. Absorbances were plotted versus respective concentrations and linear regression analysis was performed on the resultant curves. Correlation coefficients were found to be 0.999 and 0.999 for Pioglitazone Hydrochloride and Glimipride respectively (figure: 5, figure: 6).

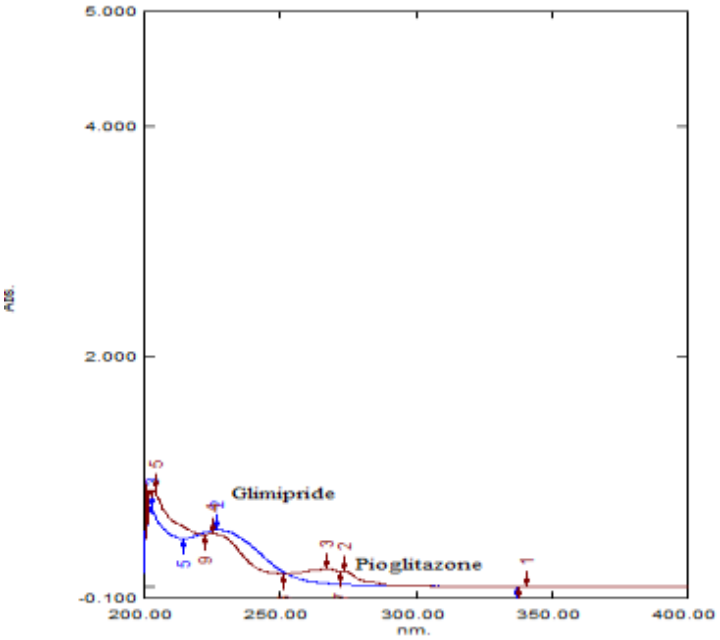

Figure: 3: Overlain Normal spectra Pioglitazone Hydrochloride (10 µg/ml) and Glimipride (10µg/ml) in methanol

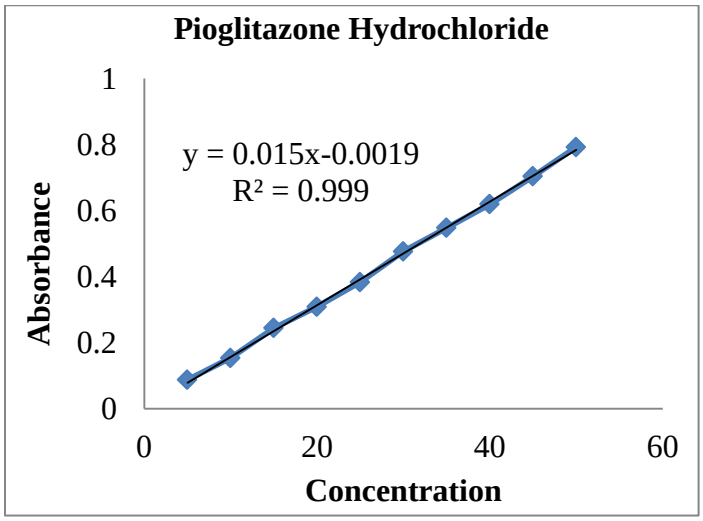

Figure 5: Calibration graph of Pioglitazone Hydrochloride at 267nm

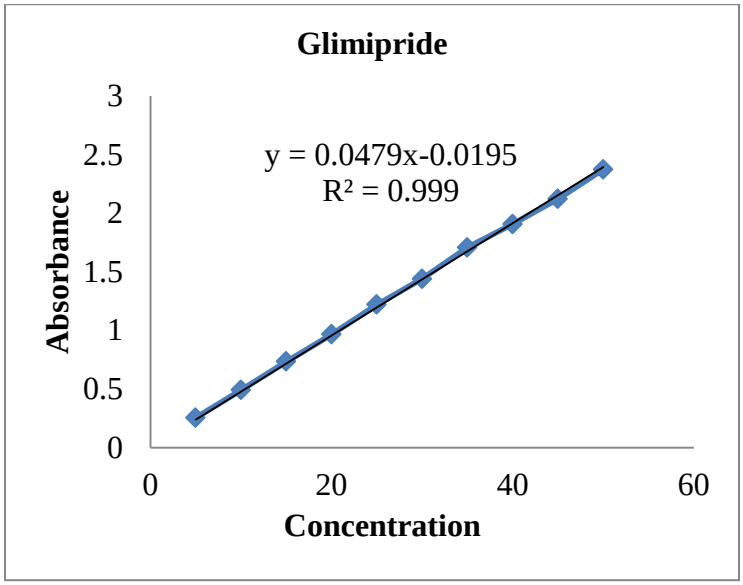

Figure: 6: Calibration graph of Glimipride at 227nm

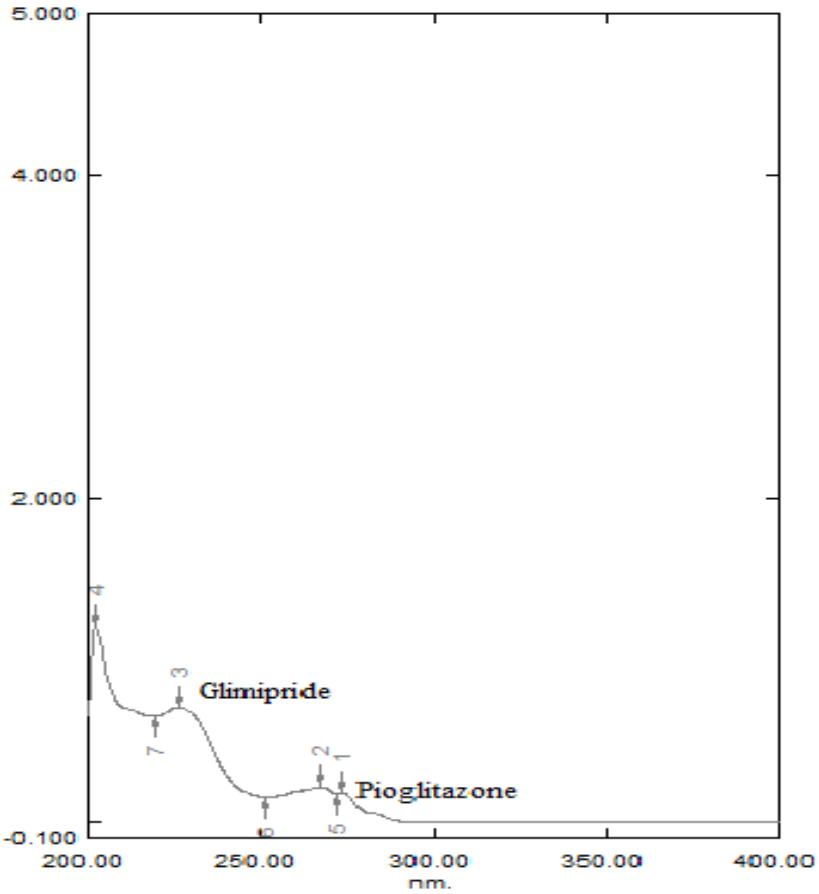

Figure 4: UV Spectra of formulation (15 µg/ml Pioglitazone hydrochloride and 2µg/ml Glimipride)

Precision

The precision of the analytical method was studied by multiple sampling of the homogenous sample. The precision was done at two levels (intraday and inter day). Intraday precision was done by analyzing the intermediate concentration of each drug (Pioglitazone Hydrochloride 15µg/ml and Glimipride 2µg/ml) for six times. Interday precision was measured over three consecutive days for the same drug concentrations. The %RSD values were found to calculated for each of them and the low RSD values indicate that the method is precise. The results of intraday precision were found to be 0.47, 1.16 for Pioglitazone Hydrochloride and Glimipride and the results of interday precision were found to be 1.35, 0.89 for Pioglitazone Hydrochloride and Glimipride.

Accuracy

Recovery studies were carried out by applying the method to drug sample to which known amount of standard Pioglitazone Hydrochloride and Glimipride corresponding to 80, 100 and 120 % of label claim had been added. At each level of the amount three determinations were performed. The results were found to be 99.4%, 101.5%, 99.2% for Pioglitazone Hydrochloride and 99.5%, 100.5%, 101.9% for Glimipride.

Sensitivity

LOD and LOQ decide about the sensitivity of the method. LOD is the lowest detectable concentration of the analyte by the method while LOQ is the minimum quantifiable concentration. LOD and LOQ were calculated by standard calibration curves. LOD and LOQ were found to be 1.56 µg/ml, 4.7µg/ml for Pioglitazone Hydrochloride and 1.1µg/ml, 3.3µg/ml for Glimipride.

Table 1: Summary of validation parameters

Parameters	Pioglitazone Hydrochloride	Glimipride
Linearity range (µg/ml)	5-50	5-50
Correlation coefficient	0.9991	0.999
Slope	0.0157	0.0479
Intercept	0.0019	0.0195
LOD (µg/ml)	1.5	1.1
LOQ(µg/ml)	4.7	3.3
Recovery (%)		
80	99.4%	99.5%
100	101.5%	100.5%,
120	99.2%	101.9%
Precision (RSD%)		
Intraday (n=6)	0.47	1.1
Interday (n=6)	1.3	0.89

Analysis of Marketed Formulation

Twenty Pioglar-G tablets each containing 15mg of Pioglitazone Hydrochloride, 2mg of Glimipride were weighed, average weight was calculated and powdered. A quantity equivalent to 15mg of Pioglitazone Hydrochloride and 2mg of Glimipride was weighed and transferred in to 10ml volumetric flask. It is extracted with methanol. The volumetric flask was sonicated for 3mins to affect the complete dissolution of the drugs and the solution was made up to the volume with methanol and filtered. Suitable aliquots of formulation were prepared and scanned to obtain concentration of the two drugs in the linearity range. The concentration of each analyte was determined using the simultaneous equation (Figure.4) (Table 2).

Table 2: Analysis of marketed formulation

Drug	Amount labeled(mg)	Amount found (mg)	% Assay	%RSD
Pioglitazone Hydrochloride	15	15.2	101.1	0.46
Glimipride	2	2.02	101	0.14

*Mean of three observations

CONCLUSION

The evaluation of obtained values suggests that the proposed UV Spectrophotometry methods provide simple, precise, rapid and quantitative analytical method for determination of Pioglitazone Hydrochloride and Glimipride in tablet dosage form. After validating proposed method as per ICH guidelines and Correlating the obtained values with the standard values, satisfactory results were obtained. The sample recoveries in all Formulations were in good agreement with their respective Label claims and they suggested no interference of formulation excipients in the estimation. Hence, the method can be easily and conveniently adopted for routine estimation Pioglitazone Hydrochloride and Glimipride in tablet dosage form.

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