Research Article

VALIDATED FIRST ORDER DERIVATIVE UV SPECTROPHOTOMETRIC VALLEY DETECTION METHOD FOR THE DETERMINATION OF PIOGLITAZONE

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ABSTRACT

A simple, precise and economical procedure has been developed for estimation of Pioglitazone in bulk drug and pharmaceutical dosage form, Using UV- spectrophotometer. As there are no reported methods for the UV methods for Quantitative evaluation of first order valley detection method for Pioglitazone in bulk as well as tablet dosage form, there was a need to expand novel methods to analyze the drugs using Methanol as a solvent. Pioglitazone has maximum absorbance at 234 nm. Pioglitazone obeys Beer's law in concentration range 15-75µg/ml. The recovery studies verified accuracy of the purposed method; result validated as per ICH guideline and results were found satisfactory and reproducible. The method was successfully performed for the estimation of Pioglitazone in tablet dosage form without the interference of common excipients.

Keywords: Pioglitazone, First order derivative method, valley determination.

INTRODUCTION

Pioglitazone is a prescription medicine used to treat diabetes mellitus. It belongs to the class of thiazolidinediones, which lower the blood sugar levels. It is used in type 2 diabetes alone or in combination with other drugs. It improves sensitivity to insulin in muscle and adipose tissue and inhibits hepatic gluconeogenesis also improves glycemic control while reducing circulating insulin levels. It works by making up the body's sensitivity to insulin, a typical hormone that helps manage blood sugar levels. Pioglitazone is not used to treat type 1 diabetes (situation in which the body does not produce insulin and, thus, cannot control the amount of sugar in the blood) or diabetic ketoacidosis (a severe condition that may increase acidity if high blood sugar is not controlled). Pioglitazone is an oral antidiabetic agent belonging to the class of thiazolidinediones ¹.

Chemical Structure of Pioglitazone

Pioglitazone [(±)-5-[[4-[2-(5-ethyl-2- pyridinyl) ethoxy] phenyl] methyl]-2, 4-] thiazolidinedione mono-hydrochloride belongs to a different chemical class and has a different pharmacological action than the sulfonylureas, metformin, or the α-glucosidase inhibitor².

On literature review, it was found that RP-HPLC method for determination of Pioglitazone, analysis of Pioglitazone using RP-

HPLC in tablet dosage form³⁻⁵, analysis of Pioglitazone by HPLC ^{6, 7}, UV spectrophotometric method ⁸⁻¹¹ have been reported for determination of Pioglitazone. But there is no first order derivative UV Spectrophotometric valley detection method so far reported for the determination of Pioglitazone. Hence, investigation of new analytical methods is in need for the quantitative estimation of Pioglitazone.

MATERIALS AND METHODS

Materials

Shimadzu 1800 spectronic UV Spectrophotometer with 1cm matched quartz cells was used for data collection and analysis. Methanol was used as a solvent for drug substance.

Methodology

Preparation of Standard Stock Solution

The standard stock solution was prepared by transferring 25 mg Pioglitazone in to a 100 ml volumetric flask. 100 ml methanol (CH₃OH) was transferred in to this volumetric flask then dissolved. The volume was made up to the mark with methanol to give a solution containing 1000 µg/ml Pioglitazone. From this volume 0.5 ml was move to 25 ml volumetric flask and the volume was adjusted to the mark with the help of Methanol to give a solution containing 100 µg/ml of Pioglitazone.

Determination of λ max

Accurate volume 1.5 ml of standard stock solution of Pioglitazone was shifted to 50 ml volumetric flask & the volumes were adjusted to the mark with similar solvent to get the solution of concentration 15 µg/ml. After that the prepared solution was

scanned in the UV range 220-250 nm. The λ max was found to be 234 nm. The spectrum of Pioglitazone was recorded and shown as Figure 1.

Selection of Analytical Wavelength Range

By the use of Shimadzu 1800 spectronic UV-Visible Spectrophotometer the derivative spectra of Pioglitazone were taken at N=8 & the standard solutions of Pioglitazone in Methanol (15 μ g/ml each) subjected to a scan 220 nm to 250 nm. The λ max was found to be at 220nm. For the Pioglitazone calibration curve of was found to be linear at 234nm. Beer's law obeyed in the concentration range of 15-75 μ g/ml.

Stability of Drug in Selected Solvent

The stability of the drugs in the selected solvent was determined by measuring the absorbance of the drug solutions (30 μ g/ml) at different time interval. The absorbance was measured after every 5 and 15min. The stability data is given in table 1.

Linearity

From the standard stock solution of Pioglitazone, appropriate aliquots were pipette out into 25 ml volumetric flask and dilutions were made up with methanol to obtain working standard solution of Pioglitazone 15, 30,45, 60, 75 μ g/ml. The difference in amplitude of Pioglitazone were measured in the first order derivative mode with n=8 of instrument at 234 nm. The calibration plot of the drug Pioglitazone was plotted. The concentration range over which the drug followed linearity was chosen as an analytical concentration range i.e. 15- 75 μ g/ml for Pioglitazone. (Table 2, Figures 2 to 6).

Validation of Proposed Method

Estimation of Drug from Dosage Form: (Tablet Assay Study)

Brand name- **PIOZ®-7.5**

Standard

For the possibility of projected method for evaluation of Pioglitazone in marketed pharmaceutical formulations, the process is preliminary tried for evaluation of drugs in standard bulk sample.

Exactly weighed 25 mg of Pioglitazone was conveying to 100 ml volumetric flask, after that dissolved in methanol by shaking and quantity was adjusted to mark by the same solvent. Then 5 ml was shifted to 50 ml volumetric flask & then volume was adjusted to up to the mark with the same solvent to achieve the concentration 100 μ g/ml. From that accurate stock solution 1.5 ml was transferred to 25 ml volumetric flask & volume adjusted to mark with the same solvent to obtain the concentration 15 μ g/ml. At 234 nm the absorbance of the solution was recorded and results are reported.

Sample

For analysis of marketable tablet formulation; brought the marketed brands tablet strips of Pioglitazone. Total weight of the all tablet was recorded. Afterward separately take 3 tablet weights, for the projected work 25 mg drug was used so the fourth tablet is added by appropriate weigh. Crush the tablet by using

mortar. Then calculated weight to be taking followed by prepare the 100 μ g/ml stock solution. Prepare the 15 μ g/ml solution and take the absorbance at 234 nm. Results are shown in table 3.

Accuracy (Recovery Test)

For the recovery experiment was studied by Accuracy. By adding known amounts of tablet, the recovery experiments were performed. The recovery was performed at three levels, 80, 100, and 120 % of Pioglitazone standard concentration. Recovery samples were prepared in before mentioned procedure. For every recovery level three samples were prepared. The percentage recoveries were calculated by using formula and the solutions were analyzed.

$$\% \text{ Recovery} = \frac{\text{Observed amount of compound in sample}}{\text{Amount of all compound present in sample}} \times 100$$

The Results of accuracy parameter of Pioglitazone are shown in Table 4.

Precision

Assay of method precision was evaluated by carrying out three independent assays of test sample of Pioglitazone. By the use of four different analysts the intermediate precision of the method also evaluated. The Assay values obtained by four analysts were summarized in the following Table 5.

RESULTS

The standard solutions of Pioglitazone in Methanol subjected to a scan at the series of wavelengths of 220 nm to 250 nm at First order derivative valley detect method and the derivative spectra were taken at N=8 using Shimadzu 1800 spectronic UV-Visible spectrophotometer. And absorbance maxima found at 234 nm. The calibration plot of Pioglitazone was found to be linear at conc. Range 15 to 75 μ g/ml at 234nm. There for, it was clear that Pioglitazone can be determined in presence of methanol with no intervention of any irrelevant substance in pharmaceutical products.

DISCUSSION

With the intention of determining the practicability of the developed technique for the assessment of commercially available brands (**PIOZ®-7.5**) of medicinal formulations, the technique was initially attempted on bulk drugs in their synthetic mixture sample as well as concentrations were estimated. Then the technique was subjected to the assay of in marketed dosage forms and satisfactory results were attained within the appropriate limits as per the content of the label claim for Pioglitazone. The newly developed method was validated as per the international guidelines and parameters. The novel method for the quantitative investigation of Pioglitazone was subjected to different validation parameters like specificity and selectivity in presence of formulation additives and excipients, studied for Linearity and range at different levels of concentrations and calibration standards where the determination range was optimized, accuracy was proved by recovery studies at different concentration levels, precision was established through inter day precision studies, where the samples were subjected to changed conditions other than optimized parameters.

Table 1: Stability Data

Sl. No.	Time (min)	Absorbance
1	0	-0.071
2	5	-0.079
3	10	-0.079

Table 2: Standard Calibration Table

Sl. No.	Concentration of Pioglitazone (µg/ml)	Absorbance at 234 nm
1	15	-0.037
2	30	-0.071
3	45	-0.102
4	60	-0.132
5	75	-0.171

Table 3: Assay of Pioglitazone in Tablet formulation

Amount Taken (mg/tab)	Amount found (mg/tab)	Amount found (%)
7.5	7.4	95.34
7.5	7.3	100.65
7.5	7.6	100.55
7.5	7.6	99.28
7.5	7.4	100.65
	Mean	99.294
	SD	2.2852
	CV	0.0230

Table 4: Results of accuracy parameter of Pioglitazone

Level of % Recovery	Label Claim (mg/tablet)	Amount of standard added (mg)	Total amount recovered (mg)	% Recovery	% mean Recovery	SD	CV
80	7.5	60	59.88	99.8	99.93	0.1178	0.0011
80	7.5	60	60.02	100.03			
80	7.5	60	59.98	99.96			
100	7.5	75	74.23	98.97	99.60	0.5575	0.0055
100	7.5	75	75.02	100.02			
100	7.5	75	74.87	99.82			
120	7.5	90	88.99	98.87	99.61	0.6478	0.0065
120	7.5	90	90.03	100.03			
120	7.5	90	89.96	99.95			

Table 5: Determination of Precision

Sample Number	Assay of Pioglitazone as % of labeled amount			
	Analyst-1	Analyst-2	Analyst-3	Analyst-4
1	99.80	100.37	99.60	100.23
2	99.45	99.25	100.70	100.12
3	100.12	99.40	99.28	99.50
4	99.10	99.71	99.82	99.02
5	99.38	100.10	99.68	99.05
Mean	99.57	99.766	99.816	99.584
S.D.	0.398554	0.468967	0.532428	0.57335
CV	0.003975	0.004700	0.005334	0.005757

Figure 1: Spectrum of λ max of Pioglitazone

Figure 2: Calibration Curve of Pioglitazone

Figure 3: First derivative spectrum of Pioglitazone concentration 15 µg/ml

Figure 4: First derivative spectrum of Pioglitazone concentration 30 µg/ml

Figure 5: First derivative spectrum of Pioglitazone concentration 45 µg/ml

Figure 6: First derivative spectrum of Pioglitazone concentration 60 µg/ml

Figure 7: First derivative spectrum of Pioglitazone concentration 75 µg/ml

CONCLUSION

From the above experimental studies, it can be concluded that First Order Derivative valley detect method by UV spectrophotometry instrument developed for estimation of Pioglitazone. The proposed methods for the selected drugs were found to be precise and accurate. The most important features of spectrophotometric methods are their rapidity and simplicity. Results of validation parameters demonstrate that these performed analytical procedures are suitable for its intended purpose and meet the criteria defined in ICHQ2A/B guidelines. The method is an excellent alternative to HPLC methods for routine analysis and accurate and rapid than the zero order UV spectrophotometric method.

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